



**Brandeis**

INNOVATION



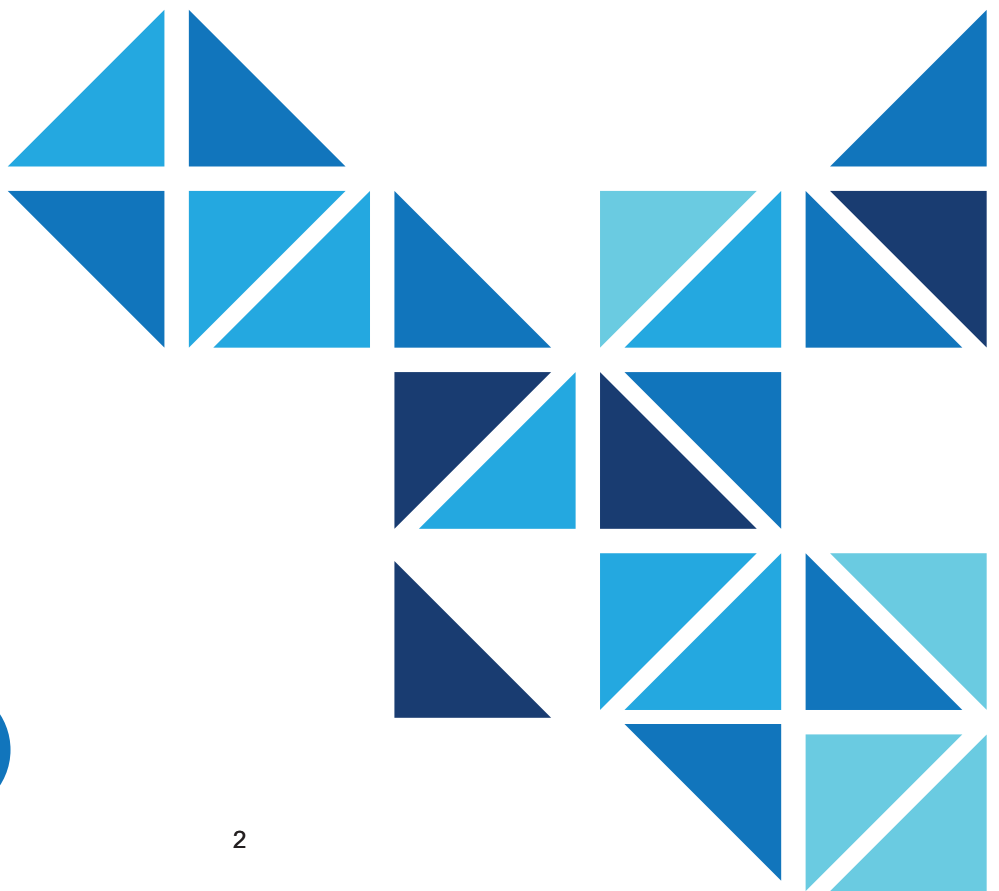
# **Brandeis Technologies Available for Licensing 2022**

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# Therapeutics, Diagnostics, & Drug Discovery



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# Neutralize Covid-19 through Encapsulation by DNA Origami Shells

## SEEKING

Exclusive licensing partner and/or sponsored research funding

## PATENT TITLE

DNA ORIGAMI SUBUNITS AND THEIR USE FOR ENCAPSULATION OF FILAMENTOUS VIRUS PARTICLES

## INVENTORS

Seth Fraden, et al.

## PATENT STATUS

Pending:  
Provisional Application

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2020-034

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### Background:

Nanomaterials have already played a key role in the fight against viruses. Now the urgency of the COVID-19 pandemic is generating interest in engineering nanomaterials that can themselves halt viruses in their tracks, rather than just acting as delivery vehicles for drugs or vaccines.

The virus enveloping shells, recently developed by us at Brandeis and collaborators at the Technical University of Munich, are made from DNA origami building blocks that self-assemble into octahedral (O) or icosahedral (T=1) shells. Using the same symmetry-based design principles that are exploited by natural virus capsids, we have designed shells with sizes ranging from 8 to 180 triangular building blocks, which assemble with exquisite fidelity and high yields up to 95%. The self-assembly is driven by tunable lock and key type interactions that allow exceptional control over shell geometry, stability, and assembly kinetics. Viral antibodies can be attached to precise locations on the inside or outside of the shells, ensuring assembly around targeted viruses with high efficiency and specificity. The system will provide a route to broadly applicable virus deactivation by engulfing whole viruses in protective shells to block virus-cell interactions.

The proposed device in this invention to use nanoengineering for an unconventional antiviral concept: rather than targeting viral proteins individually by small molecules or antibodies as is currently the norm, this novel approach is to engulf whole viruses within de novo designed macromolecular shells to block interactions between virus and host cells. The key advantage of this approach is that blocking infection requires just one binding event between the virus and encapsulating shell. In contrast, the traditional antibody approach for covid-19 requires that most of the ~100 viral surface Spike glycoproteins be bound due to their large functional redundancy in cell attachment and endosomal membrane fusion. This stringent requirement allows viruses to develop resistance through mutations that reduce antibody affinity. The claimed approach is more potent and leaves little room for escape by mutation because it envelops the entire virus through multivalent interactions. The large size of the DNA shells (internal diameter 160nm) allows designing up to 300 binding sites and ensures that multiple sites can simultaneously interact with the target virus. Due to this high multivalence, DNA shells can incorporate different antibodies, even with low affinity, and still bind multiple covid-19 variants over a broad range of conditions. Moreover, some sites on the shell can mount additional virus-binding moieties that enhance specificity or inactivate enclosed viral glycoproteins. This approach could also prevent viral resistance because it is much harder for viruses to evolve resistance against multiple treatment moieties simultaneously.

### Summary:

- This invention is an antiviral strategy that rely on DNA-based nanostructures to trap viruses
- They can potentially be formulated quickly and have activity across a broad range of virus families

### Advantages:

- The key advantage of this approach is that blocking infection requires just one binding event between the virus and encapsulating shell
- This approach is more potent than traditional ones and leaves little room for escape by mutation since it envelops the entire virus through multivalent interactions
- This approach could prevent viral resistance as it is much harder for viruses to evolve resistance.

### Scientific Publications:

- "Programmable icosahedral shell system for virus trapping". Sigl, C., Willner, E. M., Engelen, W., Kretzmann, J. A., Sachenbacher, K., Liedl, A., Kolbe, F., Wilsch, F., Aghvami, S. A., Protzer, U., Hagan, M. F., Fraden, S. and Dietz, H. Nature Materials, (2021) DOI: 10.1038/s41563-021-01020-4.



# Novel Method for Small Molecule Inhibitors to Induce Protein Degradation

## SEEKING

Licensing or collaborative research partner

## PATENT TITLE

Small Molecule Targeted Protein Degradation

## INVENTORS

Lizbeth Hedstrom, Deviprasad Gollapalli, Marcus Long

## PATENT STATUS

Issued: US 9,765,019

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1053

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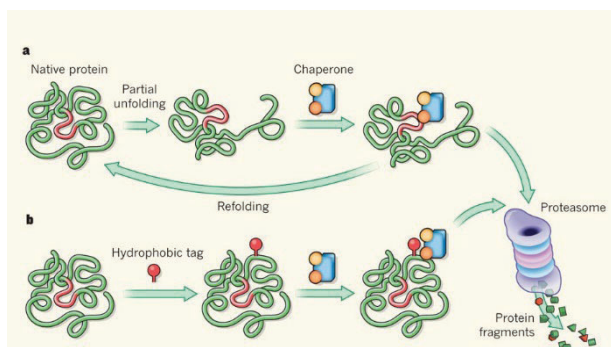
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## Small Molecule Targeted Protein Degradation

Numerous human diseases are driven by specific proteins, and small molecule protein inhibitors are pharmaceutical products heavily used in the healthcare industry. The dearth of newly approved drugs in the past decade reflects the challenges faced by the pharmaceutical industry. Although advances in genomics have identified many proteins that are implicated in disease, many of these proteins especially those that are not enzymes are not currently viable drug targets. In fact, it has been estimated that only about 15% of the human proteome is 'druggable' with small molecules.

The team of Dr. Hedstrom at Brandeis University has pioneered a novel method of developing modified small molecule inhibitors that can induce protein degradation. This technique has been validated using in vitro cell culture and has shown robust and selective degradation of protein targets.

This broadly-applicable invention may lead to the development of a novel line of drugs for diseases covering a major fraction of existing pharmaceutical market, including cancers, genetic, metabolic and neurodegenerative diseases. This invention can change previously undruggable targets into druggable targets therefore may produce novel drugs covering new disease area.



Brandeis OTL is seeking partnership from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this platform technology and its applications.

### Advantages:

- Broadly-applicable
- Robust endogenous protein down-regulation
- No genetic modification required
- Easy and cheap to synthesize

### Scientific Publication:

- Inhibitor Mediated Protein Degradation (2012). Long *et al.* [Chem Biol.19\(5\):629-37. PMID: 22633414](#)
- Boc3 Arg-linked ligands induce degradation by localizing target proteins to the 20S proteasome (2016). Shi *et al.* [ACS Chem Biol.11\(12\):3328-3337. PMID: 27704767](#)



# Novel Small Molecule Compositions to Treat Microbial Infection

## SEEKING

Licensing or collaborative research partner

## PATENT TITLE

Compounds and methods for treating mammalian gastrointestinal microbial infections

## INVENTORS

Lizbeth Hedstrom, Gregory Cuny, Suresh Gorla, Mandapata Kavitha

## PATENT STATUS

Issued: US 9,447,134

## LICENSING STATUS

Worldwide rights available

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Case 1115

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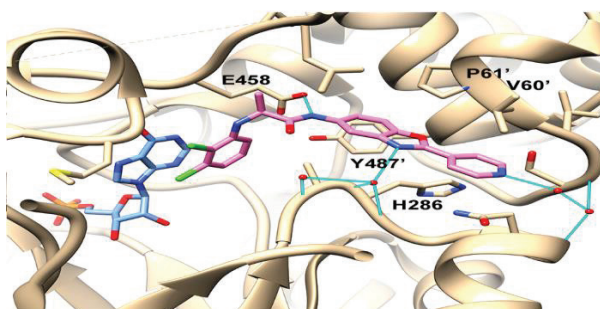
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## IMPDH inhibitors selectively prevent guanine synthesis in microbes

The invention available for licensing is a family of phthalazone, urea and benzoxazole-based small molecule compounds that treat these infections by inhibiting *Cryptosporidium* IMPDH (Cp IMPDH) activity. We have found that these compounds selectively inhibit Cp IMPDH activity in parasites to effectively shut down their purine salvage pathway and thus preventing the synthesis of new guanine nucleotides required for cell division. However, our compounds have little effect on the host's own cellular IMPDH activity. Our novel antimicrobial agents strongly inhibit the proliferation of *Cryptosporidium* oocysts when tested in a mouse model of acute cryptosporidiosis and appropriately co-localize in highest concentrations within intestinal cells where the parasite resides.

Pre-clinical results suggest our novel compounds and/or their optimized derivatives can be used to more effectively treat *Cryptosporidium* infections in mammals, while not causing liver toxicity or perturbing the host's natural gut microbiota. From our preliminary experiments *in vitro*, these same compounds also inhibit the growth of *Staphylococcus aureus* and *Mycobacterium tuberculosis* and thus show promise for use as possible broad spectrum antimicrobial agents in improving human and veterinary care.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.



### Summary:

- Novel antimicrobial compositions that inhibit protozoan and bacterial IMPDH
- Proven efficacy *in vivo* using a standard mouse model of acute cryptosporidiosis
- Additional results *in vitro* show broad spectrum growth inhibition of *Staphylococcus aureus* and *Mycobacterium tuberculosis* strains

### Scientific Publication:

- Repurposing *Cryptosporidium* Inosine 5'-monophosphate Dehydrogenase Inhibitors as Potential Antibacterial Agents. (2014). PMID: 25147601
- *Mycobacterium tuberculosis* IMPDH in complexes with substrates, products and antitubercular compounds. (2015) PMID: 26440283
- A novel cofactor binding mode in bacterial IMP dehydrogenases explains inhibitor selectivity. (2015) PMID: 25572472



# Inhibitors of Cystein Proteases

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Thiocarbonate- and Thiourea-  
based inhibitors of cysteine  
proteases

## INVENTORS

Lizbeth Hedstrom  
Marcus Long  
Ann Lawson

## PATENT STATUS

ISSUED 10,017,463

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1143

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## Inhibitors of deubiquitinating proteases

### Background:

We have discovered that isothiocyanate, thiocarbamate and thioimidocarbonic acid diester compounds can inhibit cysteine proteases, including deubiquitinating proteases (DUBs) such as USP9x, USP5, USP14, UCH37 and UCHL3, cathepsin C, papain and ficin. Cysteine proteases regulate many important physiological processes, and are potential targets for the treatment of many diseases, including inflammation, arthritis, osteoporosis, gingivitis, cancer, neurodegeneration and infection. DUBs are targets for the treatment of cancer, neurodegeneration and infection.

Cathepsin C is a target for inflammatory and autoimmune diseases. These compounds will be immediately useful as tools for the investigation of the cathepsin C and ubiquitin pathways. These compounds will also form the basis for development of chemotherapy for many diseases. These compounds are related to naturally occurring compounds that have anti-cancer activity. The currently available cysteine protease inhibitors tend to be reactive compounds that irreversibly modify other proteins in addition to their targets, and therefore exhibit nonspecific toxicity. There are few specific inhibitors of DUBs. The compounds reported here display good potency and selective toxicity in cell-based assays. There have been related developments by others: Cysteine protease inhibitors in general, and DUB inhibitors in particular, are very active areas of research.

There are many examples of general inhibitors of cysteine proteases. However, we know of no other groups working on thiocarbamate, isothiocyanate or thioimidocarbonic acid diester-based inhibitors. Naturally occurring isothiocyanates are produced from glucosinolates in cruciferous vegetables such as broccoli. These naturally occurring isothiocyanates are recognized as anti-cancer agents. There are reports that isothiocyanates inhibit the prototypical cysteine protease papain (see below). However, isothiocyanates are not known to be DUB inhibitors. It should be noted that isothiocyanates are known to modify proteins at amino groups, but these reactions occur at high pH. There are also no reports of thioimidocarbonic acid diesters inhibiting cysteine proteases, though there are reports of the related dithiocarbamates as protease inhibitors. We know of no reports of thiocarbamates as cysteine protease inhibitors, though they are known to be serine protease inhibitors.

### Summary:

- Cysteine proteases regulate many important physiological processes, and are potential targets for the treatment of many diseases, including inflammation, arthritis, osteoporosis, gingivitis, cancer, neurodegeneration and infection
- These compounds are related to naturally occurring compounds that have anti-cancer activity.
- There are few specific inhibitors of DUBs.

### Advantages:

- The currently available cysteine protease inhibitors tend to be reactive compounds that irreversibly modify other proteins in addition to their targets, and therefore exhibit nonspecific toxicity. There are few specific inhibitors of DUBs. The compounds reported here display good potency and selective toxicity in cell-based assays

### Scientific Publications:

- "A Novel Cofactor-binding Mode in Bacterial IMP Dehydrogenases Explains Inhibitor Selectivity." (2015) PMID: PMC4342496
- The antibiotic potential of prokaryotic IMP dehydrogenase inhibitors (2011) PMID: PMC5036587





# Cancer Therapy via Allosteric Modulation of Aurora A Kinase

## SEEKING

Licensing partner for  
commercialization

## PATENT STATUSES

- US 11,104,741 (Issued),  
17/380,704
- US 2019/0,038,582  
(allowed)

## INVENTORS

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## LICENSING STATUS

Worldwide rights available

## BRANDEIS REFERENCES

Cases 1229 and 1232

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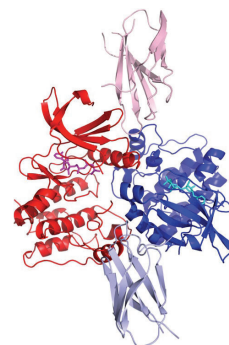
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## New treatment approach using antibody mimetics binding to the PIF-pocket of Aurora A kinase inhibits enzyme activity and causes cell death

### Background:

Aurora A (AurA) is a Ser/Thr kinase overexpressed in a wide range of human cancers including breast, colon, ovary and skin malignancies. It coordinates mitotic division not only through regulating centrosome maturation and duplication, but also through directly impacting spindle microtubule formation in later stages of mitosis. In order to localize to spindles and coordinate proper progression of mitosis, AurA must bind to, and be allosterically activated by interactions within its regulatory Pif pocket from the microtubule-associated protein TPX2 (Targeting Protein for Xklp2). Without this binding, AurA is not activated nor localized to the spindles and leads to cell death. A drug that blocks TPX2 binding and specifically reduces the activity of AurA kinase would be a powerful new anticancer therapy.

Pif pocket domains are not highly conserved among human Ser/Thr kinases and thus provide novel targets for the identification of new, highly-specific inhibitors with fewer off-target side effects than drugs directed to the more highly conserved active sites. Our invention is the discovery of monobodies (Mbs) with high binding affinity to the Pif pocket of AurA kinase which inhibit enzyme activity by modulating the allosteric conformation of its N-terminal  $\alpha$ C-helix within the catalytic domain but away from the active site. Mbs are synthetic binding proteins developed from highly tailored combinatorial libraries constructed on a small, non-immunogenic human fibronectin-based scaffold.



The interaction dynamics and mechanism of action for inhibitory Mbs were analyzed using high resolution x-ray crystallography, isothermal titration calorimetry, and NMR studies. Four major structural features were identified in effectors that differ between activating and inhibitory Mbs. The AurA-Mb interactions were confirmed *in vivo* by expression of GFP-Mb fusion constructs in both HEK293 and HeLa cells where the inhibitory Mbs disrupt translocation of AurA to spindles and cause cell death. Inclusion of small molecule inhibitors that specifically target the ATP-binding pocket in addition to use of Mbs binding to the Pif-pocket further improves inhibition of kinase activity while decreasing toxic side effects.

### Summary:

- Monobodies (Mbs) have been identified which bind with nM to low  $\mu$ M affinity to the hydrophobic Pif pocket in the N-terminal lobe of Aurora A (AurA) and allosterically modulate its kinase activity
- Inhibitory Mbs bind and “lock” the  $\alpha$ C-helix of the catalytic domain an inactive conformation
- When expressed in mammalian cells, Mb inhibitors co-localize with AurA kinase and prevent interactions with TPX2 which block microtubule spindle localization and lead to cell death
- Allosteric inhibitor Mbs targeting AurA represent a new approach in treating cancers

### Advantages:

- High affinity biologic approach that specifically shuts down enzyme activity of AurA kinase
- Very stable due to lack of disulfide bonds and non-immunogenic due to fibronectin backbones

### Related Scientific Publications:

Zorba *et al.* (2014) Molecular of Aurora A kinase autophosphorylation and its allosteric activation by TPX2. *eLife* 3:e02667. DOI: 10.7554/eLife.02667.

Pitsawong *et al.* (2018) Dynamics of human protein kinase Aurora A linked to drug selectivity. *eLife* 7:e36656. DOI: <https://doi.org/10.7554/eLife.36656>



# Oligosaccharide-Oligonucleotide Vaccine

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Methods for the Development of  
Vaccines Based on  
Oligosaccharide-Oligonucleotide  
Conjugates

## INVENTORS

Sevan Habeshian, Lizbeth  
Hedstrom, Isaac Krauss, Iain  
MacPherson

## PATENT STATUS

Issued:

U.S. Patent No. 9,080,169

U.S. Patent No. 10,378,017

## LICENSING STATUS

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## BRANDEIS REF.

Case 1052

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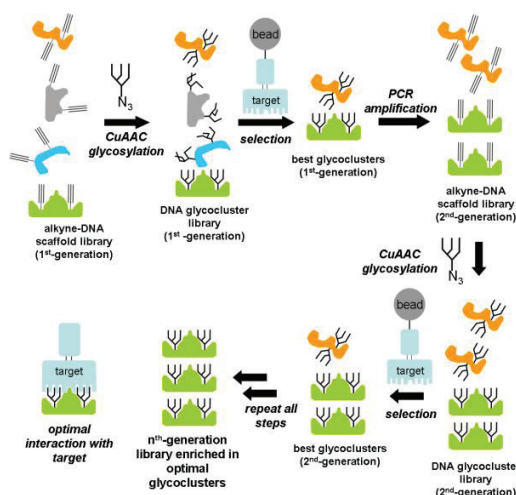
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## Develop target-specific antibody using oligosaccharide-oligonucleotide conjugates

Certain monoclonal antibodies have therapeutic potential against a particular disease, even though similar antibodies seldom or never arise during disease progression in most humans. In such cases, a "reverse immunology" approach would be desirable, in which an immunogen is designed which structurally mimics the epitope of the therapeutically useful monoclonal antibody. Immunization with this epitope mimic would then elicit an antibody response mimicking the monoclonal antibody.

The success of this strategy depends on the extent to which one can design a molecule that is a good structural and conformational mimic of the native epitope. Carbohydrates are necessary epitopes component for antibody binding. Carbohydrates are flexible and may exhibit different conformational profiles when attached to structures other than those present in the actual target protein. Good vaccine can be produced, if the target protein epitope can be faithfully mimicked

using backbone of carbohydrates embedded in the oligonucleotide framework.



The invention relates to a method of directed evolution of a large library of carbohydrate-oligonucleotide conjugates, and then a therapeutically-useful monoclonal antibody is used to bind those members of the library which best resemble its native epitope. Through amplification or diversification of the best binders from the first library, the best epitope mimics are selected from subsequent library generations to provide improved binders. The carbohydrate-oligonucleotide conjugates obtained from the process present carbohydrates in an environment similar to that of the natural epitope. Such a

compound, when formulated with the appropriate immunogenic carrier and adjuvant, would constitute a vaccine. In this invention, we utilized the oligonucleotide framework and power of the selection process to synthesize chemically modified oligonucleotides attached to an unmodified region that retains the information required for the amplification and regeneration necessary for the selection process. We used this method to select glycan-modified aptamers that bind monoclonal antibody (Mab) 2G12, which neutralizes HIV.

Though this invention can be used to design vaccines against HIV, it can also be used to discover vaccines against any other diseases for which therapeutically useful antibodies are known to bind to a carbohydrate structure, cancer antigens, for instance, RAV12. Moreover, this invention also enables rapid discovery of oligosaccharide-oligonucleotide conjugates which could specifically disrupt the binding of any known glycoprotein-glycoprotein or protein-glycoprotein interaction in which the binding involves the carbohydrates.

### Advantages:

- A novel method to generate carbohydrate-oligonucleotide conjugates to produce vaccine
- High throughput library screening by utilizing a "reverse immunology" approach
- A successful strategy for biotech/pharmaceuticals based on exhaustive antigen epitope space

### Scientific Publication:

- "Multivalent glycocluster design through directed evolution." PMID: PMC3900255



# High Temperature SElection with Modified Aptamers (SELMA)

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

High temperature selection of nucleotide-supported carbohydrate vaccines and resulting glycosylated oligonucleotides

## INVENTOR

Isaac Krauss

## PATENT STATUS

### Issued:

U.S. Patent No. 10,378,017

### Pending:

U.S. Patent Application No. 16/538,291

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1153 and 1303

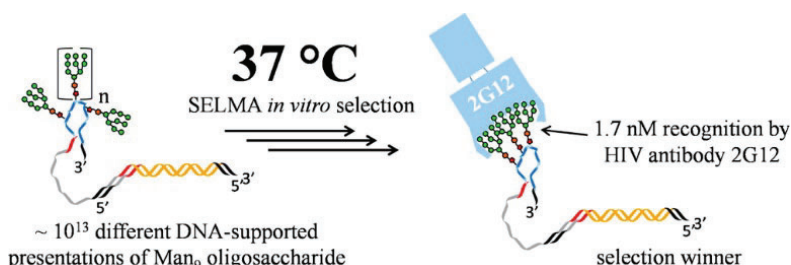
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## Evolution of DNA-Supported Oligomannose Clusters Tightly Recognized by HIV bnAb 2G12

Previous HIV vaccine approaches, mostly using whole HIV proteins, have failed because they stimulate antibodies which can only neutralize the HIV strain used to make the vaccine. Among several challenges is HIV's famously rapid mutation rate which leads to viral diversity, recent studies also have shown that up to 20% of HIV-positive individuals nevertheless produce "broadly-neutralizing" antibodies (bnAbs), work by binding to the conserved portion of the HIV protein or its carbohydrate surface, i.e., features which are essential for viral survival and therefore must remain present in all strains. Our unconventional vaccine materials are carbohydrate/DNA conjugates, but appear very promising in that HIV antibodies bind to them extremely tightly, which suggests that they are good mimics of the HIV virus and could be good HIV vaccine candidates.



The strategy based on a directed evolution method (SELMA) is used to develop DNA-supported clusters of carbohydrates in which the geometry of clustering is optimized for strong recognition

by a lectin of interest. As an optimization of the original SELMA method, we achieved dramatically stronger target recognition (100-fold) with fewer glycans (2-3 fold). Compared to the previous application of SELMA, the current glycoclusters contain fewer glycans (3-4 vs. 5-10 in the past), yet bind to the 2G12 HIV antibody target with Kd's as low as 1.7 nM (vs. 150-500 nM Kd's in the past). These glycoclusters are recognized by 2G12 as tightly as is the HIV envelope protein gp120, and they are the first constructs to achieve this tight recognition with the minimal number of Man9 units (3-4) necessary to occupy the binding sites on 2G12. They are thus of interest as immunogens that might elicit broadly neutralizing antibodies against HIV.

The invention shows that SELMA-based glycocluster selection, with the temperature increased to 37 °C, affords low-valent Man9 clusters whose affinity for 2G12 matches that of gp120 both thermodynamically and kinetically. The high temperature 37°C selection winners are not only of higher affinity (1.7-16 nM vs 150-500 nM) but also contain fewer glycans than room temperature selection winners (3-5 vs 7-10).

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### **Advantages:**

- An optimized method to generate carbohydrate-oligonucleotide conjugates to produce HIV vaccine at 37°C
- High temperature selection affords higher affinity and contains fewer glycans than room temperature
- A successful strategy for biotech/pharmaceuticals based on exhaustive antigen epitope space

### **Scientific Publication:**

- "High Temperature SELMA: Evolution of DNA-Supported Oligomannose Clusters Which Are Tightly Recognized by HIV bnAb 2G12". *J. Am. Chem. Soc.*, **2014**, 136 (5), pp 1726–1729.
- "Directed Evolution of 2G12-Targeted Nonamannose Glycoclusters by SELMA". *Chemistry*. **2013** Dec 16;19(51):17291-5.





# Directed Evolution of Multivalent Glycopeptides Tightly Recognized by HIV Antibody 2G12

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT STATUS

### Issued:

U.S. Patent No. 10,544,412 titled "Directed Evolution of Multivalent Glycopeptides that Tightly Bind to Target Proteins"

U.S. Patent No. 10,563,193 titled "Multivalent Glycopeptides that Tightly Bind to Target Proteins"

### Allowed:

U.S. Patent Application No. 16/740,750 titled "Multivalent Glycopeptides that Tightly Bind to Target Proteins"

## INVENTORS

Isaac Krauss, Satoru Horiya

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1154/1177/2019-025

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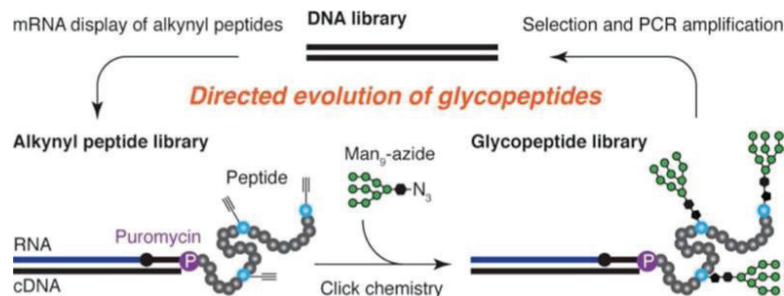
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## Background

Antibody 2G12, isolated from an HIV positive individual, binds and neutralizes a broad range of HIV strains, and provides sterilizing immunity against HIV challenge in macaque models of infection. The recent approach, SELMA, tackles the problem of designing 2G12 epitope mimics by applying a directed evolution-based strategy in which a DNA backbone evolves to optimally cluster the epitope glycans. The directed evolution of glycopeptides, can give rise to both HIV and cancer vaccine design, especially in vitro selection. The recent development in phage display with chemically modified phages enabled selection of peptides 5-mer sequences containing a single central mannose monosaccharide from  $\sim 10^6$  sequences. By incorporating multiple glycans in the carbohydrate HIV epitopes, this invention allows access to multivalent glycopeptides containing several glycans at variable positions, supported by a significant peptide framework.

The method combining mRNA display with unnatural amino acids using "click" chemistry allows in vitro selection of multivalent glycopeptides to design potential vaccines against HIV. From libraries of  $\sim 10^{13}$



glycopeptides containing multiple man<sub>9</sub>glycan(s), variants are selected to bind HIV broadly neutralizing antibody 2G12 with picomolar to low nanomolar affinity. This is comparable to the strength of the natural 2G12-gp120 interaction, and is the strongest affinity achieved with constructs containing only 3-5 glycans. These glycoclusters are recognized by 2G12 as tightly as is the HIV envelope protein gp120, and they are the first constructs to achieve this tight recognition with the minimal number of Man<sub>9</sub> units (3-4) necessary to occupy the binding sites on 2G12. They are thus of interest as immunogens that might elicit broadly neutralizing antibodies against HIV.

The invention shows that SELMA-based glycocluster selection, with "click" chemistry to attach Man<sub>9</sub> azides to the library alkynes while the DNA encoding the random library is transcribed and translated. The process is repeated until multivalent glycopeptides are obtained, which have high-affinity for the target lectin.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Advantages:

- An optimized selection method to produce carbohydrate-oligonucleotide conjugates based HIV vaccine
- Achieved tight recognition to HIV broadly neutralizing antibody 2G12 with the minimal number of Man<sub>9</sub> units
- A successful strategy for both HIV and cancer vaccine development in vitro

### Scientific Publication:

• "Directed Evolution of 2G12-Targeted Nonamannose Glycoclusters by SELMA". *Chemistry*. **2013** Dec 16;19(51):17291-5. doi: 10.1021/ja500678v.

• "DNA display of folded RNA libraries enabling RNA-SELEX without reverse transcription." *Chem. Commun.* **2017** Mar 2; 53(19):2878-2881. doi: 10.1039/c6cc09991b.



# DNA Display of Folded RNA Libraries Enabling RNA-SELEX without Reverse Transcription

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

DNA Display of Folded RNA  
Libraries Enabling RNA-SELEX  
without Reverse Transcription

## INVENTOR

Isaac Krauss, Iain MacPherson

## PATENT STATUS

Pending: U.S. Patent Application  
No. 16/486,248

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1342

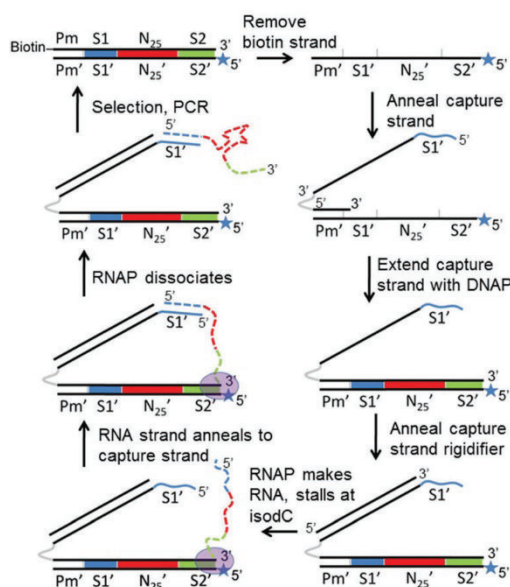
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## Directed Evolution of Glycopeptides Using a RNA Backbone

RNA-SELEX has been introduced as a way to circumvent reverse transcription step during systematic evolution of RNA ligands by exponential enrichment to physically attach folded RNA libraries to their encoding DNA. This method will be useful in the discovery of RNA aptamers and ribozymes containing base modifications that make them resistant to accurate reverse transcription. Limitations to standard aptamer libraries (nuclease sensitivity, limited chemical diversity) have been overcome by the use of non-natural nucleotide analogs. This invention presents a method termed SELECTION of Modified Aptamers, or SELMA, allowing for the incorporation of large modifications into DNA libraries, which was successfully used to obtain multivalent glycoclusters that mimic a conserved epitope on the HIV envelop protein gp120. To increase efficiency of reverse transcription in base modifications and overcome the obstacles to utilize two different types of enzymes (RNA polymerase and reverse transcriptase) to tolerate the modified bases, the method successfully circumvents the need to generate and select a RNA libraries for introduction of alkyne-modified RNA analogues and post-transcriptional click modification in an RNA-version of SELMA.



By utilizing physical attachment of folded RNA libraries to their encoding DNA, this invention is presented as a way to circumvent the reverse transcription step during systematic evolution of RNA ligands by exponential enrichment (RNA-SELEX). This method circumvents the need for reverse transcription in the amplification of RNA libraries and could be applied to base modifications for which reverse transcription is inefficient.

The invention shows a verified method for DNA display of RNA. The benefits of using RNA in selections (structural diversity, amenability to 2' modifications for nuclease resistance) can be coupled with substantial post-transcriptional modification in a SELMA-type experiment. Stringency was then increased by lowering the thrombin concentration from 10 to 1 nM and shortening incubation time from 1 hour to 5 minutes; after the 10th round of selection the

library was cloned and 10 members sequenced and analyzed for thrombin binding.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Advantages:

- An innovation for DNA display of RNA to circumvent the reverse transcription step during RNA-SELEX
- Effectively displayed RNA library that could bind to human thrombin, with preferred secondary structures
- A successful RNA library generation strategy allows the selected aptamers adopt a preferred conformation
- Selection cycle is fast and straightforward since the display method uses commercially available materials

### Scientific Publication:

- "DNA display of folded RNA libraries enabling RNA-SELEX without reverse transcription". *Chem. Commun.*, 2017,53, 2878.



# Selection of Modified Aptamers with Fluorinated GlycoRNA Aptamers

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

DNA DISPLAY OF FOLDED RNA  
LIBRARIES ENABLING RNA-  
SELEX WITHOUT REVERSE  
TRANSCRIPTION

## INVENTORS

Isaac Krauss

## PATENT STATUS

Pending:  
US 63/194,002

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2020-043

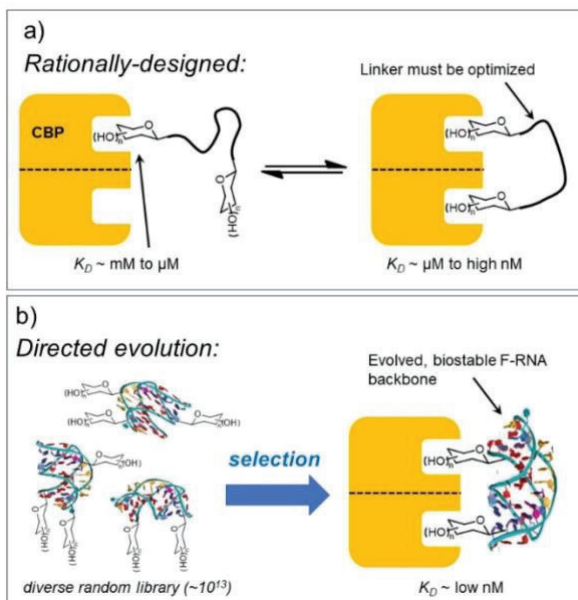
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### Background:

Many events in host-pathogen recognition, cell adhesion and cell signaling are mediated by carbohydrate-protein interactions. Therefore, the design or discovery of carbohydrate structures that can faithfully mimic or interrupt interactions with carbohydrate binding proteins (CBPs) has potentially broad applications in medicine, including the development of vaccines, immunomodulatory agents, diagnostics, and anti-adhesion drugs against cancer and other diseases.



Whereas CBPs typically have low affinity ( $K_D \sim \text{mM to } \mu\text{M}$ ) for individual glycan units, high affinity interactions are achieved through multivalent interactions with glycan clusters. Rather than using rational design and medchem to optimize multivalency to match the target binding sites, the invention claimed here is a new method for directed evolution of carbohydrate clusters assembled on 2'-deoxy-2'-fluoro RNA (F-RNA) backbones. The invention demonstrates that this method can evolve tight binders of the HIV antibody 2G12,11 a target with four glycan binding pockets that is of interest in HIV vaccine design.

Previously, we have clustered carbohydrates on libraries of DNA

aptamer or peptide backbones and developed methods to genetically encode and amplify these libraries. RNA has a more diverse structural repertoire than DNA, motivating the display of glycan clusters on RNA backbones. Although RNA is highly susceptible to nuclease degradation, F-RNA exhibits increased serum stability.

### Summary:

- The invention describes a novel platform for design of multivalent carbohydrate cluster ligands by directed evolution, in which serum-stable 2'-fluoro modified RNA (F-RNA) backbones evolve to present the glycan in optimal clusters.
- This method is validated by the selection of oligomannose (Man9) glycan clusters from a sequence pool of  $\sim 10^{13}$  that bind tightly to broadly neutralizing HIV antibody 2G12.

### Advantages:

- 2'-deoxy-2'-fluoro RNA (F-RNA) exhibits increased serum stability while traditional RNA backbones are highly susceptible to nuclease degradation.
- RNA has a more diverse structural repertoire than DNA, motivating the display of glycan clusters on RNA backbones.

### Scientific Publications:

- "Directed Evolution of 2'-Fluoro-Modified, RNA-Supported Carbohydrate Clusters That Bind Tightly to HIV Antibody 2G12." J. Am. Chem. Soc. 2021, 143, 23, 8565–8571



# Sulfur-Substituted Oligomannose Derivatives for Vaccines

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Sulfur-substituted oligomannose  
derivatives for vaccines and other  
applications

## INVENTORS

Isaac Krauss, Leiming Tian

## PATENT STATUS

Pending:  
Provisional Application

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2021-035

## CONTACT

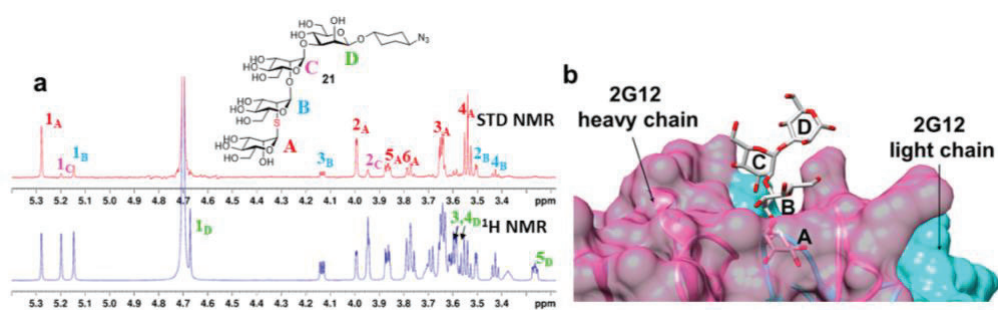
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### Background:

Carbohydrate or glycoconjugate vaccines are in use or development for prevention of bacterial infections, cancer and HIV. In HIV vaccine development, there is significant interest in elicitation of antibodies that can bind to the Man $\alpha$ 1 $\rightarrow$ 2Man moieties of high mannose (Man9GlcNAc2) glycans; however, it has been shown that, for glycoconjugate vaccines, mannosidase trimming degrades this motif so that the antibody response is directed against the glycan core or other structures in the glycoconjugate.

A possible solution to this problem is chemical stabilization of the Man $\alpha$ 1 $\rightarrow$ 2Man linkage against enzymatic hydrolysis, in particular using sulfur in the glycosidic linkage. Indeed, antibodies raised against some S-linked glycan analogs exhibit cross-reactivity with the natural oxygen-linked sugars but such analogs have not been tested in the case of oligomannose vaccines.



**Figure 1.** Binding analysis of S-Man4 to HIV broadly neutralizing antibody 2G12. a) STD-NMR spectrum of S-Man4 (21) with 2G12 IgG. Bottom spectrum (blue) shows the reference 800 MHz  $^1\text{H}$  NMR whereas the top (red) shows corresponding STD spectrum. See supporting information for details. Numbers indicate selected assignments by carbon number and ring letter. b) Crystal structure for all O-linked Man4 (22) bound to 2G12 (PDB ID 6MSY).

This invention demonstrates a facile synthetic route to Man3 and Man4 derivatives with a non-reducing-terminal sulfur linkage that is highly resistant to enzymatic degradation. These derivatives are recognized by an HIV antibody, 2G12, through contacts that are similar to those it makes with the natural oligomannose structure. This synthetic strategy should be readily amenable to preparation of higher branched stabilized oligomannose analogs, suitable for immunogenicity studies in the near future.

### Summary:

- The invention describes a facile synthetic route to Man3 and Man4 derivatives with a non-reducing-terminal sulfur linkage that is highly resistant to enzymatic degradation.
- This invention makes possible and confirms the reducing terminal S-linkage confers complete stability against *x. manihotis* mannosidase.

### Advantages:

- The synthetic route introduced by the invention can be readily amenable to preparation of higher branched stabilized oligomannose analogs
- Sulfur-substituted sugar makes possible to produce HIV vaccine that is highly resistant to enzymatic degradation.

### Scientific Publications:

- "Synthesis of Mannosidase-Stable Man3 and Man4 Glycans Containing S-linked Man $\alpha$ 1 $\rightarrow$ 2Man Termini." Org. Lett. 2021, 23, 8, 3053–3057





# Use of DBH Inhibitors for Long Term Memory Enhancement

## SEEKING

Exclusive licensing partner for commercialization

## PATENT TITLE

DBH Inhibitors for Treating or Preventing Memory Loss

## INVENTOR

John Lisman

## PATENT STATUS

### Issued:

U.S. Patent No. 10,441,573

U.S. Patent No. 10,821,097

### Pending:

PCT/US2016/065896 in Canada

Serial No. 3,007,641 and EP

Serial No. 16873949.8

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1161

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## Mobilization of noradrenergic fibers to produce hippocampal dopamine

### **Background:**

The neuromodulator dopamine is required in the hippocampus for long-term memory formation. However, dopaminergic innervation in the hippocampus is sparse while there is an abundance of noradrenergic fibers. Since noradrenaline is synthesized from dopamine by the enzyme dopamine beta-hydroxylase (DBH), it is now believed that dopamine in the hippocampus could be supplied by co-release from noradrenergic fibers. The source of noradrenergic fibers, the locus coeruleus, strongly degenerates early in the course of Alzheimer's Dementia (AD).

The invention is based on the hypothesis that deterioration of hippocampus-dependent declarative memory in AD patients may be caused by insufficient co-release of dopamine by noradrenergic fibers due to degeneration of the noradrenergic system. It suggests the chronic use of a DBH inhibitor drug (Nepicastat – manufactured by Biotie Therapeutics Corp.) can enhance memory by driving the surviving noradrenergic fibers to produce more dopamine to support memory formation. Nepicastat was developed as a selective inhibitor of DBH for treating PTSD and cocaine addiction but was abandoned in Phase 2 efficacy studies due to a failure in reaching clinical end points at inhibiting alcohol metabolism.

The invention has been first tested in C57Bl/6 mice where it was proven that chronic oral administration of Nepicastat (50-200 mg/kg) for two weeks decreased the formation of noradrenaline in hippocampus and cortex in a dose-dependent manner. However, it selectively, in a dose-dependent manner, increased levels of dopamine only in the hippocampus (2-5 times the levels found in controls) while cortical dopamine levels were not changed. A long-term (6 months) experiment in a mouse model of AD (mutant strain Tg2576) then showed that hippocampus-dependent contextual fear memory was strongly impaired in Tg2576 mice but returned to almost wild type level following chronic (5 months) oral treatment with Nepicastat (50 mg/kg) and Droxidopa (400 mg/kg). Droxidopa (also known as L-DOPS), an artificial precursor of noradrenaline, was used to compensate for the decreased levels of noradrenaline by the DBH inhibitor, Nepicastat via a DBH-independent enzymatic pathway. L-DOPS is an FDA-approved synthetic amino acid precursor used for treating several diseases and available from multiple commercial manufacturers.

HPLC analysis of hippocampal tissues of these mice after the end point showed that indeed Nepicastat strongly decreased the levels of noradrenaline but increased hippocampal dopamine content. Droxidopa rescued reduced noradrenaline levels and unexpectedly increased production of dopamine to an even greater extent. The increase in contextual fear memory co-varied with hippocampal dopamine content but not with noradrenaline levels. Neither dopamine nor noradrenaline levels co-varied with indicators of AD such as soluble and insoluble amyloid-beta content (ELISA) and amyloid-beta oligomers (Erenna). The brain tissue plaque depositions (immunohistochemistry) were negligible. The lack of change in AD indicators may be due to early age of Tg2576 mice by the end of experiment (8-8.5 months).

### **Summary:**

- Use of dopamine beta hydroxylase (DBH) inhibitors (e.g. disulfiram or Nepicastat) to prevent or delay memory loss associated with certain neurodegenerative diseases
- Treatment increases dopamine levels within the hippocampus to support memory formation by preventing noradrenergic axons from converting dopamine into noradrenaline via normal pathways
- Proof-of concept testing has been completed in a mouse model for Alzheimer's Disease

### **Advantages:**

- DBH inhibitor drugs, disulfiram and Nepicastat, have already proven safe for use in humans
- Addresses the result of dopamine-secreting axons lost during neurodegenerative disease progression and can be used in combination with other drugs that targeting cause of the disease



# A Novel Therapy for Epilepsy- Rebuilding Inhibition in the Epileptic Brain

## SEEKING

Licensing partner and/or research collaborator

## PATENT TITLE

Methods of Modulating Gabaergic Inhibitory Synapse Formation and Function.

## INVENTORS

Suzanne Paradis, Anna Moore, Marissa Juzirian

## PATENT STATUS

Issued: US 10,626,163

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1116

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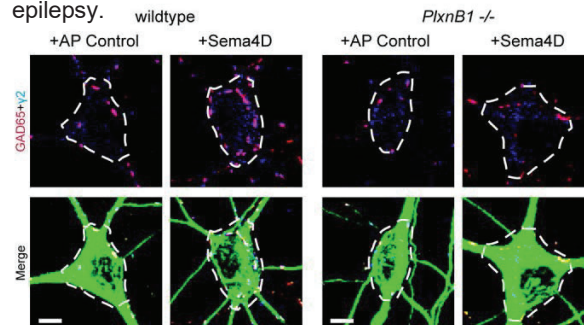
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## Modulating GABAergic synapses via the Sema4D-PlexinB1 interaction to restore the balance of excitation and inhibition in brain.

Currently, millions of Americans suffer from epilepsy and fully 1/3 of these patients do not respond to available treatments. Researchers at Brandeis University have discovered that the Sema4D-PlexinB1 interaction may be harnessed as a novel strategy for the treatment of seizure disorders.

A key aspect of neuronal circuit formation is achieving the proper balance of excitation and inhibition (E/I) within the circuit. A given neuron, through its synaptic connections, either excites or inhibits other neurons in the circuit, thus establishing this balance. Disruptions to the E/I balance can have pathological consequences for circuit function as demonstrated by the manifestation of devastating neurological disorders, including epilepsy and Autism Spectrum Disorders (ASD).

The current invention is a novel approach to treating disorders such as epilepsy that would restore the normal E/I balance in network activity by permanently increasing the number of inhibitory synapses. Treatment of hippocampal cultured neurons with the protein Sema4D, acting through its receptor PlexinB1, causes a rapid increase (i.e. within 30 minutes) in the density of functional GABAergic synapses. It was also discovered that Sema4D could rapidly drive inhibition in the context of aberrant neuronal hyperexcitability induced in an organotypic hippocampal slice culture model of epilepsy. Researchers demonstrated that acute Sema4D treatment rapidly (within 2 hours) abates the hyperexcitability found in these slices. The effect of Sema4D treatment on seizures has been tested in two standard mouse models of epilepsy.



The researchers are interested in finding industry partners to pursue issues around drug production and delivery. For example, Sema4D is a large polypeptide that is unlikely to cross the blood brain barrier, thus making it a poor drug candidate.

Nonetheless, these experiments are important proof of principle

examining the in vivo effects and anti-seizure potential of driving inhibitory synapse formation in rodent models, using Sema4D administration as a tool.

This research also has therapeutic implications for other neurological disorders, such as ASD, where a shift in E/I balance is thought to represent the underlying pathology.

### Advantages:

- This approach could be beneficial to preventing the establishment of epilepsy, halting its progression, or suppressing hyperexcitability during a seizure event
- It is conceptually different from current anti-epileptic drugs most of which seek to ameliorate seizures by temporarily increasing the function of existing inhibitory synapses

Our idea is simple and has high impact potential: on command, we instruct neurons to assemble more inhibitory synapses in the brain, thus suppressing seizures and/or preventing epileptogenesis.

### Scientific Publication:

- Juzirian et al. "The class 4 Semaphorin Sema4D promotes the rapid assembly of GABAergic synapses in rodent hippocampus." (2013) J Neurosci. 33: 8961-73.



# Treatment of RAS-related Cancers by Blocking Palmitoylation

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Cancer Therapy

## INVENTORS

Ruibao Ren  
Benjamin Cuiffo

## PATENT STATUS

Issued: US 9,220,723

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1051

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## Inhibitors of RAS palmitoyl-acyl transferases block oncogenic signaling

### Background:

RAS small GTPases act as molecular binary switches in signal transduction regulating cell proliferation, survival and differentiation via multiple downstream effector pathways including RAF-MEK-ERK and PI3K-AKT. The mammalian RAS family includes three genes that encode four proteins - HRAS, NRAS, KRAS4A and KRAS4B – which are over 90% identical in the first 166 amino acids but diverge at their C-termini which contains sequences to target homologues to specific microdomains and effector pathways in cells. Aberrant activation of RAS signaling pathways is commonly observed in transformed cells with about 30% of all cancers found to have RAS mutations. Activating mutations of HRAS are relatively rare in cancers (3%) while KRAS mutations occur most frequently (85%) followed by NRAS (12%).

Cancers with RAS mutations are the most difficult to treat and refractory to current targeted drug therapies. Our invention is the finding that palmitoylation by palmitoylacyltransferases on RAS proteins at their C-terminal residue(s) upstream of the conserved CAAX motif is essential for oncogenesis. This modification is believed to localize RAS members to the proper regions on plasma membranes for supporting activation of downstream signaling pathways. While still retaining the ability to bind GTP, palmitoylation-defective N- and KRAS oncogenic mutants fail to fully transform cells. Drugs that reduce or block this modification by modulating the activity of key palmitoylacyltransferases would be new targeted approaches needed to address both NRAS- and KRAS4A-associated cancers.

Our new class of inhibitor drugs would be most useful in the treatment of those cancers associated with oncogenes upstream of RAS signaling pathways (e.g. neurofibromin 1-associated cancers; melanomas; BCR/ABL-positive cancers; B-acute lymphoblastic leukemia). Additionally, aberrant NRAS activation is particularly common in certain hematological cancers. Among myeloid malignancies, activating mutations of NRAS are found in 20-40% of acute myeloid leukemia, myelodysplastic syndrome, chronic myelogenous leukemia, multiple myeloma and myelomonocytic diseases, including chronic myelomonocytic leukemia and juvenile myelomonocytic leukemia.

### Summary:

- Palmitoylation plays critical roles in both NRAS- and KRAS4A-mediated leukemogenesis
- Therapies preventing palmitoylation can be used for effectively treating RAS-related cancers
- While completely blocking PI3K-AKT downstream signaling for N- and KRAS, preventing palmitoylation differentially effects RAF-MEK-ERK activation and only blocks signaling for NRAS
- Modulatory drugs can be RNAi-inducing agents, antibodies, siRNA, or small chemical molecules

### Advantages:

- Cancer cells having activated RAS that require palmitoylation for oncogenesis are particularly sensitive to therapy with fatty acid synthase inhibitors (which is normally silent in adult cells)
- Targeted therapies to palmitoyl-acyl transferases are less toxic to cells than farnesyltransferase and geranylgeranyl transferase inhibitors which have proven too toxic to be clinically useful

### Publications:

B. Cuiffo and R. Ren (2010) Palmitoylation of oncogenic NRAS is essential for leukemogenesis. *Blood* 115(7):3598-3605.

Zhao et al. (2015) Roles of palmitoylation and the KIKK membrane-targeting motif in leukemogenesis by oncogenic KRAS4A. *Journal of Hematology and Oncology* 8:132-145.



# Method to Identify Patients Responsive to ICE-Inhibitor Therapies

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

ICE-Cleaved Alpha-Synuclein as a Biomarker

## INVENTORS

Dagmar Ringe  
Gregory A Petsko  
Queyen Hoang

## PATENT STATUS

Issued: US 9,116,157

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1070

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## Use of $\alpha$ -synuclein cleavage by caspase-1 as a biomarker for treatment

### Background:

Alpha-synuclein ( $\alpha$ Syn) is primarily found in brain tissues making up to 1% of all cytosolic proteins in neurons and is predominantly expressed in the neocortex, hippocampus, substantia nigra, thalamus and cerebellum. Fibrillization, aggregation and overexpression of  $\alpha$ -synuclein is believed to play a major role in the degeneration of dopaminergic neurons in synucleinopathy diseases such as Parkinson's disease, dementia and multiple system atrophy. Lewy bodies, which are the abnormal intracellular aggregates found in the dying neurons of Parkinson's disease patients, consist mainly of ubiquitin mixed with misfolded full-length  $\alpha$ Syn and a truncated form containing only its N-terminal 120 amino acids generated by protease cleavage. Inhibition of  $\alpha$ Syn cleavage represents an attractive strategy for preventing Lewy body formations and arresting synucleinopathies. While the larger N-terminal 120 amino acid fragment is believed to nucleate the toxic protein aggregations *in vivo* leading to cell death, the shorter ~20 amino acid C-terminal fragment is released freely from cells.

Based on the inventors' novel finding that the 120 and 20 amino acid cleavage fragments of  $\alpha$ Syn are generated *in vivo* by the protease caspase-1 (also referred to as interleukin-1 beta converting enzyme or ICE), our opportunity available for licensing is a diagnostic method to identify target patient populations having synucleinopathy diseases who are likely to respond favorably to treatment with caspase-1 inhibitor drugs. Caspase-1 is a member of the cysteine protease family of enzymes and located in inflammasomes where it becomes activated in response to environmental toxins, oxidative stress and infections. Our method consists of analyzing a patient's tissue sample (e.g. blood) for the presence of the C-terminal 20 amino acid cleavage fragment of  $\alpha$ Syn that typically is undetectable in normal subjects. Those patients found to have elevated levels of this cleavage fragment would be ideal candidates for treatment therapies using caspase-1 inhibitors.

Caspase-1 is the only known protease capable of cleaving  $\alpha$ Syn *in vivo* into its two protein fragments associated with synucleinopathies. The inventors identified caspase-1 as the responsible isozyme using RNAi knockdown experiments in yeast and human neuronal cell culture models. Caspase-1 proteolysis of  $\alpha$ Syn, fragment aggregation and motor-function impairments were prevented *in vivo* using the ICE inhibitors VX765 (Vertex Pharmaceuticals) or NCGC00185682 (NIH) in mouse models of synucleinopathy diseases.

### Summary:

- Diagnostic method to determine which patients having a synucleinopathy disease would likely respond to treatments using caspase-1 (ICE) inhibitor drugs
- Methodology is based on detecting the presence of a 20 amino acid C-terminal proteolysis  $\alpha$ Syn fragment in patient samples (which is normally absent in samples from unaffected subjects)
- Target patient populations for this method are persons with Parkinson's or Lewy body diseases

### Advantages:

- Targets treatment based on disease causation from  $\alpha$ Syn aggregation and neuronal cell toxicity

### Publications:

Wang *et al.* (2016) Caspase-1 causes truncation and aggregation of the Parkinson's disease-associated protein  $\alpha$ -synuclein. *Proc Natl Acad Sci* 113(34):9587-92.

Bassil *et al.* (2016) Reducing C-terminal truncation mitigates synucleinopathy and neurodegeneration in a transgenic model of multiple system atrophy. *Proc Natl Acad Sci* 113(34):9593-8.





# Improved PCR Primer Strategy for Identifying DNA Variants

## SEEKING

Licensing partners for commercialization

## PATENT TITLE

Compositions and Methods for Nucleic Acid Based Diagnostic Assays for Variable Sequence Targets

## INVENTORS

Kenneth Pierce,  
John Rice and  
Lawrence Wangh

## PATENT STATUS

Issued  
US 9,850,529

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1068

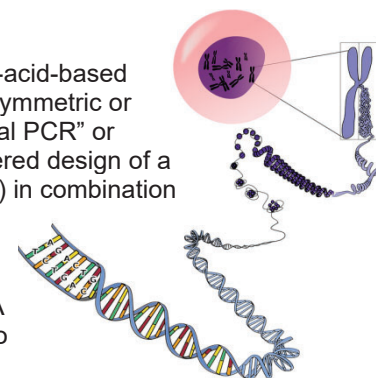
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## Detects presence of all related sequence targets in a single PCR run

### Background:

The invention is an improved method for carrying out nucleic-acid-based diagnostic assays in a single reaction chamber using either symmetric or asymmetric PCR reactions (e.g. "Linear-After-The-Exponential PCR" or LATE-PCR). The key to this method's success is the engineered design of a set of multiple, low-concentration "Initiator Primers" (iPrimers) in combination with a partially homologous consensus primer at a concentration at least 5 times higher. Such primer sets can replace one or both primers of a typical primer pair. The method improves the ability to efficiently amplify DNA or RNA targets with a wide range of sequence variations compared to other consensus primer or degenerate primer methods.



A set of iPrimers can have any or all of the sequences of multiple strains of microorganisms, subtypes of genes, and gene homologues/orthologues within the test sample and are designed to have melting temperatures similar to that of the consensus primer, ensuring amplification of any variant during the first PCR cycles. The consensus primer is preferably designed based on thermodynamic properties to improve the homology with all iPrimers in the set and ensure continued amplification and detection.

The technology can be used in a variety of research, clinical and screening applications that are designed to identify unknown strains of microorganisms or homologues/orthologues of genes in biological samples. The inventors have demonstrated their invention using a detection assay for members of the CTX-M beta-lactamase gene family found in antibiotic-resistant bacteria.

### Summary:

- An improved method for symmetric and asymmetric PCR reactions in diagnostic assays that uses multiple primers in a single tube for simultaneous amplification of multiple related targets
- Allows for detection of 1, 2 or more nucleic acid sequences in a single sample where a consensus primer contains substitutions at multiple positions
- The consensus hybridizes with multiple family members and is present at a higher molar concentration (>5X) than the iPrimers which are designed to bind specific targets
- The priming method is compatible with any probe detection method
- Incorporation of primer-target hybridization thermodynamics results in increased sensitivity

### Advantages:

- Incorporation of this amplification method into kits and related thermocycler systems enables rapid detection of multiple microorganism strains, subtypes or gene variants in a single reaction
- Well suited for amplifications with small reaction volumes and low copy number targets
- Overcomes limitations from existing assays by allowing the amplification of all strains/subtypes with the sample and thus detection of a wider range of variable sequences in a single reaction

### Scientific Publications:

Pierce, K.E. and Wangh, L.J., 2015, Low-concentration initiator primers improve the amplification of gene targets with high sequence variability. *Methods Mol Biol* 1275: 73-89.



# Detection of Sequence Variations within Populations using Non-Symmetric PCR at the Near Digital Level

## SEEKING

Licensing partners for commercialization

## PATENT TITLE

Detecting Mutations in DNA

## INVENTORS

Adam Osborne  
Lawrence Wangh and  
John Rice

## PATENT STATUS

Issued: US 9,637,790

## LICENSING STATUS

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## BRANDEIS REF.

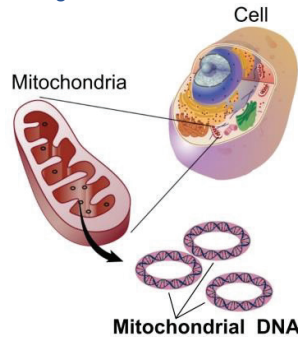
Case 1073

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## Temperature-dependent signatures created by mismatch tolerant probes

### Background:



Mutations in mitochondrial DNA (mtDNA) can result as a side-effect of age, environmental hazards, genetic susceptibility, diet, drug exposure or a combination of causes. These mutations have been correlated with human diseases such as diabetes, Huntington's, cancer, Parkinson's, bipolar disorder, chronic fatigue syndrome, amyotrophic lateral sclerosis and Alzheimer's. However, no specific point mutation has been linked to the onset of a disease. It is hypothesized that the buildup of random mutations over time in the multiple genomes of the mitochondria leads to dysfunction of the organelle and then onset of disease. In order to be able to observe the accumulation of mutations over time, current techniques require analysis of typically 1 to <10 mtDNA molecules which is expensive to carryout.

The technologies for licensing are novel methods for asymmetric amplification and fluorescence detection of the mutational load in nucleic acid target sequences including non-nuclear DNA (e.g. mtDNA, chloroplast DNA, episomal DNA) as well as RNA, cDNA, and genomic DNA. These methods utilize single-tube, multiplex polymerase chain (PCR) reactions on mixed samples which each contain one or more target specific primer pairs for DNA amplification. These reactions also contain 1 or more probe pair sets that hybridize to adjacent sites within the target, though probe pairs need not be next to each other, and each have covalently attached to it either a fluorescent compound ("Signaling Probe") or a non-fluorescent complementary quencher moiety (e.g. dabcyI or Black Hole Quencher; "Quencher Probe"). The Signaling Probe will not fluoresce unless bound to the amplified single-strand target sequence. The signal is eliminated by the fluorophore and quencher moiety whenever both probes are bound to their adjacent sites on the target sequence.

Mutational load is determined by analyzing the differences in fluorescence for the hybridization curves. Signals can be acquired either as the reaction temperature is decreased (annealing) or increased (melting). The Signaling Probes and Quencher Probes are both mismatch tolerant and can hybridize to sequences that contain 1 or more substitutions where those with greater variation from the target's complementarity lowers the melting temperature ( $T_m$ ) of the probe-target hybrid. Differences in  $T_m$  can be used to differentiate mutations accumulating in the target DNA sequence.

The invention has been enabled for the detection of human mtDNA mutations within cytochrome c oxidase subunit 2, NADH dehydrogenase subunit 1 and the hyper variable 2. The mtDNA of mice, rats, and the Nile rat (used to study diabetes) have also been amplified using this technology.

### Summary:

- Novel methods for identifying mutational loads in target DNA sequences using single-tube, asymmetric PCR reactions on mixed biological samples (specifically enabled for mtDNA)
- Mutations are detected by analysis of the temperature-dependent fluorescence signatures created by the annealing or melting of signal/quencher probe pairs to the single-stranded target
- Methods are broadly applicable to human and animal genomic and other complex DNA samples

### Advantages:

- Allows for amplification of targets and detection of multiple mutations in a single PCR reaction
- Overcomes limitations of prior analysis methods which can obscure the presence of mutations due to target DNA having methylated stretches of nucleic acids

### Citations:

Osborne *et al.* (2013) "AZT Treatment Increases mtDNA Mutations in HepG2 and CCD-1112Sk Cells." J AIDS Clin Res 4: 250. doi: 10.4172/2155-6113.1000250

Osborne *et al.* (2014) "Palm Fruit Juice Mitigates AZT Mitochondrial Genotoxicity and Dose-Dependent Cytotoxicity." J AIDS Clin Res 5: 400. doi:10.4172/2155-6113.1000400



# Enzyme-Instructed Self-Assembly of Antineoplastic Hydrogels

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

Antineoplastic Hydrogels, and Enzyme-Instructed Preparations Thereof

## INVENTORS

Yuan Gao, Yi Kuang, Bing Xu

## PATENT STATUS

Issued:

U.S. Patent No. 8,658,600

U.S. Patent No. 9,408,921

## LICENSING STATUS

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## BRANDEIS REF.

Case 1029

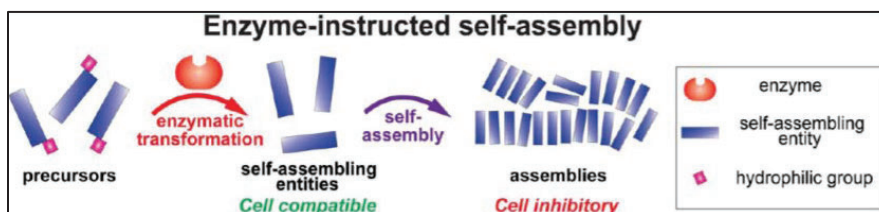
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## Nanofibers of therapeutic molecules act as a drug delivery vehicle

Cancer remains a major challenge to the public health. Therefore, there exists a need for more effective cancer treatments. To improve anti-cancer efficacy and to counteract chemotherapeutic side effects, drug carriers that improve the water solubility of anti-cancer drugs and target tumor cells have been developed. However, conventional drug delivery systems require a polymer matrix, which suffers from degradation and low biocompatibility and low drug capacity.

The current invention overcomes these limitations with nanofibers based on enzyme-triggered self-assembly of small molecules, providing a powerful method to create molecular hydrogels of clinically-used therapeutics without compromising their bioactivities. As both the delivery vehicle and the drug itself (taxol), these molecular nanofibers have tremendous potential as anticancer nanomedicines.



Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Summary:

- A novel self-assembling peptide motif composed of an enzymatically cleavable group is covalently connected to an anti-cancer drug (taxol) to form the precursor
- Upon an enzymatic reaction, the novel precursor transforms into a hydrogelator, which self-assembles into nanofibers and affords a supramolecular hydrogel of a pharmaceutical agent
- To treat cancer, tumors, malignancies, neoplasms, or other dysproliferative diseases, these low-molecular weight hydrogels release the encapsulated drugs upon degradation

### Advantages:

- This platform technology improves the safety and efficacy of anti-cancer drugs
- Enzyme-instructed self-assembly is a facile strategy for generating the supramolecular hydrogels of molecules that inherently have poor solubility in water
- Molecular hydrogels of these hydrophobic drug molecules serve as delivery systems for long term or local delivery of anticancer drugs for chemotherapy
- Unlike conventional drug delivery systems, this invention does not require a polymer matrix

### Scientific Publications:

- "Enzyme-Instructed Self-Assembly: A Multistep Process for Potential Cancer Therapy." (2015) *Bioconjugate Chem.* 26, 987-999. DOI: 10.1021/acs.bioconjchem.5b00196
- "Enzyme-Instructed Molecular Self-assembly Confers Nanofibers and Supramolecular Hydrogel of Taxol Derivative." (2009) *J. Am. Chem. Soc.* 131, 13576-13577. DOI: 10.1021/ja904411z



# Multifunctional Hydrogels of Nucleopeptide and Glycopeptide

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Supramolecular Nanofibers and  
Hydrogels Based on Nucleic Acids  
Functionalized with Nucleobases

## INVENTORS

Bing Xu

## PATENT STATUS

Issued:

U.S. Patent No. 10,093,674

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1088

## CONTACT

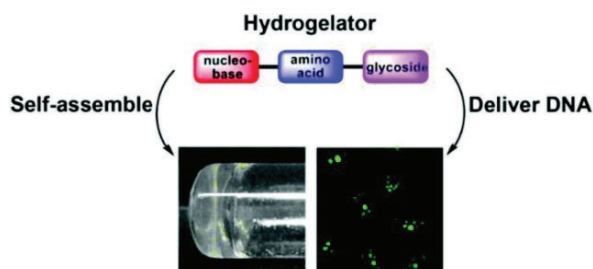
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## Sophisticated soft nanomaterials mimic natural extracellular matrices with high biocompatibility for tissue engineering

### Background:

Every year, millions who suffer from tissue loss or failure as a result of accidents or disease rely on alternative biomedical materials to regenerate living, healthy, and functional tissues. Engineered tissue scaffolds have been developed for cellular regeneration, wound healing, and diseased tissue treatment. Unfortunately, natural and synthetic polymers currently serving as these scaffolds are limited by separation and purification roadblocks, at the same time, bring cytotoxicity and demonstrate poor responsiveness to biological cues.



The solution to these problems lies in the current invention. Facile conjugation of small peptides with nucleobases and/or glycosides generates a new kind of supramolecular hydrogelator that mimics extracellular matrices for tissue engineering with high biocompatibility. Composed of fundamental biological building blocks, these low molecular weight hydrogelators may be used for many biomedical applications, including cell culturing, tissue engineering, enzyme and non-viral gene, and cancer immunotherapy.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Summary:

- To produce biomaterial comprised of a nucleobase, an amino acid, and/or a glycoside, each component is covalently coupled through a series of facile NHD activations
- Upon triggered by a change in pH or by an enzyme, the nucleopeptide or glycopeptide biomaterials self-assemble in water to afford biocompatible and bio-stable hydrogel
- Cell proliferation and rapid wound healing is promoted by contacting a plurality of cells with the supramolecular structures of the nucleopeptide and/or glycopeptide hydrogels
- The supramolecular nanofibers or hydrogels may be further functionalized to behave as a substance-hydrogel drug delivery vehicle to cells for viral infection or cancer treatment

### Advantages:

- The tunable nucleopeptide backbone enables facile structural manipulation to produce various glycol-nucleopeptide and nucleopeptide derivatives for a multitude of biomimetic applications;
- These hydrogel are resistant to protease degradation while showing high mechanical strength and prominent viscoelastic properties
- Cell penetrating abilities for DNA and RNA delivery offers a new non-viral vector for gene therapy
- Effective, safer and cheaper than traditional polymers in tissue engineering and drug delivery





# Aggregates of Small Molecules Selectively Inhibit Tumor Growth

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

INHIBITION OF TUMOR  
GROWTH WITH AGGREGATES  
OF SMALL MOLECULES

## INVENTORS

Yi, Kuang  
Bing, Xu

## PATENT STATUS

Issued:  
U.S. Patent No. 10,308,682

## LICENSING STATUS

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## BRANDEIS REF.

Case 1123

## CONTACT

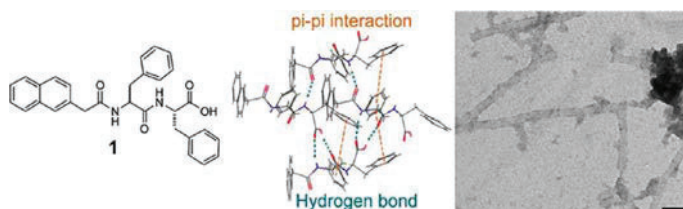
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## Self-Assembly of Hydrophobic Peptides Impede Cytoskeleton Dynamics

### Background:

Cancer and Alzheimer's disease are major threats to the public health. While both diseases are still being understood, epidemiological and clinical studies suggest that there is an inverse association between cancer and Alzheimer's disease. For example, several groups have suggested that cancer and Alzheimer's disease may share same genes (e.g., TP53 and PIN1) and biological pathways (e.g., Wnt) related to activation and deregulation of the cell cycle. The intriguing inverse association has stimulated the current invention to address the mechanisms which may lead to novel therapies to both diseases.

The invention discloses a novel paradigm of anticancer agents selectively prevent mitosis and inhibit cell proliferation. This platform invention achieves several merits including, (i) the said hydrophobic, self-assembling, small monomers are designed to form molecular aggregates to biophysically and morphologically resemble aberrant protein in Alzheimer's disease; (ii) the elevated micropinocytosis of cancer cells, as a part of the Warburg effect, enables selective accumulation of molecular aggregates within the cell to induce cell death, while stromal cells and neuronal cells, having low uptake of designed monomers, can remain viable; (iii) the molecular aggregates can be co-administrated with taxol or nocodazole to synergistically induce apoptosis of some drug-resistant cancer cells (e.g. T98G); (iv) the peptidic nature of designed monomer prevents long term accumulation and chronic toxicity; (v) the invention has a well-established synthetic route to ensure fast, low-cost, and easily scaled-up production.



The invention available for licensing is a library of hydrophobic, self-assembling small molecules which specifically target cancer cells and inhibit tumor growth. The diversity of small molecular fibril aggregates offers abundant opportunity for generating other functional entities. Furthermore, the inhibitory effect on tumor growth has been tested on nude mice with xenograft tumors by injection. The molecular aggregates significantly inhibited tumor growth over 20 folds comparing to the control during 20 days without inducing inflammation response in skin tissue or any other side effects. The findings illustrate the power of these novel anticancer agents, and potentially benefit the therapeutic research for both cancer and neurodegenerative diseases.

### Summary:

- A library of hydrophobic, self-assembling small molecules selectively inhibit tumor growth *in vivo*
- Self-assembled molecular aggregates biophysically & morphologically resemble aberrant protein
- Co-administration with taxol or nocodazole induces synergistic apoptosis of drug-resistant cells

### Advantages:

- The peptidic nature of designed monomer prevents long term accumulation and chronic toxicity
- Exploiting an established synthetic route to ensure fast, low-cost, and easily scaled-up production

### Scientific Publications:

- "Prion-like Nanofibrils of Small Molecules (PriSM) Selectively Inhibit Cancer Cells by Impeding Cytoskeleton Dynamics." JBC **289**, 29208-29218 (17 Oct 2014) doi: 10.1074/jbc.M114.600288



# fMLF-Based Supramolecular Hydrogels Prolong Inflammation Response

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

SUPRAMOLECULAR HYDROGEL OF fMLF-BASED MOLECULES AND USE THEREOF

## INVENTORS

Bing Xu  
Fan Zhao  
Hongbo R Luo  
Jingyu Li

## PATENT STATUS

Issued:  
U.S. Patent No. 10,232,037

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1152

## CONTACT

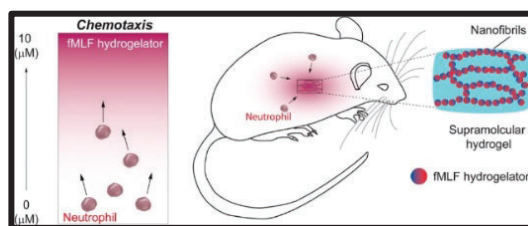
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## Hydrogels of chemoattractants preserve neutrophil activity for immunomodulation

### Background:

Neutrophils play a key role in combatting infection in the human body. Efficient local accumulation of neutrophils depends on gradients of N-formyl peptides, such as N-formyl-L-methionyl-L-leucyl-L-phenylalanine (fMLF), to signal neutrophils to the site of infection or disease. As a chemoattractant, fMLF has been used in aqueous or heterogeneous solutions for inducing acute inflammation to slow tumor growth or treat bacterial infections. However, current fMLF delivery methods have relatively weak and transient effects and suffer from burst release and low capacity payload.



The innovative approach developed to obviate these limitations incorporates fMLF into D-peptides to create self-assembling hydrogels of multifunctional chemoattractants that maintain their potent chemotactic activity towards neutrophils. As self-delivery-drugs, the fMLF-hydrogels hold promise as cancer therapies, treatment for microbial infections, and vaccine adjuvants. The modular aspects of these scaffolds can be further implemented towards neutrophil chemotaxis inhibition, rather than promotion, for chronic inflammation and pain treatments.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications

### Summary:

- D-peptides conjugated to immunogenic N-formyl peptides (i.e., fMLF) self-assemble into hydrogel
- The fMLF-hydrogels induce sustained release of chemoattractants, leading to neutrophil accumulation at the site of administration
- Administering fMLF-hydrogels at tumor site promotes innate immune response & inhibits growth
- The fMLF-hydrogels shrink tumor size when injected intratumorally every 48 hours
- Effective to treat bacterial infection, reduce sepsis, and promote resolution of septic condition
- Replacing fMLF with formyl peptide receptor (FPR) antagonists inhibits neutrophil activation for treating undesirable inflammation and pain

### Advantages:

- Immunomodulating hydrogels are structurally tunable scaffolds to treat diseases and infections
- fMLF-hydrogels of D-peptides are proteolytically stable, prolonging the sought therapeutic effects
- Self-delivery method allows high capacity payload, eliminate burst release, and sustain treatment
- The hydrogels may be tailored to apply to prosthetic devices or organs to remove biofilms
- Low administration frequency of fMLF- or FPR-hydrogels reduce cost and patient discomfort

### Scientific Publication:

- "De Novo Chemoattractants Form Supramolecular Hydrogels for Immunomodulating Neutrophils In Vivo." *Bioconjugate Chem.*, **2014**, 25 (12), pp 2116–2122. DOI: 10.1021/bc5004923



# Pericellular Nanonets Collect Cancer Cell Exosomes

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

Synthetic peptides, enzymatic formation of pericellular hydrogels/nanofibrils, and methods of use

## INVENTORS

Bing Xu, Junfeng Shi, Yi Kuang, Xuewen Du, Jie Zhou

## PATENT STATUS

Issued: U.S. Patent No. 11,155,576

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1157

## CONTACT

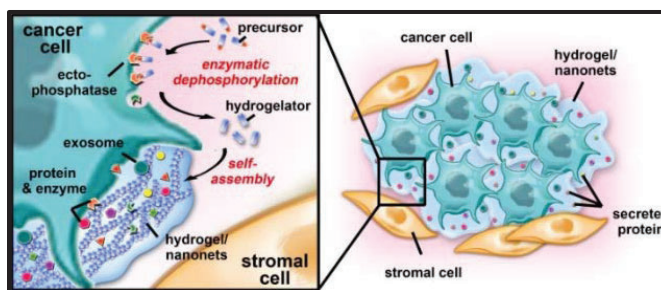
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## A cutting-edge diagnostic tool: selective formation of pericellular nanonets on cancer cell surface entrap secretome

### Background:

Traditional chemotherapy or molecular therapy has been rendered inadequate as cancer treatments, due to the ever-growing complexity of cancer cells, which leads to cancer drug resistance and metastasis. Moreover, accurate and reliable early cancer detection techniques involving exosome analysis for novel biomarker discovery and identity is lacking, further contributing to the rising mortality rate caused by cancer. Therefore, it is imperative to develop innovative approaches to overcome cancer and drug resistance.



The current invention integrates enzymatic transformation and self-assembly of D-peptide derivatives into a novel cancer theranostic technique to improve early cancer detection and cancer treatment. Nanonets of D-peptidic hydrogels selectively form within the pericellular space of cancer cells to simultaneously inhibit target cell survival and entrap cancer cell secretomes, for accurate mapping and discovery of cancer biomarkers and elimination of cancer drug resistance.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Summary:

- Hydrogel precursors comprised of several amino acids, with a plurality of aromatic amino acids which are either phosphorylated, sulfated, or covalently bound to an ester-moiety
- The precursors become hydrolyzed upon exposure to overexpressed ectoenzymes
- The enzymatically active peptides self-assemble into nanonets on the targeted cell surfaces
- Inhibit cancer cell migration and proliferation, while entrapping secretomes within the nanonets
- Covalent conjugation of a fluorophore may be integrated for imaging on live cells

### Advantages:

- These molecular nanofibers actively prevent cancer cell proliferation and collect cancer cell exosomes, serving as a novel diagnostic tool for cancer nanomedicine;
- Enzymatic formation of molecular nanofibrils inhibits survival of drug-resistant cancer cells
- Deepens understanding of cancer progression and accelerates cancer biomarker discovery
- The procedure is simple and eliminates the need for additional purification or concentration steps
- A low-cost diagnostic method for high yields of secretome with relatively short incubation time



# Novel Magnetic Nanoparticles Selectively Target Cancer Cells

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

ENZYMATICALLY RESPONSIVE  
MAGNETIC PARTICLES AND  
THEIR USE

## INVENTORS

Bing Xu  
Xuewen Du  
Jie Zhou

## PATENT STATUS

Issued:  
U.S. Patent No. 10,857,243

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1162

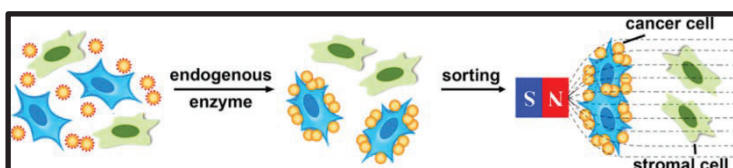
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## Platform technology for cell sorting, cancer diagnostics and therapeutics

### Background:

Cell sorting has become an important sampling method for isolating specific cells from a mixed population, contributing many biomedical advances. Unfortunately, sorting mammalian cells requires complicated and expensive instruments and reagent, such as the most widely used cell sorting method, fluorescent activated cell sorting (FACS). Magnetic cell sorting is a promising alternative technique, but as it stands, is an ill-defined process due to the non-specific protein binding to modified magnetic beads. Thus, there exists a need for an inexpensive cell sorting method that will contribute to low-cost diagnostics and treatment.



The current invention is a new approach that eliminate both the high cost of FACS and involvement of specific ligand receptor interactions. Designed

around in inherent difference between cancer and normal cells, overexpression of ectophosphatases, this method employs magnetic nanoparticles (MNp) that are modified to selectively sort and inhibit cancer cells from a mixed cell population without the extra expense. This facile, highly selective, and low cost process will lead to the use of MNPs in many biomedical applications.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications

### Summary:

- Conjugated to MNp, the amino acid residue contains a enzymatically responsive cleavable moiety
- Mixed cell population comprising normal and cancerous cells are treated with the MNp conjugates
- Overexpressed ectoenzymes on the cancer cell surface hydrolyze the cleavable moiety of the MNp, selectively labeling cancerous cells over normal ones
- The labeled cancer cells are magnetically separated from mixed population under magnetic field
- Selective adherence of the hydrolyzed MNp is also sufficient to inhibit cancer cell survival
- The high selectivity of adherence can generate better cell imaging by enhancing contrast

### Advantages:

- Enzymatically triggered adhesion of MNPs selectively to cancer cells can be utilized in biomedical applications: cell sorting, cell separation, imaging and disease diagnostics and treatment
- MNPs perform better than nanoparticles loaded with cisplatin<sup>1</sup> as cancer therapeutics
- Unlike FACS, this invention eliminates the need of labelling cells with fluorescent proteins
- Reducing the cost, increasing product stability and improving cell sorting efficacy
- The invention is straightforward to enable and does not require expensive set-up or antibodies

### Scientific Publication:

- "Enzymatic Transformation of Phosphate Decorated Magnetic Nanoparticles for Selectively Sorting and Inhibiting Cancer Cells." *Bioconjugate Chem.*, **2014**, 25 (12), pp 2129–2133. DOI: 10.1021/bc500516g





# EISA of a Tyrosine-Cholesterol Conjugate Selectively Kill Cancer Cells

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Enzyme-Instructed Assemblies of  
a Tyrosine-Cholesterol Conjugate  
Selectively Kill Cancer Cells

## INVENTORS

Bing Xu, Huaimin Wang

## PATENT STATUS

Issued: U.S. Patent No.  
11,040,108

## LICENSING STATUS

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## BRANDEIS REF.

Case 1273

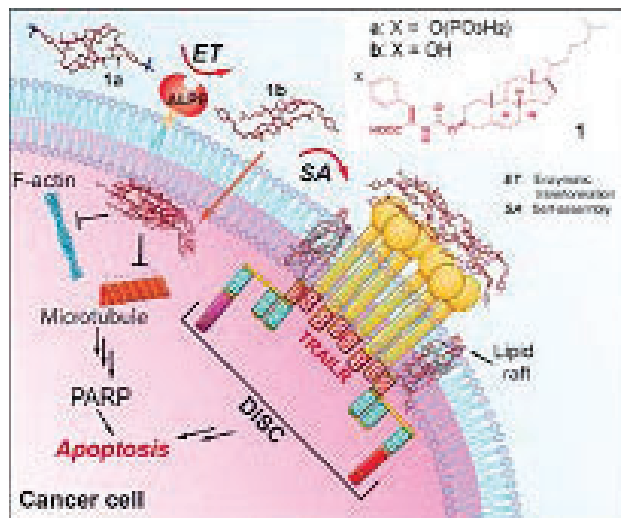
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## EISA of tyrosine-cholesterol conjugate activates extrinsic and intrinsic cell death signaling

This invention introduces a new platform of single amino acid-cholesterol conjugate that selectively inhibiting cancer cell by the overexpressed enzyme. This system could find various applications in inhibiting drug resistant cancer (e.g., ovarian cancers), to serve as a platform for combination therapy, drug delivery, or as a vaccine to modulate immune system, thus it potentially holds many therapeutic possibilities.



A finding of a tyrosine-cholesterol conjugate which could selectively form aggregate outside/intracellular environment by the overexpressed enzyme of cancer cell is utilized to selectively control the fate of cancer cell while not damage normal tissue. Alkali phosphatase which overexpressed from several cancer cell lines dephosphorylate a precursor of a tyrosine-cholesterol conjugate to trigger the self-assembly of the aggregator and to generate toxic aggregates selectively either around or inside specific cancer cells that overexpress phosphatase. Several other amino acid-cholesterol conjugates were also tested to confirm the specificity of

tyrosine. Comparing with the commercial drug cisplatin, the tyrosine-conjugate also exhibited better therapeutic effect against cisplatin resistant cancer cell (A2780cis). This discovery of enzyme instructed assembly of tyrosine cholesterol conjugate presented new applications of amino acid cholesterol conjugate such as controlling cancer cell death, inhibiting drug resistance cancer cell, immune therapy and drug delivery. Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications

### Summary:

- A novel platform of single amino acid-cholesterol conjugate that selectively inhibits cancer cell;
- The tyrosine-cholesterol conjugate which could form aggregate outside/intracellular environment by the overexpressed enzyme is utilized to selectively control cancer cell fate while not damage normal tissue.
- Based on the advantage of selectivity, the platform has great potentials in applications such as cancer cell drug resistance inhibition, immune therapy and drug delivery.

### Advantages:

- The invention pioneers in selective inhibition of cancer cell by the self-assembly of single amino acid-cholesterol conjugate or peptide-cholesterol conjugate;
- The present invention serves as a successful demonstration to inhibit cancer cell lines including cisplatin drug resistant cancer cell;
- This work illustrates a new way for developing efficient nanomedicine against drug resistant cancer as the first study to use EISA for modulating lipid rafts.

### Publications:

- H.M Wang et al. "Enzyme-Regulated Supramolecular Assemblies of Cholesterol Conjugates against Drug-Resistant Ovarian Cancer Cells." J. Am. Chem. Soc., 2016, 138 (34), pp 10758–10761. DOI: 10.1021/jacs.6b06075.



# Mitochondria Targeting Kills Cancer Cell without Acquired Drug Resistance

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

EISA coupled with mitochondria targeting to selectively kill cancer cells without acquired drug resistance

## INVENTOR

Bing Xu

## PATENT STATUS

Pending:

U.S. Patent Application No. 16/476,183

## LICENSING STATUS

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## BRANDEIS REF.

Case 1311

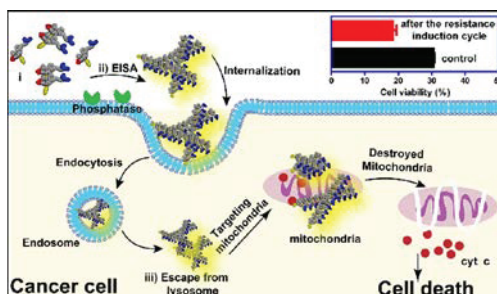
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## High selectivity in mitochondrial targeting of cancer cell via enzymatic cleavage

Targeting organelles by modulating the redox potential of mitochondria is a promising approach to kill cancer cells that minimizes acquired drug resistance. However, it lacks selectivity because mitochondria perform essential functions for (almost) all cells. This invention shows that enzyme-instructed self-assembly (EISA), a bioinspired molecular process, selectively generates the assemblies of redox modulators (e.g., triphenyl phosphonium (TPP)) in the pericellular space of cancer cells for uptake, which allows selectively targeting the mitochondria of cancer cells. The attachment of TPP to a pair of enantiomeric, phosphorylated tetrapeptides produces the precursors (L-1P or D-1P) that form oligomers. Upon dephosphorylation catalyzed by ectophosphatases (e.g., alkaline phosphatase (ALP)) overexpressed on cancer cells (e.g., Saos2), the oligomers self-assemble to form nanoscale assemblies only on the surface of the cancer cells. The cancer cells thus uptake these assemblies of TPP via endocytosis, mainly via a caveolae/raft-dependent pathway. Inside the cells, the assemblies of TPP-peptide conjugates escape from the lysosome, induce dysfunction of mitochondria to release cytochrome c, and result in cell death, while the controls (i.e., omitting TPP motif, inhibiting ALP, or removing phosphate trigger) hardly kill the Saos2 cells. Most importantly, the repeated stimulation of the cancers by the precursors, unexpectedly, sensitizes the cancer cells to the precursors.



acquired drug resistance. The invention also the first time to report controlling peptide self-assembly inside organelle of mitochondria of live cells, which provides new opportunity for therapeutics against cancer and some immune-deficient disease. Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

## Summary:

- A novel molecular-targeted therapeutic system by integrating special control of cytotoxic agents by EISA;
- A bioinspired molecular process, selectively generates the assemblies of redox modulators (TPP) in the pericellular space of cancer cells for uptake, allows selectively targeting the mitochondria of cancer cells.
- Based on the advantage of selectivity, the platform has great potentials in applications such as cancer cell drug resistance inhibition, immune therapy and drug delivery.

## Advantages:

- Achieves high selectivity in mitochondrial targeting of cancer cell;
- The first example to integrate subcellular targeting and spatial control of the assemblies of non-specific cytotoxic agents by EISA as a promising molecular process for selectively killing cancer cells;
- A new way for developing efficient nanomedicine without inducing acquired drug resistance.

## Publications:

- H.M Wang et al. "Integrating Enzymatic Self-Assembly and Mitochondria Targeting for Selectively Killing Cancer Cells without Acquired Drug Resistance." J. Am. Chem. Soc., 2016, 138 (49), pp 16046–16055. DOI: 10.1021/jacs.6b09783



# Instant Formation of Supramolecular Hydrogels by Short Peptide and Bioactive Small Molecules

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

RAPID FORMATION OF SUPRAMOLECULAR HYDROGELS BY SHORT PEPTIDE AND BIOACTIVE SMALL MOLECULES

## INVENTORS

Bing Xu  
Huaimin Wang

## PATENT STATUS

Pending: U.S. patent application 16/639,467

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1339

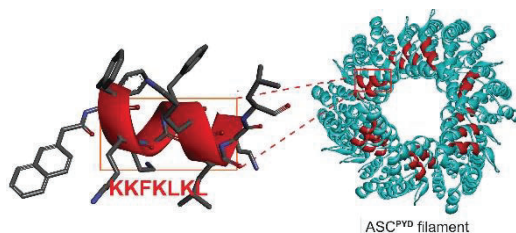
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### Background:

The invention describes a novel method of fast hydrogelation based on short peptide triggered by small bioactive molecules. The invention not only illustrates a fundamentally new way to form hydrogels that with controlled morphology, but also suggests an unprecedented approach to engineer molecular assemblies based on short peptides for many other applications, such as wound healing, drug delivery, 3D cell cultures, immune adjuvant controlling immune responses of small molecules.



To solve the key step for applications such as wound healing, tissue engineering and 3D cell culture, fast gelation of hydrogel based on short peptides is proposed as a novel designed peptide sequence NapFFKKFKLKL by utilizing small bioactive molecules such as pyridoxal phosphate, pyridoxal, folic acid, ATP, ADP, AMP and phosphorylated tyrosine to induce fast gelation process. The peptides consist of three key parts: i) the epitope of KKFKLKL, a conserved surface of residues that play critical roles for oligomerization of the hASCPYD. ii) Lysine, the most employed amino acid in proteins, not only serves as an active site for the formation of Schiff-base in biological system, but also introduces positive charge to the peptides for interacting with the phosphate on pyridoxal phosphate. iii) Nap-FF is a well-established building block for promoting self-assembly both in aqueous solution and biological milieu. As the demonstration of correlating assemblies of peptides and the relevant protein epitopes, this work shows a bioinspired approach to develop supramolecular structures modulated by endogenous small molecules.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Summary:

- This invention describes a novel approach to self-assemble peptides and relevant protein epitopes intrigued by endogenous small bioactive molecules to develop various supramolecular structures;
- The fast gelation is achieved by utilizing pyridoxal phosphate, pyridoxal, folic acid, ATP, ADP, AMP and phosphorylated tyrosine to induce gelation process of a novel designed peptide sequence NapFFKKFKLKL;
- Based on the advantage of fast gelation, the system has great potentials in applications such as wound healing, tissue engineering and 3D cell culture.

### Advantages:

- The invention would be more biocompatible and much faster comparing to other strategies for instant gelation by using small endogenous molecules;
- The present invention serves as an efficient method to design short peptides that adopt conformations such as helical and random-coil other than most common beta-sheet conformation;
- The bioactive small molecules in this system can also serve as a cell compatible trigger for crosslinking the pre-exist nanofibers of other peptides or drugs to form instant hydrogel.

### Scientific Publications:

- "Instant Hydrogelation Inspired by Inflammasomes." (2017) DOI: 10.1002/anie.201702783
- "Nucleopeptide Assemblies Selectively Sequester ATP in Cancer Cells to Increase the Efficacy of Doxorubicin" (2018) DOI: 10.1002/anie.201712834



# Branched Peptides for Enzymatic Assembly and Mitochondria Drug Delivery

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

BRANCHED PEPTIDES FOR ENZYMATIC ASSEMBLY AND MITOCHONDRIA DRUG DELIVERY

## INVENTORS

Bing Xu; Hongjian He

## PATENT STATUS

Issued:  
U.S. Patent No. 11,191,724

Pending: U.S. Patent Application  
No. 17/537,418

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Cases 2018-002 & 2020-001

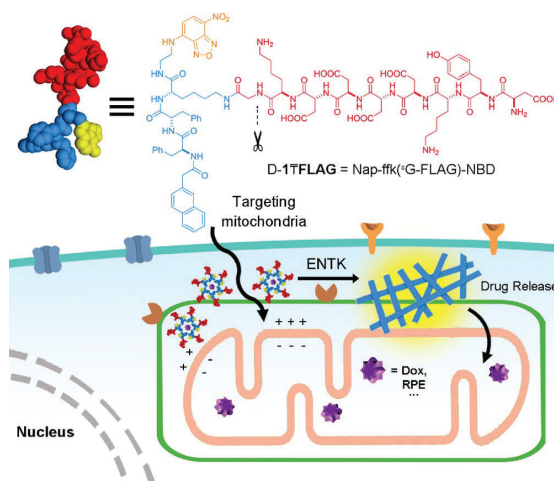
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### Background:

This invention introduces a new platform technology accomplishing mitochondria-targeting cargos delivery to selectively inhibit or rescue different types of cells. Due to the importance of mitochondria for living cells, the branched peptides have the potential to control the fate of cells, via delivering diverse bifunctional molecules to mitochondria. The targeting delivery of cytotoxic drugs to mitochondria may significantly increase the toxicity, while the mitochondrial accumulation of some bioactive molecules (e.g. pifithrin- $\mu$ ) may rescue normal tissue from radiotherapy.

To meet the need of mitochondria-targeting cargos delivery, a branches peptide is designed to control the fate of cells, either inhibit or rescue, via delivering diverse bio functional molecules to mitochondria. The generation of supramolecular hydrogel via branched peptides upon the addition of a serine protease: enterokinase (ENTK). The said peptide consists of 3 fragments: i) the FLAG-tag DYKDDDK, as the substrate of ENTK for proteolysis, ii) a hydrophobic peptide moiety which self-assembles into nanofibers after the cleavage of FLAG-tag, and iii) a Glycine, as the spacer for I and ii. The enzymatic cleavage of the hydrophilic FLAG branch by ENTK turns the branched peptide hydrogelator to nanofibers, resulting into supramolecular hydrogel. The merit of this invention is, to carry multiple negative charges and can escape from endosome after rapid cellular uptake and specifically accumulate in mitochondria. Bioactive molecules, such as proteins and anti-cancer drugs, can be encapsulated by the branched peptides and eventually delivered to mitochondria.



### Summary:

- This invention describes a novel targeting delivery of cytotoxic drugs to mitochondria may significantly increase the toxicity to control cell fate;
- The branched hydrogelator is specifically designed with three fragments including the FLAG-tag DYKDDDK, a self-assembling hydrophobic peptide moiety, and a spacer linking these two parts;
- This novel approach for mitochondria targeting drug delivery demonstrates rapid cellular uptake and specific accumulation in mitochondria in vitro.

### Advantages:

- The invention reports a new possible mechanism for targeting mitochondria other than traditional lipophilic and cationic molecules;
- This work illustrates a new approach to encapsulate bioactive molecules, such as proteins and anti-cancer drugs, into the designed branched peptides and eventually get delivered to mitochondria;
- The invention introduces a mitochondrion –specific drug delivery of cargo molecules by the FLAG-tagged precursors which is promising for various application in biomedicine.

### Scientific Publications:

- "Enzymatic Cleavage of Branched Peptides for Targeting Mitochondria." (2018) DOI: 10.1021/jacs.7b11582





# Peptide-conjugated Prodrugs with Enhanced Efficacy for Inhibiting Bacteria

## SEEKING

Exclusive licensing partner and/or sponsored research funding

## PATENT TITLE

PEPTIDE-CONJUGATED

Licensing partner and/or sponsored research funding  
PRODRUGS

## INVENTORS

Bing Xu  
Jiaqing Wang

## PATENT STATUS

Pending;  
PCT/US2020/051410

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2019-038

## CONTACT

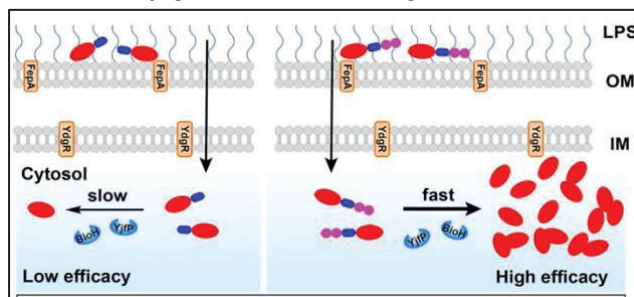
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### Background:

Antimicrobial drug resistance demands novel approaches for improving the efficacy of antibiotics, especially against Gram-negative bacteria. This invention reports that conjugating a diglycine (GG) to an antibiotic prodrug drastically accelerates intrabacterial ester-bond hydrolysis required for activating the antibiotic.

The emergence of multidrug resistant (MDR) bacteria remains a serious problem in biomedicine. However, the antibiotic supply in clinical pipeline is limited. Therefore, there is an urgent need for developing new antimicrobial approaches against MDR bacterial pathogens. In comparison to developing a new drug which requires years of extensive testing, modifying existing antibacterial drug to form derivatives with the higher efficacy is much more rapid, lower-cost and safer. In this invention, the strategy is to conjugate a series of peptides to a prodrug of antibiotics and efflux pump inhibitors, or use aminoacetonitrile to modify C-terminal of peptides as well. The efficacy of these conjugates was tested against E.coli. for the antimicrobial activity. Besides, the cytotoxicity of these conjugates was confirmed against several mammalian cell lines including bone marrow cells, hepatocyte cells and kidney cells. This work illustrates that peptide conjugation modulates intrabacterial hydrolysis for increasing antibiotic efficacy against bacteria.



The conjugation of peptides is an effective strategy for accelerating the hydrolysis catalyzed by intrabacterial esterases and enhancing the efficacy of antibiotics. The discovery should help develop new antimicrobial prodrugs more selective to bacteria, thus increasing efficacy and decreasing adverse effects of drugs.

### Summary:

- This invention describes a novel strategy of conjugating GG to succinate prodrugs of antibiotics to enhance the efficacy and improves the safety of the existing antibiotics;
- The rapid intrabacterial hydrolysis serves as a useful approach for countering the efflux pumps or other bacterial machineries;
- The conjugation of GG to an antibiotic prodrug is an effective strategy for accelerating enzymatic prodrug hydrolysis and enhancing the antibacterial efficacy of antibiotics.

### Advantages:

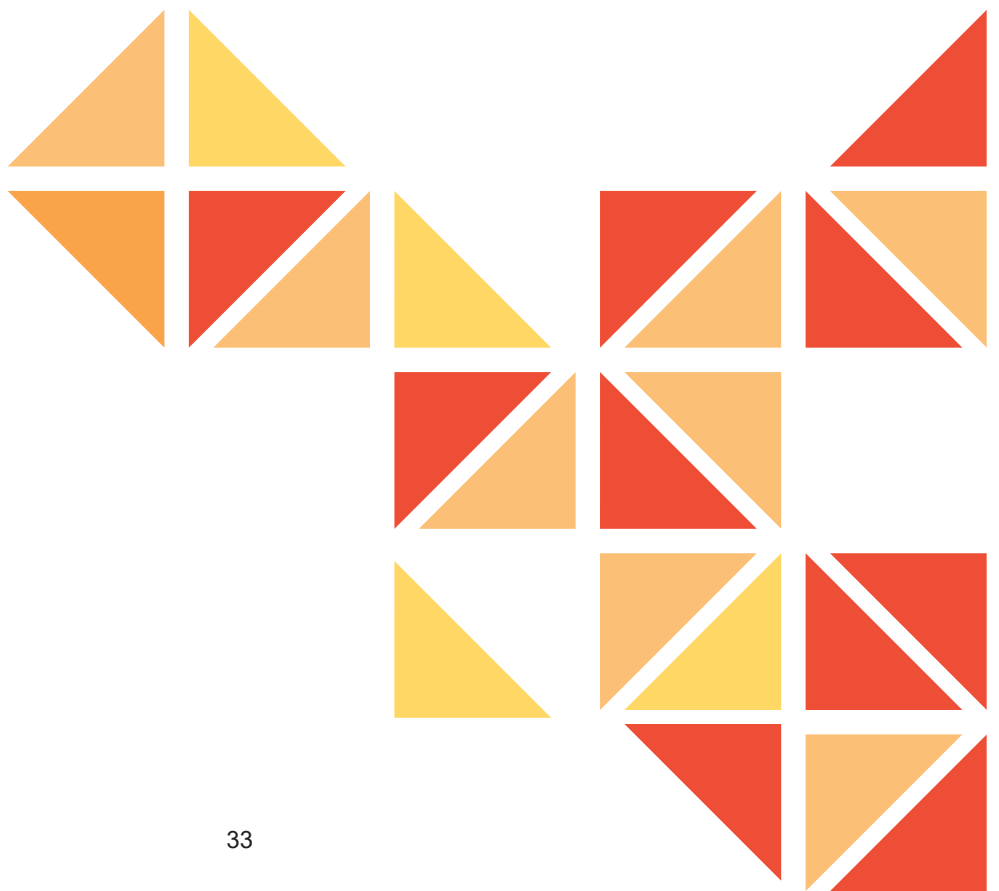
- The invention reports an antibiotic prodrug drastically accelerates intrabacterial ester-bond hydrolysis required for activating the antibiotic;
- The conjugate prodrug exhibits lower cytotoxicity to bone marrow stromal cells than chloramphenicol;
- The dipeptide conjugation modulates intrabacterial hydrolysis for increasing antibiotic efficacy and reducing adverse drug effects.

### Scientific Publications:

- " Diglycine Enables Rapid Intrabacterial Hydrolysis for Activating Antibiotics against Gram-negative Bacteria." *Angew Chem Int Ed Engl* 2019 Jul 29;58(31):10631-10634. doi: 10.1002/anie.201905230.



# Research Tools & Materials



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# Catalytic Asymmetric Umpolung Reactions of Imines

## SEEKING

Licensing partner for commercialization

## PATENT STATUS

### Issued:

U.S. Patent No. 8,722,891 titled "Conjugate Addition Reactions Using Bifunctional Cinchona-Alkaloid-Based Catalysts"

U.S. Patent No. 10,836,761 titled "Cinchonine-Derived Catalysts and Methods of Using Same"

## INVENTORS

Wu, Yongwei  
Deng, Li

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1024 and 1240

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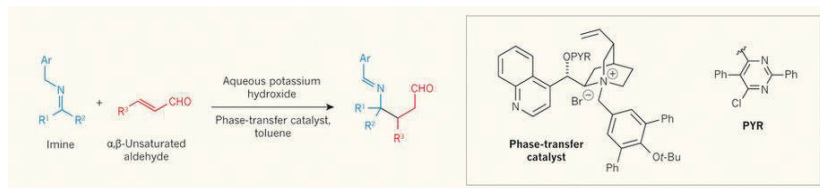
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## New chiral phase transfer catalysts promote highly efficient asymmetric reactions of imines and enals

### Background:

Methods for the spatially selective assembly of molecules containing nitrogen to improve cell permeability, water solubility and biological interaction are of considerable interest for drug discovery. This invention has developed a procedure that achieves a reversal of the natural electrostatic polarization (umpolung) in a highly chemoselective, regioselective and enantioselective manner. The present invention describes the discovery and development of new chiral phase transfer catalysts that promote highly efficient asymmetric reactions of imines and enals. The reaction provides a conceptually new and practical approach towards the synthesis of chiral amino compounds.

The invention discloses an analogous catalytic strategy that allows the enantioselective synthesis of nitrogen-containing compounds from imines to contribute in drug discovery research. Evolved from a widely accepted concept of using one enantiomer of a base to isomerize imines, the invention performs better than other current catalysts by exploiting a different C-C bonding forming reaction. They used a chiral 'phase-transfer' catalyst, developed from a quinine compound that was originally derived from *Cinchona* plants, to shepherd the base from an aqueous solution to the immiscible organic solution in which the reaction occurs, thus enabling the transformation, and also inducing enantioselectivity. The reaction products are modified versions of imines (Figure), and can be readily converted into a variety of other nitrogen-containing compounds.



The invention available for licensing is a group of novel phase transfer catalysts which break the limitation that only highly activated imines could be used in the reaction. The new catalysts allow a wide variety of imines to participate with nearly equal facility. Furthermore, the reaction proceeds with remarkable enantioselectivity, and yields the amine products with high fidelity. It is also easy to set up and tolerates air and moisture from the atmosphere. The findings illustrate the power of catalyst development for organic synthesis, and provide a straightforward route to chiral amines, which ultimately benefit the drug discovery research.

### Summary:

- A method enables highly chemoselective, regioselective and enantioselective umpolung reaction
- The discovery and development of chiral phase transfer catalyst promote highly efficient reaction
- These asymmetric reactions of imines provides a novel and practical approach to drug discovery

### Advantages:

- The catalyst widens the variety of imines to react with easily set-up and highly tolerant facility
- Remarkable enantioselectivity and high yields with this uncomplicatedly synthesized catalyst

### Scientific Publications:

- "Catalytic asymmetric umpolung reactions of imines." *Nature* **523**, 445-450 (23 July 2015)  
doi:10.1038/nature14617



# Cinchonium Betaines as New and Powerful Catalysts for Asymmetric Proton Transfer Catalysis

## SEEKING

Licensing partner for commercialization

## PATENT STATUS

Issued:

U.S. Patent No.

10,888,853 titled "Cinchonium Betaine Catalysts and Methods of Using Same"

U.S. Patent No.

10,836,761 titled "Catalysts for Olefin Isomerization"

## INVENTORS

Wu, Yongwei; Xiao, Zhou; Deng, Li

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1299 and 2017-050

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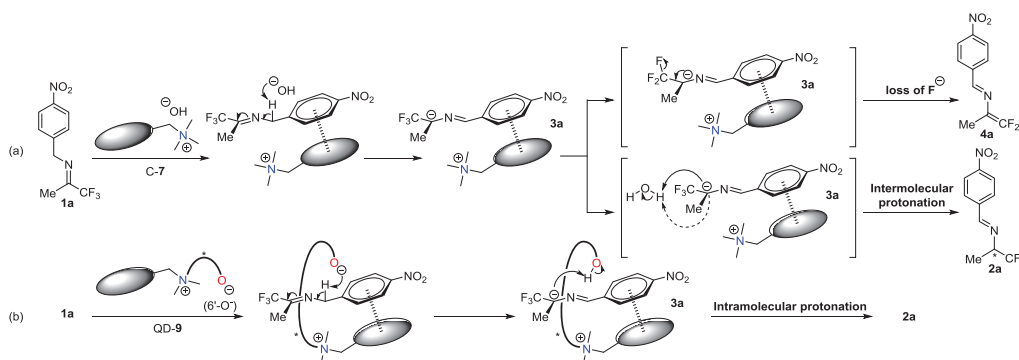
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## The Development of a Practical Enantioselective Isomerization

Chiral organic catalysts containing both hydrogen bond donor and acceptor could facilitate biomimetic 1,3-proton transfer catalysis to promote highly enantioselective olefin and imine isomerizations. These enantioselective isomerizations provide new access to valuable chiral building blocks such as  $\alpha$ ,  $\beta$ -unsaturated butenolides,  $\alpha$ -amino acids,  $\alpha$ ,  $\beta$ -unsaturated cyclohexenones and trifluoromethylated amines. Among these studies, the realization of the first highly enantioselective isomerization of trifluoromethyl imines with DHQ-a stands as a conceptually significant progress as DHQ-a achieved efficient catalytic chiral recognition of non-enolate carbanions for asymmetric reactions.

The invention discloses a new class of cinchonium betaine catalysts bearing both a base moiety and an aromatic moiety. These cinchonium betaines were found to promote proton transfer catalysis with 1000-5000 turnovers per 24 hours, thereby enabling us to realize highly efficient enantioselective isomerization of trifluoromethyl imines to provide a practical access to optically active trifluoromethylated amines. Notably the catalyst QD-9c promoted an unprecedented isomerization of  $\alpha$ ,  $\beta$ -unsaturated imine in excellent enantioselectivity and yield. It is noteworthy that the reaction proceeded without the formation of the 1,3-proton transfer product. The scope of the reaction was readily extended to aryl trifluoromethyl imines.



The invention available for licensing is a new class of catalysts for enantioselective proton transfer catalysis. These new catalysts afforded remarkably high catalyst turnover rate for the promotion of asymmetric isomerizations of trifluoromethyl imines. Consequently, a broad range of alkyl, alkenyl and aryl trifluoromethyl imines could be converted in a highly enantioselective manner into either enantiomers of the corresponding optically active trifluoromethylated amines with typically 0.02 to 0.10 mol% of the cinchonium betaines. The invention provides a general scoped simple protocol for reaction execution and product isolation with an extraordinarily low catalyst loading, which ultimately benefits the drug development.

### Advantages:

- A class of catalysts for enantioselective proton transfer catalysis with high turnover rate
- The development of enantioselective proton transfer catalysts promote highly efficient reaction
- The catalysts provide general scope, simple protocol for reaction execution and product isolation
- An extraordinarily low loading render this transformation very practical for asymmetric synthesis

### Scientific Publications:

- "Catalytic asymmetric umpolung reactions of imines." *Nature* **523**, 445-450 (23 July 2015) DOI:10.1038/nature14617
- "Cinchonium betaines as efficient catalysts for asymmetric proton transfer catalysis: the development of a practical enantioselective isomerization of trifluoromethyl imines." *J. Am. Chem. Soc.*, **2016**, 138, 12297-12302. DOI: 10.1021/jacs.6b08727



# Cold Stage for Cryo Super-Resolution Fluorescence Light Microscopy

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Cooling systems and methods for cryo super-resolution fluorescence light microscopy and other applications

## INVENTORS

David DeRosier, Charles Ingersoll  
Marc Nahmani, Gina Turrigiano

## PATENT STATUS

Issued: U.S. Patent 9,784,962

Pending: PCT/US2013/059748

Japan under JP2015-532093

Europe under EP13837090.3

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Worldwide rights available

## BRANDEIS REF.

Case 1095

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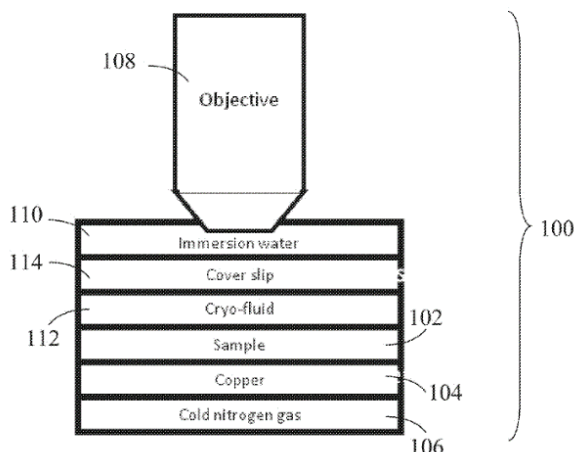
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## PALM microscopy cryo-stage preserving specimen grid for cryo-EM

This invention discloses a unique light microscope cryo-stage design to meet the rapid development of cryo-EM technology. Ever since the importance of cryo-EM has been acknowledged by 17' Nobel prize, the protein structure analyzed by the technology has also been encouraged and sponsored by NIH in two initiative facilities. We have designed a device that can be used for super-resolution PALM microscopy with 'resolution' in the nm range while preserving the specimen grid for subsequent cryo-EM. The unique feature is that our cold stage is designed to be used with a high numerical aperture, water immersion objective, which is operating at room temperature while the frozen hydrated grid remains below -135 Celsius, which maintains vitreous ice.



Conventional light microscopy with its resolution of about 200 nm is inadequate to study the organization of biological molecules (e.g., proteins) whose dimensions are generally less than 10 nm. Super-resolution fluorescent microscopy methods allow one to localize the position of an isolated switchable fluorophore by determining the center of distribution of the fluorescent photons. Thus the super-resolution mainly is limited by the number of photons collected and motion of the fluorophores during the repeated cycle of activation and mapping. Using microscopy at cryogenic temperatures, e.g., below -135 Celsius has several beneficial

effects related to improving resolution. However there is presently no super-resolution cryogenic microscope assembly which can be used with a conventional light microscope without compromising the imaging resolution or performance of the microscope.

In the present prototype, the cold stage works surprisingly well while balancing the accurate cold. Having reached cryo-temperature, the temperature stability is within a degree over times on the order of an hour and perhaps longer. The drift is minimal about 1 or 2 microns over a similar period. The field of view in the camera is about 80 microns meaning that items of interest remain in view during a run. The rate of drift is slow allowing one to correct for drift. Corrections for drift are a separate albeit necessary matter.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Summary:

- A novel cold stage for maintaining a desired steady state temperature during cryo-EM screening
- The device designed for utilizing in super-resolution PALM microscopy
- Achieves high resolution in nm range while preserving the specimen grid for subsequent cryo EM

### Scientific Publications:

- "High-numerical-aperture cryogenic light microscopy for increased precision of superresolution reconstructions." *PNAS* **2017**, 114 (15) 3832-3836. DOI: 10.1073/pnas.1618206114



# Hierarchical Self-Assembly of Non-Amphiphilic Colloidal Membranes

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Aligned Arrays of Nanorods and Methods of Making and Using Them

## INVENTORS

Edward Barry, Zvonimir Dogic, Michael Hagan, Daniel Perlman, Yesheng Yang

## PATENT STATUS

Pending:

U.S. Patent Application No. 14/354,258

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1019

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## Aligned monolayer nanorods for electronic or semi-conductor devices

### Background:

Nanostructured materials have the potential to facilitate a new generation of electronic or semi-conductor devices, as well as the potential for use in filtration systems and biosensors. Important prerequisites to realization of these devices include the ability to assemble and align nanorods over large length scales ( $>1 \text{ mm}^2$ ) and tune physical properties of the final assemblages, including the density of rods and the inter-particle spacing between rods. Nanorods are a class of anisotropic particles with properties that are geometrically identical to that of a cylinder or spherocylinder; these particles are characterized by a well-defined length (L) and diameter (D). When made soluble and properly stabilized against coagulation stemming from strong attractive van der Waals interactions, nanorods can be dispersed in solution and will behave as colloidal particles. The solution-based self-assembly of monolayer and multi-layer arrays of aligned rodlike colloids was recently reported by E. Barry and Z. Dogic on PNAS 107(23): 10348-10353, 2010. This invention specifically targets the issue of generalizing such method for arbitrary conditions and components, including varying polymer sizes and compositions, solvent conditions, or varying degrees of flexibility, electrostatic charge, contour length, diameter, or combinations thereof of the rod-like molecules. In order to extend this method to other systems, such as those composed of nanorods, the current invention helps to elucidate a greater understanding of the underlying principles involved in this assembly pathway and introduce the means by which it can be generalized and extended to cover a far greater range of component compositions and sizes.

The invention available for licensing relates to a method for assembling homogenous rod-like molecules or particles into aligned monolayer arrays. The method comprises forming multi-layer structures from more than one monolayer with adjustable internal properties of the arrays, such as the density of and inter-particle spacing between rods (porosity), the crystallinity or fluidity (regularity), or elasticity of the array. The assembled array may comprises of viruses absorbing metal ions or semi-conducting material onto their surface. The surface of the virus may have been biomineralized therefore producing pores with adjustable distance between each other, and various pore regularity.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Advantages:

- First demonstration of nanorod alignment in liquid medium
- Self-assembly with tunable physical properties
- Can be used to make or perform other functions than implicitly described examples

### Applications:

- Electronic or semi-conductor devices
- Potential for use in filtration systems and biosensors

### Scientific Publication:

- "Entropy driven self-assembly of nonamphiphilic colloidal membranes." **PNAS** 2010, 107 (23) 10348-10353. <https://doi.org/10.1073/pnas.1000406107>





# In Situ Generation of Chlorine Dioxide

## SEEKING

Licensing partner and/or  
sponsored research funding.

## PATENT TITLE

Method of Humidity-Controlled  
Generation of Chlorine Dioxide in  
Polymers and super absorbent  
Hydrogels

## INVENTORS

Christopher J. Doona  
Irving R. Epstein  
Florence Feehely  
Kenneth Kustin

## PATENT STATUS

### Issued:

U.S. Patent No. 10,626,016

### Pending:

U.S. Patent Application No.  
16/776,789

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US rights available

## BRANDEIS REF.

Case 2017-059

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## Method of Humidity-controlled Generation of Chlorine Dioxide in Polymers and super absorbent Hydrogels

### Background:

Chlorine dioxide is a well-known bleaching agent for paper pulp of flour and is also a well-known biocidal or anti-microbial agent for a broad spectrum of microorganisms in decontamination applications for bacterial spores, viruses, phage, mold, fungi and other pathogens. Benefits to using chlorine dioxide as a disinfectant are that it is effective, compatible with most materials, safe for users and the environment, and associated is user friendly. However, possible hazards associated with this disinfectant include the possibility of explosion in the condensed phase as a high concentration liquid. Additionally, chlorine dioxide cannot be pre-generated and shipped/transported in trucks or other vehicles to distant locations for use. Rather, it must be generated on-site for use in decontamination and disinfections. The present invention allows for the in situ generation of chlorine dioxide.

We present a method for a dry chemical composition in polymer substrates to rapidly and conveniently absorb moisture in humid environments, then safely and controllably produce chlorine dioxide to prevent mold, mildew, and pathogen growth that degrades textiles or other surfaces. This method provides an alternative to bio-decontaminate *Bacillus anthracis* Sterne spores on individual protective fabrics using chemicals in the liquid or gaseous state. By using a novel chemical composition and method to produce chlorine dioxide from dry precursors imbedded in media that absorbs water in humid environments, a reaction occurs that produces a disinfectant which kills mold, mildews, and other contaminating microorganisms on textiles.

Using this method, chlorine dioxide is produced for particular utility for production in-container, in-enclosure, and in an enclosed space. This chemical disinfectant method allows for a wide latitude for convenience, simplified logistics, and technological advantages over the existing art for textiles.

### Summary:

- Chlorine dioxide can be produced for use in an enclosed container where it previously could not be.
- Chlorine dioxide can be made cheaper and more easily, and can also be transported more simply.
- Can be used to prevent mold/ microbial growth on textiles for clothing, uniforms, or interior of cars.

### Advantages:

- Improved, convenient, portable method for decontaminating microbiologically contaminated surfaces of textiles.
- Can be used in humid environments.
- Can be used in contained environments.
- This anti-microbial textile may be used to reduce incidences of rashes, irritations, and infections involved with wearing uniforms or other textiles that aren't laundered for prolonged periods.



# Rechargeable Functionalized Fabrics that Self-Clean

## SEEKING

Licensing partner and/or sponsored research funding.

## PATENT TITLE

SELF-DECONTAMINATING,  
SELF-DEODORIZING TEXTILES  
AND SURFACES AND  
METHODS OF MAKING AND  
USING THE SAME

## INVENTORS

Christopher J. Doona  
Irving R. Epstein  
Florence Feehery  
Kenneth Kustin

## PATENT STATUS

Pending  
PCT/US2020/048490

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## BRANDEIS REF.

Case 2020-002

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### Background:

There is a critical need for self-decontaminating, self-deodorizing, self-disinfecting, and/or self-cleaning surfaces, particularly for textiles used in individual protective garments, to respond to two types of threats: i) communicable diseases and antibiotic-resistant pathogens in hospitals, healthcare, and nursing settings, and ii) chemical and biological warfare agents. In both cases, it is crucial to protect the health care professionals providing services, patients, emergency first-responders, deployed military personnel, and others from potential exposure to etiologic agents or disease-carrying vectors, and to prevent contaminated clothing from acting as a source of further spread of contamination to themselves or anyone else.

Without self-decontamination as an inherent feature of the protective garment, disposal of the clothing after brief exposure (30-60 min) to the harmful chemical or biological agent is recommended. In fact, training is required to effectuate the safe donning, doffing, and disposal of protective garments to prevent contamination of the wearer or their surroundings. Additionally, there are unwanted consequences of utilizing protective garments that may: hinder mobility or cause over-heating and dehydration of the wearer; cause cross-contamination; or create excessive costs by disposing of garments after a single use.

This invention uses a novel chemical method to functionalize various surfaces with a stimuli-responsive hydrogel polymer that responds to external stimuli by taking up, storing, and controllably releasing gaseous or aqueous chlorine dioxide ( $\text{ClO}_2$ ) for the purposes of inactivating harmful microorganisms, neutralizing odors, or preventing cross-reactions with storage container surfaces. In clothing or garments, the stimuli-responsive hydrogel polymer could initiate the release of disinfectant to self-decontaminate microorganisms that cause infections or rashes and irritations on the wearer, and to self-deodorize the garment from sweat, body odors, or by-products of microbial metabolism.

Chlorine dioxide ( $\text{ClO}_2$ , with the Cl atom in the +4 oxidation state) is a potent alternative to household bleach (hypochlorite with Cl in the +1 oxidation state), because  $\text{ClO}_2$  is environmentally-friendly, compatible and non-corrosive with most materials and surfaces including clothing and footwear and more effective at lower doses in destroying a broad spectrum of pathogens and spoilage microorganisms without these organisms acquiring resistance, such as bacterial cells, bacterial spores (including *Bacillus anthracis* Sterne and *Clostridioides difficile*, the notorious pathogen in hospitals and nursing care settings), yeasts, molds, mildews, fungal spores, and viruses.

There are many applications and needs for textiles and plastic packaging with improved self-decontaminating, self-disinfecting, self-deodorizing, self-cleaning, self-stabilizing properties that this present invention addresses. In addition, a study of the inactivation of coronavirus (severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2, the causative virus of COVID-19) by this  $\text{ClO}_2$  technology could offer promising possibilities for eliminating this pathogenic virus when airborne or on contaminated surfaces.

### Advantages:

- This invention reports a novel chemical method of creating self-decontaminating and self-disinfecting fabrics that are effective, practical and economical;
- This invention can satisfy unmet needs for self-clean textiles during a global pandemic;
- It is an improved, convenient, portable method for decontaminating microbiologically contaminated surfaces of textiles;
- This anti-microbial textile may be used to reduce incidences of rashes, irritations, and infections involved with wearing uniforms or footwear for prolonged periods without access to laundering.



# High Throughput Screening Chip for Optimal Protein Crystallization

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Microfluidic Devices for Investigating  
Crystallization

## INVENTORS

Seth Fraden, Michael Heymann,  
Markus Ludwig

## PATENT STATUS

Issued: 10,365,188

Continuation Pending: 16/447,369

## LICENSING STATUS

US Rights Available

## BRANDEIS REF.

Case 1113

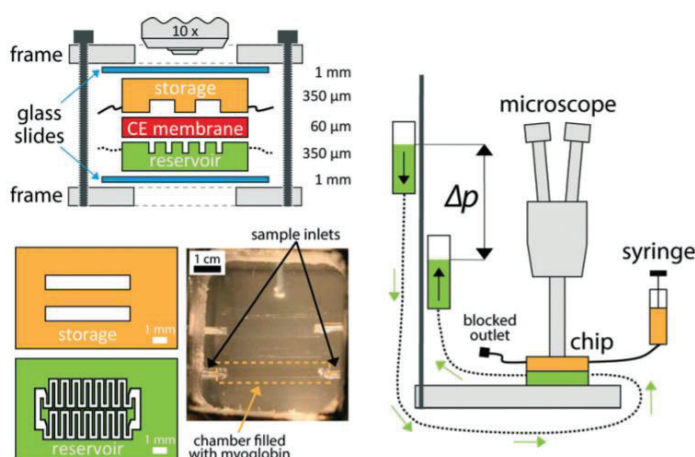
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## Modular Phase Chip for Determining Optimal Protein Structure for Drug Design

In drug design and in many areas of medical research the knowledge of protein structure is fundamental. Finding these structures requires growing a crystal of the target protein and collecting X-ray diffraction images. Current technologies for protein crystallization are not optimized. They consume large amounts of the protein, which can be precious, they are laborious and the quality of the data obtained depends greatly on the skill of the experimenter. We have developed microfluidic devices to simplify the process of protein crystallization.



Our PhaseChip allows high-throughput screening for optimal crystallization parameters and significantly reduces the required amount of sample protein. In addition, it allows versatile manipulation of the crystallization kinetics, which is the key to grow defect free crystals that yield high-resolution structures. Furthermore, in current practice, crystals are manually harvested, cryo-protected and frozen to  $-196^{\circ}\text{C}$  to reduce radiation damage prior to X-ray experiments. This process induces strain in the crystal which reduces the resolution of the obtained structures significantly. Using our X-ray transparent Chip, we diffract in-situ, avoiding handling and cryo-protection of the crystals entirely. This reduces labor and improves crystal quality.

Our devices can be categorized into the consumables segment. Their advantages compared to standard methods make the protein crystallization business much easier, independent from the experimenter and high-throughput. As a new technology our devices promise to induce changes on the market.

Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Scientific Publication:

- "Room-temperature serial crystallography using a kinetically optimized microfluidic device for protein crystallization and on-chip X-ray diffraction." (2014) PMID: 25295176
- "Cross polarization compatible dialysis chip" (2014) PMID: 25105977



# Methods for Generation and Storage of Isolated Droplets

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

Devices for Simultaneous  
Generation and Storage of  
Isolated Droplets, and Methods of  
Making and Using the Same

## INVENTORS

Seth Fraden

## PATENT STATUS

Issued: U.S. Patent No.  
10,836,761

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1238

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## Microfluidic Device for Obtaining Better Quality Crystals for Protein Crystallization

### Background:

The present invention relates to a method for simultaneous generation and storage of isolated droplets of aqueous solutions. To date, existing methods used to determine the optimal concentrations for achieving protein crystallization have included mixing macro-portions of multiple aqueous solutions. This mixing occurs in testing trays called crystallization trays which have several chambers and contain the mixtures of proteins at various concentrations. The disadvantage of the current method is that often due to the macro sized volume of these testing trays, it becomes cost prohibitive to test out multiple solution concentrations at one time. Additionally, in conventional protein X-ray crystallography, a large crystal is required in order to obtain a complete data set.

Our invention is based on an emulsion-based serial crystallographic technology in which nano-litre sized droplets of protein solutions and encapsulated in oil and stabilized by surfactant. Serial crystallography takes the opposite approach to traditional X-ray crystallography techniques of developing one large crystal. In this instance, a complete diffraction set is assembled from a large number of individual diffraction frames acquired from small single unoriented crystals that are not cryoprotected. Our microfluidic device based contains multiple sequences of capillary valves and storage chambers that simply and robustly generate and store aqueous solutions in chambers that are isolated from one another by oil. The microfluidic chip is able to generate drops in a serial fashion. The device has the capability of allowing different chemicals to be added without mixing, or alternatively, will allow for chemicals to be added to the mix in pre-determined quantities set by the geometry of the device.

This emulsion-based serial crystallographic technology, in which nano-litre sized droplets of protein solution are encapsulated in oil and stabilized by surfactant works by allowing the first crystal in a drop to be nucleated and this small volume then generates a negative feedback mechanism that lowers the supersaturation. This mechanism is exploited to produce one crystal per drop. Diffraction data are measured, one crystal at a time, from a series of room temperature crystals stored on an X-ray semi-transparent microfluidic chip, and a 93% complete data set is obtained by merging single diffraction frames taken from different unoriented crystals. This process is cheaper and provides better quality crystals for protein crystallization over the current methods.

### Summary:

- Useful for protein crystallization or other applications requiring formulation and storage of many small samples of nano-liter volumes.
- Eliminates cross contamination between samples.
- Cheaper method to test for the optimal concentration of protein.
- Crystals can be small which increases the potential for growing crystals in the first place.
- The present method avoids the roughly tenfold increase in crystal mosaicity typically encountered during cryoprotection and eliminates the need to search for cryoprotectant conditions.

### Scientific Publications:

- "Room-temperature serial crystallography using a kinetically optimized microfluidic device for protein crystallization and on-chip X-ray diffraction" IUCrJ. 2015 September 01; PMID: 25295176





# Microfluidic Chip for Crystallization and X-ray Crystallography

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

FLUIDIC DEVICE, INJECTOR SYSTEM, AND METHODS OF MAKING AND USING THE SAME

## INVENTORS

Seth Fraden  
Ali S. Aghvami

## PATENT STATUS

Pending:  
U.S. Patent Application No. 17/289,636

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Cases 2019-005/2020-006

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## Microfluidic Chip for high throughput protein crystallization screening

### Background:

Our microfluidic chip for Protein Crystallization and X-ray Crystallography can provide pharmaceutical companies and life scientists with a cost effective and fast approach for determining the high-resolution protein structure by X-ray crystallography. Our design is a liquid handling chip with multiple advantages over current microfluidic chips. It is built from inexpensive bio-compatible material via a rapid fabrication procedure and it can be altered as needed based on the customer need. Production of high-resolution structures of proteins is one the main steps in structure-based drug design. Although cost reduction and efficiency improvements are the important benefits of structure-based drug design, the lack of generalized methods for high quality, fast and low-cost crystal production is still a major struggle in this process. Microfluidics, as a powerful liquid handling tool that reduces the amount of solution in a screening experiment to nanoliters have been introduced to the protein crystallization market earlier. Existing methods of determining optimal concentrations for achieving the crystallization of various proteins include mixing macro-portions of multiple aqueous solutions. The mixtures are traditionally made by mixing the multiple aqueous solutions in testing trays, generally called crystallization trays. The testing trays have several mixture chambers, which contain the mixtures at various concentrations. These mixtures are then analyzed for protein crystallization. Often, due the macro-sized volume of these testing trays, it is cost prohibitive to test out multiple solution concentrations, as many types of proteins are exceedingly expensive

Our innovation is an x-ray transparent microfluidic chip for protein crystallization which is less expensive, easier to operate and more performant in comparison to the current market solutions. By commercializing this device and introducing it to the market, pharmaceutical companies and life scientists will reduce the time and money spent to determine the high-resolution structure of proteins from x-ray diffraction, which is a current bottleneck in structure-based drug discovery.

The present invention is an inexpensive, x-ray transparent microfluidic chip for protein crystallization. For many medical and biological applications, such as pharmaceutical engineering, the molecular structure of a protein is essential. The most accurate way to determine protein structure is X-ray crystallography, a process that requires the analysis of X-ray diffraction patterns of protein crystals. However, protein crystallization remains challenging because each protein has its own phase diagram, thus, many different conditions should be tried to find the optimal conditions for protein crystallization. Our technology addresses four core challenges in protein crystallization; it (1) screens chemical conditions for protein crystal stability, (2) produces crystals using optimized processing kinetics, (3) obtains structure with room temperature crystals, and (4) avoids crystal handling by diffracting on chip. On-chip X-ray diffraction has been demonstrated for our protein crystallization chips. Prototypes of our first design have been made and have been tested for protein crystallization with one specific solution.

### Advantages:

- X-ray diffraction can be done on the microfluidic chip, therefore there is no extraction step.
- Less protein required
- Entire process can be done at room temperature.
- The microfluidic chip is made from cheap biodegradable material, therefore this process is no cost prohibitive like the alternative microfluidic chips.



# Methods to Identify New Compounds for Controlling Insects

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Methods of Identifying Insect-TRPA-1 Modulators

## INVENTORS

Paul Garrity and Kyeongjin Kang

## PATENT STATUS

Issued

US 9,488,640 and US 9,986,740

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1054

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## Differential thermo- and chemo-sensing stimulated by TRPA1 isoforms



### Background:

Highly temperature-responsive Transient Receptor Potential (TRP) cation channels mediate thermosensation, noxious chemical detection and other homeostasis functions in all animals ranging from insects to humans. TRPs are a large family of channels with 27 different human and 13 different fly homologues. Like their mammalian TRP-counterparts, the TRPA1 channels in *Drosophila melanogaster* act as both thermal and chemical sensors, responding to warmth (above ~25-27°C) and sensing noxious chemicals. TRPA1 channels within the brain modulate the fly's preference for temperatures compatible with survival (18-32°C) while those within gustatory chemosensors function to inhibit ingestion of electrophiles and reactive chemicals that incapacitate the fly (e.g. isothiocyanate and N-Methyl Maleimide).

The invention is the finding that *Drosophila* actually possess two TRP protein isoforms, TRPA1(A) and TRPA1(B), with each having distinct amino termini but the same carboxy-terminal ankyrin and transmembrane domains. TRPA1(A) is expressed in the fly's proboscis which houses the TRPA1-expressing chemosensors while TRPA1(B), the previously described gene, is predominantly expressed elsewhere in the head where the TRPA1-expressing thermosensors of flies are located.

TRPA1(A) and TRPA1(B) isoforms are conserved in other hematophagous insects including *Aedes aegypti* and *Culex quinquefasciatus* mosquitos and *Pediculus humanus corporis* lice which transmit dengue, West Nile fever and typhus, respectively. The differentiation in function between the channel isoforms provides two new distinct TRPA1 molecular targets for disrupting behavior in disease vector, agricultural, horticultural and parasitic pest control (for use in aerial crop dusting; environmental sprays; topical lotions/sprays).

### Summary:

- Cell-type segregation of the two TRPA1 isoforms confers thermal vs. chemical sensitivity in flies.
- TRPA1(A) expressing neurons in proboscis only respond to noxious chemicals but not warmth while TRPA1(B)-expressing neurons within the head retain both thermal and chemical sensitivity.
- The reduction in thermosensitivity for TRPA1(A) is due to a unique N-terminal region that contains several key amino acid mutations from TRPA1(B) protein that modulate its lower activity.
- The invention provides methods to identify new compounds that modulate TRPA1(A) cation channel activity for use in pest control by inhibiting the feeding behavior in larvae, pupae or adults.

### Advantages:

- TRPA1 isoforms are conserved in malaria-causing mosquitos and other insects suggesting that all utilize similar mechanisms for discriminating host-derived warmth from chemical repellants.
- Compounds that preferentially modulate insect TRPA1 but not human TRPA1 can be used as novel agents for pest control without causing irritation or other biological effects in mammals.

### Scientific Publications:

- "Modulation of TRPA1 thermal sensitivity enables sensory discrimination in *Drosophila*." (2011) Nature 481, 76-80. Doi:10.1038/nature10715.



# Novel targets identified for modulating insect survival behaviors

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Methods for modulating insect hygro- and /or thermosensation

## INVENTORS

Zachary Knecht,  
Paul Garrity and  
Lina Ni

## PATENT STATUS

Pending  
US 11,198,875

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1276

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## Hygro-& thermosensation responses are conserved across arthropods

### Background:

Signaling through the ionotropic receptors (IRs) located on the surfaces of hair-like sensilla structures in the antennae, legs and heads of insects allow them to detect changes in the environment which are essential for survival including avoiding desiccation, reproduction activities, and host/prey identification. IRs are a large family of highly conserved cation channels located in the dendrites of sensory neurons in invertebrate and are a subfamily of the related ionotropic glutamate receptors (iGluRs) conserved from plants to animals.



Using *Drosophila melanogaster* as a model system, the inventors have shown that IR-heteromeric complexes consisting of IR25a/IR93a/IR40a and IR25a/IR93a/IR68a located in the sacculus of antennae are critical in mediating hygropreferences and those flies expressing mutant loss-of-function forms of IR25a, IR93a or IR40a will lack normal

hygrosensory responses. The inventors also identified for the first time another IR-heteromeric complex in the antenna of insects, IR25a/IR93a/IR21a, which is essential for detecting cues required for cold avoidance and those flies expressing loss-of-function mutant forms of IR25a, IR93a, or IR21a will lack normal thermosensation.

Since these antennal IRs are highly conserved across diverse arthropod species but not in mammals, our technology provides new targets and assay methods for identifying novel compounds (i.e. inhibitors, agonists and antagonists) that will modulate thermo- and hygrosensory behaviors. These compounds can be incorporated into aerosols, sprays and lotions to attract, repel or kill disease vectors, agricultural / horticultural parasites, and annoying insects. The IR-heteromeric complexes covered by the patent claims modulate survival responses in both larval and adult insect stages suggesting potential for uses as broad spectrum pest control agents.

### Summary:

- Thermo- and hygrosensation responses of insects are essential for survival and reproduction
- Novel heteromeric complexes of IRs have been identified in the larvae and adult stages of *Drosophila* that mediate moisture sensitivity and cold temperature behavioral responses
- These multimeric IR signaling complexes are highly conserved across arthropod species
- IR25a, IR93a, IR40a, IR68a and/or IR21a can be used, alone or in combination, in assays to identify new agents for controlling the survival or reproduction of pests and disease vectors

### Advantages:

- New pesticides will have species specificity but without strong resistance selection pressures
- Assays will target two highly conserved environmental sensing pathways essential for survival
- No known strategies currently in the market to exploit these moisture and temperature sensors

### Scientific Publications:

"Distinct combinations of variant ionotropic glutamate receptors mediate thermosensation and hygrosensation in *Drosophila*." Knecht *et al.* eLife **2016**;5:e17879. [Doi: 10.7554/elife.17879](https://doi.org/10.7554/elife.17879)

"Distinct ionotropic receptor-dependent moist and dry cells control hygrosensation in *Drosophila*." Knecht *et al.* eLife **2017**;6:e26654. [Doi:10.7554/eLife.26654](https://doi.org/10.7554/eLife.26654)

"Mosquito heat seeking is driven by an ancestral cooling receptor" Greppi *et al.*, Science **2020**, 367:681-684. <https://doi.org/10.1126/science.aba4484>



# Photo-switchable Adhesives

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

Light-responsive temporary adhesives

## INVENTORS

Grace Han  
Mihael Gerkman  
Eli Kengmana  
Xiang Li

## PATENT STATUS

Pending;  
PCT/US2020/031340

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2019-041

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## Background

Organic photo-switching systems absorb solar radiation, store energy in chemical bonds, and release it in the form of thermal energy upon triggering. The capability of the system to store energy for a variable time frame (hours, days, weeks) and the triggerable release of the stored energy present exciting opportunities in solar energy harvesting and potential applications in de-icing of windshields and windows, wearable heating devices, and general heating systems.



A novel class of light-responsive molecules was discovered to show adhesive properties which can be modulated by the irradiation with UV light (Figure 1(a)). The process of UV-activated structural change of a spiropyran photo-switch that leads to the change of adhesive strength; (b) A schematic of two substrates melt-bonded by a photo-switchable adhesive layer. The pre-adhesive powders are first melted to bond substrates, and the debonding process is triggered by the irradiation with UV. This

debonding process is gentle and leaves negligible residue of adhesives on the substrate.

Micron-thick silicon wafers break throughout multiple patterning steps involving bonding to carriers and subsequent debonding. Current acrylic temporary adhesives have fixed adhesive strengths and require peel-off process during which residue remains and additional chemical treatments/flipping processes increase the failure rate. For example, a well-known temporary adhesive used for silicon wafer backgrinding process is 3M Liquid UV-Curable Adhesive, which is limited in that three additional chemical treatment steps are required for the debonding process: LTHC release layer, dicing tape, and peel-off tape are applied for its removal.

The temporary adhesive will be tested for silicon wafer processing steps as the initial application. Our temporary adhesive technology could potentially be implemented in packaging tapes and hanging strips, which could be removed easily and cause little damage to the substrate such as packages and walls. The specific light-activated debonding and the lack of residue from removal will be favorable for recycling and home decoration.

The designed light-responsive adhesives are advantageous in that the glue can be selectively removed from the desired substrate (i.e. silicon wafer), through one-step specific triggering procedure. A more gentle process leads to lower rates of substrate damage, which produces a higher yield of finer quality industrial products. Because the debonding process is triggered by light, it could be operated locally and controlled more precisely with a narrow beam of light enabling meticulous work such as the detachment of micron-scale components on electronics for the optimization of multi-step assembly and the customization of intricate devices.

## Summary:

- A precisely controlled and locally operated glue utilizes detachment through light trigger
- UV regulated debonding is gentle and leaves negligible residue of adhesives on the substrate

## Advantages:

- The light-responsive adhesives can be removed from various substrates via one-step
- Potential applications of this invention include de-icing of windshields and windows, wearable heating devices, and general heating systems





# Functional Heat Storage Materials for Heating Engine Oil

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

Thermal storage materials and applications thereof

## INVENTORS

Grace Han  
Mihael Gerkman  
Yuran Shi  
Jennifer Taufan

## PATENT STATUS

Pending:  
PCT/US2020/051410

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2019-042

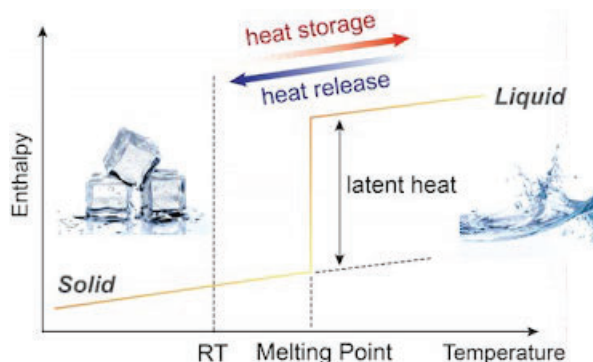
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## Background

We develop composites of phase-change materials (PCMs) and light-responsive molecules, which absorb the waste heat generated from a running engine, store the heat overnight, and release the heat instantly to warm up the engine once triggered by blue LED light. We design an optimized and custom-designed oil pan integrating the composites, which provides an instant source of heat ( $\sim 300$  J/g) to cold oil when triggered.

The majority of damage in engine components occurs during a cold start, due to the frozen/viscous oil in the engine at low temperatures. Our primary product will be a double-layered engine oil pan with an outer layer filled with heat storage materials (i.e. PCMs) which release heat when optically triggered. The owners of gas or diesel-powered vehicles and the corporations that operate oil-lubricated machinery, such as airplane engines and boat engines that are impacted by cold weather, will be our major potential customers.



The heat storage and release materials can be also used for domestic water heating systems. The heaters installed near rooftop can absorb excess solar heat during daytime and release it after sundown to generate hot water without operating gas-fueled boilers.

Commercially available oil pan heaters (300 W), for example, Peterson dipstick heaters and Kat's oil pan

heaters, cost up to \$200, and the installation service is purchased at dealerships due to the challenging self-installation. Typically, they take 3-4 hours to charge and spend  $\sim 300$  kWh of electricity per winter.

Our invention utilizes heat recycling storage materials that are eco-friendly, operate at zero cost after the initial installation, and most importantly warm up engine oil instantly once triggered. This will pose an immediate impact on electricity bill of car owners, CO2 emission associated with the electricity generation, and the everyday life of car owners residing in cold climate. We have designed and synthesized new light-responsive dopants which are the part of PCM composites that can operate at various temperatures. We are currently testing the heat storage and release properties of new composites in a small scale, and we plan to optimize the PCM/dopant types and composition in order to implement the materials to engine oil heating devices.

## Summary:

- An optimized and customizable oil pan provides an instant source of heat to cold oil upon trigger
- Commercial solution takes 3-4 hours to charge and spend  $\sim 300$  kWh of electricity per winter
- The innovative heat recycling storage materials are eco-friendly, and operate at zero cost

## Advantages:

- The invention utilizes heat recycling storage materials that are eco-friendly, operate at zero cost
- The oil pan can warm up engine oil instantly once triggered
- This engine add-on could tremendously cut-off electricity bill of car owners residing in cold climate
- The long term benefits include CO2 emission reduction, engine preservation, and sustainability





# Solar Heat Collector Modules for Long-Term Energy Storage

## SEEKING

Licensing partner and/or  
sponsored research funding

## PATENT TITLE

SUNLIGHT-ACTIVATED PHASE  
CHANGE MATERIALS FOR  
CONTROLLED HEAT STORAGE  
AND TRIGGERED RELEASE

## INVENTORS

Grace Han  
Yuran Shi

## PATENT STATUS

Pending:  
PCT Application No.  
PCT/US2022/014950

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2021-007

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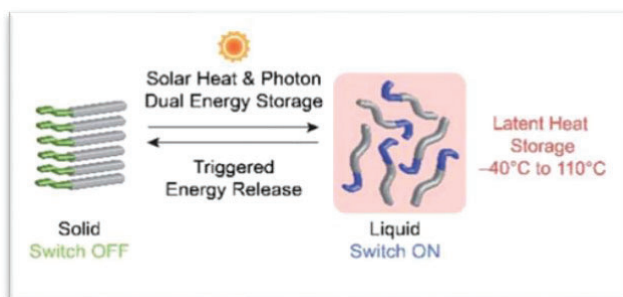
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### Background:

According to the U.S. Energy Information Administration report in 2019, the residential energy consumption is ~740 billion kWh per year on average, which is 25% of total yearly energy usage. There exists, therefore, a critical need to improve the efficiency of residential heating systems and to reduce the fossil fuel consumption by providing a renewable energy source for heating. The accomplishment of this task will help to achieve the aim of reducing 50% of greenhouse gas in a decade, announced by the U.S. government in accordance with the global effort.

The invention claimed here is a solar thermal energy storage device that can complement the conventional heating methods for residential applications. Sunlight is the most abundant, renewable, and clean source of photons and thermal energy, which has made a remarkable contribution to the electricity generation through photovoltaics. However, the intermittent nature of sunlight limits the energy generation to only during the daytime, thus necessitating a means of energy storage. The Han group has recently developed state-of-the-art phase change materials (PCMs) that are capable of controllably storing solar energy and releasing it in the form of heat through their chemical and physical changes. The PCMs can store up to 0.7 MJ/L of heat for 2 months without loss and release the stored energy on demand, which cannot be achieved using conventional heat storage materials that exhibit extremely short storage time in the range of minutes to hours.



The proposed device in this invention can be installed on a rooftop and connected to a boiler system. The device will store solar energy during the day, controllably release it at night or when needed, and transfer the heat to water, providing space heating and hot water for buildings. We anticipate that 1 kg of PCMs is able to heat 3 L of water from room temperature to 56 °C, offering a

comparable performance to that of commercial boiler systems. Harnessing solar energy and storing heat in a controllable fashion will enhance the energy efficiency of buildings by reducing the consumption of electricity, oil and gas via diurnal or seasonal energy load shifting, which will significantly reduce energy expenses in residential or commercial buildings.

### Summary:

- The invention provides a solution to utilize phase change materials to controllably store solar energy and release it in the form of heat on demand
- The new materials exhibit the absorption of visible light (530-625 nm) instead of UV to undergo phase transition and store latent heat

### Advantages:

- The photo-controlled phase transition by the absorption of natural solar spectrum is achieved for the first time, without the need for high intensity UV light sources, which distinguishes this invention from the previous work
- The photo-controlled phase transition solves the problem of uncontrolled loss of thermal energy by preserving the liquid phase as well as the stored latent heat for an extended period of time and over a wide range of temperatures, even at subzero temperatures.

### Scientific Publications:

- "Sunlight-Activated Phase Change Materials for Controlled Heat Storage and Triggered Release" Y. Shi, M. and G. G. D. Han\* et al. J. Mater. Chem. A 2021, 9, 9798-9808.



# Drug Development Based on a Protein's Energy Landscape

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Biophysical Platform For Drug Development Based On Energy Landscape

## INVENTOR

Dorothee Kern

## PATENT STATUS

Pending

United States Application Serial No.15/524,181 (published as US-2017-0356024-A1)

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REFERENCES

Cases 1175

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## Rational drug design through analysis of conformational dynamics

### Background:

A fundamental pitfall in current drug development processes is a lack of understanding of the detailed biophysical mechanisms that make inhibitors successful. Our invention is a novel strategy for developing new high affinity and specific drug inhibitors through analysis the unique energy landscapes underlying the regulatory features of a target protein's active site. These methods involve predicting the transition rate of conversion between an "initial binding" conformation and an "induced fit" conformation after an agent contacts the active site of a protein. Those agents that increase the stability of the induced fit conformation for the active site (when compared to stability induced by a physiologic reference agent) are identified as good candidates for having strong and specific inhibitory binding. The agents identified in screening assays can be small molecules, polypeptides, peptides or peptide mimetics.

Protein kinases are attractive therapeutic drug targets because different signaling cascades can be selectively regulated by inhibiting individual kinases and they are often deregulated in many cancers. However, there are more than 500 human protein kinases and they all share a high level of similarity in their active sites which makes it difficult to design drug inhibitors that are specific to a particular kinase for an anticancer therapy.

The drug discovery platform has been enabled by examining the energy landscapes for the drug inhibitor-target protein interactions and resulting induced fit step transition rates for both Tyr and Ser/Thr kinases, specifically the binding kinetics for Gleevec-Abl kinase and Danusertib-Aurora A kinase pairs. The results show the energy landscape of ligand binding is complex and the conformational selection step weakens the overall inhibitor affinity, while an induced fit step tightens the affinity in relation to the amount of equilibrium shift in the kinase/inhibitor drug complexes.

### Summary:

- A new approach for identifying better drug inhibitor compounds that exploits the dynamic nature of proteins and targets these dynamic parts for engaging them in induced fit steps
- Method highlights the importance of induced fit step transitions to select for drugs with increased selectivity (thereby minimizing off-target effects) and higher binding affinities to the target protein
- The integrated platform combines conformational flexibility data obtained from NMR spectroscopy dynamics, fast fluorescence binding kinetics, crystallography structures, enzyme kinetics, ancestral sequence reconstructions and/or molecular dynamics simulation

### Advantages:

- Platform focuses on sites in target proteins crucial for binding in different dynamic states (i.e. free and when bound to compounds) and does not rely on the conformation of a single static structure
- Our novel drug design approach solves the problems for how to design new inhibitor drugs that will have very high affinity, long on-target residence times and very high specificity

### Related Scientific Publications:

Agafonov *et al.* (2014) Energetic dissection of Gleevec's selectivity towards human tyrosine kinases. *Nature Structural and Molecular Biology* 10:848-853. doi: 10.1038/nsmb.2891

Wilson *et al.* (2015) Using ancient protein kinases to unravel a modern cancer drug's mechanism. *Science* 347(6224):882-886. doi: 10.1126/science.aaa1823

Pitsawong *et al.* (2018) Dynamics of human protein kinase Aurora A linked to drug selectivity. *eLife* 7:e36656. DOI: <https://doi.org/10.7554/elife.36656>



# Novel and Optimized Cryo-EM Sample Preparation with PicoCell™

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Freezable fluid cell for cryo-electron microscopy

## INVENTORS

Joel R Meyerson, Jungwon Park

## PATENT STATUS

Pending:

PCT/US2017/064831 pending  
16/466,860 in United States  
CA3046200 in Canada  
17878807.1 in Europe  
201780075756.4 in China  
10-2019-701836 in South Korean

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1307

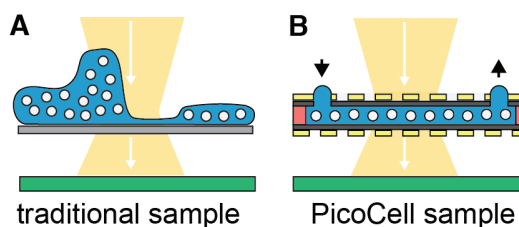
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## Rapid, efficient, blot-free, and low-cost sample optimization for cryo-EM

Cryo-electron microscopy (cryo-EM) is emerging as the preferred method to determine 3D protein structures in biomedical research and drug discovery. The method's importance was acknowledged with the 2017 Nobel Prize in Chemistry. Cryo-EM is performed by taking pictures of frozen proteins using an electron microscope, then processing the images with a computer to create a 3D structure of the protein. This method thereby enables atomic-resolution molecular structures under native conditions and without the need for crystallization. We have a novel nanofabricated invention, PicoCell™, to address the problems with cryo-EM sample preparation, enhance automation in cryo-EM workflows, and push cryo-EM to the next frontier.



Our device targets a central problem in existing cryo-EM workflows – the process of freezing proteins in a thin film of water before imaging. Current technology for preparing these thin ice samples is associated with an array of problems rooted in lack of control over sample geometry, uniformity, and environment (**LEFT**). The new technology we present uses a nanofabricated chamber that gives full control over sample preparation, thereby ensuring consistency and reproducibility for every sample (**RIGHT**). Additionally, slits in the top of PicoCell™ nanochamber allow for passive protein loading by capillary action, thereby eliminating traditional blotting and reducing the protein material requirements over 1,000-fold. Our innovation thus delivers a low-cost, blot-free approach that accelerates automation while smoothly incorporating into existing cryo-EM workflows. We also envision that these features will make cryo-EM easier to use, and thereby broaden the cryo-EM market.

Prototype testing has shown the viability of the core technology. The design was conceived for scalable manufacturing by leveraging existing semiconductor manufacturing processes. We anticipate the mature incarnation of PicoCell™ will help breach current problems in cryo-EM and open new scientific and commercial opportunities. Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications.

### Summary:

- A novel re-imagining of sample preparation to accelerate cryo-EM workflows
- Uniform sample thickness without blotting, and reduces the quantity of target protein needed by 1,000-fold
- Use of mature nanofabrication techniques keeps Cryo EleMent™ manufacturing costs low
- Consumable, one-time-use design

### Advantages:

- Fast sample optimization, low screening time, and increased sample reproducibility
- Blot-free approach reduces quantity of protein needed for 3D structure determination
- Eliminates air-water interface to improve protein orientations and distributions
- Versatile design provides for product line diversification



# Improved Gene Silencing through Use of Organic shRNAs

## SEEKING

Licensing partners for commercialization

## PATENT TITLE

Organic small hairpin RNAs

## INVENTORS

Nelson Lau  
Mei Zeng  
Suzanne Paradis  
Marissa Kuzirian

## PATENT STATUS

Issued: US 9,777,277

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1137

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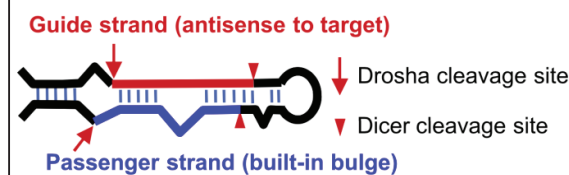
## Advanced design strategy increases efficiency and decreases costs

### Background:

Technologies harnessing the endogenous cellular phenomenon of RNA interference (RNAi) are uniquely capable of regulating gene expression *in vivo*. This power derives from practitioners' ability to present small guide RNAs to a cell's native RNA Induced Silencing Complex (RISC) and thereby target any native messenger RNA for degradation. Short hairpin RNAs (shRNAs) are attractive RNAi technology because they are expressed by vector-based transgenes and therefore not diluted with cell division or RNA turnover.

Current shRNA methods for gene silencing are inefficient and unpredictable. Practitioners often must buy and test panels of candidate shRNAs against their gene targets, and occasionally, the entire panel will fail. This is because the primitive design of current shRNAs allows for imprecise cleavage of the RNA hairpin, which in turn allows non-guide RNAs to enter the RISC and produces off-target effects on gene expression.

### The Organic shRNA (OshR) design



The organic shRNA (OshR) platform of our invention overcomes these deficiencies by incorporating distinct elements of endogenous inhibitory microRNAs (miRNAs) to more closely mimic their natural structure and results in improved shRNA performance. These features ensure proper cleavage and the biased

accumulation of the designated guide strand 3–50-fold over the passenger strand. Additionally, a rational design workflow specifically for OshRs allows effective constructs to be created against any target gene.

The performance of OshRs has been proven in immortalized cells. We are seeking licensing partners to develop kits or pharmaceutical compositions for commercializing this technology. Paired with our proprietary workflow, such fully-contained kits would provide a cost-effective and time-saving solution for suppressing genes otherwise refractory to RNAi manipulation.

### Summary:

- Flexible OshR design for use in silencing any target gene of interest which contains, in 5' to 3' order:
  - a 5' *constant stem* sequence,
  - a 22 base *guide strand* that is the reverse complement of the target sequence,
  - a *constant stem loop*,
  - a 20 base *passenger strand* that is the near-reverse complement of the guide sequence and
  - a 3' *constant stem* sequence
- Specific mis-match sites are introduced on the passenger strand of the shRNA where base 19 is mutated to be a mis-match relative to the guide strand and also bases 11 and 12 are deleted
- Design ensures precise cleavages of the hairpin by the Drosha and Dicer enzymes

### Advantages:

- Transparency: Practitioner controls and tracks the design workflow
- Near-optimal RNA biogenesis: Preferential guide strand accumulation of 3–50x over passenger strand, approaches 3–300x rate observed for endogenous miRNA-30a-5p
- More reliable: Off-target effects are significantly reduced allowing interpretation of phenotypes with confidence
- More cost-effective: Eliminates need to validate commercial shRNA panels or conduct parallel screenings

### Reference:

Zeng, M, Kuzirian, MS, Harper, L, Paradis, S, Nakayama, T, Nelson, L. (2013) Organic small hairpin RNAs (OshR): a Do-It-Yourself platform for transgene-based gene silencing. *Methods*. 63:101-109.





# Cas9 Fusions Improve DNA Repair in CRISPR-based Systems

## SEEKING

Licensing partner

## PATENT TITLE

Modified CAS9 Compositions and Methods of Use

## INVENTORS

Nelson Lau

## PATENT STATUS

Issued

US 11,111,508

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1166

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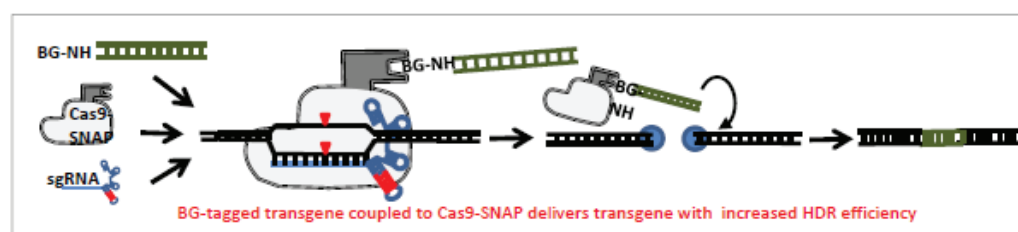
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## Cas9-SNAP tethered transgenes increase rates of homologous DNA recombination

### Background:

CRISPR/Cas9-based genome modifications are being heralded as revolutionary breakthroughs for advancing the speed, cost-effectiveness and promise for development of innovative gene therapies, model organisms and biomedicines. One of the most critical steps in the modification process after Cas9 cuts the double-stranded DNA at a specific location in the genome is the stable incorporation of the large transgene into the target site. However, this repair step is a random, inefficient and low frequency event, typically occurring with an integration efficiency rate of <1% to under 10%, depending on the CRISPR system used.



The invention available for licensing is a method to improve the rate of homologous DNA recombination (HDR) repair through the use of a recombinant Cas9 protein fused to SNAP-tag, a 20 kDa mutant of the DNA repair protein O<sup>6</sup>-alkylguanine DNA alkyltransferase. This fusion protein physically brings the repair transgene DNA template with it to the target gene location which contains the double-stranded break made by the CRISPR/Cas9 systems thereby greatly increasing the repair efficiency.

The Cas9-SNAP tag fusion polypeptide has been generated by the inventor and successfully tested in a mammalian human embryonic kidney cell system (HEK293T cells) for its ability to increase CRISPR/Cas9 transgene repair efficiency. When compared to use of wild-type (WT) Cas9, the improved Cas9-SNAP tag nuclease provides an approximately two-fold increase in transgene integration efficiency.

### Summary:

- The invention is a method to increase DNA repair efficiency in CRISPR-based genomic modification systems by expressing in target cells the following essential kit components:
  - a vector containing Cas9-SNAP fusion protein,
  - a sgRNA, and
  - a suitable transgene for incorporation into a genome
- Proof-of-concept successfully tested in vivo using CRISPR/Cas9 system in HEK293T cells

### Advantages:

- Use of Cas9-SNAP tag fusion nuclease increases integration efficiency 2-fold over WT Cas9
- This platform is particularly suited for inserting long DNA sequences into both constitutive and inducible endogenous loci to generate novel human cell lines for the study of important biological processes

### Scientific Publication:

- “DNA templates with blocked long 3' end single-stranded overhangs (BL3SSO) promote bona fide Cas9-stimulated homology-directed repair of long transgenes into endogenous gene loci”. Bandyopadhyay et al., [G3, 2021, 11\(8\), jkab169](#).





# High Throughput Video *Drosophila* Behavior Monitoring System

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

High Throughput Video *Drosophila* Behavior Monitoring System

## INVENTORS

Michael Rosbash, Hyung J Jung, Fang Guo

## PATENT STATUS

Issued: US 11,058,093

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1231

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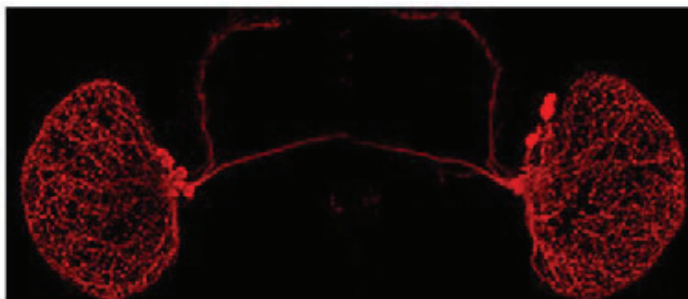
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## High Throughput Video *Drosophila* Behavior Monitoring System

We have developed a high-throughput, real-time video recording system combined with optogenetic stimulation for recording *drosophila* activity. Flies are loaded to standard 96-well plates with food, and the locomotor behavior video-tracked. A pair of LEDs with a specific wavelength for optogenetic stimulation is symmetrically placed above the plate. The timing, frequency and intensity of LED light pulses can be controlled by an Arduino Uno Board or Raspberry Pi. This setup (video recording and optogenetics) can be further combined with a bioluminescence plate reader, which uses luciferase as reporter of neuronal activity or transcriptional activity.

The invention allows the stimulation and recording of neuronal activity within discrete neurons, and it also couples these manipulations/measurements to fly behavior. Notably, the system will function for many days, allowing measurements of sleep-wake as well as circadian cycles. It can provide a standard method for researchers to control and record the activity of animals like flies, and it allows researchers to precisely and noninvasively stimulate neuronal activity in a living fly. This system can be used by neuroscience labs to screen for genes and neuronal circuits involved in different fly behaviors (sleep, circadian rhythms, courtship, aggression). This system also can be used for screening drugs that might target those behavior disorder by using *drosophila* as a disease model.



This invention is superior to the current *Drosophila* activity monitor (DAM) with regards to the fact that the current system (DAM) has many blind spots which are insensitive to tiny movements of the flies. In contrast, our video recording setup can capture what the flies are doing with exact timing and over a very long period of time. Our option will be far cheaper than the current DAM system. Moreover, recycling and waxing the DAM board behavior tubes are labor-intensive. Our device will cost less, and we use a standard commercial 96-well plate. This is much simpler and less labor-intensive system for loading the flies. Lastly, the flies loaded in the DAM system tubes become unhealthy quickly because the small amount of food in the tubes dries out quickly. In contrast, flies in a 96-well plate can live for weeks since each well contains a large amount (300ul) of food.

### Summary:

- Flies in our system live longer due to increase food availability in the 96-well plate.
- Our technology can record triple the number of flies as the current DAM system.
- Our Technology can couple with a bioluminescence plate reader in order to couple real-time neuronal activity or transcriptional activity to the fly's behavioral status.

### Scientific Publication:

• "Clk post-transcriptional control denoises circadian transcription both temporally and spatially." Nat Commun. 2015 May. PMID: 25952406



# Novel Technique for RNA-Binding Protein Analyzation Method

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Compositions and methods for identifying RNA Binding Polypeptide Targets

## INVENTORS

Michael Roshbash  
Aoife McHahon  
Weijin Xu  
Hua Jin

## PATENT PENDING

US 2019-0390186

EU 16909733.4

## LICENSING STATUS

Worldwide rights available

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Case 1306

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## Easier, Faster, and Accurate Method to identify RNA-Binding Proteins

**Background:** An innovative technique to effectively analyze RNA-Binding Proteins with fewer cells to shorten the drug discovery process.

Many efforts have been made to accurately identify drug targets for neurological diseases, yet there are still many challenges to decrease time-to-market. There are links to abnormalities in RNA-Binding proteins (RBP) with numerous human diseases such as Parkinson's, autism, and Amyotrophic Lateral Sclerosis (ALS). Post-transcriptional regulation of gene expression is mediated by a host of proteins that bind to pre-mRNA and mRNA for correct splicing, localization, and translation of cellular components to occur. Currently approximately 10% of protein-coding genes in humans are RBPs, yet the pathological mechanisms and targets for RBPs are undetermined. Identifying targets and RBP-RNA interactions for these debilitating diseases is a crucial component for effective treatments.

Traditional methods of RBP target identification, typically immunoprecipitation of target RNAs, are generally performed on mixed tissues. This can lead to issues such as post-lysis in vitro association of RBPs with spurious targets, and dramatic changes in results with seemingly subtle differences in experimental conditions. The long list of candidate targets has little overlap between labs. A more sophisticated method includes CLIP (crosslinking and immunoprecipitation) still has several disadvantages including a requirement for a high-affinity, specific antibody, the inefficiency of crosslinking, and requirements for large amounts of material. CLIP was first described in 2005 and no cell-specific experiments identifying cell-specific RBP targets have yet been published.

The invention available **TRIBE** (Targets of RNA-Binding Proteins Identified by Editing) allows researchers to effectively analyze these proteins with greater accuracy in a cost-effective and faster manner. The invention available for licensing will help in identifying cell-specific RBP targets via fusion polypeptides.

### Summary:

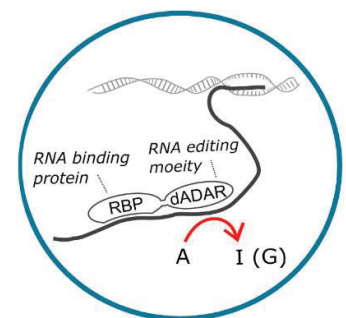
- Approximately 10% of protein-coding genes in humans are RBPs
- CLIP requires a high-affinity, specific antibody and the inefficiency of crosslinking, and requiring large amounts of material
- **TRIBE** provides greater accuracy in a cost-effective and faster manner

### Advantages:

- No additional reagents required
- Shorter experiment time (3 days vs. 8 days)
- Low false-positive rate
- Requires 10,000-fold less material

### Scientific Publications:

- McMahon, Aoife C., et al., *TRIBE: Hijacking an RNA-Editing Enzyme to Identify Cell-Specific Targets of RNA-Binding Proteins*. Cell, 2016. **165**(3): p. 742-753.
- Xu, W., R. Rahman, and M. Rosbash, *Mechanistic implications of enhanced editing by a HyperTRIBE RNA-binding protein*. RNA, 2018. **24**(2): p. 173-182.
- Rahman, R., et al., *Identification of RNA-binding protein targets with HyperTRIBE*. Nature Protocols, 2018. **13**(8): p. 1829-1849.



**TRIBE: Target of RNA-binding protein Identified By Editing**



# EZ Amp- Simple DIY Current Measuring Tool

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Current Meter

## INVENTORS

Hermann F. Wellenstein, Paul Keselman

## PATENT STATUS

Issued: US 8,922,193

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1050

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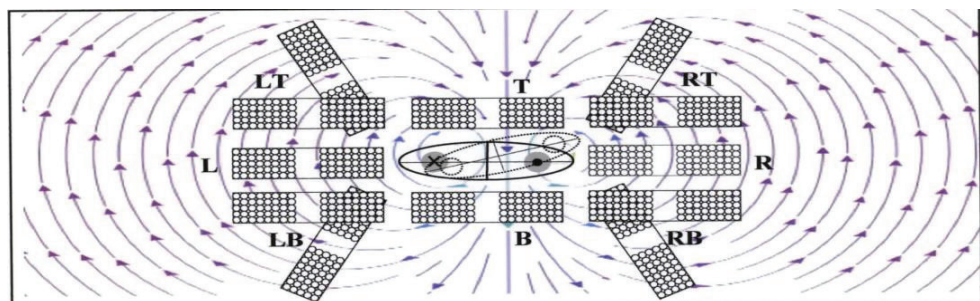
## A New Current Meter

### Background:

In electrical engineering, a device to measure current is a clamp or current-probe with two jaws that open and allow clamping around an electrical conductor. This allows the electrical current in the conductor to be measured without having to make physical contact with it, or having to disconnect it for insertion through the probe. An electrical meter with an integral current clamp is known as a clamp meter, clamp-on ammeter, or tong tester. Currently, several types of clamp meters exist which include: Rectifier, Split Ferrite Ring, iron Vane, Hall-Effect, and Open Jaw.

Conventional clamp meters have certain shortcomings the most notable of which is that only one conductor is passed through the probe, requiring the conductors of multi conductor cables to be separated before the current in one conductor can be measured. Electrical installation codes for commercial and residential properties forbid the opening of cables or the separating of wires. If more than one conductor were to be passed through, the measurement would be the vector sum of the currents flowing in the conductors which could be very misleading depending on the phase relationship of the currents. In particular, if the clamp is closed around a two-conductor cable carrying power to the equipment, where the same current flows down on conductor and up the other, then the conventional meter will falsely provide a reading of zero. Conventional current clamp meters have been available for many years and are an accepted method of non-intrusive current measurement. However, these instruments can only measure current in a single core-cable, requiring multi-core cables to be separated before one core can be measured. Where these current meters fail, the present invention excels in that it takes advantage of the magnetic field pattern surrounding a multiple-conductor cable to provide accurate readings of AC current using simple and inexpensive components.

Current in multi-core cables can be measured without the need to split cores by using an array of magnetic sensors to determine the magnetic field pattern surrounding the two, three, or four-core cable and computing the current flowing in each conductor from this magnetic field profile. Our technology is a device and procedure to measure the alternating electric current in a multi-conductor cable. The current meter disclosed here has only a small number of coils (one or two) and uses a large number of turns in each coil to obtain a robust signal output. Our current meter can have a coil geometry and placement that may be optimized with respect to certain parameters with the optimal arrangement being achieved when an output signal is strong and accurately proportional to the electric current in the cable while also being insensitive to small displacements between the cable and meter.





# Active Cross-Linkers for Chemomechanical Polymers

## SEEKING

Licensing partner and/or sponsored research funding

## PATENT TITLE

Olymeric materials having active cross-linkers, methods for making them, and use thereof

## INVENTORS

Bing Xu, Ye Zhang

## PATENT STATUS

Issued:

U.S. Patent No. 9,920,147

U.S. Patent No. 10,519,265

## LICENSING STATUS

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## BRANDEIS REF.

Case 1140

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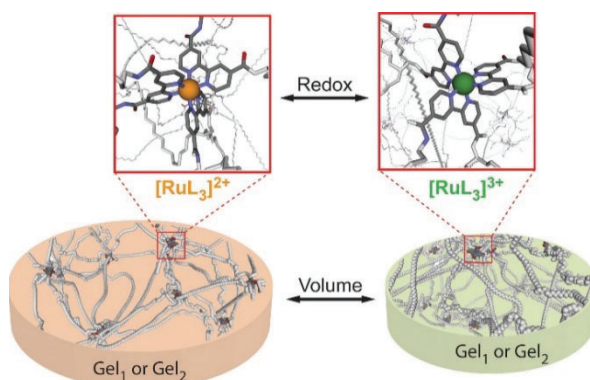
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## Novel hyper-cross linkers generate redox-active and shape-changing soft materials

Stimuli responsive shape changing soft materials (e.g., gels, elastomers, rubbers) have broad technological application. But there is limited method to produce such materials except memory alloys and temperature responsive gels. This invention describes a new method to generate stimuli responsive shape changing soft materials based on the development of active crosslinkers, that is, the crosslinkers of the polymer networks themselves to respond to stimuli, thus causing the shape/volume changes of the polymer networks that act as the component of soft materials. We show an example of this concept by producing a gel that changes volume due to the chemical reduction and oxidation. This invention should be applicable for all active crosslinkers to develop active gels as chemomechanical materials, multiply the diversity of active materials, and construction of gels that change volumes to actuating flows in a channel.



Inspired by the process of converting chemical energy into mechanical motion in the cytoskeleton of muscle cells, we developed an active cross-linker based on the tris(bipyridine) ruthenium complex  $[\text{Ru}(\text{bipy})_3]^{n+}$  for the construction of novel polymer. Benefited from this hyper cross-linker's role as a redox catalyst for a well-established chemical oscillator, namely the Belousov-Zhabotinsky (BZ) reaction, we used  $[\text{Ru}(\text{bipy})_3]^{n+}$  and N,N'-methylenebis(acrylamide) (BIS) based active cross-linker and two distinct monomers, N-isopropylacrylamide (NIPAAm) and

allylamine, for the polymerization that results in active hydrogels. We characterized the physiochemical, structural properties to achieve the self-oscillatory polymer with drastic volume changes between oxidized and reduced states. Additionally, we also used a photo-polymerization process to fabricate the optimal cross-linked active gel with the cross-linker and monomer in a molar ratio of 0.004.

This work provide a simple, however, powerful and general way to construct active soft materials compared to present technology. By applying our techniques, active materials were generated based on different types of polymer backbones and presented drastic different chemomechanical behaviors compared to present materials. This work also illustrates a new way to control molecular architecture for active materials in which the active hyper crosslinkers of the polymer network command the materials properties, which leads to a new way for making active soft materials. Brandeis OTL is seeking statements of interest from parties interested in licensing and/or sponsoring collaborative research to further develop, evaluate, or commercialize this technology and its applications

### Summary:

- A novel platform of hyper active polymer hydrogel that benefits from a redox-active novel cross-linker
- Our simple yet powerful strategy generates the drastic different chemomechanical soft materials
- Molecular architecture for active polymers can be precisely designed and controlled by adjusting molar ratio

### Advantages:

- The invention presents a new way to control molecular architecture of polymer with novel cross-linker
- The self-oscillatory polymers are hyper active to stimuli with robust ability to change shape/volume

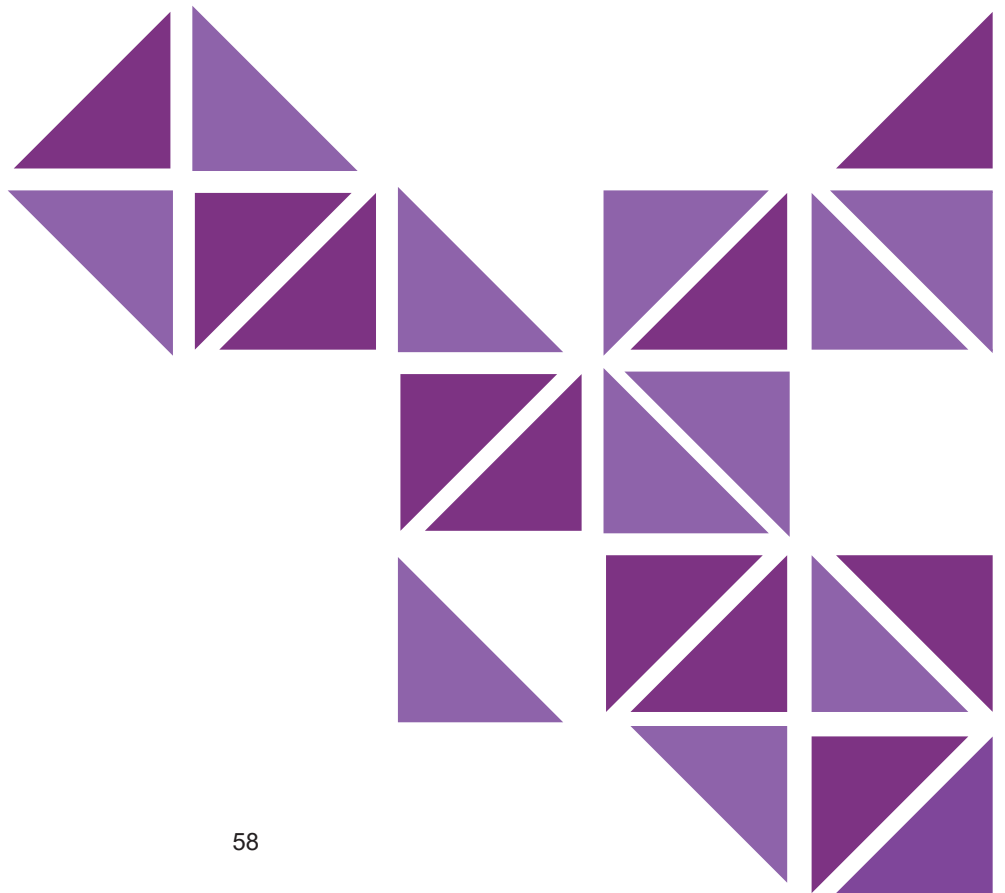
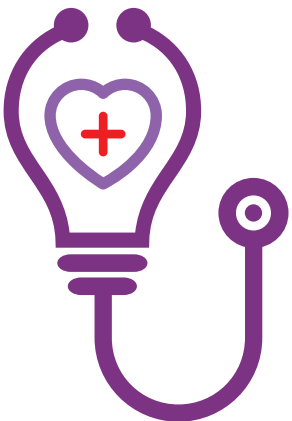
### Publications:

- Y. Zhang et al. "Active Cross-Linkers that Lead to Active Gels." *Angew. Chem. Int. Ed.* 2013, 52, 11494 –11498. DOI: 10.1002/anie.201304437.





# Medical Devices & Adaptive Technologies





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Mapping the Human Eye	63



# Better Back Brace Design for Treatment of Scoliosis Patients

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Adjustable Back Brace and Methods for Use Thereof

## INVENTOR

Ingrid Marko

## PATENT STATUS

Pending

US application 16/608,092

## LICENSING STATUS

US Rights Available

## BRANDEIS REF.

Case 1349

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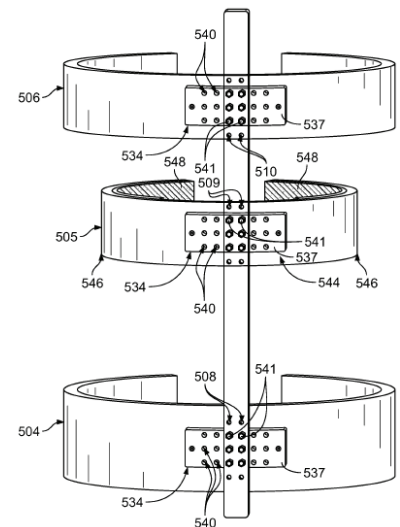
## Jointed brace is adjustable to correct spine curvatures as children grow

### Background:

Scoliosis is a spine disorder that affects 2-3% of the population (~9 million in the U.S. alone) and is observed more frequently in young girls than boys at a rate of 7:1. If left untreated, progressive spinal curvature can induce physical deformities and cause health risks affecting both heart and lung functions. Treatment options range from the use of stiff back braces in those patients with earlier diagnoses (or less severe cases with less than 40° curve angle) to higher risk corrective surgeries for patients with higher curvature angles. Children diagnosed with scoliosis are recommended to wear back braces up to 23 hours per day while they are still growing for optimal therapy to try to prevent further curvature from occurring.

The current standard of care for patients is the use of either the Boston or Charleston back brace for treating moderate to severe scoliosis in children aged 6-16 years. These brace designs aim to stop curvature from progressing and are usually custom fitted for each patient's body, but do not have high success rates. The lead times for production typically range from several weeks to several months and each can cost on the order of several thousand dollars to purchase. The problem with the use of these types of braces is that they are not adjustable to account for the growth of children or curvature progression, sometimes leading to further musculoskeletal damage if the incorrect forces are applied to the spine from the use of ill-fitted or outgrown devices.

Our invention is a novel back brace design for scoliosis patients consisting of upper and lower components that tightly conform to the body around the chest and hip regions, while being connected along the back using an attached rod, to apply tension to the spinal curves. The attachment points of the rod are adjustable both laterally and vertically on each of the upper and lower brace pieces so that the corrective forces can be periodically changed, as needed, by the physician during the treatment period as the child grows. In an alternative design, a third or middle brace can be added to the waist region for certain patients where the three conforming braces are then connected using two horizontally and vertically adjustable rods to optimize spinal corrective pressures. The doctor can adjust the tension on the spine based on positioning of these one or two rods and thus allowing better fit during growth over a 5-10+ year period.



### Summary:

- Two improved adjustable back brace designs for providing corrective forces to scoliosis patients
- Novel brace designs that allow for periodic adjustments during the treatment period of 5-10+ years and will maintain a constant, custom fit as the child with scoliosis grows

### Advantages:

- Design eliminates the long production wait time for obtaining a new, larger device once the child out-grows a custom fit brace thus avoiding damage from the use ill-fitted braces or their lack of use
- Adjustable nature reduces overall cost of treatment through the purchase of fewer devices and better application of corrective forces



# WorkingWell: A Support App for Neurodivergent Employees

## SEEKING

Licensing partner and/or  
Collaborator

## PRODUCT TITLE

WorkingWell App

## INVENTORS

Joanne Nicholson

## INTELLECTUAL PROPERTY

Copyright/Software

## BRANDEIS REF.

Case 2020-008

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## App Supporting Workplace Success

### Background:

The disparities in employment for individuals living with mental health conditions such as schizophrenia, bipolar disorder, and major depressive disorder have been well documented, as have the benefits of work for these individuals. Employment provides daily activity and routine, and opportunities for building social supports, with positive impact on self-esteem and independence, social integration, and community participation.

Supported employment service delivery models have demonstrated robust success in promoting competitive employment among these individuals. Although supported employment services have demonstrated effectiveness in helping individuals achieve the goal of competitive employment, sustaining employment presents additional challenges. Symptom severity and limitations in neurocognitive capacities, interpersonal skills, motivation to work, and self-efficacy undermine job tenure. In-person supported employment services are not routinely provided on the job, creating a gap in support for individuals with mental illness who are actively working.

The WorkingWell mobile app has been developed in response to the need for accessible follow-along supports for individuals with mental health conditions who are actively employed. The app was developed through the collaborative efforts of researchers, providers, individuals living with these conditions, an Expert Advisory Panel (including supported employment trainers and providers), and experienced app designers. It was informed by user experience design. Iterative cycles of usability testing were conducted individually, side-by-side, and in focus groups as content, information architecture, and navigation were developed. The principles underpinning the app were drawn from evidence-based supported employment. WorkingWell has been adapted for use by autistic individuals with autistic individuals, with relevance for a broader group of neurodivergent users.

### Summary:

- WorkingWell is built upon years of research in partnership with multiple mental health agencies and further improved based on the feedback from diverse stakeholders and end-users
- Mobile app provides accessible, as-needed employment support for individuals with mental illnesses
- It can work as stand-alone app or integrated into an existing system or employment supports

### Benefits:

- WorkingWell will enhance job tenure and employee retention, especially among individuals with mental health conditions and autistic people.
- Supports like WorkingWell can help in inducting workforce which currently sitting on the sidelines

### Scientific Publications:

- Nicholson J, Wright SM, Carlisle AM, Sweeney MA, McHugo GJ. "The WorkingWell Mobile Phone App for Individuals With Serious Mental Illnesses: Proof-of-Concept, Mixed-Methods Feasibility Study". JMIR Ment Health 2018;5(4):e11383. doi: 10.2196/11383





# SNAPCAP: Special Needs and Arthritic Practical Swim Cap

## SEEKING

Licensing partner for commercialization.

## PATENT TITLE

Specialized swim cap for wearers with special needs and dexterity issues.

## INVENTORS

Rebecka Lauren Sokoloff

## PATENT STATUS

Issued US. 10,869,516

## LICENSING STATUS

US Rights Available

## BRANDEIS REF.

Case: 2020-039

## CONTACT

### Inventor:

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## A New and Unique Swim Cap for All Individuals, Regardless of Abilities

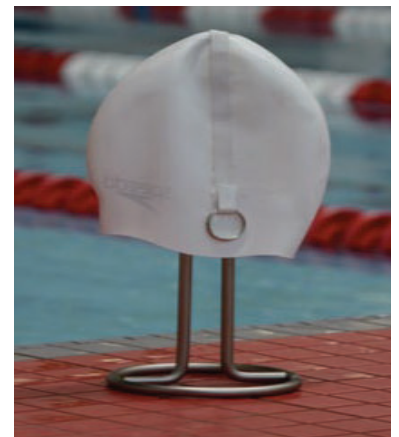
### **Background:**

A swim cap is a fitted garment, typically made out of silicone and latex, for the head of a competitive and recreational swimmer. The purpose of a swim cap is to protect the hair and ears from water and chlorine. In addition, swim caps reduce drag while swimming, which is incredibly important for competitive athletes. Putting on a swim cap involves immense musculoskeletal maneuvering. An individual need to have the ability to place their fingers within the cap, pulling it over their head and ears, and adjusting it around the ears. Over time, the caps shift affecting the goggles, hair, ears, and purpose.

The current state of swim caps is concerning, particularly for individuals with special needs, arthritis, and dexterity issues. Over time, as swim caps are stretched, pulled, and exposed to chlorine chemicals, the material breaks down and becomes fragile. Additionally, depending on the strength of the individual and the force they use to put it on, keep it on, and take it off, the cap may rip it as they take it off. This can happen during leisure swims, practice, and/or competitions. Since swim caps are necessary in the sport of swimming, they need to be frequently replaced. This is very costly and frustrating.

Swimmers with special needs often struggle placing the fingers within the cap, pulling it over the head, and then adjusting it around the ears. Most of the time, the cap either slides off, does not secure the goggles or hair, or rips. Feedback from regular swimmers also suggest that they end up constantly ripping and struggling with swim caps because of this process.

Given this problem, the inventor has created and developed SNAPCAP, a swim cap that is both beneficial and unique providing a better solution that would be less frustrating and costly. The current design has been optimized to provide an elastic band inside of the cap which connects two metal rings that sit above the ear. The rings allow for the wearer to place their fingers within it and pull the cap over the head without tearing the cap. In addition, during a practice or meet, the individual has the ability to adjust the cap with minimal effort and ripage. The inventor has produced the prototype and tested them in the water successfully.



### **Summary and Advantages:**

- Able to put on, keep on, and take off a swim cap with minimal musculoskeletal maneuvering.
- Elevates the frustration for the swimmers during leisure, practice, and competition swims.
- Allows individuals to spend less money replacing swim caps.
- Promotes a more welcoming and happy pool deck.



# Mapping the Human Eye

## SEEKING

Licensing partner for  
commercialization

## PATENT TITLE

Systems and Methods for  
Surveying the Sclera of the Eye

## INVENTORS

Hermann Wellenstein

## PATENT STATUS

US 10,881,293

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1250

## CONTACT

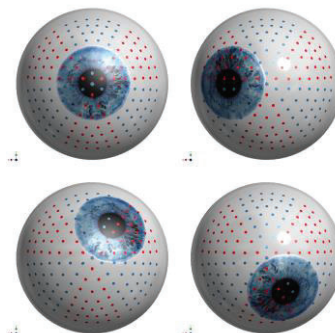
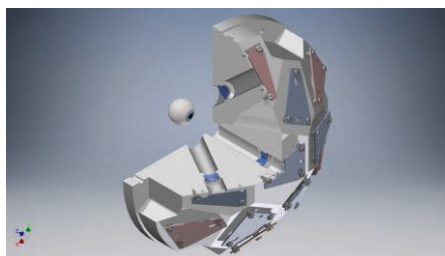
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## Sclervey: A New Device to Survey the Sclera

### Background:

Corneal diseases cause debilitating suffering in patients and leads to severely impaired vision or blindness. The visions of the affected patients cannot be corrected with ordinary glasses or contact lenses due to the fact that the shape of the cornea is no longer a simple, smooth surface. In order to fully restore vision to the patients suffering from complex corneal diseases, a prosthetic replacement of the ocular surface (PROSE), developed by Boston Foundation for Sight, is used. PROSE is the treatment process used to design custom fitted scleral lenses. The prosthesis forms a seal on the sclera holding a saline solution between the damaged tissues creating a "new cornea" thus restoring vision. Currently, the fitting process is done by trial and error, requiring multiple sessions and trial lenses. The present invention, Sclervey, surveys the sclera quickly and without any contact. Sclervey maps the sclera to tens of micron precision and provides clinicians and technicians with the data necessary to design custom fitted lenses to seal the sclera with high precision.

Sclervey uses six LED arrays arranged on a block positioned with the eye at the center of projection in order to obtain a uniform grid of 163 light spots on the surface of the eye. Six CCD cameras (plus one in the center) mounted inside a plastic spherical shell view the dot projection such that each dot is visible to two or more cameras, and stereo geometry reduces two imaged into a 3D surface. The camera pairs are utilized to conduct stereo imaging which leads to a 3D reconstruct of the light spots on the surface of the eye. The sclera must be surveyed in sections where the patient is cued (via a blinking light) to look in four directions: straight ahead, right, up left, and down left. At each position, a little more than a third of the sclera is exposed to the projected spots and mapped. Each surveyed section overlaps with the adjacent sections and neighboring sections are stitched together using image stitching software. Sclervey will make PROSE treatment more efficient, cost effective, and will improve patient experience by reducing the number of fitting sessions.



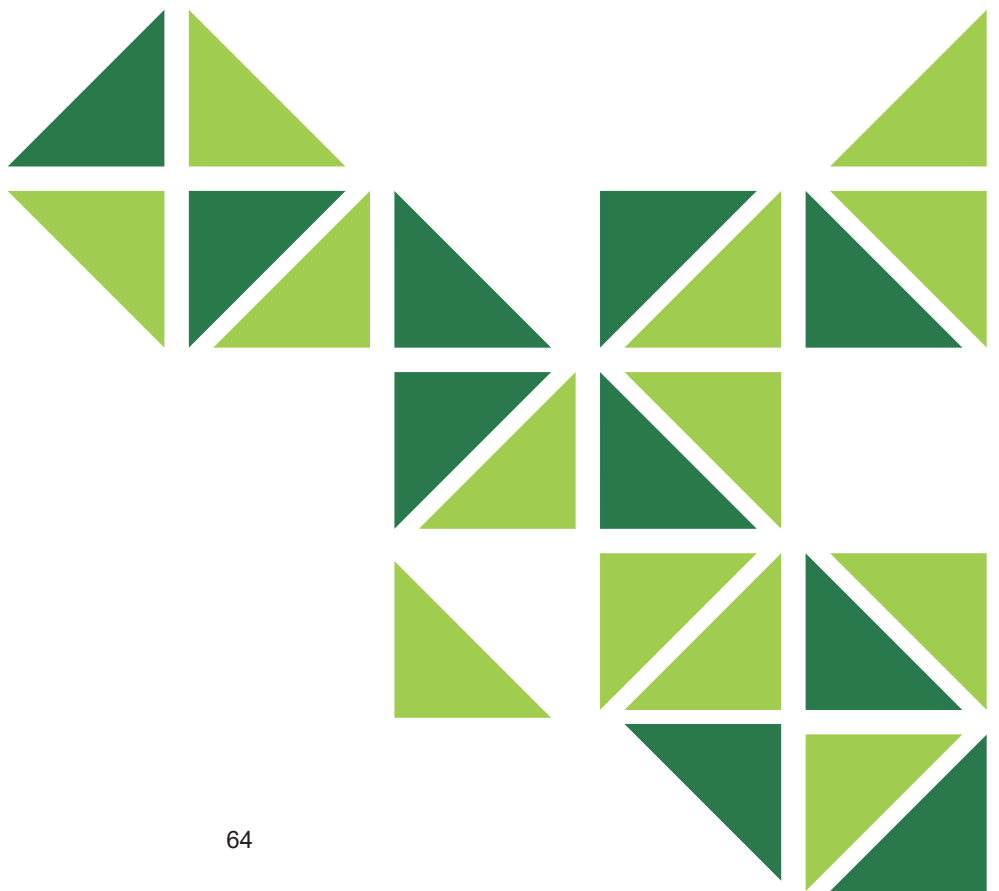
### Advantages:

- Sclervey will make PROSE treatment more efficient and cost effective.
- Sclervey will improve patient experience by reducing the number of fitting sessions.





# Functional Foods/ Dietary Supplements



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# Edible Fat Blends for Lowering LDL Cholesterol Levels in Blood

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Balanced Myristate- and Laurate-containing Edible Oils

## INVENTORS

Daniel Perlman  
Kenneth C. Hayes

## PATENT STATUS

### Issued:

US 9,491,955, US 8,617,634,  
US 8,114,461

## LICENSING STATUS

Rights available Worldwide

## BRANDEIS REF.

Case 1017

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## Novel fat blends for use in food products to promote heart health

### Background:

Dietary fats are important for maintaining good health. Clinical studies have established a link between the types of fatty acids consumed in diets with the levels of high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol found in blood. HDL is considered to be the “good” cholesterol while LDL is often referred to as the “bad” cholesterol where higher levels of total serum cholesterol and LDL are associated with higher incidence of cardiovascular diseases (e.g. heart attacks or strokes). Most experts now agree ingestion of saturated fatty acids (SFAs) (e.g. myristic, lauric, palmitic and stearic fatty acids) raise LDL and total cholesterol levels in blood while ingestion of polyunsaturated fatty acids (PUFAs) (e.g. linoleic acid) lowers those levels. Monounsaturated fatty acids (MUFAs) are more neutral in their effects.

The current opportunity available for licensing is the use of a balanced blend of dietary SFAs (i.e. myristic acid and/or lauric acid; formed either naturally or by enzymatic and chemical interesterification) combined with linoleic acid (C18:2) at specific concentrations in commercial food preparations. Since our bodies cannot produce linoleic acid, this essential PUFA must be provided in healthy diets or else some vital functions could be compromised (blood clotting, wound healing and inflammation). Furthermore, our balanced blended fat mixtures containing linoleic acid at 10-35% promote healthy blood lipoprotein profiles via lowering LDL cholesterol, raising HDL cholesterol and decreasing triglyceride levels.

The edible blended fat compositions covered by our patent claims are palatable ingredients for use in human, domestic pet and livestock food products and can be marketed to promote optimal health and reduce risks of cardiovascular disease when consumed consistently over a period of weeks. Potential commercial uses in food product manufacturing including cooking oils, spreads, margarines, shortenings, condiments (salad dressings, mayonnaises, barbecue sauces), baked goods (bread; tortilla; pastry; cake; cookie; bars) and dairy products (milk; yogurt; cheese).

### Summary:

- Invention is a blended dietary fat product containing:
  - 10 to 35% by weight linoleic acid (C18:2)
  - 15 to 55% by weight SFAs and
  - At least 10% by weight MUFAs

- Modulates the harmful effects of SFAs found in hard fats having a Mettler drop point higher than palm kernel oil (shea butter; soy bean oil; palm midfraction; palm oil; palm stearin; natural high-stearic fat; fully-hydrogenated vegetable oil)

- Currently commercialized in the United States and Canada in margarine and nut spreads

### Advantages:

- Formulation versatility allows for products to be commercialized in solid or liquid formulations
- Consistent consumption over time reduces one's risk of developing coronary heart disease by:
  - Increasing HDL levels
  - Decreasing LDL level
  - Lowering total serum cholesterol
  - Improving fasting glucose levels
  - Decreasing serum triglyceride levels





# Blended Fats and Oils for Reducing LDL and VLDL Cholesterols

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Vegetable Oil Composition Containing Palm Mid-fraction Fat and Method of Reducing Plasma Cholesterol

## INVENTORS

Daniel Perlman  
Kenneth C. Hayes

## PATENT STATUS

Issued: US 8,809,388; US 8,906,959; US 9,144,245

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1117

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## Blends made from palm mid-fraction fat combined with linoleic acid

### Background:

Over 50 years of clinical research has established a clear link between the types of dietary fats (triglycerides) consumed and their ability to modulate total cholesterol levels (TC) found in blood. Common hardening/hardstock fats used in commercial food processing (e.g. palm oil, palm mid-fraction, stearin fats), are high in saturated fatty acids (SFA) that are associated with raising TC in blood including both low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C). HDL-C is considered to be the "good" cholesterol while LDL-C and very low density lipoprotein cholesterol (VLDL-C) are often referred to as the "bad" cholesterol since higher levels of TC, VLDL-C and LDL-C are all linked to higher incidences of cardiovascular disease. Adding the appropriate amount of polyunsaturated fatty acids (PUFA) in the form of linoleic acid (18:2n6) favorably impacts the metabolism of lipoproteins.

The current invention for commercialization covers novel blended dietary fat compositions for food processing that contain palm mid-fraction hardstock fat combined with sufficient levels of linoleic acid to enhance lipoprotein metabolism. In fact, such fat blends can promote the lowering of LDL-C and VLDL-C in blood plasma without lowering HDL-C when consumed regularly over a period of weeks. Surprisingly, palm mid-fraction as the hardstock fat blended with oils rich in PUFA is found to be more effective at reducing TC in subjects than other palm oil products and hardstock fats. The latter includes whole palm oil, palm stearin, partially hydrogenated trans-containing fats and interesterified fats that often contain SFA or a trans-fatty acid at the middle (sn-2) position in the triglyceride molecule, negatively affecting LDL-C and HDL-C metabolism.



As was the case with the original SMART BALANCE blend of four natural oils, these newer heart-healthy blends contain sufficient solid fat content to harden the products at room temperature while still maintaining the cholesterol-lowering effect provided by the one or more functional polyunsaturated vegetable oils. The resulting blended fat and oil compositions with different melt points have multiple commercial uses in food manufacturing including margarines, table spreads, cooking oils and fats, shortenings, baked goods, frying oils, dairy products (e.g. cheese, yogurt, milk), fat-containing confectionary goods, mayonnaises, condiments and salad dressings.

### Summary:

- The opportunity is a healthy blended fat or oil product for use in processed foods containing:
  - At least one palm mid-fraction fat (10-22% )
  - At least one unsaturated vegetable oil (60-90%) and
  - A final 15-45% linoleic acid [18:2n6] content based on the total weight of all fatty acids
- Effective vegetable oils used in the food manufacturing processes include safflower, olive, corn, canola, sunflower, soybean, cottonseed and peanut oils
- Blended products are fluid at 35° C while forming solid or semi-solid products at 20° C

### Advantages:

- Formulation versatility allows for solid or liquid forms for use in many types of processed foods
- Beneficially improves lipoprotein profile in blood plasma by replacing conventional dietary fats
- Consistent consumption reduces one's risk of developing coronary heart disease by:
  - Decreasing LDL level
  - Decreasing VLDL level and
  - Lowering total serum cholesterol



# Palm Fruit Juice Protects DNA From Damage Caused by Drugs and Age-related Diseases

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Treatment of DNA damage and mitochondrial dysfunction using palm fruit juice

## INVENTORS

Lawrence Wangh  
Adam Osborne  
KC Hayes  
Ravigadevi Sambanthamurthi

## PATENT STATUS

Issued: US 10,813,972;

EP 2953639

## LICENSING STATUS

United States and European rights available

## BRANDEIS REF.

Case 1121

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## Polyphenols reduce reactive oxygen species leading to fewer mutations

### Background:

Mitochondrial dysfunction and mitochondrial DNA (mtDNA) damage can occur naturally over time during the aging process but can also be induced as side-effects by the drugs used to treat serious diseases, including tuberculosis and cancer. One of the most commonly used anti-retroviral drugs to treat HIV/AIDS (zidovudine or AZT) is known to cause damage to the mitochondrial genome and any mitigation of this permanent side-effect would significantly benefit the long term health of patients.

Our invention introduces palm fruit juice (PFJ) as a novel natural product for preventing and treating mitochondrial dysfunction due to mtDNA and genomic DNA damage. PFJ is a water soluble by-product of oil extraction from the fruit of the oil palm (*Elaeis guineensis*) that is rich in antioxidant phenolics and other phytochemicals. PFJ has been found to exhibit a high scavenging activity for hydrogen peroxide, the main reactive oxygen species (ROS) produced in excess by defective mitochondria. The antioxidants in PFJ reduce the level of intracellular ROS and lower the level of oxidative stress in cells which in turn decreases the number of DNA-associated breaks and mutational events that accumulate upon repair. Such mutations have been correlated with a higher incidence of mitochondrial dysfunction and age-related diseases, such as diabetes, cancer, Parkinson's and Alzheimer's. PFJ can be delivered as a nutraceutical, alone or in conjugation with drug therapies.

Our results *in vitro* using the human liver carcinoma cell line HepG2 revealed AZT exposure for 30 days induced up to a 9-fold increase in mutations as compared to normal culture media. When PFJ was added in combination to AZT exposure, the number of mutations significantly decreased by 35% when compared to AZT alone. PFJ was additionally found to mitigate the cytotoxic effects of AZT after exposure to increasing concentrations over the course of a 6-day period. Similar benefits in reducing drug-induced mtDNA mutational loads were also observed by comparing the effects of PFJ on HepG2 cells after exposure to the drug isoniazid (INH) which is commonly used to treat patients having tuberculosis infections.

Our results suggest that antioxidant phenolics from PFJ can be used as a functional food ingredient in beverages or as a supplement in nutraceutical or therapeutic orally delivered products while not causing cytotoxicity. We are seeking exclusive partners to commercialize this technology with proposed marketing claims for treating or preventing mitochondrial dysfunction, genomic DNA damage and mtDNA mutations resulting as long-term side effects caused by exposure to nucleoside reverse transcriptase inhibitor and isoniazid drugs, chemotherapy, and radiation. Brandeis University holds the exclusive licensing rights in the United States and Europe for the use of PFJ to prevent DNA damage.

### Summary:

- PFJ contains natural polyphenols for treating or preventing mtDNA damage, mitochondrial dysfunction and genomic DNA mutations caused by aging, disease and drugs
- The mitigating effects on mtDNA and genome DNA damage was shown in human liver carcinoma cells along with an observed reduction in ROS to relieve oxidative stress levels

### Advantages:

- Easily incorporated as a synergistic agent into therapeutic product formulations
- Widely available as a low-cost bi-product of palm oil milling with variable delivery forms
- Addresses long-term side-effects of certain drugs (e.g. AZT for HIV/AIDS; INH for tuberculosis)

### Scientific Publications:

"Palm Fruit Juice Mitigates AZT Mitochondrial Genotoxicity and Dose-Dependent Cytotoxicity." (2014) *Journal of AIDS & Clinical Research* 5:400.







# Carrot Fiber to Prevent Metabolic and CV-related Diseases

## SEEKING

Commercialization partner for manufacturing and sales

## PATENT TITLE

Fruit or Vegetable Pomace  
Composition and Use as Blood  
Glucose Modulator and Anti-Diabetic  
Agent

## INVENTORS

Daniel Perlman  
Kenneth C. Hayes

## PATENT STATUS

Issued: US 10,596,213

Pending: US 16/783,962

- Europe Serial No. 16860705.9
- Canada Serial No. 3,002,388

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1186

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## A low cost, natural dietary fiber all-natural ingredient for foods, beverages, and dietary supplements

### Background:

The market for dietary fibers in foods and beverages is expected to reach \$6.5 billion by 2022 and includes diverse health and wellness applications for weight loss, gut health, blood sugar control and lowering cholesterol levels. Changes in taste and quality preferences for the growing number of health conscious consumers as well as aging global populations are driving industry's needs to introduce new and better sources of functional fibers.

Carrot pomace powder (CPP) has potential to be at the top of this list as a leading new source of functional dietary fibers. It is currently considered a "waste product" of carrot juice production; however, we have found CPP isolated using our proprietary process to be highly enriched in both soluble and insoluble fibers (greater than 50% by weight) while maintaining a low sugar-to-fiber ratio in the final composition. CPP dramatically improves mammalian carbohydrate metabolism when tested in the male Nile rat model of Type II Diabetes, including lowering blood glucose, cholesterol and triglyceride profiles while also reducing fat accumulation and weight gain. Its health and wellness benefits were found to be more effective than comparable levels of two other leading commercial healthy dietary fibers – insoluble cellulose and soluble inulin. CPP exerts its effects by beneficially altering carbohydrate uptake and the cecal microflora composition within the gastrointestinal tract.

Complementing its superior performance as a functional dietary fiber, CPP is also cost effective and easy to incorporate into manufacturing processes. We are currently seeking partners to commercialize our novel CPP ingredient in functional food and beverage applications, nutritional supplements and nutraceutical products which target a diet-based approach to delay or prevent carbohydrate-related metabolic and cardiovascular diseases, including obesity, pre-diabetes, diabetes, metabolic syndrome, hyperlipidemia and hypercholesterolemia.

CPP is an ideal fiber source for use in human and companion animal diets.

### Summary:

- Carrot pomace is the by-product or "waste" material left after carrots have been juiced
- Excellent new dietary fiber for use in functional foods, beverages and health supplements
- Novel dietary ingredient for reducing blood glucose, cholesterol and triglyceride levels
- Additional wellness benefits include supporting a healthy gastrointestinal microflora profile
- Phase I human study currently underway tracking blood glucose & GI responses over 4 weeks



### Advantages:

- Higher balanced fiber source over other options (>50% by weight soluble and insoluble fibers)
- Superior blood glucose control and lower incidence of diabetes when tested against several other leading dietary fibers in animal models, including cellulose, resistant starch and inulin
- Promotes a protective gut flora profile relative to controls for developing Type 2 Diabetes
- All natural, non-GMO, sustainable fiber source that is gluten-free, and digestive well tolerated
- An abundant and cost-effective ingredient with easy and scalable manufacturing



# Edible Phytosterol-Containing Fat Blends for Promoting Heart Health

## SEEKING

Licensing partners for commercialization

## PATENT TITLE

Prepared Foods Containing Triglyceride-Recrystallized Non-Esterified Phytosterols

## INVENTORS

Daniel Perlman, Kenneth C. Hayes and Andrzej Pronczuk

## PATENT STATUS

### Issued:

- US 6,638,547
- US 7,144,595
- US 7,575,768
- US 7,709,038
- US 8,187,657

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2000-1102

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## Cholesterol-reducing phytosterol-containing fat blends in foods

### Background:

Plant phytosterols (i.e. plant sterols and stanols, including beta-sitosterol, beta-sitostanol, campesterol, campestanol, stigmasterol, stigmastanol, brassicasterol, brassicastanol, clionasterol and clionastanol) have been shown to lower serum LDL cholesterol levels in subjects by inhibiting absorption of cholesterol in the small intestine. Appreciable benefits from their incorporation into processed foods was thought to only occur by dissolving the phytosterols in an edible oil or other permissible solvent or emulsifier.



Our opportunity provides a more bio-effective form of phytosterols for use in fortifying fat-containing prepared foods without the need for microcrystalline powdered forms or exogenous solubilizers, emulsifiers or other dispersant additives. We have found heat-solubilizing non-esterified phytosterols in fat or oil, followed by cooling, results in the recrystallization of a binary complex of triglycerides and phytosterols. In addition to having higher bioavailability, these compositions decrease the oxidation of polyunsaturated-containing fats used in prepared foods.

Our phytosterol-fat blends are palatable ingredients for use in processed food products marketed to promote health and wellness by reducing one's risk of cardiovascular disease. Potential product uses include cooking oils, margarines, shortenings, spreads (peanut butter or other seed, kernel and nut butters), condiments (salad dressings, mayonnaises, barbecue sauces), baked goods, dairy (cheese and other fat-containing products), fried snacks (French fries; potato chips; corn chips), and dietary supplements.

### Summary:

- A blended dietary fat or food product that lowers LDL cholesterol levels in blood serum and liver which contains at least one edible fat and 3%-50% by weight natural (non-ester) phytosterols
- Increases bioavailability of phytosterols *in vivo* and thus reduces dosing requirements
- LDL cholesterol lowering effects were shown in 3 animal studies and 2 human clinical studies
- Products can be in the form of: Dietary supplements (capsule, pill or wafer forms); Nutraceutical fat ingredients in prepared foods; Spreads, butters and creams; Cooking oils and shortenings
- Blended products are fluid at 35° C while forming solid or semi-solid products at 20° C

### Advantages:

- Natural (non-esterified) phytosterol-containing fat blends that are free of exogenous emulsifiers
- Simplified processing, lower caloric content and more cost-effective food manufacturing (i.e. avoids use of chemically modified, microcrystalline and/or more perishable formulations)
- Stabilizes fats and oils from oxidation / rancidity during cooking and storage for longer shelf life

### Scientific Publications:

Hayes *et al.* (2002) "Free phytosterols effectively reduce plasma and liver cholesterol in gerbils fed cholesterol." *J. Nutrition* 132:1983-1988.

Hayes *et al.* (2004) "Nonesterified phytosterols dissolved and recrystallized in oil reduce plasma cholesterol in gerbils and humans." *J. Nutrition* 134:1395-1399.

Hayes *et al.* (2005) "Free phytosterols facilitate excretion of endogenous cholesterol in gerbils." *J. Nutr Biochemistry* 16:305-311.

Kunces *et al.* (2013) "Triglyceride recrystallized phytosterols in fat-free milk improve lipoprotein profiles more than unmodified free phytosterols in hypercholesterolemic men and women." *J Amer College Nutr* 32:234-242.



# Phenolics in Palm Fruit Juice for Alleviating Diabetic Symptoms

## SEEKING

Commercialization partners in food, beverage, pharmaceutical and nutraceutical sectors

## PATENT TITLE

Methods for the treatment or prevention of Diabetes Mellitus and other metabolic imbalances

## INVENTOR

Kenneth Hayes, Kalyana Sundram, Ravigadevi Sambanthamurthi, and Yew Ai Tan

## PATENT STATUS

Issued:

US 8,071,143; US 9,326,957

EP Patent No. 2299364

## LICENSING STATUS

All rights available in United States and Europe

## BRANDEIS REFERENCE

Case 20060802

## CONTACT

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## Novel dietary solution to correct blood glucose and lipid metabolism

### Background:

Numerous studies have suggested regular consumption of plant-derived bioactive phytochemicals may be able to delay or prevent the onset of serious cardiovascular and metabolic diseases through their anti-inflammatory and antioxidant effects. Palm fruit juice (PFJ), the water-soluble by-product after oil extraction from the fruit during the milling process, is surprisingly a natural source rich in phytochemicals, in particular bioactive phenolic compounds ("oil palm phenolics" or OPP).



Our invention is the use of OPP from PFJ as prophylactic or therapeutic dietary supplements in humans and animals. We have discovered OPP possess anti-hyperglycemic and anti-hyperlipemic properties when provided in the regular diets of animals genetically-prone to developing type II diabetes.<sup>1</sup> Following 12-weeks of consumption, diets supplemented with PFJ lowered fasting blood glucose levels ~5.4 fold in older diabetic animals (i.e. 650 mg/dL vs. 120 mg/dL) and resulted in overall levels near those of their non-diabetic controls fed either water or PFJ (i.e. <100 mg/dL). Similarly, these diabetic animals had severely elevated triglycerides, high VLDL levels and low HDL levels while those in the diabetic group given PFJ had plasma lipid profiles essentially normal and nearly identical to their non-diabetic controls. At necropsy, additional differences in organs, such as increased kidney size, increased liver size and the wasting of fat deposits associated with advanced diabetes, were observed in the diabetic animals given water. However, these changes were not observed in the diabetic group fed PFJ which had organs and fat deposits similar to those in the non-diabetic control group. Regular long term consumption of PFJ over a 9-month period also prevented the onset of diabetes and had no detrimental effects when fed to healthy young animals with normal blood glucose levels. This is not surprising as extracts from boiled palm fruit in the *Elaeis* genus have long been regularly consumed by African populations, resulting in an OPP intake on the order of ~300 mg/d, predominantly added as an ingredient for soups and stews.<sup>2</sup>

We are seeking partners to commercialize this technology with marketing claims including methods for treating diabetes mellitus (type 1, type 1.5 and type 2), gestational diabetes, genetic defects of  $\beta$ -cell function or insulin action, pre-diabetes and metabolic syndrome.

### Summary:

- PFJ is a cost-effective source of dietary phenolics including cinnamate and benzoate derivatives
- Proven effective in reducing blood glucose and lipid levels when tested in the Nile rat model
- Reduces glucose absorption, improves insulin sensitivity and enhances insulin secretion *in vivo*
- Shows no ill effects in animals and tested in a Phase I clinical trial by Malaysian Palm Oil Board
- Darker brown in color with a sweet yet slightly bitter taste easily masked by sweetening agent
- Easily incorporated as a functional ingredient into foods for in humans, pets and farm animals

### Advantages:

- **Green technology** generated as a by-product of palm oil production - the world's No. 1 edible oil<sup>3</sup>
- Abundant, low cost sourcing by concentrating OPP from water waste created during oil milling
- Versatile nutraceutical / pharmaceutical delivery options in pill, powder, gel or liquid formulations

### References:

1. Bolsinger, Julia et al. Anti-diabetic effects of PFJ in the Nile rat (*Arvicantis Niloticus*). J Nutri Sci; 2014; 3:e5. doi:10.17/jns.2014.3.
2. Nti CA. Household dietary practices and family nutritional status in rural Ghana. Nutr Res Prac; 2008; 2, 35–40
3. <https://www.statista.com/statistics/263933/production-of-vegetable-oils-worldwide-since-2000>



# Beneficially Stabilized Probiotics in Fat-Containing Spreads

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Probiotic Anhydrous Fatty Food-stuffs and Methods of Making Same

## INVENTOR

Daniel Perlman

## PATENT STATUS

Issued:  
US 10,532,076

## LICENSING STATUS

Worldwide rights available

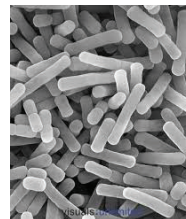
## BRANDEIS REF.

Case 1176

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## Method of stabilizing probiotic bacteria in nut, seed & bean butters



### Background:

Probiotics have become a major factor in the choice of foods by health-conscious consumers and provide a number of benefits, including limiting the growth of pathogenic gut bacteria, reducing bloating, controlling symptoms from lactose intolerance, improving bowel regularity and enhancing nutrient absorption. Global demand in the probiotic food market sector is expected to grow at a 7.4% CAGR and exceed \$55 billion in annual revenues by 2024 due to increased awareness, expanded access, and consumer preferences for natural products. However, a major impediment to growth for the industry is the limited shelf life due to the viability of health-promoting bacteria in most food products.

Our technology enables cheaper and faster manufacturing of low water activity fat-containing probiotic spreads and butters made from nuts, seeds and beans, including products made from peanuts, hazelnuts, almonds, chia seeds, soybeans and sesame seeds. Typically, a slurry is made from freeze-dried probiotic bacteria and an edible oil. The slurry is subsequently blended into a warm nut/seed/bean butter around the time of addition of a structuring fat and before packaging. In addition to significantly improving the long-term survival of microorganisms over a 12-month period (1-3 logs higher survival) and extending shelf life, our technology ensures uniform physical distribution of the probiotic particles throughout the product. Probiotic stability has been demonstrated during room temperature storage so that product shipping, storage and sale do not require refrigeration. Eliminating cold storage in the value chain is important for both consumer and sales convenience and economy (e.g. difficulty spreading cold butters; shelving costs for retailers; transportation for manufacturers). Long term viability of probiotic bacteria was tested over a 12-month period measuring the number of colony forming units (CFU) from the bacterial genera *Lactobacilli* and *Bifidobacteria* stored at 4°C and 20°C in multiple low water activity fat-based foods including peanut butter, anhydrous butterfat and palm fat.

### Summary:

- Novel manufacturing methods for healthy butters and spreads made from blends of anhydrous probiotic bacteria and low water activity fat-containing foods made from nuts, seeds or beans
- Butters and spreads containing a structuring fat are combined with anhydrous probiotic bacterial slurries in vegetable oil prior to crystallization of the structuring fat
- Provide long-term uniform distribution of probiotic particles throughout the product
- 75-100% bacterial survival for products stored for 12-month at room temperature (20°C)
- Total increased CoGs estimated to be approximately \$0.02 for a 16 oz. jar of peanut butter containing 14 servings with each serving providing approximately  $10^9$  CFU

### Advantages:

- Stable low water activity fat environment maintains probiotics in a dormant state
- Methods eliminate cold storage requirements for maintaining long-term bacterial viability
- Bacteria are uniformly suspended in the product to provide consistent delivery per serving





# Coffee Bean Flour Preserves Antioxidants and Caffeine



## SEEKING

Licensing partner for manufacturing and/or sales

## INVENTOR

Daniel Perlman

## PATENT STATUS

### Issued:

US 9,210,948: "Par-baked and Milled Coffee Beans for Use in Foods, Beverages and Dietary Supplements"

US 9,936,717: "Method of Preparing Par-baked and Milled Coffee Beans for Use in Foods, Beverages and Dietary Supplements"

US 10,278,405: "Par-Baked Coffee Bean Compositions for Use in Antioxidant-containing Products"

EP 3021684

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 1134

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## JavaPower® - Par-baked for Maximizing the Benefits of Green Coffee

### Background:

Green coffee extract from unroasted coffee beans has attracted worldwide attention as a dietary supplement. Chlorogenic acid (CGA) antioxidants found in green coffee beans are clinically proven to beneficially modulate sugar metabolism and insulin response as well as may also lower risks for cardiovascular disease, cancer and certain neurodegenerative conditions.<sup>1-3</sup> However, green coffee beans have an unpleasant flavor profile and are difficult to mill which necessitates packaging of green coffee extract in capsules. While roasting improves the flavor, aroma and color of the beans as used for coffee beverages, this process unfortunately degrades CGA.

The current invention relates to a new method for partially baking ("par-baking") green coffee beans and milling them into a fine flour that not only preserves the CGA and other nutrient levels but also retains the caffeine. The ingredient has a low cost of production with multiple commercial uses including food, health/wellness, personal care and dermatological products. The flour is palatable as an ingredient in healthy foods and beverages including coffee, tea, ice cream, smoothies, energy snacks, breakfast bars, baked desserts, breads, cereals and other edible goods. It can be used as a coffee alternative where ~4 grams flour provides the same caffeine content as a cup of coffee. The milled par-baked coffee bean powder can be packaged as tablets or capsules at varying doses. Alternatively, the coffee bean flour may be combined with skinceuticals or cosmetics for its beneficial antioxidant effects on skin.



### Summary:

- Green coffee beans are partially baked at temperatures significantly lower than traditional roasting
- Up to 4X more CGA in par-baked vs. regularly roasted beans (~8.6-11% w/w CGA by chemical & UV analyses)
- Milled beans have unexpected characteristics - nutty flavor, golden tan color and limited moisture content
- Par-baking renders the tough green beans easier to mill, allowing for production of flours having any desired particle size
- Controlled residual moisture enables rapid flour dispersal and release of CGA into aqueous foods
- Ideal for adding to foods without any gritty mouth feel
- Powder can be manufactured from organic and/or decaffeinated beans using various coffee species

### Advantages:

- Formulation versatility allows for use in foods, beverages, gels, pills, capsules and personal care products
- Improved flavor & aroma when compared to green coffee beans with low moisture content to prolong shelf life
- Easily flavor-modified with sugar, high intensity sweeteners, flavor extracts, and other ingredients
- CGA beneficially modulates sugar uptake, insulin response, and other biological indices
- Unlike roasted coffee, the light color of milled par-baked coffee minimally alters food product appearance
- Benefits of par-baked bean flour over coffee cherry flour:
  - Generally Recognized As Safe (GRAS)
  - High CGA antioxidant and caffeine content
  - Higher caffeine content (= traditional roasted beans)
  - Minimally changes the color and flavor of products





## Nutritional Data Sheet - JavaPower®

**DESCRIPTION:** Coffee Bean Flour (CBF) made from partially-baked (par-baked) beans can be used as an ingredient in food, beverage, energy, sports performance, dietary supplement, cosmetics, skincare and face/body/hair personal care products. The flour can be milled to different particle sizes and reconstitutes rapidly in all products. The particles are rounded in shape, mustard yellow in color and have a nut-like aroma, texture similar to fine flours and antioxidant levels equivalent to green coffee beans.

### BASED ON 100 GRAMS

Chlorogenic Acid (Caffeoylquinic Acid) Isomers in Robusta Coffee Beans (% w/w) <sup>1</sup>			
Analyte	Green Beans <sup>2</sup>	Par-Baked Beans <sup>3</sup>	Light Roast Beans <sup>4</sup>
iso-1-Chlorogenic Acid	0.487	<b>0.524</b>	0.049
iso-2-Chlorogenic Acid	0.572	<b>0.450</b>	0.035
iso-3-Chlorogenic Acid	0.576	<b>0.716</b>	0.059
krypto-Chlorogenic Acid	0.651	<b>0.980</b>	0.382
neo-Chlorogenic Acid	0.481	<b>0.733</b>	0.300
n-Chlorogenic Acid	4.63	<b>4.50</b>	0.648
Total Chlorogenic Acid	7.397	<b>7.903</b>	1.473

<sup>1</sup> Analytical results by chemical analysis

<sup>2</sup> Moisture content 11%, w/w

<sup>3</sup> Moisture content 4%, w/w

<sup>4</sup> Moisture content <1%, w/w

Amino Acid Profile (ppm)	
Alanine	542
Aspartic Acid	1150
Glutamic Acid	2240
Glycine	711
Histidine	252
Isoleucine	468
Leucine	971
Lysine	519
Methionine	140
Phenylalanine	638
Proline	606
Serine	539
Threonine	407
Tyrosine	383
Valine	622

**QUALITY CONTROL:** This product is manufactured in accordance with a GMP and HACCP based Quality Assurance Program

### CERTIFICATION:

KVH Kosher and Pareve.

### PROXIMATE DATA: (per 100g)

Total Calories..... 384

Calories from fat..... 41  
Calories from carbohydrate..... 258  
Calories from protein..... 85

% Moisture, max..... 4.6  
% Protein, as is..... 21.3  
% Fat, max..... 4.5  
% Carbohydrates..... 64.6  
% Ash..... 5.0  
% Fat by GC..... 4.5  
% Caffeine..... 2.4

### MICROBIOLOGICAL DATA:

Standard Plate Count, max..... 20,000/g  
Coliform..... < 10/g  
E. Coli..... < 10/g  
Staphylococcus..... < 10/g  
Salmonella..... Negative  
Yeast..... 340/g  
Mold..... 10/g

### PREPARATION INSTRUCTIONS:

Add CBF to hot water with stirring until a desired paste consistency is reached:

Parts by Weight:  
Thick Paste 1CBF: 1.5 water  
Flowable Paste 1CBF: 2 water

### Bakery and Extrusion Applications:

Replace a portion of flour in recipes to approx. 1:1 with CBF using a 5% - 10% dry weight basis substitution

### Levels of Caffeine & Antioxidants:

A 50g serving of food containing 2.5g CBF provides approximately 60mg caffeine and 200mg CGA antioxidants comparable to ½ cup of brewed coffee

### TYPICAL ANALYSIS: (per 100g)

Total Fat (g) 4.5  
Cholesterol (mg) <1.0  
Total Carbohydrate (g) 64.6

Dietary Fiber, insoluble (g) 61.0  
Total Sugar (g) 3.6  
Sucrose (g) 3.6  
Lactose (g) <0.1  
Protein (g) 23.0  
Sodium (mg) 2.7  
Calcium (mg) 103.0  
Iron (mg) 24.7  
Potassium (mg) 1.7  
Magnesium (mg) 0.16  
Zinc Trace  
Copper Trace

### Fatty Acid Profile (100%)

Saturated Fat 40.5%  
Monosaturated Fat 15.2%  
Polyunsaturated Fat 44.4%  
Trans Fat 0.01%

### Ingredients: Par-baked coffee bean flour

**Storage and Shelf Life:** Stable for up to two years at ambient temperature

### Order Minimums and special orders:

Contact New England Coffee associate for packaging sizes, other bean species and organic sourcing

Coffee <i>Bean</i> Flour versus Coffee <i>Cherry</i> Flour (per 10g)		
	Bean Flour	Cherry Flour
Total Calories	38	35
Fat	4 Cal	0 Cal
Carbohydrate	26 Cal	28 Cal
Protein	9 Cal	4 Cal
Total Carbs	6.5g	7.0g
Dietary Fiber	6g	6g
Protein	2g	1g
Fat	0.5g	0g
Caffeine	240mg	---
CGA antioxidants	790mg	---

The information contained herein is correct to the best of our knowledge. The recommendations contained in this bulletin are made without guarantee or representation as to results. We suggest that you evaluate these recommendations and suggestions in your own laboratory prior to use. Our responsibility for claims arising from breach of warranty, negligence, or otherwise, is limited to the purchase price of the material. Samples for evaluation are available from New England Coffee, 100 Charles Street, Malden, MA. 02148 Toll Free: 1-800-225-3537 <https://www.newenglandcoffee.com/javapower-coffee-bean-flour/>



# Novel Phytosterol-Glycerine Microparticles for Promoting Heart Health

## SEEKING

Licensing partners for commercialization

## PATENT TITLE

Liquid Crystalline Phytosterol-Glycerine Complex for Enhanced Bioavailability and Water Dispersal

## INVENTOR

Daniel Perlman

## PATENT STATUS

Issued:

- US 8,460,738
- US 8,921,351

## LICENSING STATUS

All commercialization rights are currently available

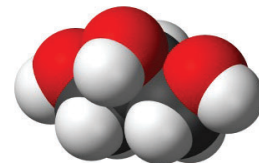
## BRANDEIS REF.

Case 1138

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## Improved cholesterol-reducing natural phytosterol formula for dietary supplements, foods and beverages



### Background:

Phytosterols are naturally occurring water-insoluble molecules commercially isolated from vegetable and tree oils. Natural phytosterols include both non-ester (chemically unmodified) sterols and stanols such as beta-sitosterol, beta-sitostanol, campesterol, campestanol and other species. In spite of their limited bioavailability, these substances have been shown to modestly lower plasma LDL cholesterol levels following ingestion by inhibiting the absorption of dietary cholesterol in the small intestine. Phytosterols are normally purified from edible oils as hydrophobic crystals with poor dispersibility in foods and beverages. As a result, obtaining any appreciable health benefit from their incorporation into beverages and processed foods typically requires either redissolving the phytosterols in edible oils or combining them with substantial amounts of emulsifiers for dispersal. On a molecular scale, the substantial size of crystalline phytosterol particles limits their effectiveness at binding cholesterol in the GI tract and decreases their ability to maintain stable suspensions in beverages.

Our technology available for licensing provides a novel binary molecular complex produced by mixing heating natural (non-esterified) phytosterols with glycerine, a natural and edible liquid. This process produces highly dispersible micron-sized particles having a new and unique liquid-crystalline structure. The glycerine does not act as an emulsifier or solvent but rather as a spacer between phytosterol molecules that blocks undesirable crystallization. The novel liquid-crystalline complex is more readily water-dispersible and more easily incorporated into beverages, foods and dietary supplements without the need for adding caloric fats or aggressive dispersing agents.

The novel phytosterol-glycerine composition can be used as an ingredient to promote cardiovascular health in dietary supplements, e.g., soft chews, or in processed food and beverage products. Potential commercial uses in processed foods include health and wellness beverages (smoothies, shakes, nutraceuticals), dairy products (milks, yogurt, cheese, sour cream), and condiments (salad dressings, mayonnaises, sauces, catsup, mustard, relishes, soups, pasta sauces, pizza sauces and dessert sauces).

### Summary:

- Edible liquid-crystalline phytosterol complex for use in dietary supplements, beverages and processed foods containing glycerine and a phytosterol and/or phytostanol
- Increases dispersibility of phytosterols thereby increasing bioavailability while reducing dose requirements
- LDL cholesterol-lowering fat-free supplement or food additive formula with *in vivo* efficacy demonstrated with soft chew dietary supplement formulations in one animal study and two small human clinical studies
- Can be optionally combined with an emulsifier such as a monoglyceride during heating to form an even more highly dispersible formulation for aqueous systems.

### Advantages:

- A fat-free complex of natural (non-esterified) phytosterols and natural glycerine
- More cost-effective and shelf-stable ingredients for dietary supplements and processed foods (i.e. avoiding use of rancidity-prone fatty acid ester formulations or fine phytosterol powders)
- Formulation versatility for delivering phytosterols into diverse consumer products including soft chew supplements, beverages, solid foods, soups, and condiments
- Regular consumption reduces risk of developing heart disease by lowering plasma LDL cholesterol levels



# Optimized Coffee Particle Grind Sizes for Single-Serve Pods

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Truncated Gaussian Distribution of Coffee Particles, Cartridge Assemblies, and Uses Thereof

## INVENTOR

Daniel Perlman

## PATENT STATUS

Issued:  
US 9,155,319

## LICENSING STATUS

All rights are currently available

## BRANDEIS REF.

Case 1169

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## Enhanced extraction efficiency requires 20% less coffee for same taste

### Background:

Single serving disposable coffee filter cartridges and their automatic brewing machines have become a popular, efficient and convenient way of brewing coffee beverages on-demand. However, the overall process of brewing in 25-50 seconds combined with low pressure heated water is challenging and best results are obtained by carefully balancing coffee particle grind sizes and rates of water flow through the pod to optimize the extraction of flavor, caffeine, color, anti-oxidants and other nutrients from the beans. If the particle sizes are too small in pods used for current brewing machines, they clog the filter and prevent or slow brewing. If the particle sizes are too large, extraction is inefficient during brewing and more coffee must be used in each individual pod in order to obtain similar amounts of caffeine, nutrients, aroma and taste.



Our invention provides a simple solution to increase the amount of natural components extracted from a given amount of coffee in a single serving filter cartridge. We have found the optimal weighted average particle size (WAPS) for large scale grinds packaged into the pods averages ~450 microns. The brewing efficiency can be further improved by "truncating" the Gaussian particle size distribution to remove particles larger than 500-600 microns using commercial high-throughput sieve-shakers (e.g. US Standard No. 30 or 35 opening) or air classifying. This additional step lowers the WAPS to ~350 microns.

The additional sieving process removes 30-35% of the larger coffee particles by weight from the grind. However, we have found that these largest particles actually release only half of their potential extractable components during the short single serve brewing process when compared to the smaller-sized sieved particles. In order to maximize cost of goods (COGs) and manufacturing investments, all larger particles can be re-directed into other ground coffee products used in drip and percolator brewing machines. Our proprietary process provides a cost-savings of 15-20% per unit through decreased raw ingredient requirements.

### Summary:

- Coffee particles >500 microns are less efficient for extracting soluble components in 25-50 sec. brews with smaller particles extracting 15-40% more efficiently using low pressure heated water
- Most commercial coffee pods tested have 1/3 to 2/3 by weight of particle sizes >500 microns
- Our invention optimizes the weighted average particle sizes in single serve pods (~450 microns)
- Extraction efficiency is further optimized by removal of particles >500-600 microns by adding a sieving step during manufacturing process prior to packaging the coffee into filter cartridges

### Advantages:

- Low cost solution for maximizing coffee bean sales by decreasing cost of goods and increasing gross margins (i.e. uses less coffee in each cup for same brewed taste)
- Alternatively increases brew strength per unit weight as compared to non-size-selected grinds
- Simple manufacturing modification that increases optimal particle size w/w yield by 20%
- Larger particles can be removed using small footprint, high capacity commercial shaker-sieves



# Novel Glass Wine Bottle Having a Dripless Lip Design

## SEEKING

Licensing partner for  
commercialization

## PATENT TITLE

"Glass Wine Bottle"

## INVENTOR

Daniel Perlman

## PATENT STATUS

Pending

U.S. Design Patent

Application No. 29/649,503

## LICENSING STATUS

U.S. rights available

## BRANDEIS REF.

Case 1170

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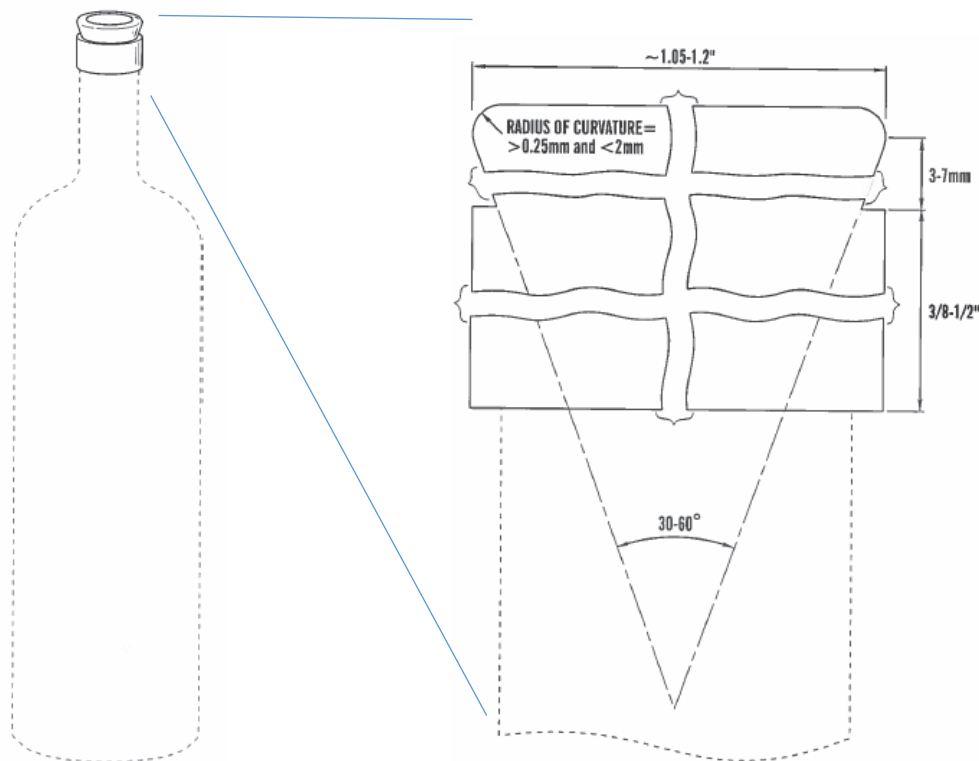
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## Conically-tapered design for bottle tops closed with corks and stoppers

### Background:

Our invention is the modification of the upper neck portion of glass wine bottles to include a conically-tapered region of 3-7 millimeters positioned below the upper lip edge but above the neck collar. Inclusion of this conical taper significantly decreases the formation of droplets and allows for drip-free pouring without the use of additional extraneous devices.

The outer edge of the lip on our wine bottle designs can be sized larger than or equal to the outer circumference of the neck collar. The conical angle formed by the conically-tapered lip region can vary from 30° to 60° and the size of the neck collars is typically 3/8" to 1/2".



### Summary:

- A conical taper added below the lip region prevents liquid from dripping down the sides of bottles
- Though enabled for wine, the design works on all glass bottles topped with corks and stoppers

### Advantages:

- Allows for drip-free pouring without the use of extraneous drip-guards or need for edge-wiping





# Novel Flow Guide and Air Channel Design Enables Drip-free Pouring

## SEEKING

Licensing partner for commercialization

## PATENT TITLE

Drip-free glass bottles having a circumferential channel and methods of making and using such bottles

## INVENTOR

Daniel Perlman

## PATENT STATUS

Issued: USSN 10,239,672

Pending:

PCT No. PCT/US2017/033012, EU

Application No. 17800056.8, and

US Application No. 16/272,765

## LICENSING STATUS

US and EU rights available

## BRANDEIS REFERENCE

Case 1300

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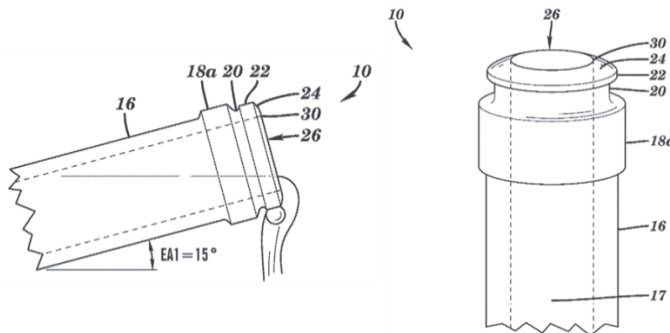
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## A drip-free glass bottle design for wines and other precious liquids



### Background:

Connoisseurs and restaurateurs have long been annoyed by wine dripping down the sides of glass wine bottles. They have addressed that problem by adding anti-drip spouts or cloth wraps in an effort to avoid staining tablecloths and tabletops. By studying the flow of wine from bottles using slow motion video, Dr. Perlman has identified and finally solved this dripping problem by modifying a small exterior portion of the conventional wine bottle's neck.

Our licensing opportunity exploits an innovative neck design that effectively solves the problem of wine dripping without compromising the strength or internal architecture of conventional commercial glass bottles. The design introduces a novel 1-2mm wide liquid flow guide below the bottle's lip edge that effectively holds onto the last wine droplet as the pouring stream ends. The guide is positioned to retain that droplet directly above an abutting ~2mm wide by ~1mm deep circumferential channel, i.e. groove, that blocks the wine droplet from running down the side of the bottle. The dimensions of the flow guide and air channel in combination with the shape and smoothness of the pouring lip are critical for functionality.

Although we describe the improved architecture for wine bottles, our technology can also be applied to other glass storage bottles for which drip-free pouring of valuable liquids is desirable. Other manufactured glass bottles that could benefit from our invention include those used for fine scotches or whiskeys; balsamic vinegars; olive oils; liquid pharmaceuticals; strong acids/bases; and other caustic liquids.

### Summary:

- Novel bottle architecture exploits a balance of capillary adhesion against capillary flow of a liquid droplet under the force of gravity as a liquid flows over the upper lip edge and flow guide, and the droplet encounters a circumferential channel that blocks downward movement of the droplet

- Video of pouring from drip-free bottles:

<http://www.brandeis.edu/now/2017/march/wine-bottle-perlman.html>

- Named as one of "The 17 Most Amazing Science Moments in 2017" by CTVNews.ca

- Prototype glass wine bottles have been commercially manufactured

### Advantages:

- Functional drip-free design is independent of:

- Angle of pour;
- Size and fullness of bottle;
- Alcohol content of liquid

- Eliminates the need to use any exogenous anti-dripping devices

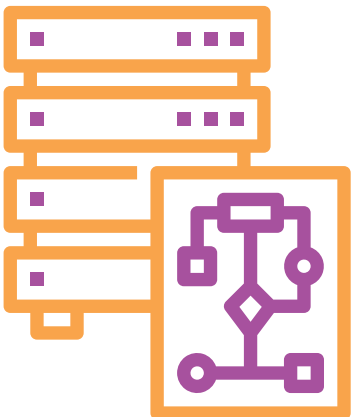
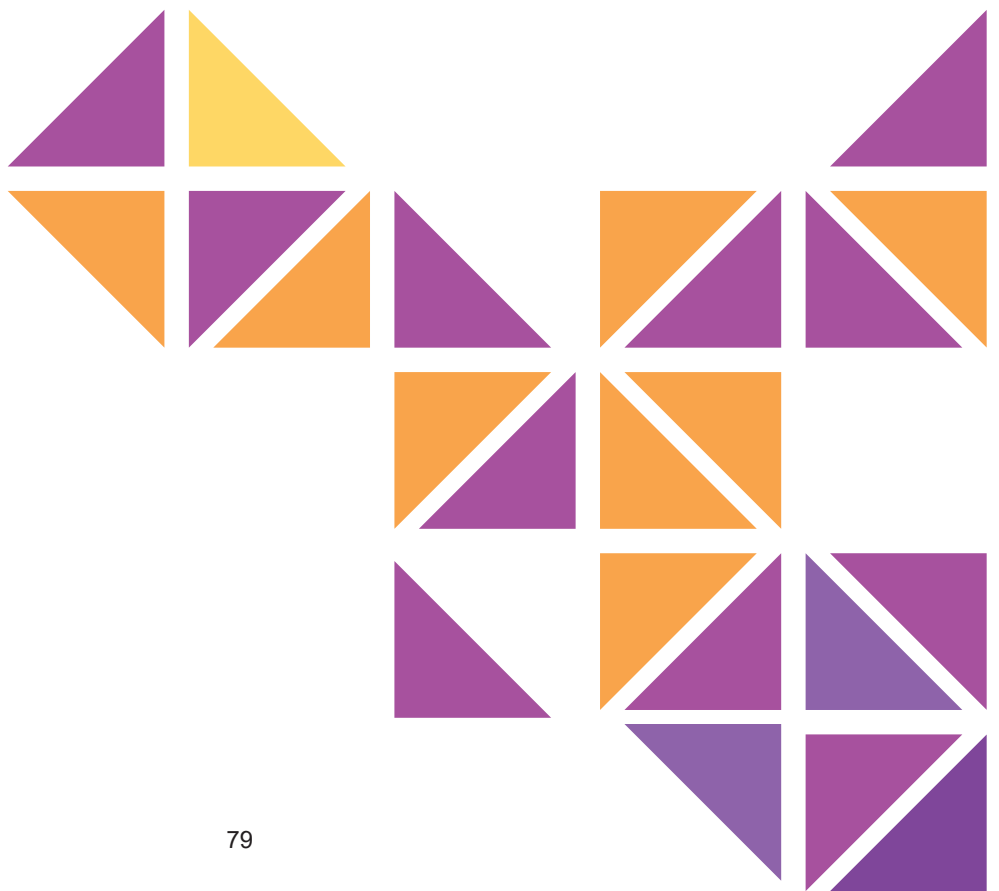
- Can be used in bottles topped with screw thread caps or corks







# Data Science



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# Predictive Model for Food Safety

## SEEKING

Licensing partner for  
commercialization

## PATENT TITLE

**Method for Microbiological  
Quasi-Chemical Kinetics  
Growth-Death Modeling in Food**

## INVENTORS

Christopher Doona

## PATENT STATUS

Issued: 10,437,909

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1239

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## Method for Modeling Growth-Death Kinetics in Food

### Background:

This invention relates to the field of predictive modeling to ensure the microbiological safety and extended shelf life of foods; additionally, to a quasi-chemical mathematical modeling method which is used as a tool for predictive microbiology evaluation of microorganism population dynamics based on an understanding of chemical reaction pathways that are intrinsic to these organisms in support of the safe design of food product formulation and food processing conditions.

To predict the ideal conditions for modeling, we looked into how bacteria populations grow and die in response to the factors influencing a food products. Intrinsic factors of the food include physical properties such as pH, water activity, salinity, and the presence of anti-microbial constituents. Extrinsic factors are also considered, which refer to properties of the external environment, such as storage temperature, relative humidity, ambient pressure, and applied processing conditions, all of which influence microbial survivability.

Current prediction models for analyzing bacterial population dynamics turned to equations developed previously from theories of treating human and animal population dynamics in their effort to model microorganism growth curves and death curves. These models were characterized by parameters such as per capita birth rate, sustainable population, which are not useful for describing the growth and death of unicellular microorganisms. Missing from the current prediction models are criteria that evaluate in a manner that reflects the underlying biochemical and biological bases of these changes.

This technology addresses the biochemical reasons underlying changes in microbial population dynamics. The Quasi-chemical model is a mechanistic based mathematical model that applies appropriate sequences of chemical reactions or biochemical processes to more accurately and meaningfully represent the molecular mechanisms of bacterial anabolism, catabolism, cellular signaling (i.e. quorum sensing) and lethality that result in growth-death behavior and offers several technological advantages over anthropomorphic models invoked by early investigators or other empirical models currently in use. In predictive microbiology, predictive models provide food technologists and non-mathematical experts with convenient food safety tools to determine the survivability of microorganisms in response to food formulations designed to control growth or in response to process conditions intended to limit or destroy pathogenic bacterial populations wherever they may originate. The data characteristic of bacterial population dynamics are collected, characterized, and referred to in terms of quantitative parameters using mathematical models or equations.

This information can be used to predict how or whether the microbial population will evolve in time, and will be particularly beneficial for food shelf life safety analysis.

### Advantages:

- Determines the microbial population changes based on biochemical factors.
- Predicts the shelf life of foods and/or the microbial growth cycles on surfaces or foods.
- Can be used to predict how or whether a particular microbial population will evolve in time.



# Relational Coordination Survey-A Tool to Enhance Work Productivity

## AVAILABILITY

End-user license (EULA) & Non-exclusive licenses in all fields

## PRODUCT TITLE

RC Survey Tool

## AUTHOR

Jody Hoffer Gittell

## INTELLECTUAL PROPERTY

Copyright

## BRANDEIS REF.

Case 1141

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## RC Survey Tool

**Background:** Relationships shape the communication through which coordination occurs, for better or for worse. Research findings suggest that the strength of relational coordination ties among participants in a work process predicts outcomes that are critically and strategically important for organizations. These outcomes include quality, efficiency, customer satisfaction, workforce resilience, well-being, learning and innovation. Research findings also identify the structures that support relational coordination, providing guidance on how to build and sustain it in real organizations.

**Relational coordination is communicating and relating for the purpose of task integration.** These mutually reinforcing communication and relationship ties form the basis for coordinated collective action, driving performance outcomes. Relational coordination is particularly relevant when work is interdependent, uncertain and time constrained.

**Summary:** The RC Survey is a tool that enables organizations to understand where relationships are strongest and weakest across roles in a focal work process. This brief assessment can serve as one of the first diagnostic steps in improving performance or as a way to evaluate the effectiveness of an intervention.

### Features:

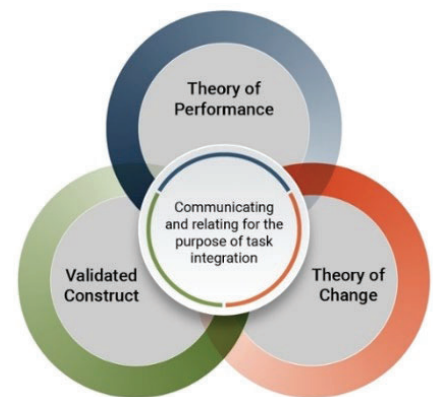
- A fully validated, network measurement tool that includes seven questions and a network structure based on the theory of relational coordination.
- It has been translated into a variety of languages.
- The tool can be customized to any work process, from small co-located teams to large complex multi-level systems.
- The survey can be administered via a web link and generally takes 10 to 20 minutes to complete, depending on the number of groups and additional questions included.

### Advantages:

- The RC Survey has been successfully implemented in a variety of industries and sectors worldwide.
- Outcomes include efficiency and financial outcomes, quality and safety outcomes, client engagement, worker engagement as well as learning and innovation.
- This tool enables users to **assess** performance, **discover** specific areas for change, and **develop** solutions unique to their particular needs and circumstances.

### Scientific Publications:

- Gittell, J.H., Ali, H.N. (2021). Relational Analytics: Guidelines for Analysis and Action. Routledge.
- Bolton, R., Logan, C.K., Gittell, J.H. (2021). Revisiting Relational Coordination: A Systematic Review. Journal of Applied Behavioral Science.
- Gittell, J.H., Hajjar, L. (2019). Strengthening Patient-Centered Care in the VHA: A Relational Model of Change. Journal of General Internal Medicine, 1-4.
- Gittell, J. H., Seidner, R., Wimbush, J. (2010). A Relational Model of How High-Performance Work Systems Work. [Organization Science, 21\(2\), 490-506.](#)
- Gittell, J.H. (2002). Coordinating Mechanisms in Care Provider Groups: Relational Coordination as a Mediator and Input Uncertainty as a Moderator of Performance Effects. Management Science, 48(11), 1408-1426.
- Gittell, J. H., Fairfield, K. M., Bierbaum, B., Head, W., Jackson, R., Kelly, M., ... Zuckerman, J. (2000). Impact of Relational Coordination on Quality of Care, Postoperative Pain and Functioning, and Length of Stay: A Nine-Hospital Study of Surgical Patients. Medical Care, 807-819.





# Integrate Multiple Hypothesis Tests to Control False Discovery Rate

## SEEKING

Licensing or collaboration partner  
for commercialization

## PATENT TITLE

Integrate Multiple Hypothesis Tests  
to Control False Discovery Rate

## INVENTORS

Pengyu Hong, Yuanzhe Bei

## PATENT STATUS

Pending:

US 11,055,304

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1159

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## Optimization algorithm to formulate FDR control with high-dimensional data

False discovery rate (FDR) control is essential for identifying significant features in analyzing high dimensional datasets (e.g., genome-wide datasets). Conventional FDR controlling methods use single type of statistical hypothesis test in each analysis. Each type of statistical test has its own advantages in detecting different aspects of differential information. To fully utilize the advantages of different statistical tests, this invention discloses a new statistics *Composite-Index* that combines multiple statistical tests and formulates FDR control as a machine learning problem. This invention also develops an algorithm *Composite-Cut*, which implements a special case of the above concept.

*Composite-Cut* integrates multiple base statistics into *Composite-Index* to maximize the utilization of differential information, which makes *Composite-Cut* substantially more powerful in detecting differential features, especially, those with subtle signals. A series of comparisons on simulated datasets, DNA Microarray datasets, and RNA-seq gene expression datasets has been conducted to demonstrate that *Composite-Cut* significantly outperforms existing approaches, such as, the Benjamin-Hochberg approach, the Storey approach, Significance Analysis of Microarrays, voom, limma, DSeq/DSeq2, PoissonSeq, edgeR, NBSeq, EBSeq, baySeq, ShrinkSeq, and so on. The results were endorsed by various supplementary analyses, such as, literature search, gene ontology enrichment analysis, gene set enrichment analysis, survival analysis, dependency analysis, and classification analysis. Literary evidence suggests that the genes called significant only by *Composite-Cut* are indeed relevant to the underlying biology. *Composite-Cut* has ability to dig deeper into data and is more sensitive to subtle yet statistically significant evidence while defying the effects of noise. The experimental results also validated that *Composite-Cut* was capable of identifying relatively more subtle changes (e.g., features with small fold-changes). Such subtle changes were showed to be relevant to the underlying biology. In complex systems, detecting subtle changes can be extremely important because the systematic aggregation and propagation of subtle changes at upstream can cause dramatic downstream effects, which are easier to detect. This invention brings such a capability which ultimately will lead to more insight, discovery, and knowledge in practice.

The invention can be widely practiced to analyze other types of high-dimensional datasets, which require multiple comparisons correction, in many fields including biotech, healthcare, pharmaceutical, finance, and so on. The executable of *Composite-Cut* can be downloaded from <http://www.cs.brandeis.edu/~hong/CC/> for non-commercial purpose only.

### Summary:

- Composite-Index is developed to combine multiple statistical tests and formulate FDR control;
- The algorithm, Composite-Cut has been implemented in a software which is available to test;
- Robustness and effectiveness are backed up by various supplementary analyses, such as literature search, Gene Ontology enrichment analysis, and clinical data analysis.

### Advantages:

- Can be practiced and accommodated in fields including biotech, healthcare, pharmaceutical, and finance;
- Better performance in analyzing high-dimensional data & identifying subtle yet meaningful changes.

### Scientific Publication:

- Y.Z. Bei and P.Y. Hong. "Robust differential expression analysis by learning discriminant boundary in multi-dimensional space of statistical attributes." BMC Bioinformatics (2016) 17:541. DOI: 10.1186/s12859-016-1386-x





# GlycoDeNovo - Modeling Method for Glycan Structures

## SEEKING

Licensing partner and/or research collaboration

## PATENT TITLE

System and Method for Determining Glycan Topology Using Tandem Mass Spectra

## INVENTORS

Pengyu Hong, Cheng Lin

## PATENT STATUS

Pending

16/616,831 (v1)

63/294,681 (v2)

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2017-051; 2022-003

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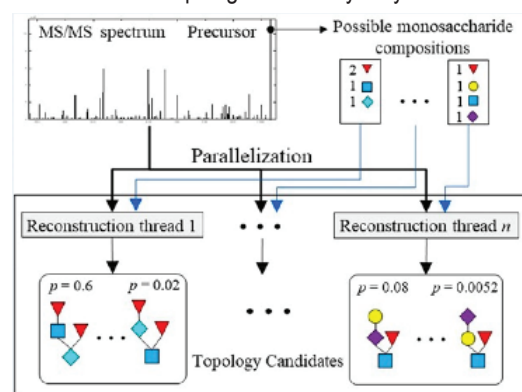
## A Method for de novo Reconstructing Glycan Structures from Mass Spec Data for Use in Bio-Pharmaceutical Design

### Background:

Glycosylation is a common modification by which a glycan (or oligosaccharide) is covalently attached to a target biomolecule such as protein and lipids. Glycosylation serves important purposes in many biological processes, including protein folding and clearance, cell adhesion, and immunological responses among others. Additionally, glycosylation is one of the key factors that determine the solubility, stability, and efficacy of many biopharmaceuticals.

Glycan structure identification is essential to understanding the roles of glycans in various biological processes, however it is a challenging task due to the vast number of topologies that they may assume even for a moderate sized glycan.

Currently, mass spectrometry has become of the most powerful tools for determining glycan structures. Several processing tools exist for determining the topologies of glycans using mass spectrometry (catalog-library approach that searches experimental mass spectra against pre-built glycan databases, brute-force search methods, such as STAT) but they have many limitations which restrict their application to a small number of glycans. Currently, there is a need for a reconstruction method that has a reduced computational complexity, and a method which does not rely on a database of only known glycans.



This invention overcomes the drawbacks by providing systems and methods for achieving a de novo method for reconstructing glycan topologies from experimental MS data. The de novo method reconstructs possible glycan topologies in a bottom up way by building an interpretation-graph that interprets some non-precursor peaks as B or C ions and specifies how to interpret each B or C ion by appending one or more preceding B and or C ions to monosaccharide. Additionally, this invention is a machine learning tool that may learn fragmentation patterns to assist in selecting the correct glycan topology from a candidate set of proposed structures.

This method has been further developed (GlycodeNovo.v2) which makes further improvements to the previous version. First, the researchers use the precursor mass measured for a peak that likely corresponds to a glycan to determine its potential compositions, which are used to constrain the search space, enable parallel computation, and hence speed up topology reconstruction. Second, they developed a procedure to calculate the empirical p-value of a reconstructed topology candidate.

### Advantages:

- It is equipped with a paradigm shift invention that uses machine learning to learn fragmentation rules/patterns to distinguish different fragmentation ions in mass spec data, which can be used to better rank the topology candidates inferred from mass spec data
- The computational complexity is significantly lower than previously reported methods and results in lower and more efficient computation time.

### Scientific Publications:

- "GlycoDeNovo – an Efficient Algorithm for Accurate de novo Glycan Topology Reconstruction from Tandem Mass Spectra". Hong et al., *J. Am. Soc. Mass Spectrom.* 2017, 28, 11
- "GlycodeNovo2: An Improved MS/MS-Based De Novo Glycan Topology Reconstruction Algorithm". Chen et al., *J. Am. Soc. Mass Spectrom.* XXXX, XXX, XXX-XXX.



# OptMark- A Tool for Assessing Query Optimizers

## SEEKING

Licensing or Collaboration partner  
for commercialization

## PATENT TITLE

A Profiling and Quality  
Assessment Tool for Query  
Optimizers

## INVENTORS

Olga Papaemanouil

## PATENT STATUS

US Pending  
US 2020/0142894

## LICENSING STATUS

US rights available

## BRANDEIS REF.

Case 1346

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## OptMark

### Background:

Query optimizers are one of the most complex components of a database management system. Optimizers are responsible for discovering the most efficient way to process a user's query. Existing performance assessment approaches for database engines produce a performance assessment of the query run-time system rather than its query optimizer. Currently there are no tools for evaluating the quality of query optimizers. To address this challenge, researchers at Brandeis University have introduced OptMark, a system for profiling and evaluating the quality of a query optimizer.

OptMark is a toolkit that quantifies the quality of a query optimizer, independently of any other component of the database management system. Our toolkit is able to accomplish this by two ways: first, by decoupling the quality of an optimizer from the quality of its underlying execution engine; and second, by evaluating independently both the effectiveness of an optimizer and its efficacy.

OptMark evaluates the relative performance factor in order to provide an insight into the quality of the optimizer's purposed plan compared with other alternative plans. The evaluation process of this metric requires us to generate a set of alternative plans and collect their execution times. OptMark relies on query hints to affect the optimizer's choice to select a specific plan, however the plan that gets executed may not be the one specified in the hint-based query. It is hard to detect before execution whether a plan is executed as the one specified by the query hints. The execution plan can be manually compared to the hint-based query after execution to check if they are the same, however that would never be efficient with a big workload. Therefore, it would be useful if there is a general approach to check if the execution plan is the same as the one specified by the query hints independently of DBMSs.

OptMark's approach for evaluating the effectiveness of an optimizer involves reporting the three effectiveness metrics absolute performance factor, relative performance factor, and optimality frequency. OptMark is able to report the relative and absolute performance factor of a given profiling query by generating and executing a sample of plans compared with the optimizer chosen plans.

### Advantages:

- First toolkit that separates the assessment of the system component from other components, making it possible to compare different optimizers.
- Allows for the comparison of different versions of the optimizer of the same data management system and for the comparison of optimizers of different data management systems.
- It is minimally invasive to the database management system being used.

### Scientific Publication:

OptMark: A Toolkit for Benchmarking Query Optimizers, Zhan Li, Olga Papaemmanouil, Mitch Cherniack. In Proceedings of 25th ACM International Conference on on Information and Knowledge Management (CIKM 2016). [\[pdf\]](#)



# Releasing Cloud Databases from the Chains of Performance Prediction Models

## SEEKING

Licensing and/or collaboration partner for commercialization

## PATENT TITLE

Systems, Methods, And Media for Distributing Database Queries Across a Metered Virtual Network

## INVENTORS

Olga Papaemmanouil, Ryan Marcus

## PATENT STATUS

Pending

US 2020-0219028

## LICENSING STATUS

Worldwide rights available

## BRANDEIS REF.

Case 2017-056

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## Discovering Database Queries Through Performance Prediction Models

### Background:

Infrastructure-as-a-Service (IaaS) providers offer low cost and on-demand computing and storage resources, allowing applications to dynamically provision resources by procuring and releasing them depending on the requirements of incoming workloads. Compared with traditional datacenters, this approach allows applications to avoid static over provisioned, or under provisioned, systems by scaling up or down for spikes, or decreases, in demand. This is realized by a "pay as you go" model of these services cloud, in which applications pay only for the resources used and only for as long as they are used.

However, taking advantage of these benefits remains a complex task for data management applications, as deploying and scaling an application on an IaaS cloud requires making a myriad of resource and workload decisions. Typically, developers must make decisions about how many machines to provision, which queries to route to which machines, and how to schedule queries within machines. Minimizing (or even predicting) the cost of each of these decisions is a complex task, as the resource availability of each machine and the execution order of the queries within them have great impact on the execution time of query workloads.

Most IaaS providers leave it to users to manually instigate a scaling action when their application becomes popular or during periods of decreased demand, and allow users to deploy custom strategies for dispatching workloads to reserved machines. Therefore, in many real-world applications, scaling and workload distributions decisions are made based on rules-of-thumb, gut instinct, or, sometimes, even past data. Even when application developers grasp the complexity of cloud offerings, it is often still difficult to translate an application's performance goal (e.g., queries must complete within 5 minutes, or the average latency must be less than 10 minutes) into a cost effective resource configuration and workload distribution solution. Status quo solutions, such as scaling based on rules-of-thumb, human-triggered events or techniques that rely on a query performance prediction models, fail to fully achieve the promise of IaaS-deployed cloud databases. Humans may be drastically incorrect or inaccurate when attempting to predict the best times to scale and what scale to use. Latency prediction-based techniques suffer from a large range of accuracy problems that worsen with scale and unknown query types, inherently undermining the main objective: estimating the cost of using cloud resources while meeting performance goals.

Our invention here relates to Methods, Systems and media for distributing database queries across a metered virtual network are provided, the method encompassing: receiving a first query at a first time; selecting a first virtual machine to execute the first query using probabilistic models that each correspond to one of a plurality of virtual machines; receiving information indicating the cost of executing the first query based at least in part on the execution time of the first query by the first virtual machine; providing an observation to each of the plurality of probabilistic models, wherein the observation includes at least information about the cost of executing the first query, and information about an action selected by the probabilistic model in connection with the first query; and reducing, over time, the costs of executing queries received after the first query based on the observations.

### Advantages:

- Eliminates human error when scaling workload distributions.
- Avoids latency prediction-based techniques which allows for higher accuracy and better odds at achieving the main objective.

### Scientific Publication:

Releasing Cloud Databases from the Chains of Predictions Models. Ryan Marcus, Olga Papaemmanouil. In Proceedings of the 8th Biennial Conference in Innovative Data Systems Research (CIDR 2017). [\[pdf\]](#)



# Skippy: Enabling Long-Lived Snapshots of the Long-Lived Past

## SEEKING

Licensing partner for  
commercialization

## PATENT TITLE

Device and method for enabling long-  
lived snapshots

## INVENTORS

Ross Shaull  
Liuba Shrira  
Hao Xu

## PATENT STATUS

Issued U.S. 8,583,598

## LICENSING STATUS

U.S. Rights Available

## BRANDEIS REF.

Case 20070501

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## An Efficient Method for Mapping Disk Pages of Copy-on-Write Snapshots

### Background:

Decreasing disk costs make it possible to take frequent snapshots of past storage system states and retain them for a long duration. Existing snapshot approaches offer no satisfactory solution to long-lived snapshots. Current methods include the Split snapshots and they are an approach that is promising because it does not disrupt the current state storage system in either the short or the long run. An unsolved problem has been how to maintain an efficient access method for long-lived split snapshots without imposing undesirable overhead on the storage system. Existing snapshot approaches, however, offer no satisfactory solution to long-lived snapshots. Yet, long-lived snapshots are important because, if the past is any predictor of the future, a longer-time prediction needs a longer-lived past.

Existing access techniques to versioned past data in databases and file systems rely on a “no-overwrite” update approach. In this approach, the past state remains in-place and the new state is copied, so the mappings for the past state take over the mappings of the current state all at once, rather than gradually. Although in-memory techniques exist for split snapshot system to accelerate the construction scan, this approach supports only short-lived snapshots. Thus, an access method is needed for split snapshot systems that also supports long-lived snapshots.

Skippy is a new approach that inexpensively indexes long-lived snapshots in parallel with snapshot creation. An embodiment of Skippy uses append-only index data structures to optimize writes while simultaneously providing low-latency snapshot lookup. Performance evaluations of Skippy indicate that this new approach is effective and efficient. It provides close-to-optimal access to long-lived snapshots while incurring a minimal impact on the current-state storage system. A key component of the split snapshot system that allows a storage system to run unmodified applications over snapshots in addition to the current state. This allows for the creation of maps for high frequency snapshots without disrupting access to the current state and to lookup the mappings efficiently when application code runs against long-lived snapshots.

The Skippy Mapper access method provides both low-cost snapshot mapping creation and low-cost snapshot mapping lookup for long-lived snapshots because they were disruptive in the long run. This method provides consistency by constraining the order of disk writes for snapshot mappings but allows flexible order for snapshot blocks. The flexibility enables more efficient snapshot creation. Because Skippy mapper protocol supports a common low level interface in storage systems the invention does not depend on specific storage system architecture and is applicable to different types of storage systems, databases, file systems, and content-addressable stores.

### Advantages:

- Current methods rely on specific storage system architecture and are not applicable to different types of storage systems; Skippy is applicable to different storage systems/databases.

### Publications:

- "Skippy: a New Indexing Method for Long-Lived Snapshots in the Storage Manager" by [Ross Shaull\(Brandeis\)](#), [Liuba Shrira \(Brandeis\)](#), and [Hao Xu \(Brandeis\)](#). [ACM SIGMOD Conference](#), Vancouver, CA, June 2008





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