TECHNOLOGIES AVAILABLE FOR LICENSING **2023**

Data Analytics

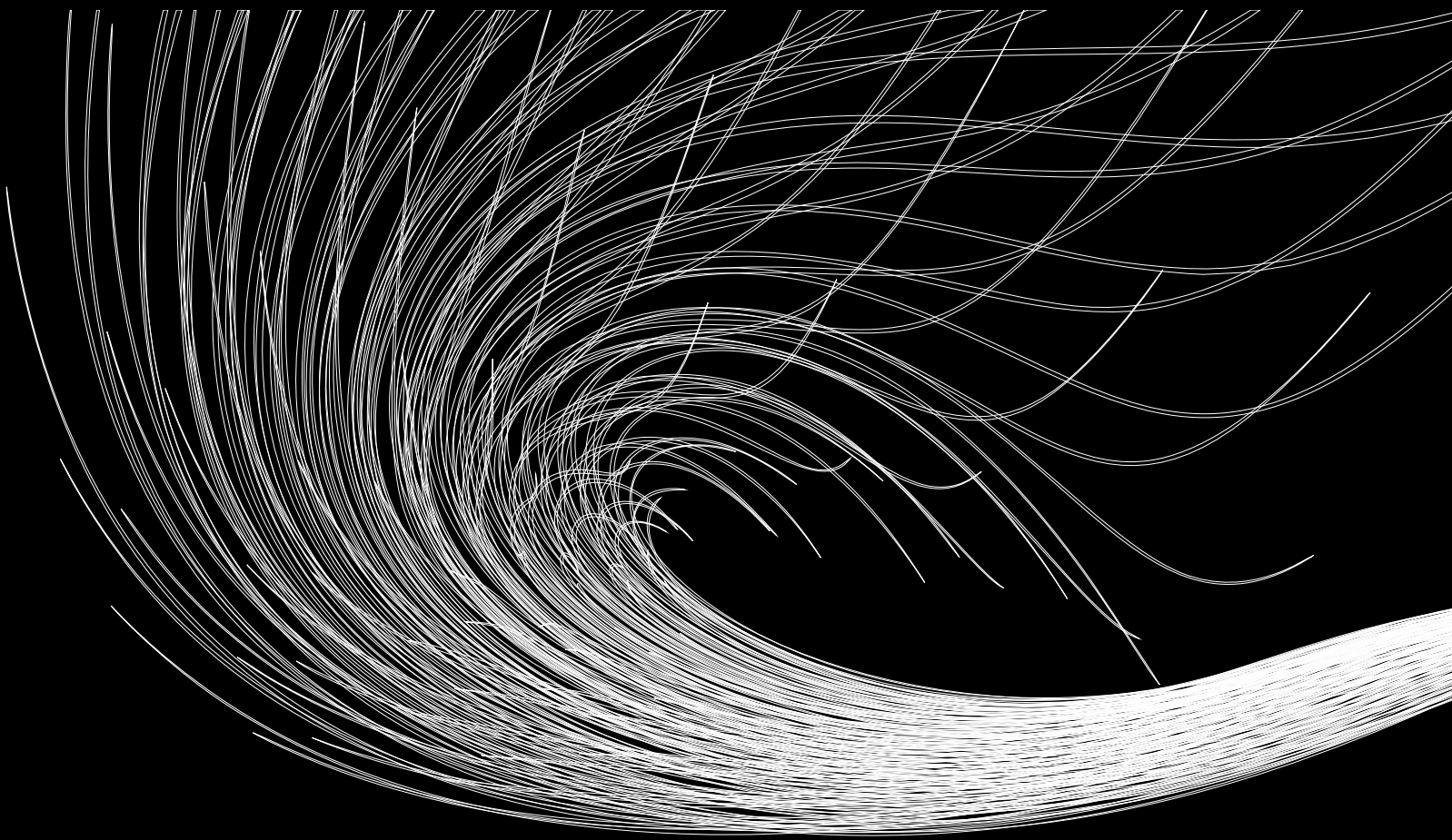
Functional Foods / Dietary Supplements

Medical Device and Adaptive Technology

Research Tools and Materials

Therapeutics, Diagnostics and Drug Delivery

Brandeis | INNOVATION



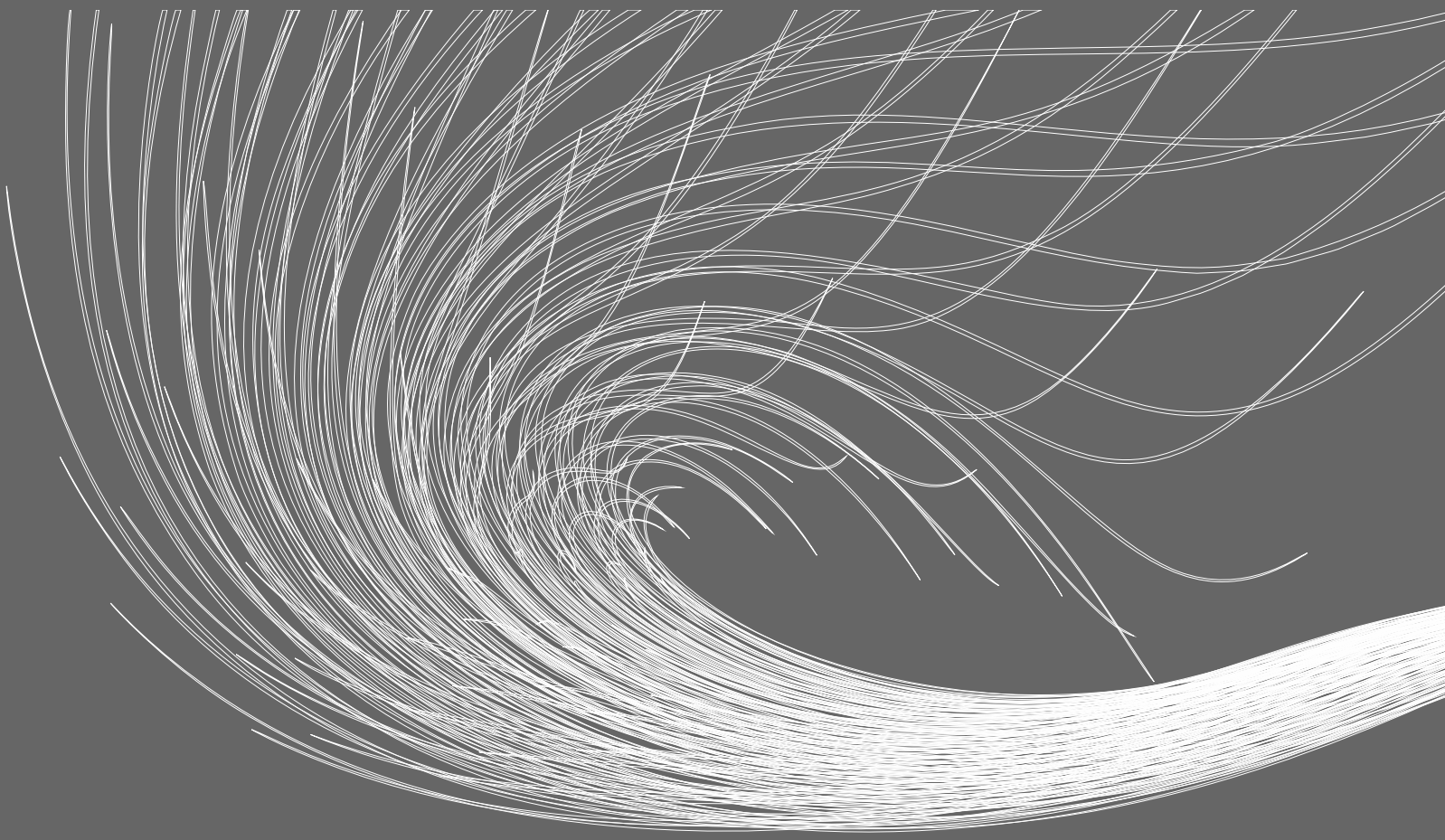
About Brandeis University's Innovation Center

Brandeis University's Innovation Center supports entrepreneurial activities across campus through our technology licensing services, innovation funding, and virtual incubator programs.

We offer training, mentorship, pitch competitions, and commercialization assistance to the entire Brandeis community of students, faculty, and staff. By doing so, Brandeis Innovation is becoming a "collision" place for interdisciplinary research and entrepreneurial teams. We comprise two distinct, yet interlinked entities: The Office of Technology Licensing and the Virtual Incubator.

Partnering with Brandeis University means tapping into our deep expertise in functional foods, neuroscience, research reagents, chemistry, therapeutics, materials science, AI, and data analytics. We have a wide variety of IP and technologies available for licensing.

Please feel free to reach out to Brandeis Innovation for more detailed information about any of our technologies and partnering opportunities. We look forward to working with you!



Contents

Therapeutics, Diagnostics and Drug Delivery

Therapeutic & diagnostic discoveries in neuroscience, oncology, infectious disease, and more. Novel drug delivery platforms with wide-ranging applications.

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1029	Supramolecular Hydrogels: Overcoming the Limitations of Traditional Drug Delivery Systems	Xu	24	●		●				●
1088	Multifunctional Hydrogels Made of Nucleopeptides and Glycopeptides	Xu	25	●						
1123	Peptides That Mimic Aberrant Proteins to Kill Cancer Cells	Xu	26	●						●
1157	New Peptide Hydrogelators for Cancer Imaging, Treatment, and Secretome Collection	Xu	27	●	●					●
1273	Enzyme-Instructed Assemblies of a Tyrosine-Cholesterol Conjugate to Selectively Kill Cancer Cells	Xu	28	●						●
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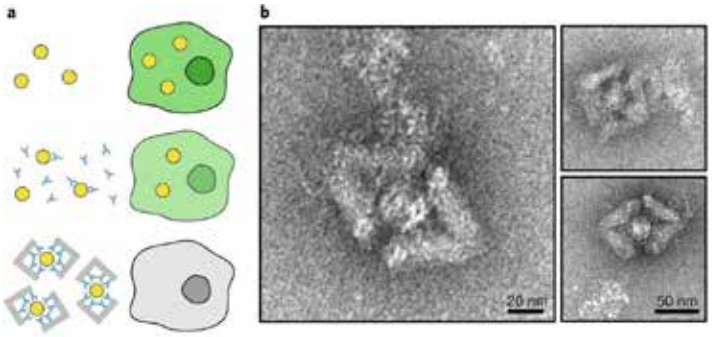
DNA Origami Shells Neutralize Viral Particles via Encapsulation

Application

Novel approach for the neutralization of viral particles and preventing infection using DNA origami

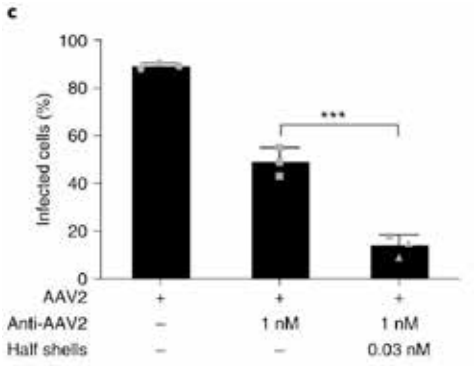


Key Benefits

- Prevents infection using single binding event between viral target and encapsulating shell
- Address viral resistance via novel preventative approach

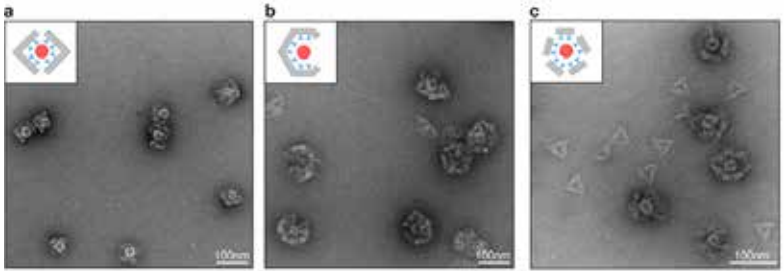
Innovation

Currently, most viral diseases lack effective treatments, and there is a scarcity of broadly applicable antiviral platform technologies. This invention describes a novel platform technology that involves trapping entire virus particles inside custom-designed macromolecular shells, thereby impeding their molecular interactions with host cells and preventing it from establishing infection. These shells can be engineered to complement a wide range of virus-binding moieties, whether independently neutralizing or not, resulting in a powerful and versatile antiviral agent. To achieve its function, the shells must be large enough to hold entire viruses while being chemically addressable for virus-specific moieties on the interior surface. The extended surface allows multivalent functionalization, enabling strong binding of target viruses even with individually weak virus-binding molecules. Complete virus coverage by the shells offers greater multivalency and binding strength, making them effective virus-neutralizing traps. The shells can be modified with various virus binders (antibodies, designed proteins, aptamers, or polymers) for targeting different viruses.



Technical Overview

Researchers from Brandeis University have developed virus enveloping shells using DNA origami building blocks. These shells self-assemble into octahedral or icosahedral shapes, ranging from 8 to 180 triangular building blocks with up to 95% assembly yield. The shells can be functionalized with viral antibodies to target specific viruses efficiently and with high specificity. This approach offers a promising method for broadly applicable virus deactivation by enclosing entire viruses in protective shells, preventing virus-cell interactions and reducing escape mutations. The large size of the DNA shells allows for up to 300 binding sites, accommodating various antibodies to effectively bind multiple covid-19 variants under diverse conditions. Some sites on the shell can be modified to enhance specificity or inactivate viral glycoproteins.



Publications

1. Programmable icosahedral shell system for virus trapping (Sigl et al. 2021). Nature Materials. PMID: 34127822
2. Geometrically programmed self-limited assembly of tubules using DNA origami colloids (Hayakawa et al, 2022). Proc Natl Acad Sci U S A. PMID: 36252043

Intellectual Property

- WO 2022/261312 | PCT/US2023/068418

Tech ID: Brandeis # 2020-034, 2022-034

Lead Inventor: Seth Fraden, Michael Hagan, Benjamin Rogers, Department of Physics, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/ecf89994-fb20-463e-85d3-5b3415914112

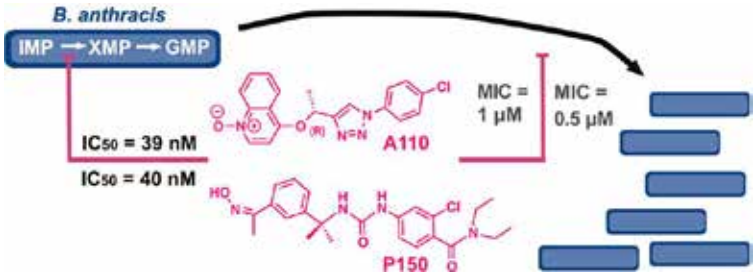
Novel IMPDH Inhibitors to Treat Microbial Infection and Fight Antibiotic Resistance

Application

A family of IMPDH inhibitor compounds and their optimized derivatives for the treatment of bacterial infection via cell division inhibition

Key Benefits

- Inhibit protozoan and bacterial IMPDH
- Unperturbed host gut microbiota
- Broad spectrum potential
- Validated in *in vivo* rodent model of acute cryptosporidiosis



Innovation

With the rise of antibiotic resistant bacteria on the rise, the arsenal of robust antibiotics available have become compromised creating a need for new targets and compounds to counter the growing threat of drug-resistant strains. While infections from strains like *Staphylococcus aureus* and *Mycobacterium tuberculosis* have always been alarming, the threat of bacteria perniciously engineered to act as biowarfare agents, such as *Bacillus anthracis*, is menacing creating another demand for more treatment options. We present a family of phthalazine, urea and benzoxazole-based small molecule compounds to treat infections caused by the protozoan parasite, *Cryptosporidium* (Cp). Our compounds inhibit Cp IMPDH activity preventing cell division halting infection. Furthermore, pre-clinical results highlight that our compounds also display treatment efficacy in the treatment of infections caused by *S. aureus* and *M. tuberculosis*. Thus, our compounds display promise as broad spectrum antibiotic agents and can improve both human and veterinary care.

Technical Overview

Organisms must be able to synthesize nucleotides in order for their cells to divide and replicate; Inosine 5'-monophosphate dehydrogenase (IMPDH) is an enzyme involved in the biosynthesis of guanine nucleotides. IMDPH is ubiquitous in eukaryotes, bacteria, archaebacteria, and protozoa; human IMPDHs are attractive targets for selectively inhibiting the immune system without perturbing the proliferation of other cells. Our compounds function as useful inhibitors of IMDPH, selectively inhibiting the parasitic version IMDPH while host IMPDH is unaffected. Our compounds shut down the parasite's purine salvage pathway by preventing the synthesis of new guanine nucleotides thus halting cell division. Our novel antimicrobial agents strongly inhibit Cp oocysts proliferation as shown in mouse models of acute cryptosporidiosis and appropriately co-localize in highest concentrations within intestinal cells where the parasite resides. Additionally our preliminary *in vitro* studies support the broad spectrum potential of our compounds by treating *S. aureus* and *M. tuberculosis* infection. Our compounds boast selectivity for parasitic enzymes while not causing liver toxicity or negatively perturbing the host's natural gut microbiota.

Publications

1. Repurposing Cryptosporidium Inosine 5'-monophosphate Dehydrogenase Inhibitors as Potential Antibacterial Agents (Mandapati et al. 2014). ACS Medicinal Chemistry Letters. PMID: 25147601
2. Mycobacterium tuberculosis IMPDH in complexes with substrates, products and antitubercular compounds (Makowska-Grzyska et al. 2015). PLOS One PMID: 26440283.
3. A novel cofactor-binding mode in bacterial IMP dehydrogenases explains inhibitory selectivity (Makowska-Grzyska et al. 2015). Journal of Biological Chemistry. PMID: 25572472.

Intellectual Property: US 9,447,134

Tech ID: Brandeis # 1115

Lead Inventor: Lizbeth Hedstrom, Professor of Biology and Chemistry, Chair of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/3d0ff77c-1614-4c6b-b97e-4c3320a13ed0

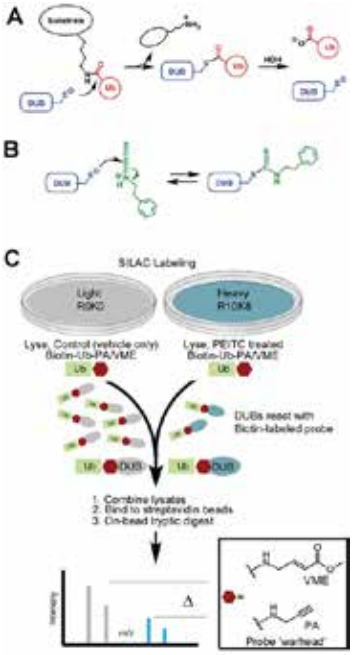
New Compounds Inhibit Cysteine Proteases with Selective Toxicity and Potency

Application

The use of cysteine protease inhibitors as a multi-functional target for treatment of a broad range of diseases such as inflammation, arthritis, osteoporosis, gingivitis, infection, neurodegenerative diseases and cancer

Key Benefits

- Specific DUB inhibition without off-target effects
- Potency and target-specific toxicity in cell based assays
- Emerging target for therapeutic discovery



Innovation

Deubiquitinating proteases (DUBs) regulate many important physiological processes and are targets for the treatment of a wide variety of diseases such as arthritis, infection, neurodegeneration, and cancer. Specifically, cysteine proteases, such as cathepsin C, can be inhibited through the use of specific diester compounds. While there are many examples of general cysteine protease inhibitors, we know of no other groups working on thiocarbamate, isothiocyanate or thioimidocarbonic acid diester-based inhibitors. Compared to current protease cysteine inhibitors that are reactive and irreversibly modify nonspecific targets resulting in nonspecific toxicity, our compounds display both selective toxicity and potency in cell-based assays. Our compounds offer an exciting research opportunity for the development of treatments for a wide range of maladies.

Technical Overview

We have discovered that isothiocyanate, thiocarbamate and thioimidocarbonic acid can inhibit cysteine proteases including DUBs such as USP9x, USP5, USp14, UCH37, UCHL3, cathepsin C, papain and ficin. For example, cathepsin C is a known target of inflammatory and autoimmune disease; thus, these compounds will function as useful tools to investigate the cathepsin C and ubiquitin pathways. These compounds can also serve as the basis for the development of novel chemotherapies for multiple modalities. Our inhibitors are related to naturally occurring compounds that have been documented to have anti-cancer agents such as naturally occurring isothiocyanates produced from glucosinolates in cruciferous vegetables such as broccoli. Furthermore, isothiocyanates have been reported to inhibit the prototypical cysteine protease papain but are not known to be DUB inhibitors. Additionally, isothiocyanates are known to be able to modify proteins in amino groups, though these reactions occur at high pH levels. There are no reports of thioimidocarbonic acid diesters inhibiting cysteine proteases, though there are reports of related dithiocarbamates as protease inhibitors. We know of no reports where thiocarbamates are being used as cysteine protease inhibitors though their function as serine protease inhibitors has been documented.

Publications

1. Identification of deubiquitinase targets of isothiocyanates using SILAC-assisted quantitative mass spectrometry (Lawson et al. 2017). Oncotarget. PMID: 28881649
2. Naturally occurring isothiocyanates exert anticancer effects by inhibiting deubiquitinating enzymes (Lawson et al. 2016). Cancer Research. PMID: 26542215

Intellectual Property

- U.S. 10,017,463 | WO2016014522A1

Tech ID: Brandeis # 1143

Lead Inventor: Lizbeth Hedstrom, Professor of Biology and Chemistry, Chair of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/10cafad2-35cb-411c-831a-3742bd14d032

Small Molecules that Target Protein Degradation

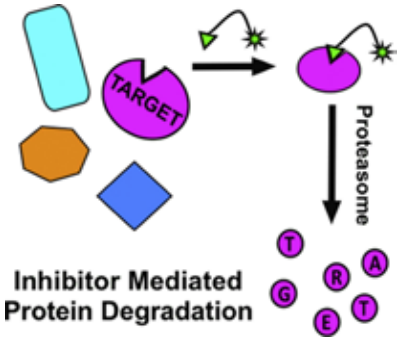
Application

A novel method of targeted endogenous protein degradation as a potential therapeutic approach using a tagged protein-binding moiety

Key Benefits

- Feasible and affordable to synthesize
- Broad applicability to scale across multiple disease classes
- Allows for robust endogenous protein downregulation
- No genetic modification required

Innovation



Treatment options for a variety of disease modalities have focused on modulating expression levels of target proteins at the transcription level; however, current methods for post-translational modulation are limited and largely rely on the expression and use of fusion proteins. While the fusion protein approach can provide useful insights into cellular processes, the need for a fusion approach can be constraining and its therapeutic potential even more limited. These limitations create an exciting opportunity to develop a small molecule strategy that can modulate protein expression opening an exciting approach for treatments like chemotherapy. Here, we present a novel development method for small molecules that function as targeted promoters for the degradation of endogenous proteins. Our approach has been validated using in vitro studies and demonstrates selective degradation of targeted proteins. Our development method is broadly applicable and presents an exciting pipeline for the design of a novel line of small molecules that can change previously undruggable targets into treatment options across a wide variety of disease classes.

Technical Overview

Numerous human diseases are caused by dysregulation in specific protein levels, activity and expression with pharmaceutical treatment approaches heavily relying on the use of small molecule protein inhibitors. The dearth of newly approached drugs in the past decade reflects the challenges faced by the pharmaceutical industry in spite of the advances in genomics identifying new protein targets implicated in disease. Sadly, many of those protein targets are not currently viable drug targets: only an estimated 15% of the human proteome is “druggable” with current small molecules. Our approach focuses on the use of compounds consisting of a protein-binding moiety that binds to a target of interest, a tag which promotes the degradation of said target, and a covalent linker which connects the moiety to the tag. These compounds present a novel approach to downregulate protein levels associated with disease states caused by excessive protein expression such as infections, inflammatory conditions, diabetes, cancer and genetic disorders. Additionally, the use of these compounds present themselves as useful research tools for investigating protein degradation and its underlying mechanisms.

Publications

1. Inhibitor mediated protein degradation (Long et al. 2012). Journal of Chemistry & Biology. PMID: 22633414
2. Boc3Arg-linked ligands induce degradation by localizing target proteins to the 20S proteasome (Shi et al. 2016). ACS Chemical Biology. PMID: 27704767

Intellectual Property:

- US 9,765,019

Tech ID: Brandeis # 1053

Lead Inventor: Lizbeth Hedstrom, Professor of Biology and Chemistry, Chair of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/1e934e72-d635-4b4d-a9ec-176b62fcce62

Pif-targeting Aurora A kinase monobodies offer new treatment approach for cancer therapy targets

Application

High binding affinity monobodies for the Pif pocket of Aurora A (AurA) kinase are intended to be licensed for commercial, enterprise, academic and research applications in cancer therapy and drug discovery

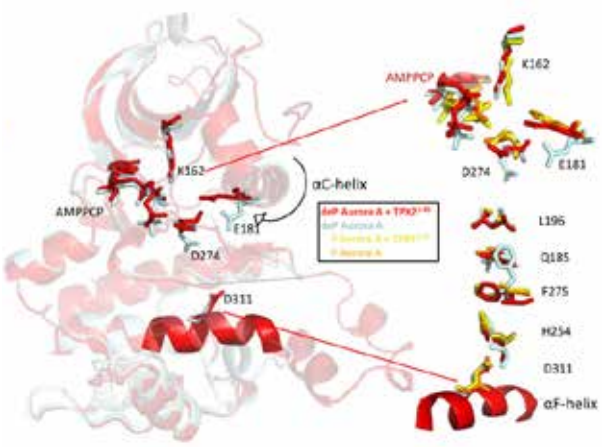
Key Benefits

- High-affinity, highly selective biological approach shut down enzymatic activity of AurA kinase
- High stability monobodies due to lack of disulfide bonds
- Synthetic, non-immunogenic proteins constructed on fibronectin scaffolds
- Ability to work in conjunction with small molecule inhibitors

Innovation

Aurora A (AurA) is Ser/Thr kinase that acts as a key regulator for mitotic events such as mitotic entry, centrosome maturation and duplication, and spindle formation. Irregularity in AurA activity has been shown to lead to cell cycle arrest when depleted while overexpression has been linked in various cancers: breast, colon, ovarian and skin. Here, the use of highly selective, non-immunogenic monobodies (Mbs) that are of highly affinity to the Pif pocket of AurA presents a novel approach to modulate enzymatic activity. By inhibiting the binding ability of the Pif pocket, AurA is not activated nor can it localize to the spindle fibers. Mbs present a novel way to study potential targets to regulate AurA activity, and have the potential to be used in conjunction with ATP-pocket small molecules, like danusertib. The use of ATP-pocket targeting kinase inhibitors in combination with our Mbs allow for a double-drugging approach. Our Pif-targeting AurA monobodies are available for licensing and will facilitate target identification and characterization of protein dynamics.

Technical Overview



Our monobodies are synthetic proteins developed from highly tailored combinatorial libraries constructed on a small, non-immunogenic human fibronectin scaffold. They function by binding with high affinity to the Pif pocket, inhibiting enzyme activity by modulating the allosteric conformation of its N-terminal αC-helix: binding at the catalytic domain but not the active site. By inhibiting the Pif pocket, TPX2 (Targeting Protein for Xklp2), a microtubule associated protein, cannot bind to AurA, kinase localization to spindles is halted and enzyme activity inhibited. Pif pocket domains are not highly conserved among human Ser/Thr kinases, thus providing novel targets for the identification of new highly-specific inhibitors with fewer off-target effects compared to drugs that bind to more highly conserved active sites.

Publications

- Molecular mechanism of Aurora A kinase autophosphorylation and its allosteric activation by TPX2 (Zorba et al. 2014). eLife. PMID: 24867643
- Dynamics of human protein kinase Aurora A linked to drug selectivity (Pitsawong et al. 2018). eLife. PMID: 29901437

Intellectual Property

- US 11,266,616 | US 11,104,741 | US 2023-0050231

Tech ID: Brandeis # 1229 & 1232

Lead Inventor: Dorothee Kern, Professor of Biochemistry, HHMI Investigator, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/592c2cf9-4799-430c-8d8d-d28987c6aab3

Oligonucleotide-Based Glycoclusters For Vaccine Design

Application

Development of Vaccine and inhibitors for biological processes that are mediated by multivalent ligand–receptor interactions, including cell adhesion, host invasion by pathogens, pathogen neutralization by host, and numerous cell regulatory signaling pathways

Key Benefits

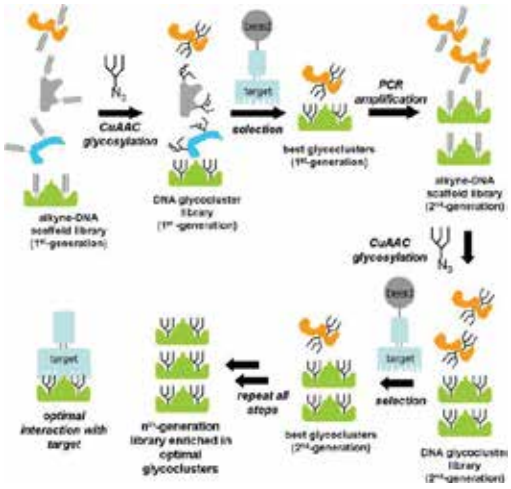
- A novel method to generate carbohydrate-oligonucleotide conjugates to produce vaccine
- High throughput library screening by utilizing a “reverse immunology” approach
- A successful strategy for biotech/pharmaceuticals based on exhaustive antigen epitope space

Innovation

This invention focuses on the importance of multivalency in carbohydrate-receptor interactions, where clustered glycans demonstrate high-avidity binding to clustered receptor sites. Although most glycocluster ligands have been designed for synthetic convenience rather than considering tertiary structure, this approach employs directed evolution to design glycocluster ligands. A library of scaffold molecules is glycosylated to generate a pool of glycoclusters, and the best glycoclusters are selected based on their binding to the target protein. These selected glycoclusters serve as templates for a second-generation library, and the process is repeated through multiple rounds to enrich the pool with high-affinity binders. DNA is chosen as the glycocluster scaffolding material due to its ease of synthesis, replication via PCR, ability to fold into diverse structures, and the feasibility of sequence-specific "glycosylation" using glycan azides and CuAAC ("click") attachment to alkyne-modified nucleobases. This approach offers a promising strategy for designing biologically active glycoclusters.

Technical Overview

This invention, as an example, used a directed evolution to find multivalent carbohydrate glycoclusters which can bind the 2G12 HIV antibody. Natural glycoclusters offers some key features which have not been widely explored in normal synthetic approaches such as: 1) glycan spacing; 2) limited glycan flexibility; 3) non-carbohydrate recognition. Therefore, the objective has been to build a library of glycosylated molecules whose tertiary design may be controlled. Through SELMA (selection with modified aptamers; designed by the inventor), DNA acts as the scaffold to support the glycoclusters, and through multiple rounds of selection the “best” binders are selected. 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.



Publications

1. Multivalent glycocluster design through directed evolution (MacPherson et al, 2011). Angew Chem Int Ed Engl. PMCID: PMC3900255

Intellectual Property

- US 9,080,169
- US 10,378,017

Tech ID: Brandeis # 1052

Inventors: Lizbeth Hedstrom, Isaac Krauss, Professors of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/7385e7dc-3739-4819-a7a4-c98e2d39b3d2

High Temperature SELMA: Glycosylated Oligonucleotide-Based Vaccine Design

Application

Development of Vaccine and inhibitors for biological processes that are mediated by multivalent ligand–receptor interactions, including cell adhesion, host invasion by pathogens, pathogen neutralization by host, and numerous cell regulatory signaling pathways

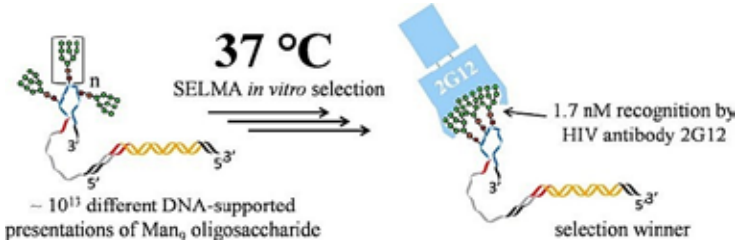
Key Benefits

- 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

Innovation

The strategy based on a directed evolution method, SELMA (Selection with Modified Aptamers), that can be used to design DNA-supported clusters of carbohydrates with optimized clustering geometry for strong recognition by a target lectin. This invention describes a modification of previously established and patented SELMA method that results in glycoclusters with significantly stronger target recognition (100-fold) and fewer glycans (2-3-fold). This technology has been used to identify specific polynucleotide-based glycoclusters for the HIV neutralizing antibody, 2G12 but can be used to design other similar vaccines or inhibitors.

Technical Overview



This SELMA strategy is an optimized version of a previously reported carbohydrate-oligonucleotide selection tool. 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 neutralizing 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).

Publications

1. High Temperature SELMA: Evolution of DNA-Supported Oligomannose Clusters Which Are Tightly Recognized by HIV bnAb 2G12 (Temme et al, 2014). J. Am. Chem. Soc., PMID: 24446826.
2. Directed Evolution of 2G12-Targeted Nonamannose Glycoclusters by SELMA (Temme et al, 2013). Chemistry. PMID: 24227340.

Intellectual Property

- US 10,378,017 | US 11,268,099 | US 10,780,150

Tech ID: Brandeis # 1153 & 1303

Inventors: Isaac Krauss, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/6851229d-c4e4-42ae-8ba5-1a9ee50b79f2

mRNA-Library Based HIV Vaccine with High-Affinity Immunogens

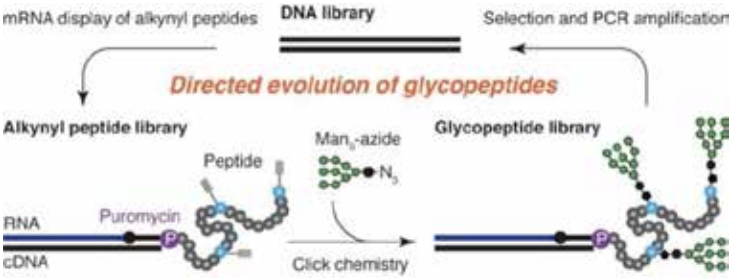
Application

A successful strategy for both HIV and cancer vaccine development in vitro

Key Benefits

- 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 Man9 units
- A successful strategy for both HIV and cancer vaccine development in vitro

Innovation



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 ~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.

Technical Overview

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 ~10^{13} glycopeptides containing multiple man$_9$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$_9$ 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 Man9 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.

Publications

1. Directed Evolution of 2G12-Targeted Nonamannose Glycoclusters by SELMA (Temme et al, 2013). Chemistry, PMC: 3896081.
2. DNA display of folded RNA libraries enabling RNAĞSELEX without reverse transcription (Macpherson et al, 2017). Chem. Commun. PMID: 28220154.

Intellectual Property

- US 10,563,193 | US 2020/0140853 | US 10,544,412 | US 11,345,912 | US 2022/0090055

Tech ID: Brandeis # 1154/1177/2019-025

Inventors: Isaac Krauss, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/1bcd5913-3c8a-41b0-bb45-f769e0c8156f

New Method for RNA-SELEX without Reverse Transcription

Application

Platform technology for the development of new drugs and diagnostics

Key Benefits

- 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

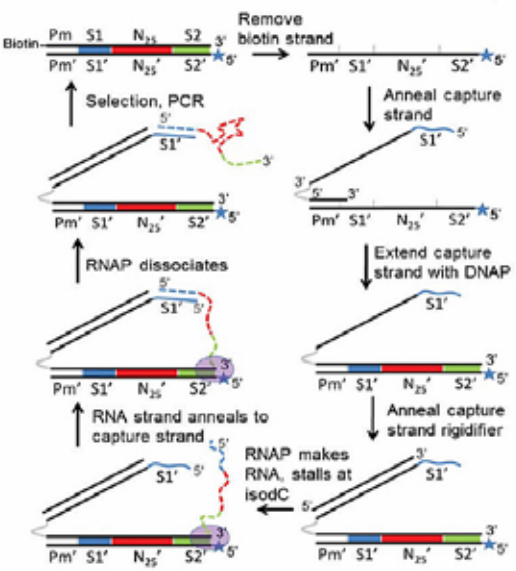
Innovation

oligonucleotide aptamers are DNA or RNA with high affinity for proteins or small molecules. Exhibiting advantages such as affinities comparable to those of antibodies, simplicity of synthesis, and general lack of immunogenicity, aptamers have found a place in the pharmaceutical market. A technique (SELEX) Systematic Evolution of Ligands by Exponential enrichment, has been used to identify specific aptamers for binding to the target ligand through multiple cycles of selection. RNA-based aptamer library provides a much larger pool because of more diverse structures and limitations to standard aptamer libraries (nuclease sensitivity, limited chemical diversity) have been overcome by the use of non-natural nucleotide analogs. However, an obstacle to development of base-modified RNA-SELEX is that it would require that two different types of enzymes (RNA polymerase and reverse transcriptase) tolerate the modified bases. This invention presents the successful generation and selection of RNA libraries in which the folded RNA is physically attached to the dsDNA that encodes it.

Technical Overview

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.



Publications

1. DNA display of folded RNA libraries enabling RNAǴSELEX without reverse transcription (Macpherson et al, 2017). Chem. Commun. PMID: 28220154.

Intellectual Property

- US 2020/0002699 | WO 2022/251651

Tech ID: Brandeis # 1342, 2020-043

Inventors: Isaac Krauss, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/e178166a-1f6e-48ce-a6e0-37910f633422

Capture-SELMA: A New mRNA Library-Based Tool for Drug-Design

Application

Biopharma including the development of vaccines, immunomodulatory agents, diagnostics, and anti-adhesion drugs against cancer and other diseases

Key Benefits

- 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

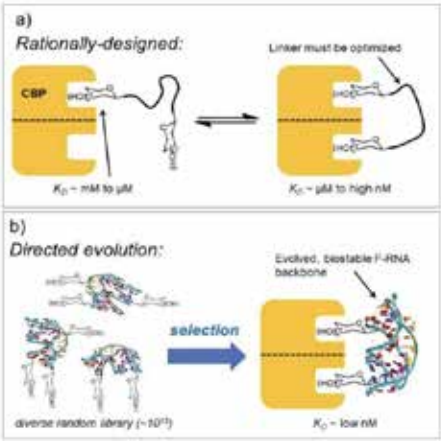
Innovation

Carbohydrate-protein interactions are essential for many biological processes. The design of carbohydrate structures that can mimic or interrupt these interactions has potential applications in medicine, such as vaccine development, immunomodulation, diagnostics, and anti-adhesion drugs. Rather than using rational design and medchem to optimize multivalency to match the target binding sites, this invention describes developing a directed evolution method to rapidly select optimal multivalent glycan clusters from extremely diverse libraries of 10^{12}-10^{13} structures using 2′-deoxy-2′-fluoro RNA (F-RNA). Such directed evolution of carbohydrate clusters on Fluoro-RNA backbone provides more serum stability to the RNA and this method can identify multi-valent glycan clusters as shown with an example of tight binders of the HIV antibody 2G12,11 a target with four glycan binding pockets.

Technical Overview

The invention is 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. CBPs usually have low affinity (Kd ~mM to µM) for individual glycan units. In this case, 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. Unlike the previous generation of SELMA (SELection of Modified Aptamers) method, in which glycan-modified DNA was covalently displayed on unmodified DNA, the current method (Capture SELMA) utilizes a capture strategy in which a nascent RNA transcript from a DNA template is non-covalently hybridized to a “capture strand”, and thus travels with its DNA template. The DNA template can be amplified by PCR, regardless of subsequent glycosylation of the RNA, without reverse transcription.

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. This method is validated by the selection of oligomannose (Man9) glycan clusters from a sequence pool of ~10^{13} that bind tightly to broadly neutralizing HIV antibody 2G12.



Publications

1. Directed Evolution of 2Ǫ-Fluoro-Modified, RNA-Supported Carbohydrate Clusters That Bind Tightly to HIV Antibody 2G12 Redman & Krauss, 2021). J.Am.Chem.Soc. PMID: 34096703

Intellectual Property

- WO 2022/251651

Tech ID: Brandeis # 2020-043

Inventors: Isaac Krauss, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/7481375f-7f05-4dc0-b238-8b0a2fa03284

Sulfur-Linked Oligomannose Derivatives for Vaccines

Application

Vaccine and therapeutic development, and immunogenicity studies

Key Benefits

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

Innovation

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 Manα1→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 Manα1→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.

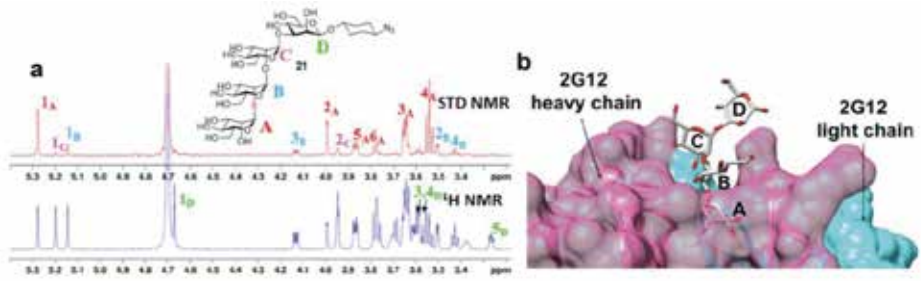
Technical Overview

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. Additionally, this invention makes possible and confirms the reducing terminal S-linkage confers complete stability against *x. manihotis mannosidase.*

Figure 1 (BELOW) – 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 1H 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).

Publications

1. "Synthesis of Mannosidase-Stable Man3 and Man4 Glycans Containing S-linked Manα1 →2Man Termini (Neralkar et al, 2021. Org. Lett. PMID: 33793242.



Intellectual Property

- WO 2022/197990

Tech ID: Brandeis # 2021-035

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Link: https://brandeis.flintbox.com/technologies/850ef8c4-4c7f-46c5-b027-efce18993f51

Use of Dopamine Beta-Hydroxylase (DBH) Inhibitors to Prevent Long Term Memory Loss

Application

The use of dopamine beta-hydroxylase (DBH) inhibitors for the treatment and delay of memory loss associated with neurodegenerative disease, disorder, or conditions

Key Benefits

- Inhibitor drugs (disulfiram, Nepicastat) alrea proven safe for human use
- Addresses loss of dopamine by axons during neurodegenerative disease progression
- Can be used in combination with other drugs
- Proof-of-concept testing completed in rodent model for Alzheimer's Disease

Innovation

Neurodegenerative diseases of the mind, like Alzheimer's Disease (AD), are hallmarked by symptoms such as memory loss. Dopamine (DA) is a critical neuromodulator required for long-term memory formation and in disease states like AD, it is hypothesized that memory decline is linked to the insufficient co-lease of DA by noradrenergic (NA) fibers. The decline in DA release may be due to the strong degeneration of the noradrenergic system in early AD progression preventing long term memory formation. We present the use of dopamine beta-hydroxylase (DBH) enzyme inhibitors as a treatment for memory loss. Since NA is synthesized from DA via DBH enzymes, the use of inhibitors would drive the surviving NA fibers to produce more DA and thus support memory formation. The chronic use of disulfiram or Nepicastat, human-approved DBH inhibitors, can prevent or delay memory loss associated with certain neurodegenerative diseases.

Technical Overview

The invention is based on the hypothesis that the deterioration of hippocampus-dependent declarative memory in AD patients may be caused by the insufficient co-lease of DA by NA fibers due to degeneration of the noradrenergic system. We have conducted proof-of-concept studies in rodent models highlighting that the chronic use of DBH inhibitors (Nepicastat, disulfiram) can increase levels of dopamine in the hippocampus. In our rodent studies, chronic oral administration of Nepicastat (50-200 mg/kg) for two weeks decreased the formation of NA in both the hippocampus and cortex in a dose-dependent manner. Nepicastat treatment selectively increased levels of DA only in the hippocampus while cortical DA levels were not changed; these effects were dose-dependent. In long-term studies using an AD rodent model (Tg2576), contextual fear memory was restored to near normal levels in the AD model when compared to healthy mice following a chronic five month oral treatment of Nepicastat and Droxidopa (L-DOPS). To account for potential decreases in NA levels, L-DOPS, an FDA-approved synthetic amino acid precursor, was paired with Nepicastat treatment. HPLC analysis of hippocampal tissue after study endpoints showed that treatment of Nepicastat strongly decreased levels of NA but increased hippocampal DA. The use of L-DOPS rescued reduced levels of NA and increased production of dopamine to an even greater extent.

Related Publications

1. The dopamine beta-hydroxylase inhibitor nepicastat increases dopamine release and potentiates psychostimulant-induced dopamine release in the prefrontal cortex. (Devoto et al. 2014). Addiction Biology. PMID: 23289939
2. Noradrenergic dysfunction in Alzheimer's disease (Gannon et al. 2015). Frontiers in Neuroscience. PMID: 26136654

Intellectual Property

- US 10,441,573 | US 10,821,097

Tech ID: Brandeis # 1161

Lead Inventor: John Lisman, Professor of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/a488d1a6-55f2-4683-9461-8cbb2a8cc0a0

Suppression PCR for Improved Rare Copy Diagnostics

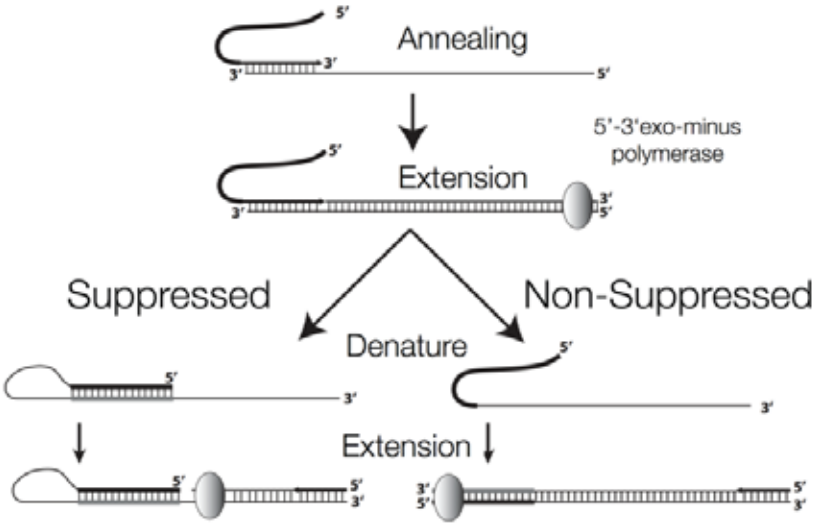
Application

Improved diagnostic design and diagnostic assays for healthcare, academic, and enterprise settings

Key Benefits

- Selective, million-fold amplification of rare sequence variants
- Outperforms existing suppression PCR methods — by up to 8000x
- Requires only conventional primers and commercially available polymerase lacking 5’-3’ activity
- Unconstrained by temperature dependence at annealing/extension phases and restriction enzyme sites in target sequence

Innovation



Patients, healthcare providers, and payers have a keen interest in faster, more accurate, and less invasive cancer diagnostic methods. The current gold standard, tumor biopsy, entails high costs and risks associated with invasive surgery, providing only a limited sample of abnormal cells. Considering the role of intratumoral genetic heterogeneity in clonal evolution, metastases, and treatment resistance, it becomes crucial to identify and analyze rare or low copy DNA mutations driving these changes for effective therapy management. Moreover, improved tests analyzing metastatic and tumor cell DNA in the bloodstream through liquid biopsies would advance oncology treatment. Despite these advancements, current PCR-based diagnostics face inherent technical constraints.

Technical Overview

The current invention introduces Nunchaku PCR as the most user-friendly and widely-deployable suppression PCR method available today. This technology employs a single upstream PCR primer with two unique binding sequences: a common 5' priming sequence shared among all variants and a 3' selective priming sequence that, after extension and denaturing, loops back to bind to the primer's 5' end. This configuration effectively hinders 5'-3' extension by a DNA polymerase lacking 5'-3' exonuclease activity, allowing for selective amplification of rare sequence variants amidst an abundance of a known sequence using the same primer sites. Even a single mismatch, such as in single-nucleotide polymorphisms (SNPs), significantly enhances extension and sequence amplification. Notably, Nunchaku suppression PCR has been successfully demonstrated in vitro.

Intellectual Property

- US 9,518,292

Tech ID: Brandeis # 1057

Lead Inventor: Sacha Nelson, Gyula and Katica Tauber Professor of Life Science, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/4624949d-aa4a-4d5c-aa1f-a17ef7790265

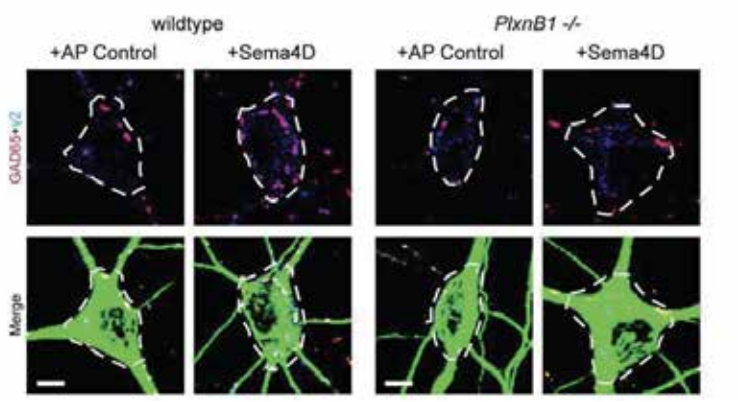
A Novel Therapy for Treating Epileptic Seizures

Application

Potential Disease areas: Epilepsy, rare diseases such as status epilepticus, Dravet syndrome, Rett syndrome, Tuberous sclerosis complex (TSC)

Key Benefits

- Prevent or halt the epileptic progression
- Suppress hyperexcitability during a seizure event
- Drives inhibitory synapse formation



Innovation

Currently, millions of Americans suffer from epilepsy and 1/3 of these patients do not respond to available treatments. 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 increasing the number of inhibitory synapses. 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.

Technical Overview

Researchers at Brandeis University have discovered that harnessing the Sema4D-Plexin B1 interaction may lead to novel treatments of seizure disorders. Treatment of hippocampal neurons with Sema4D causes a rapid increase (i.e. within 30 minutes) in the density of functional GABAergic synapses, rapidly (within 2 hours) reducing aberrant neuronal hyperexcitability in hippocampal slice cultures and two epilepsy mouse models. Nonetheless, these experiments indicate that inducing the formation of inhibitory synapses through the administration of Sema4d could result in beneficial in vivo effects and possibilities for anti-seizure treatment.

Publications

1. Semaphorin 4D induced inhibitory synaptogenesis decreases epileptiform activity and alters progression to Status Epilepticus in mice (Adel et al, 2023). Epilepsy Res. PMID: 37163910
2. Semaphorin 4D promotes inhibitory synapse formation and suppresses seizures in vivo (Acker et al, 2018). Epilepsia. PMID: 29799628
3. The class 4 Semaphorin Sema4D promotes the rapid assembly of GABAergic synapses in rodent hippocampus. (Kuzirian et al. 2013) J Neurosci. PMID: 23699507

Intellectual Property

- US 10,626,163 | Provisional patent application filed

Tech ID: Brandeis # 1116, 2023-007

Inventors: Suzanne Paradis, Professor of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/4f9e48a3-8dd9-46e6-82ed-17d515265ff3

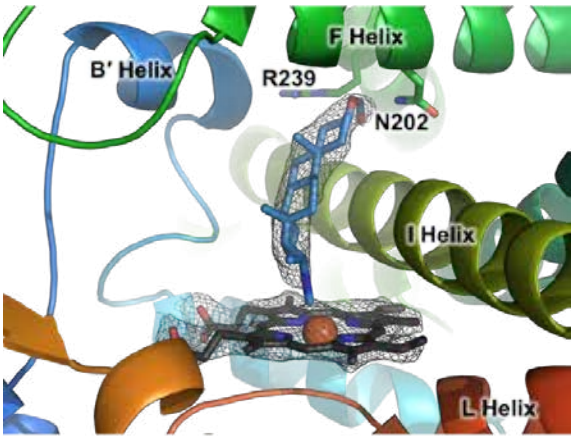
Isonitrile-Derivatives of Cytochrome P450 Inhibitors as Chemotherapy Agents

Application

In pharmaceutical formulation as a more specific chemotherapy drug for cancer therapy as well as other diseases where a specific cytochrome P450 inhibitor can be effective

Key Benefits

- Improved CYP selectivity
- Reduced dependence on the oxidation state
- Better stability in aqueous solution



Innovation

Cytochromes P450 (CYPs) are a diverse superfamily of heme-containing monooxygenase enzymes that use O2 to oxidize organic molecules, often in a highly selective manner. Cytochrome P450 (CYP) enzymes play an important role in pharmacology. They are involved in the metabolism of many drugs, including antifungals, cancer chemotherapy drugs, and HIV-suppressing drugs. CYP enzymes also play a role in the activation and metabolism of drugs. For example, CYP3A4 is responsible for the metabolism of approximately 50% of all small-molecule drugs currently available. The majority of drugs that inhibit CYP enzymes work by binding to the heme group of the enzyme. However, this type of inhibition has two major drawbacks: it is dependent on the oxidation state of the iron in the heme group, and it can lead to cross-inhibition, meaning that a molecule that inhibits one CYP is likely to inhibit others to some extent. There is a need for CYP inhibitors that have improved CYP selectivity and reduced dependence on the oxidation state of the iron in the heme group. This invention describes the isonitrile derivatives of chemotherapy agents that can stably bind to both accessible oxidation states of common monooxygenases.

Technical Overview

Alkyl isonitriles, also known as isocyanides, are a class of compounds that can bind to the heme iron of cytochrome P450 (CYP) enzymes in both oxidation states. This makes them potentially useful as pharmaceuticals, as CYP enzymes are involved in the metabolism of many drugs. In the past, the inherent reactivity of alkyl isonitriles and their instability under acidic conditions has discouraged their use in pharmaceuticals. However, the isonitrile-derivative compounds described in this invention are sufficiently stable in aqueous solutions at physiological pH, making standard binding assays feasible. These compounds also appear to remain stably complexed to the P450 heme iron for multiple hours during conversions between the ferric and ferrous oxidation states. Recent advances in the delivery of enzymatically and/or chemically labile pharmaceuticals via encapsulation and targeted delivery suggest that compounds of this type may be feasibly adapted for medicinal purposes. These advances could help overcome the challenges posed by the inherent reactivity of alkyl isonitriles, making them a more viable option for developing new drugs.

Publications

1. Publication pending

Intellectual Property

- WO 2023/028205

Tech ID: Brandeis # 2020-010

Inventors: Thomas Pochapsky, Professor of Chemistry, Brandeis University

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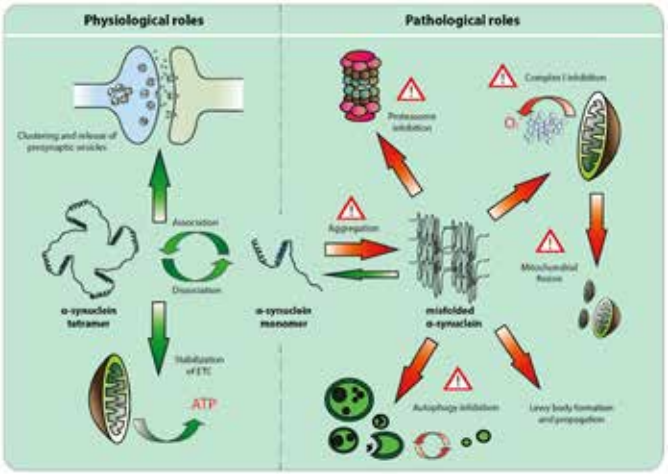
Link: https://brandeis.flintbox.com/technologies/08391c72-63c3-4ecf-96d5-ae012f11fc98

α-Synuclein as Biomarkers for Synucleinopathy and Related Diseases

Application

Diagnostic and therapeutic development for synucleinopathy and related diseases



Key Benefits

- Targets treatment based on disease causation from αSyn aggregation and neuronal toxicity

Innovation

Alpha-synuclein (αSyn) is a protein primarily found in brain tissue making up to 1% of all cytosolic proteins in neurons and is predominantly expressed in the neocortex, hippocampus, substantia nigra, thalamus and cerebellum. Mutations in αSyn expression has been linked to disease pathologies due to the fibrillization and aggregation. Parkinson's disease is a neurodegenerative disorder pathologically characterized by the presence of Lewy bodies. These abnormal intracellular aggregates are found in dying neurons and are believed to play a major role in the degeneration of dopaminergic neurons. The major components of Lewy Bodies consisting of αSyn. Here, we present that the protease, caspase-1 (ICE), cleaves αSyn in vivo and such cleavage generates more αSyn fragments that are prone to toxic aggregate formation. This discovery provides a method for identifying patients who will likely respond to an ICE inhibitor therapy approach.

Technical Overview

Lewy bodies consist mainly of ubiquitin mixed with misfolded full-length αSyn and a truncated form containing only its N-terminal 120 amino acids generated by protease cleavage. Inhibition of αSyn represents an attractive strategy for preventing Lewy body formations and arresting synucleinopathies. 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 αSyn 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 αSyn in vivo into its two protein fragments associated with synucleinopathies.

Publications

1. Caspase-1 causes truncation and aggregation of the Parkinson's diseases-associated protein α-Syn (Wang et al. 2016). PNAS. PMID: 27482083
2. Reducing C-terminal truncation mitigates synucleinopathy and neurodegeneration in a transgenic model of multiple system atrophy (Bassil et al. 2016). PNAS. PMID: 27482103

Intellectual Property

- US 9,116,157

Tech ID: Brandeis # 1070

Lead Inventor: Dagmar Ringe, Professor of Biochemistry and Chemistry Emerita, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/189d527d-4ecb-4665-b0ed-f65bb39e7c87

Treatment of RAS-Related Cancers via Palmitoylation Inhibition

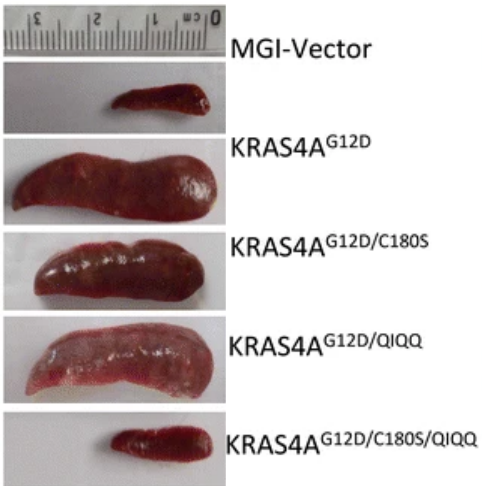
Application

Modulatory target for the potential treatment and prevention of mutant RAS-associated cancers (e.g. melanoma, leukemia)

Key Benefits

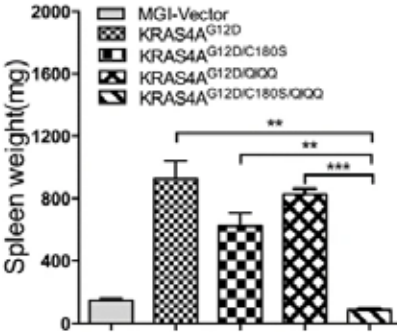
- Leverages an essential step in signal transduction required for oncogenesis
- Less cytotoxicity compared to farnesyl- and geranylgeranyl- transferase inhibitors
- Modulatory drug approaches can include RNAi-inducing agents, antibodies, siRNA, or small molecules

Innovation



Cancer is a deadly disease that accounted for nearly 10 millions deaths in 2020: nearly one in six deaths were cancer related. There is a serious need for new therapies to help treat and prevent cancer in addition to novel approaches for the identification and development of new therapeutic approaches. Mutations that lead to the constitutive activation of RAS are associated with roughly 30% of all human cancers, including both solid tumors and blood malignancies. We present a novel approach to suppress cancer transformations by inhibiting palmitoylation of RAS proteins, molecules that modulate signal transduction involved in cell proliferation, survival and differentiation. Palmitoylation, the covalent attachment of fatty acids - like palmitates - to amino acids, is a critical step in signal transduction and has been shown to be essential for leukemogenesis. Using our new class of inhibitor drugs, defective palmitoylation can be reduced or blocked by modulating the activity of key palmitoyl acyltransferases. Our drugs would be most useful in the treatment of cancers associated with oncogenes upstream of RAS signaling pathways (e.g. melanomas, etc) and in hematological cancers (e.g. leukemia, etc).

Technical Overview



RAS proteins are small GTPases that function as molecular switches in cell signal transduction pathways, transducing extracellular signals from surface receptors to the nucleus. The mammalian RAS family includes three genes that encode four proteins - HRAS, NRAS, KRAS4A and KRAS4B - which share over 90% homology in the first 166 amino acids, diverging at their C-termini. The sequences found at the C-termini target homologues to specific microdomains and effector pathways; signaling cascade activation in these pathways, such as RAF-MEK-ERK and PI3K-AKT, function to regulate cell proliferation, survival and differentiation. Cancers with RAS mutations are the most difficult to treat and refractory to current targeted drug therapies. Our invention is the finding that palmitoylation at the C-terminal residue(s) of RAS proteins upstream of conserved CAAX motifs by palmitoyl acyltransferases is essential for oncogenesis. This modification is believed to localiza RAS members to the proper regions on plasma membranes for supporting activation of downstream signaling pathways.

Publications

1. Roles of palmitoylation and the KIKK membrane-targeting motif in leukemogenesis by oncogenic KRAS4A (Zhao et al. 2015). Journal of Hematology & Oncology. PMID: 26715448
2. Palmitoylation of oncogenic NRAS is essential for leukemogenesis (Cuiffo & Ren 2010). Blood. PMID: 20200357

Intellectual Property: US 9,220,723

Tech ID: Brandeis # 1051

Lead Inventor: Ruibao Ren, Research Professor of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/b6fa8636-f4eb-43cc-809e-9bcede067d90

Nucleic Acid Based Diagnostic Assay for Variable Sequence Targets

Application

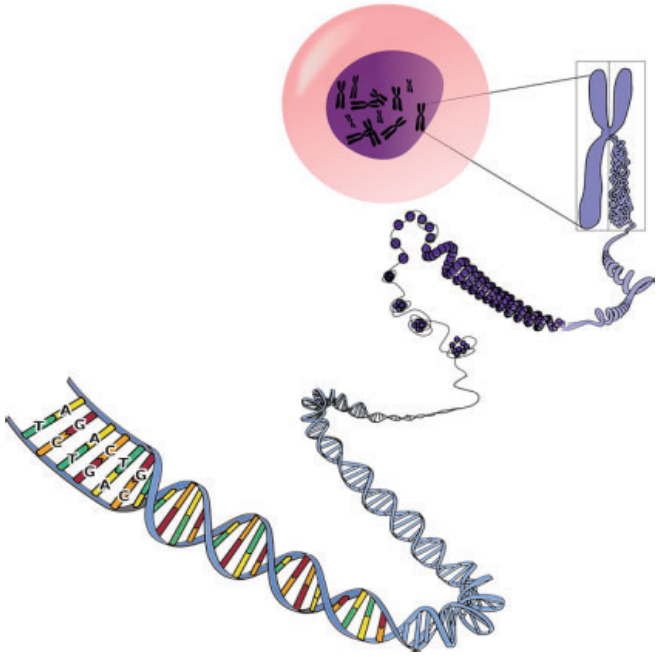
Novel methods for the detection and quantification of mutant sequence variations using non-symmetric PCR

Key Benefits

- Easily incorporated into commercial kits
- Suited for small volume reactions and low cc number targets
- Enables rapid detection of multiple microorganism strains and genes in a single reaction

Innovation

The amplification and detection of diverse strains of infectious virus, bacteria or variants within a gene family is critical for both clinical and basic research; however, it can be difficult to distinguish between gene sequences using conventional PCR as the homology between primers and a variant target sequence can be extremely low. As a result, amplification can be significantly delayed or fail entirely. We present a novel method for carrying out nucleic-acid-based diagnostic assays in a single chamber using either symmetric or asymmetric PCR reactions (e.g. Linear-After-The-Exponential-PCR" or LATE-PCR). We have engineered multiple, low-concentration "initiator primers" (iPrimers) that in combination with a partially homologous consensus primer efficiently amplify DNA or RNA targets with a wide range of sequence variations compared to other available consensus or degenerate primer methods.



Technical Overview

The invention is an improved method for carrying out nucleic-acid-based diagnostic assays. A set of iPrimers can have any or all the sequences of multiple strains of microorganisms, subtypes of genes or gene homologues and orthologs within the test sample. The primers are designed to have melting temperatures similar to that of the consensus primer thus 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. Our priming method is compatible with any probe detection method and the incorporation of primer-target hybridization results in increased sensitivity. Our method has been used in a detection assay for members of the CTX-M beta-lactamase gene family found in antibiotic-resistant bacteria.

Publications

1. Low-concentration initiator primers improve the amplification of gene targets with high sequence variability (Pierce & Wangh 2015. Methods in Molecular Biology. PMID: 25697652

Intellectual Property

- US 9,850,529

Tech ID: Brandeis # 1068

Lead Inventor: Lawrence Wangh, Professor Emeritus of Biology, Brandeis University

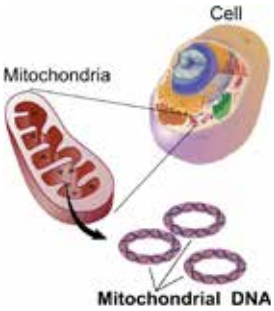
Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/4c9d8295-85b3-44ea-a559-dc332d39df26

A More Sensitive and Accurate Way to Detect Mitochondrial Mutations

Application

Novel methods for the detection and quantification of mutant sequence variations using non-symmetric PCR



Key Benefits

- Identification of mutational loads in target D
- Broadly application to humans or animals

Innovation

Mitochondria are the primary energy source of most eukaryotic cells where each mitochondrion possesses multiple copies of mitochondrial DNA (mtDNA). The mitochondrial genome includes a control region that contains the displacement loop D-loop where the process of DNA replication is initiated and gene transcription regulated. Recently, increased levels of mutations within the mitochondrial gene have been associated with several diseases including diabetes, Alzheimer's Disease and cancer. Despite the insights that detecting mitochondrial mutations may bring, a substantial technical challenge persists in detecting, characterizing and diagnosing changes in mtDNA sequences due to the very large number (10-1000s) of mtDNA molecules in each eukaryotic cell. Due to sheer volume, changes in mtDNA molecules are often "averaged out" in populations of mtDNA molecules, even in single cells creating a need for better systems and methods for characterizing these mutations to assist in biological research, drug development, drug or therapeutic impact assessment, or disease screening, diagnosis and monitoring. Our technologies provide novel methods for the asymmetric amplification and fluorescence detection of the mutation load in nucleic acid target sequences such as: RNA, cDNA, genomic and non-nuclear DNA (mtDNA, etc). Using our methods, the detection of human mtDNA mutations within cytochrome c, oxidase subunit 2, NADH dehydrogenase subunit 1 and 2 are possible.

Technical Overview

Mutations in mtDNA are a result of aging, environmental hazards, genetic susceptibility, diet, drug exposure or a combination of comorbidities and have been implicated in a wide range of human diseases. Jt is hypothesized that the buildup of random mutations over time in multiple genomes of the mitochondria leads to dysfunction of the organelle and then disease onset. Our methods allow for the amplification and detection of mutations in target nucleic acid sequences: these methods utilize single-tube, multiplex polymerase chain reactions (PCR) on mixed samples containing 1 or more probe pair sets that hybridize to adjacent sites within the target. Our probes pairs need not be next to each other and each have covalently attached to either a fluorescent compound ("Signaling Probe") or a non-fluorescent complementary quencher moiety ("Quencher Probe"; Black Hole Quencher or dabcyl acid). The Signaling probe will not fluoresce unless bound to the amplified single-strand target sequence and the signal eliminated via the fluorophore/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 and signals can be acquired either as the reaction temperature is decreasing or increasing. Differences in temperature can help to differentiate mutations accumulating in the target sequence.

Publications

1. Palm fruit juice mitigates AZT mitochondrial genotoxicity and dose-dependent cytotoxicity (Osborne et al, 2014). Journal of AIDS & Clinical Research.
2. AZT treatment increases mtDNA mutations in HepG2 and CCD-1112Sk Cells (Osborne et al, 2013) Journal of AIDS & Clinical Research.

Intellectual Property: US 9,637,790

Tech ID: Brandeis # 1073

Lead Inventor: Lawrence Wangh, Professor Emeritus of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/7abd8278-f885-473b-b8c9-6e2a51af1f1d

Supramolecular Hydrogels: Overcoming the Limitations of Traditional Drug Delivery Systems

Application

Therapeutic molecules to act as drug delivery vehicles

Key Benefits

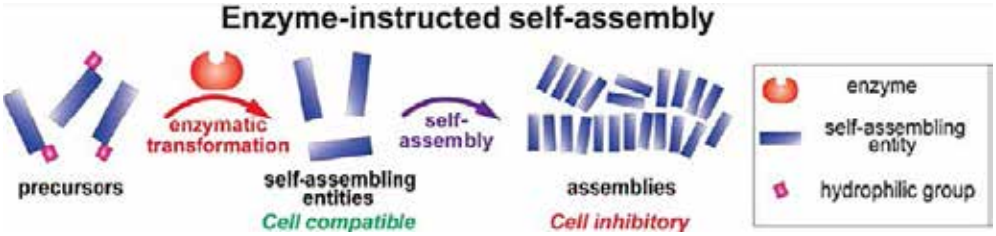
- Improves stability and efficacy of anti-cancer drugs
- Provides bio-compatible supramolecular hydrogels for drug-delivery
- Serves as a drug delivery system for both long-tem and local delivery of anti-cancer drugs
- Does not require a polymeric matrix

Innovation

Even with modern advances, treatment of cancer remains difficult. To improve anti-cancer efficacy and other limitations from chemotherapy, a new set of supramolecular hydrogels have been developed as drug carriers that improve water solubility of anti-cancer drugs and target tumor cells have been developed. Typically, drug delivery systems require a polymeric matrix which easily degrades and a low biocompatibility as well as low drug capacity. The current invention surpasses these limitations by using enzyme triggered self-assembly (EISA) to form nanofibers which act as a delivery vehicle and a drug itself (taxol). This delivery-drug hybrid provides an avenue for the application of molecular hydrogels to be used as therapeutic agents without compromising their bioactivities.

Technical Overview

A peptide therapeutic/drug delivery agent is composed of an enzymatically cleavable group and has been covalently linked to an anti-cancer drug (taxol) to form the uncleaved precursor. Upon enzymatic reaction the precursor transforms into a hydrogelator which assembles into nanofibers and by large a supramolecular hydrogel. Low molecular weight hydrogels like these release encapsulated drugs upon degradation which can be used to selectively treat cancers, tumors, malignancies, etc.



Publications

1. Enzyme-Instructed Self-Assembly: A Multistep Process for Potential Cancer Therapy (Zhou & Xu, 2015) Bioconjugate Chem. PMID: 25933032
2. Enzyme-Instructed Molecular Self-assembly Confers Nanofibers and a Supramolecular Hydrogel of Taxol Derivative (Gao et al, 2009) J. Am. Chem. Soc. PMID: 19731909

Intellectual Property

- US 8,658,600
- US 9,408,921

Tech ID: Brandeis # 1029

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/a947dbe3-5fcd-46de-84f5-69d8c6b67750

Multifunctional Hydrogels Made of Nucleopeptides and Glycopeptides

Application

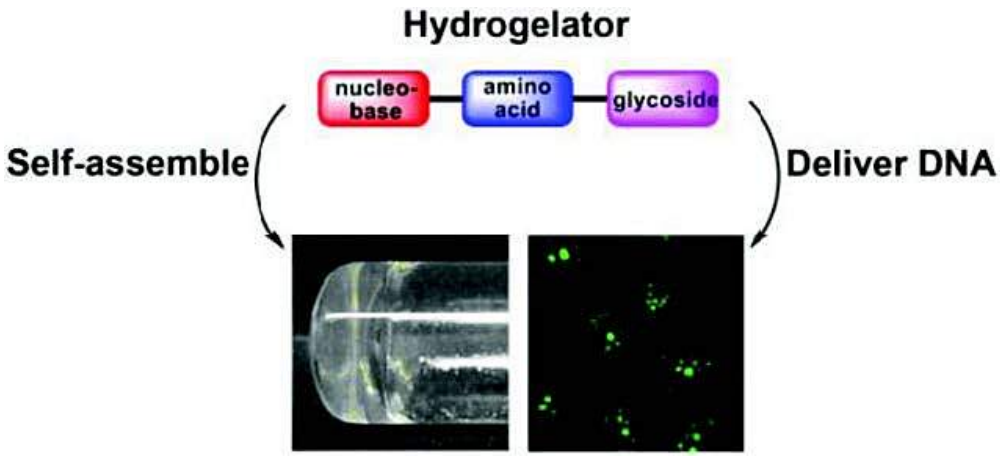
To act as soft nanomaterials to mimic the extracellular matrix for possible tissue engineering

Key Benefits

- Tunable nucleopeptide backbone for versatile structural manipulation
- Clinically suitable and resistant to protease degradation
- Effective, safer, and cost-effective alternative to conventional polymers in tissue engineering/drug delivery

Innovation

Millions rely on biomaterials for tissue regeneration post-surgery, accidents, and disease. However, current polymer scaffolds face separation, purification, toxicity, and poor responsiveness challenges. Thai invention introduces a novel approach using peptide-nucleobase/glycoside conjugates to create supramolecular hydrogelators. These hydrogelators mimic extracellular matrices, exhibiting high biocompatibility and offering cost-effective, low molecular weight solutions. Their broad applications include cell culturing, tissue engineering, non-viral gene therapy, and cancer immunotherapy.



Technical Overview

This peptide material is composed of a nucleobase, amino acid and/or a glycoside where each component can be easily coupled through NHS activation. Enzymatic reaction or pH change drives self-assembly of the peptide in water to afford a biocompatible and bio-stable hydrogel. The supramolecular structures in the hydrogel promote cell proliferation and wound healing by contact between the assemblies and various cells. These structures offer versatility as they can be functionalized to act as a drug-delivery vehicle for treating viral infections or cancer treatment.

Publications

1. Supramolecular Nanofibers and Hydrogels of Nucleopeptides (Li et al., 2011). Angewandte, PMID: 21948432

Intellectual Property

- US 10,093,674

Tech ID: Brandeis # 1088

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/912c779b-9c65-4be4-894d-32c92bf46b7b

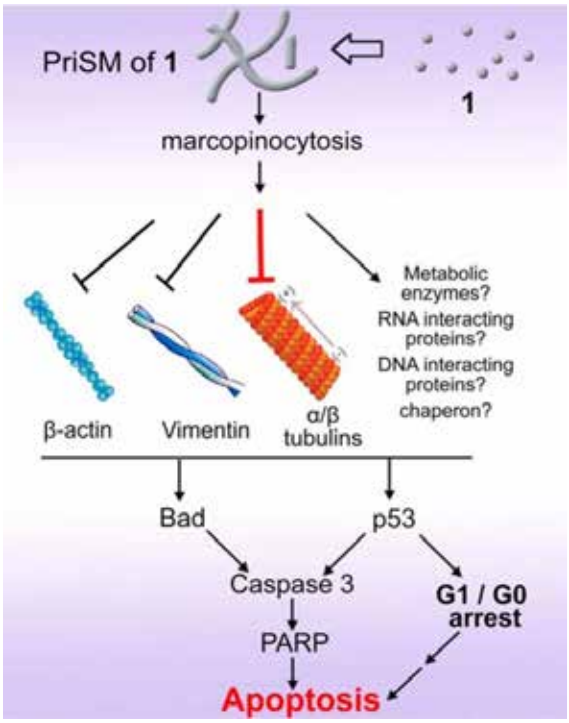
Peptides That Mimic Aberrant Proteins to Kill Cancer Cells

Application

As an anticancer agent

Key Benefits

- Peptidic design eases biocompatibility
- Can be synthesized inexpensively and easily scaled for larger production



Innovation

The invention is a library of hydrophobic, self-assembling small peptides which specifically target cancer cells and inhibit tumor growth. These Fibrillar molecular aggregates, sharing morphological and phenotypic resemblance with oligomers of abnormal proteins, are a unique feature of this invention. These aggregates form through the self-assembly of small hydrophobic molecules, effectively hindering microtubule growth. This groundbreaking mechanism, referred to as "self-assembly to interfere with self-organization," demonstrates the ability to inhibit the growth of cancer cells. The reported findings illustrate the power of these novel anticancer agents, and may benefit therapeutic research for both cancer and neurodegenerative diseases.

Technical Overview

This invention discloses a novel paradigm of anticancer agents that selectively prevent mitosis and inhibit cell proliferation. These agents are peptides that have several advantages, including:

- They can form aggregates that resemble aberrant proteins in Alzheimer's Disease.
- Cancer cells are more likely to take up these aggregates, which can lead to their death.
- These peptides can be co-administered with other drugs to synergistically kill cancer cells.
- The peptides are biocompatible and can be easily produced.

In animal studies, these peptides were found to inhibit tumor growth by more than 20 times compared to the control group.

Publications

1. PriSM Inhibits Cancer Cells by Impeding Cytoskeleton Dynamics (Kuang et al., 2014). JBC, PMID: 25157102

Intellectual Property

- US 10,308,682

Tech ID: Brandeis # 1123

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/76b55ff8-4cbf-46af-ba74-29d572aea469

New Peptide Hydrogelators for Cancer Imaging, Treatment, and Secretome Collection

Application

Cellular imaging; cancer treatment; Secretome collection and screening for identifying new biomarkers

Key Benefits

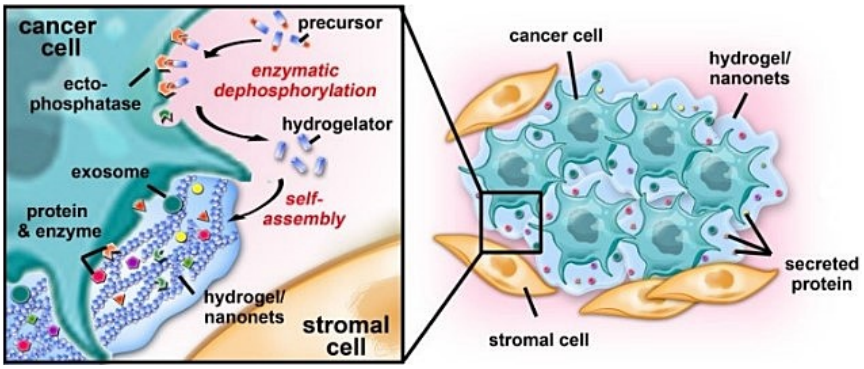
- Selectively prevent drug-resistant cancer cell proliferation
- Can deepen understanding of cancer progression and further research may accelerate cancer biomarker discovery
- Self-assembling molecule is easy to make and purify
- Low-cost diagnostic method with high yields of secretome sequestration

Innovation

Traditional chemotherapy or molecular therapy is unsuitable 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 are lacking. The current invention describes enzymatically responsive peptide hydrogelator precursors that can be used for cellular imaging, cancer treatment, and secretome collection and screening. The hydrogels can be used to track the movement of cells, visualize the expression of genes, deliver drugs to cancer cells, and collect and screen the secretome from cells.

Technical Overview

Peptides composed of several amino acids including a variety of aromatic side chains are either phosphorylated, sulfated, or covalently bound to an ester-moiety. The precursors become hydrolyzed upon exposure to overexpressed ectoenzymes on cancer cell surfaces, which in turn create nanofibril or nanonet-like structures near the surface of the target cells. These hydrogel materials inhibit cancer cell migration and proliferation while also entrapping secretomes within the nanonets. To expand the utility of these peptides, covalent conjugation of a fluorophore may be integrated for imaging on live cells. These materials, and compositions containing the same, can be used for in vitro and in vivo cellular imaging, treating cancerous conditions, collecting a secretome from a cell upon which the pericellular hydrogels/nanofibrils form as well as screening the collected secretome.



Publications

1. Pericellular hydrogel/nanonets inhibit cancer cells (Kuang et al 2014). Angew Chem Int Ed Engl. PMID: 24820524

Intellectual Property

- US 11,155,576

Tech ID: Brandeis # 1157

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/e1db3edf-39f1-450f-bfe2-b0e3041698bb

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

Application

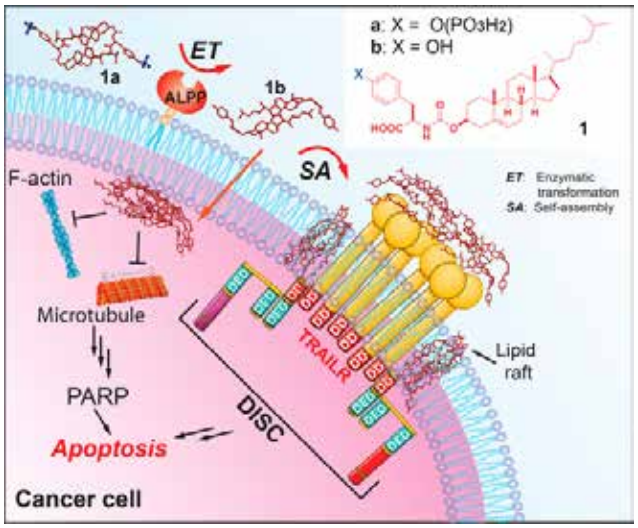
Inhibiting drug resistant cancer (e.g., ovarian cancers), potential platform for combination therapy, drug delivery, or as a vaccine to modulate immune system

Key Benefits

- Selective inhibition of cancer cells by an amino acid/peptide-cholesterol combination
- Can inhibit various cell lines including cisplatin-resistant cancer cells
- Develops a new avenue for developing efficient nanomedicine against drug-resistant cancer cells
- First study to use EISA (**E**nzyme-**I**nstucted **S**elf **A**ssembly) for modulating lipid rafts

Innovation

This invention introduces a new platform of single amino acid-cholesterol conjugate that selectively inhibits cancer cells by the overexpression of alkaline phosphatase (ALP). 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 the immune system. The invention is a tyrosine-cholesterol which can selectively form aggregates extracellularly and intracellularly. Because toxicity is dependent on the high concentration of alkaline phosphatase (ALP), normal tissue (which does not overexpress ALP) is unharmed. This discovery presents new applications of amino acid cholesterol conjugate such as controlling cancer cell death, inhibiting drug resistant cancer cells, immune therapy and drug delivery.



Technical Overview

Xu and colleagues have created a novel platform of single amino acid-cholesterol conjugates that selectively inhibit cancer cells which overexpress ALP. Several other amino acid-cholesterol conjugates were tested to confirm the specificity of tyrosine. Compared with the commercial drug cisplatin, the tyrosine-conjugate exhibited better therapeutic effect against platinum-resistant cancer cells (A2780cis). Based on the advantage of selectivity, the platform has great potential in applications such as cancer cell drug resistance inhibition, immune therapy and drug delivery.

Publications

1. Enzyme-Regulated Supramolecular Assemblies of Cholesterol Conjugates against Drug-Resistant Ovarian Cancer Cells (Wang et al., 2016). J. Am. Chem. Soc., PMID: 27529637

Intellectual Property

- US 11,040,108

Tech ID: Brandeis # 1273

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/485c00aa-160e-4c6f-bd4f-7456721d2ac2

High selectivity in Mitochondrial targeting of cancer cell via Enzymatic Cleavage

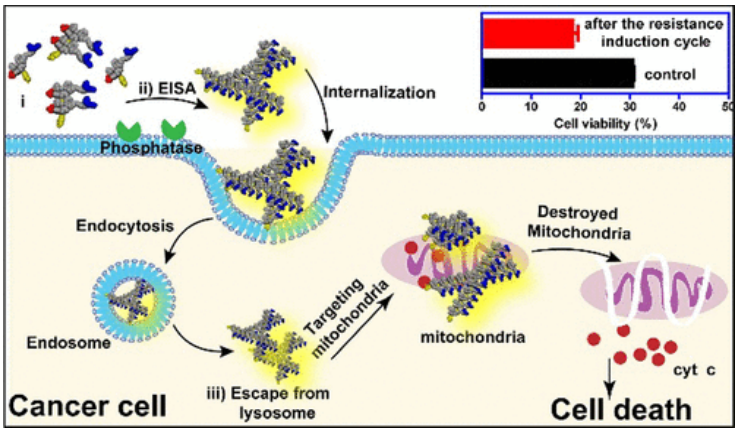
Application

Cancer cell drug resistance inhibition, immunotherapy, drug delivery, nanomedicine development, immune deficiency disease therapeutics

Key Benefits

- High selectivity in mitochondrial targeting of cancer cells
- First example to integrate subcellular targeting and spatial control of the assemblies of non-cytotoxic agents by EISA as a promising molecular process for selectively killing cancer cells
- Novel way to develop efficient nanomedicine without inducing acquired drug resistance

Innovation



Targeting organelles by modulating the redox potential of mitochondria is a promising approach to kill cancer cells with acquired drug resistance. However, it lacks selectivity because mitochondria perform essential functions for (almost) all cells. This invention, as the first to report the control of peptide assemblies in mitochondria, shows that enzyme-instructed self-assembly (EISA) selectively generates the assemblies of redox modulators (e.g., triphenylphosphonium (TPP)) in the pericellular space of cancer cells, which allows selective targeting of the mitochondria. The conceptual system has been tested ex vivo on several cancer cell lines, which provides new opportunities for therapeutics against cancer and some immune-deficiency diseases.

Technical Overview

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. Saos-2), the oligomers self-assemble to form nanoscale assemblies on the surface of the cancer cells. The cancer cells thus uptake the assemblies via endocytosis where the TPP-peptide assemblies escape from the lysosome, induce dysfunction of mitochondria to release cytochrome c, and result in cell death.

Publications

1. Integrating Enzymatic Self-Assembly and Mitochondria Targeting for Selectively Killing Cancer Cells without Acquired Drug Resistance (Wang et al., 2016). J. Am. Chem. Soc., PMID: 27960313

Intellectual Property

- US 2020/0023065

Tech ID: Brandeis # 1311

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/ae456bcf-6c5b-42e3-8b08-4e7dff396856

Supramolecular Hydrogels For Wound-Healing, Drug Delivery & 3D Cell Culture

Application

Wound Healing, tissue engineering, immune adjuvant and 3D cell culture

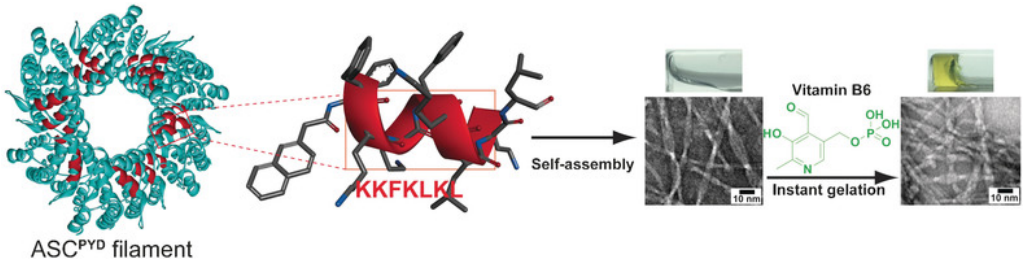
Key Benefits

- Biocompatible and much faster compared to other strategies for instant gelation
- Efficient method to design short peptides that adopt conformations such as a helix and random coil
- Molecules can also serve as a cell compatible trigger for cross-linking the nanofibers with peptides or drugs to form an instant hydrogel

Innovation

This invention describes a novel method of fast hydrogelation based on a short peptide triggered by small bioactive molecules. The peptide is capable of induced self-assembly by a bioactive molecule comprising a (i) hydrogelation-promoting amino acid sequence and (ii) an oligomerization sequence The invention not only illustrates a new way to form hydrogels 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 culture, or immune adjuvant controlling immune responses of small molecules.

Technical Overview



The hydrogel is a novelly designed peptide sequence NapFFKFKLKL and uses small bioactive molecules such as pyridoxal phosphate, pyridoxal, folinic acid, ATP, ADP, AMP to promote assembly. The peptide consists of three parts: 1) the epitope, KKFKLKL, a conserved sequence that plays critical roles for oligomerization of ASC filaments in inflammasomes. ii) lysine, serves as an active site for the formation of a Schiff base in the biological system, but also introduces positive charge to the peptides interacting with the phosphate on pyridoxal phosphate. iii) Nap-FF, a well-established building block for promoting self-assembly. As the demonstration of correlating assemblies of peptides and their relevant protein epitopes, this work shows a bioinspired approach to develop supramolecular structures, modulated by endogenous small molecules.

Publications

1. Instant Hydrogelation Inspired by Inflammasomes (Wang & Xu, 2017). Angew Chem Int Ed Engl, PMID: 28481474
2. Nucleopeptide Assemblies Selectively Sequester ATP in Cancer Cells to Increase the Efficacy of Doxorubicin (Wang et al., 2018). Angew Chem Int Ed Engl., PMID: 29451962

Intellectual Property

- US 2021/0128745

Tech ID: Brandeis # 1339

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/98f1ca4a-32e8-4c19-98e9-b5c52521737a

Branched Peptides for Enzymatic Assembly and Mitochondria Drug Delivery

Application

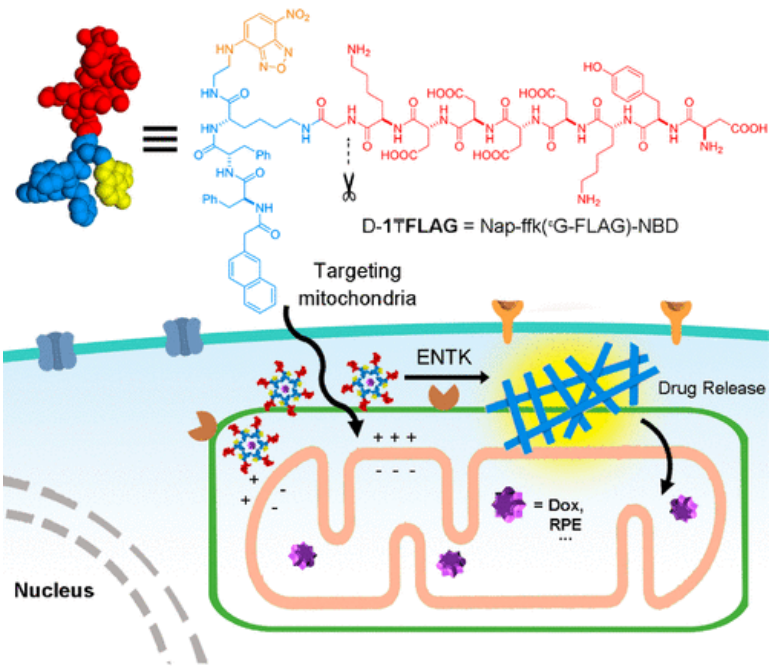
Drug delivery of bioactive molecules, such as proteins, cytotoxic drugs, and anti-cancer drugs, to mitochondria

Key Benefits

- A novel mechanism for mitochondrial targeting different from traditional cationic and lipophilic molecules
- Can encapsulate bioactive molecules for eventual delivery
- As a platform for mitochondrial targeting which can be used for other biomedical applications

Innovation

This invention introduces a new platform technology to create mitochondria-targeting cargos 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 cell fates, via delivering diverse bifunctional molecules to the mitochondria. The targeted delivery of cytotoxic drugs to mitochondria may significantly increase toxicity, while the mitochondrial accumulation of some bioactive molecules (e.g. pifithrin-μ) may rescue normal tissue from radiotherapy.



Technical Overview

To meet the need of mitochondria-targeting drugs, a branched peptide is designed to control the fate of cells, either to inhibit or rescue, via delivering diverse bio functional molecules to mitochondria. The said peptide consists of 3 fragments: i) the FLAG-tag DYDDDK, 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 branched peptide hydrogelator has multiple negative charges to traffic to the mitochondria and forms nanofibers (D-10 upon cleavage. Bioactive molecules, such as proteins and anti-cancer drugs, can be encapsulated by the branched peptides and eventually delivered to the mitochondria.

Publications

1. Enzymatic Cleavage of Branched Peptides for Targeting Mitochondria (He et al., 2018). J Am Chem Soc., PMID: 29328651

Intellectual Property

- US 11,191,724 | US 2022/0112240

Tech ID: Brandeis # 2018-002, 2020-001

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/#technologies/c539da16-2292-4da0-a319-74d0642631d7

Repurposing Antibiotics with Enhanced Efficacy

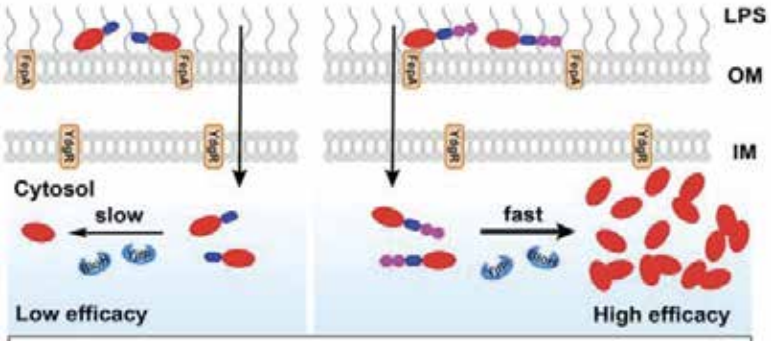
Application

Development of new antimicrobial prodrugs which are more selective to bacteria, accelerate the hydrolysis catalyzed by intrabacterial esterases and enhance the efficacy of antibiotics

Key Benefits

- Drastically accelerates activation of a known drug chloramphenicol succinate (CLsu)
- Exhibits lower toxicity to bone marrow stromal cells than chloramphenicol
- Dipeptide conjugation amd subsequent hydrolysis increases antibiotic efficacy and adverse side effects

Innovation



Multidrug resistance (MDR) is an ongoing problem as bacteria continuously evolve and become more resistant to antibiotics. This problem demands novel approaches for improving the efficacy of antibiotics, especially against gram-negative bacteria. In comparison to developing a new drug which requires years of extensive testing, modifying existing antibiotics to derivatives with higher efficacy is much more rapid, cost-effective, and safer. This invention reports that conjugating diglycine (GG) to an antibiotic prodrug (chloramphenicol), drastically accelerates interbacterial ester bond hydrolysis required for activation of the antibiotic.

The drug is effective against E. coli, and innocuous to bone marrow cells, hepatocyte cells, and kidney cells which are mainly affected by chloramphenicol during regular treatment.

Technical Overview

This invention describes a novel strategy of conjugating GG to chloramphenicol succinate (CLsu) to enhance the efficacy and improve the safety of existing antibiotics. The GG-conjugate improves the efficacy of chloramphenicol succinate from a minimum inhibitory concentration (MIC) of 200μM to 20μM. Also, through the increase of solubility and compatibility with the addition of GG and other peptides, the hydrolysis rate of CLsu increases from about half in 24hrs, to almost complete cleavage within a few hours. 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. Overall, the use of peptides in the repurposing of prodrugs seems to be a promising avenue to circumvent long FDA approval times and expand the arena of antibiotics available to the public.

Publications

1. Diglycine Enables Rapid Intrabacterial Hydrolysis for Activating Anbiotics against Gram-negative Bacteria (Wang et al., 2019). Angew Chem Int Ed Engl., PMID: 31167041

Intellectual Property

- US 2022/0387610

Tech ID: Brandeis # 2019-038

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/60c75efd-8acc-4e22-8d53-0e4b6a51c085

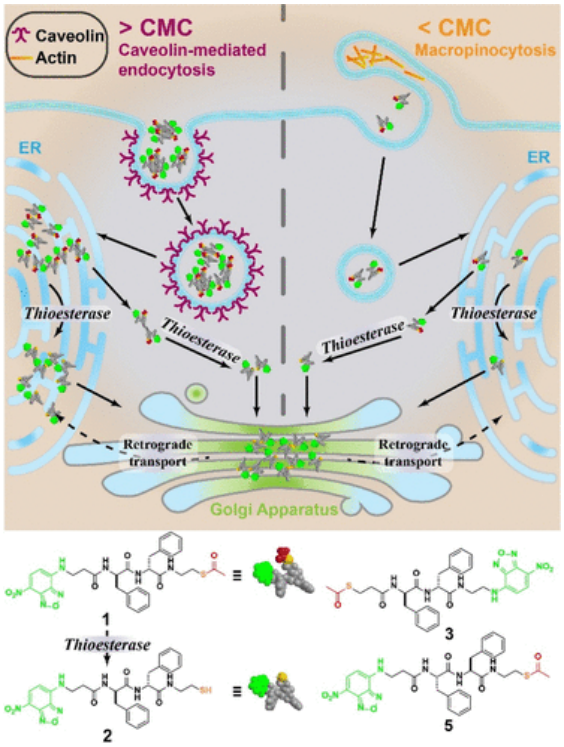
Dual Action Peptides for Ultrafast Golgi Targeting and Cancer Therapy

Application

As a reagent in live-cell imaging of the golgi apparatus across various cell lines (human, murine, and Drosophila) and delivering golgi-specific anti-cancer drugs

Key Benefits

- Fast & selective targeting of the golgi apparatus even at small concentrations
- Potent in a variety of cell lines
- Cancer growth inhibition activity at submicromolar level
- Easy linking to fluorophores and peptides for therapeutic purposes
- May be used as diagnostic tool



Innovation

The golgi apparatus (GA) is considered part of the transportation highway of the cell. Typically, the golgi has been detected by imaging molecules which have long incubation times and are only applicable to certain cell types. GA-targeting sequences are unsuitable for intercellular delivery because of their large sizes. This invention describes a couple of peptide-based molecules which can target GA rapidly at very small concentrations. The first generation thiohosphopeptide (TP) is able to image the golgi quickly and has been shown to be toxic to HeLa cells (ovarian cancer cells). After further studies and a simple chemical change from a thiophosphopeptide to a thioester (TE), a 2nd generation derivative that can be used for fast imaging and cancer therapy across various cell lines.

Technical Summary

TP and TE can image the GA very quickly. **TE** is cleaved by thioesterases, and accumulates in the golgi apparatus of various cells, while its predecessor is limited to certain cells which overexpress phosphatases. Also, the depsipeptide is cytotoxic to a number of cells which express low or moderate levels of glutathione. Both sequences however, show promise as a new way to image organelles for diagnostic and therapeutic use. PE has been shown to be effective for GA imaging at micromolar concentration and inhibit cells with IC50 in nM concentrations.

Publications

1. Enzymatic Assemblies of Thiophosphopeptides Instantly Target Golgi Apparatus and Selectively Kill Cancer Cells (Tan et al, 2021). Angew Chem Int Ed Engl. PMID: 33783926
2. Enzyme-Responsive Peptide Thioesters for Targeting Golgi Apparatus (Tan et al, 2022). JACS. PMID: 35404599

Intellectual Property

- WO 2022/174058 | Provisional application

Tech ID: Brandeis # 2021-001 & 2023-002

Inventors: Bing Xu, Professor of Chemistry, Brandeis University.

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/3b4a2d47-be35-48aa-89c3-18f2a0bf20c8

A New Class of Phosphorylated Peptides for Cancer Therapy

Application

To selectively kill osteoblasts and metastatic castration-resistant prostate cancer

Key Benefits

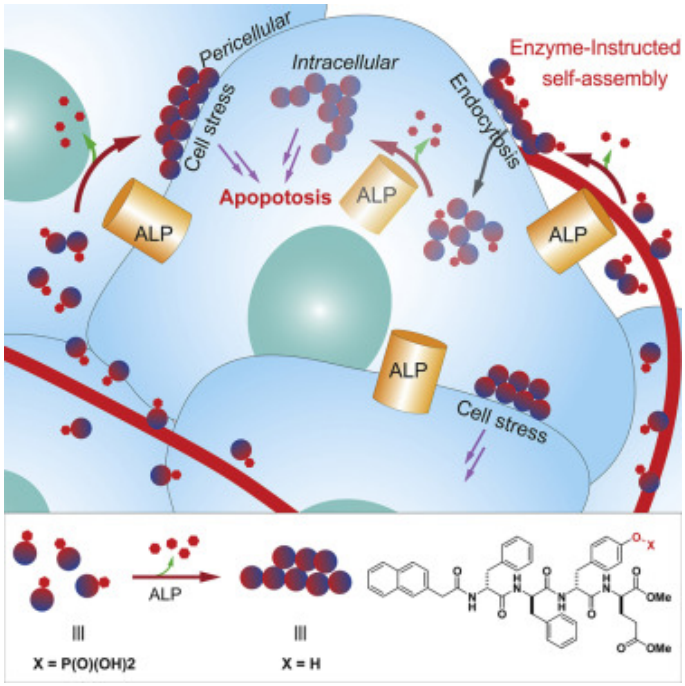
- Non-radioactive compared to current treatment
- On-site selective inhibition of osteosarcoma and prostate cancer

Innovation

Cancer immunotherapy has made significant advances, but the immunosuppressive tumor microenvironment can still make tumors unresponsive to treatment. Alkaline phosphatases (ALPs) are enzymes that are overexpressed in some cancer cells and contribute to immunosuppression. This invention uses ALPs to trigger the assembly of peptides that selectively inhibit tumors that overexpress ALPs. This is the first example of enzyme-instructed self-assembly (EISA) of peptides to target immunosuppressive tumors in vivo. This invention provides a new approach for developing novel cancer therapeutics that counter immunosuppression in the tumor microenvironment. Many peptide derivatives have been made, which are toxic to osteosarcoma (bone) cells and prostate cancer cells. These compounds show selectivity towards cancer cells, while showing low toxicity to non-cancerous bone marrow cells.

Technical Overview

Enzyme-instructed self-assembly (EISA) is an established bottom-up strategy for the formation of peptide nanomaterials. Previous technologies have used phosphotyrosine-conjugated short peptides as an enzyme-responsive trigger for initiating the self-assembly of the peptides. This invention demonstrates phosphobiphenyl carboxylic acid (pBP) as an enzyme-responsive trigger for conjugating with peptides for EISA. pBP can serve as an enzyme trigger to connect with other entities, such as dyes, drugs, and nanoparticles for drug delivery and imaging of enzyme activities. In particular, multiple pBP derivatives such as, pBP-ffOMe and pBP-ffe(OMe)$_2$, display inhibitory activity against cancer cells and observed emergent cytotoxicity against Saos-2 and SJSA-1 cancer cells in a short treatment time with low concentration.



Publications

1. Enzyme-Instructed Peptide Assemblies Selectively Inhibit Bone Tumors (Feng et al, 2019). Chem. PMID: 31552305

Intellectual Property

- WO 2023/039174

Tech ID: Brandeis # 2021-037

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/06a59c3e-6a53-478c-8897-1150f57848ab

Cell Spheroids with Enzyme-Responsive D-Peptides

Application

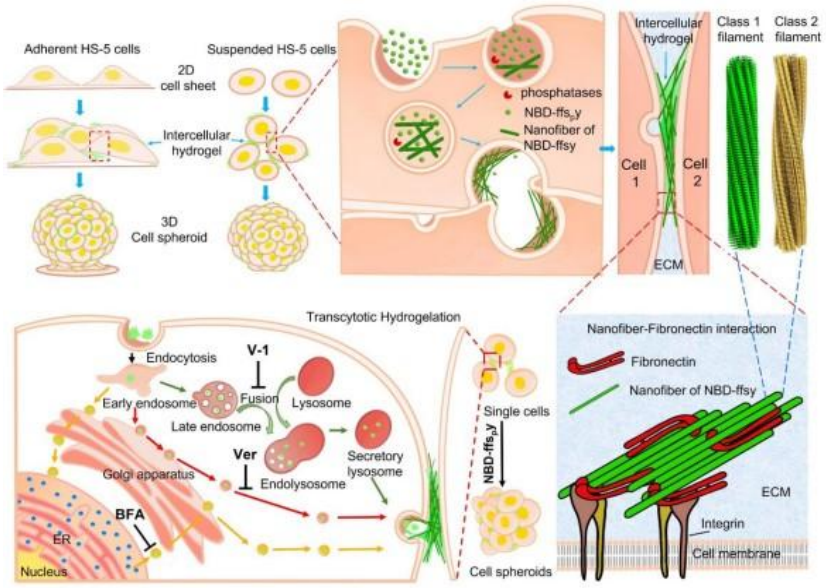
Tissue engineering, regenerative medicine, Pre-clinical drug screening and diagnostic

Key Benefits

- Biocompatible across various cell lines
- Facile method for inducing cell spheroids
- Spheroid formation is maintained by natural proteins on the cell surface rather than additives
- Gels for housing spheroids are formed *in situ* rather than separately

Innovation

In order to mimic the cellular environment of various organs and cellular structures, cell spheroids serve as a model for in vivo systems. Formation of hydrogels on the surface of cells which induce spheroid formation is a new approach in comparison to separately made spheroids and gel components. Enzyme-responsive D-peptides are a new biomimetic approach for regenerative medicine and tissue engineering. These peptides can induce cell spheroids, which are clusters of cells that are similar to those found in tissues. Spheroids can be used to study the behavior of cells in vitro, and they can also be used to create artificial matrices for tissue engineering. The development of enzyme-responsive D-peptides is a promising new technology that has the potential to revolutionize the field of regenerative medicine.



Technical Overview

A proteolytically resistant peptide is able to form a hydrogel in situ on HS-5 cells and subsequently induce cell spheroids. It is a phosphatase-responsive peptide with a fluorescent molecule attached to the N-terminal to report assembling behavior. D-phosphopeptides, being protease resistant, undergo endocytosis and endosomal dephosphorylation to generate helical nanofibres. On secretion to the cell surface, these nanofibers form intercellular gels that act as artificial matrices and facilitate the fibrillogenesis of fibronectins to induce cell spheroids. No spheroid formation occurs without endo- or exocytosis, phosphate triggers or shape switching of the peptide assemblies.

Publications

1. Cell spheroid creation by transcytotic intercellular gelation (Guo et al, 2023). Nat Nanotechnol. PMID: 37217766

Intellectual Property

- Provisional application filed

Tech ID: Brandeis # 2023-032

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/ba1bf864-17d4-46e4-8251-7a17b7d0933e

Research tools for microfluidics, drug-discovery platforms, advanced materials, imaging and more.

Research Tools And Materials

Contents

Invention Number	Invention Title	Lead PI (Last Name)	Page	Imaging	Drug Discovery	Targets	Clean Tech	Advance Materials	Measuaring Tool
2023-033	Molecular Solar Thermal (MOST) Systems for Thermal Energy Storage Only with Solid Phase	Han	55				●	●	
2021-034	The D-Hasp: New Tamper-Resistant Hasp	Hodge	56						
2022-001	High-Throughput, Quantitative Assay for Measuring Pleomorphic Virus Particle Size and Composition	Ivanovic	57	●	●				
1175	Drug Development Based on a Protein's Energy Landscape	Kern	58		●	●			
1166	Next Gen. CRISPR-Based Genome Modification System using Tethered Target Transgene	Lau	59			●			
1307	Novel and Optimized Cryo-EM Sample Preparation with PicoCell	Meyerson	60	●	●				
1137	Improved Gene Silencing using Organic Small Hairpin RNAs (OshR)	Paradis	61		●				
1231	High Throughput Video Drosophila Behavior Monitoring System	Rosbash	62		●				
1306	TRIBE: A Novel tool for the analysis of RNA-Binding Proteins (RBP)	Rosbash	63		●	●			
1050	EZ Amp- Simple DIY Current Measuring Tool	Wellenstein	64						●
1140	Active Crosslinkers for Chemomechanical Polymers	Xu	65		●	●			
1162	Novel Magnetic Nanoparticles Selectively Target Cancer Cells	Xu	66	●	●	●			
2021-036	New Biocompatible Small Molecule to Eliminate Undifferentiated Residual iPSCs	Xu	67		●				

A Breakthrough Catalytic Strategy for Creating Nitrogen-Containing Compounds

Application

Commercial and manufacturing use of nitrogen-containing compounds in drug discovery and biological interaction research

Key Benefits

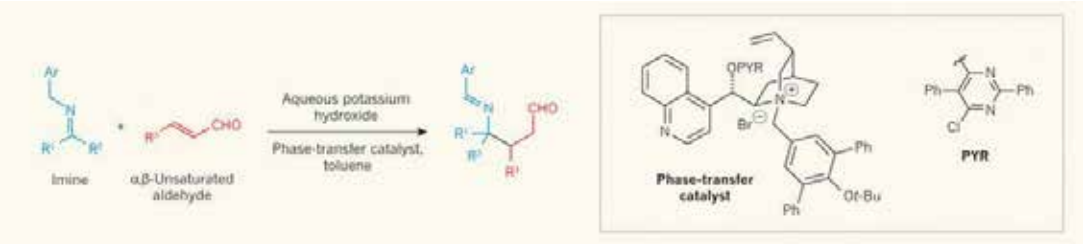
- Asymmetric reactions of imines provides a novel and practical approach to drug discovery
- Method enables highly chemoselective, regioselective and enantioselective umpolung reaction
- Widens the variety of imines to react with easily set-up, highly tolerant facility, and tolerates air/moisture
- Remarkable enantioselectivity and high yields of amine product with uncomplicatedly synthesized catalyst

Innovation

The demand for enantiomerically pure compounds has grown rapidly in recent years, due to their many advantages over racemic drug mixtures. Enantiomerically pure compounds have fewer side effects and greater potency, making them more effective and safer for patients. They are also used as intermediates for synthesis in the pharmaceutical industry. This invention introduces a novel procedure that achieves the reversal of natural electrostatic polarization (umpolung) in a highly chemoselective, regioselective, and enantioselective manner. The present innovation focuses on the discovery and advancement of chiral phase transfer catalysts that facilitate efficient asymmetric reactions involving imines and enals. This reaction presents a conceptually new and practical approach for synthesizing chiral amino compounds, offering promising prospects in the field.

Technical Overview

The invention presents a catalytic strategy for the enantioselective synthesis of nitrogen-containing compounds from imines, contributing to drug discovery research. It surpasses existing catalysts by utilizing a distinct C-C bonding formation reaction, building upon the concept of using one enantiomer of a base for imine isomerization. By employing a chiral 'phase-transfer' catalyst derived from a quinine compound found in Cinchona plants, the invention effectively guides the base from an aqueous solution to an immiscible organic solution where the reaction takes place. This enables the desired transformation while inducing enantioselectivity. The reaction products are modified imines, readily convertible into various nitrogen-containing compounds. The invention offers a group of novel phase transfer catalysts, providing a direct pathway to chiral amines that significantly benefits drug discovery research.



Publications

1. Catalytic asymmetric umpolung reactions of imines (Wu et al, 2015). Nature, PMID: 26201597.

Intellectual Property

- US 8,722,891 | US 9,006,441 | US 10,836,761

Tech ID: Brandeis # 1024 and 1240

Inventors: Li Deng, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/847a2f1f-d6d9-441d-be65-0c101d6adc74

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

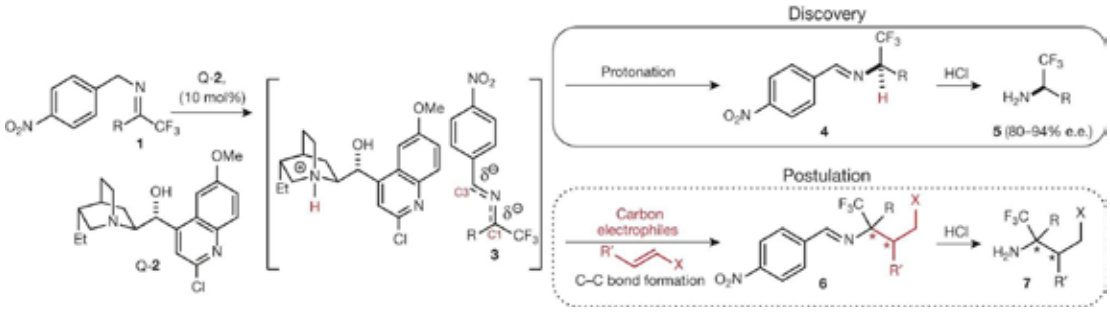
Application

Development of drugs, water treatments, and pollution prevention

Key Benefits

- High turnover class of catalysts for enantioselective proton transfer catalysis
- Development of highly efficient, reactive enantioselective proton transfer catalysts
- Provides general scope and easy-to-follow protocol for reaction execution and product isolation
- Highly practical for asymmetric synthesis due to extraordinarily low loading

Innovation



Chiral organic catalysts both hydrogen bond donor and acceptor groups enable biomimetic 1,3-proton transfer catalysis, promoting highly enantioselective olefin and imine isomerizations. These reactions offer valuable building blocks for α, β-unsaturated butenolides, α-amino acids, α, β-unsaturated cyclohexanones, and trifluoromethylated amines. Notable, the first highly enantioselective isomerization of trifluoromethyl imines with DHQ-α represents significant progress, demonstrating efficient catalytic chiral recognition of non-enolate carbanions for asymmetric reactions.

Technical Overview

The invention presents a novel class of cinchonium betaine catalysts that possess both a base moiety and an aromatic moiety. These catalysts facilitate proton transfer catalysis with impressive turnovers of 1000-5000 per 24 hours, allowing for highly efficient enantioselective isomerization of trifluoromethyl imines. As a result, optically active trifluoromethylated amines can be readily accessed. Particularly noteworthy is the catalyst QD-9c, which achieved unprecedented enantioselectivity and yield in the isomerization of α, β-unsaturated imine without generating the 1,3-proton transfer product. The reaction scope extends seamlessly to aryl trifluoromethyl imines. These new catalysts usher in a remarkable high turnover rate for promoting asymmetric isomerizations of trifluoromethyl imines, enabling the conversion of a wide range of alkyl, alkenyl, and aryl trifluoromethyl imines into optically active trifluoromethylated amines using just 0.02 to 0.10 mol% of the cinchonium betaines.

Publications

1. Cinchonium Betaines as Efficient Catalysts for Asymmetric Proton Transfer Catalysis: The Development of a Practical Enantioselective Isomerization of Trifluoromethyl Imines (Zhou et al. 2016). Journal of the American Chemical Society. PMID: 2759574.
2. Catalytic asymmetric umpolung reactions of imines (Wu et al. 2015). Nature. PMID: 26201597.

Intellectual Property

- U.S. 10,888,853 | U.S. 10,836,761

Tech ID: Brandeis # 1299 & 2017-050

Lead Inventor: Li Deng, Professor Emeritus of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/ab361f40-a5fe-45f1-ba66-53437d6275a6

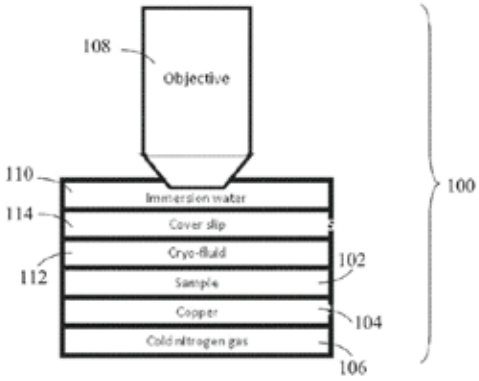
Cold Stage for Cryo Super-Resolution Fluorescence Light Microscopy

Application

Commercial licensing in academic, research, and biological organism experimentation and studies. Also interested in sponsoring collaborative research to further develop, evaluate, and commercialize this technology and its applications

Key Benefits

- Maintains a desired steady state temperature during cryo-EM screening
- Achieves high resolution in nm range and preservation of specimen grid for subsequent cryo-EM
- Designed for maintaining frozen hydrated grid (-135°C) in room temperature settings



Innovation

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. However, 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. This invention describes a unique light microscope cryo-stage device design that can be used for super-resolution PALM microscopy with high 'resolution' in the nm range while preserving the specimen grid for subsequent cryo-EM.

Technical Overview

The novel feature of this invention is that our cold stage is designed to be used with a high numerical aperture (NA), water immersion objective, which is operating at room temperature while the frozen hydrated grid remains below -135 Celsius, which maintains vitreous ice. Having reached cryo-temperature, the temperature stability is within a degree over time on the order of an hour and perhaps longer. The drift is minimal, ~1 or ~2 microns over a similar period, and slow, allowing for easy correction. The field of view in the camera is about 80 microns, meaning that items of interest remain in view during a run.

Publications

1. High-numerical-aperture cryogenic light microscopy for increased precision of superresolution reconstructions (Nahamani et al, 2017). PNAS, PMID: 28348224.

Intellectual Property

- US 9,784,962 | US 10,678,039 | EP 2,895,909 | JP 2015-529858

Tech ID: Brandeis # 1095

Lead Inventors: David DeRosier, Gina Turrigiano, Brandeis University, Department of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/c23ae70c-5738-417d-9214-24b33aeac4cf

Colloidal Membranes: A New Platform for Functional Nanomaterials

Application

Commercial and manufacturing use in electronic or semi-conductor devices, filtration systems, and biosensors devices

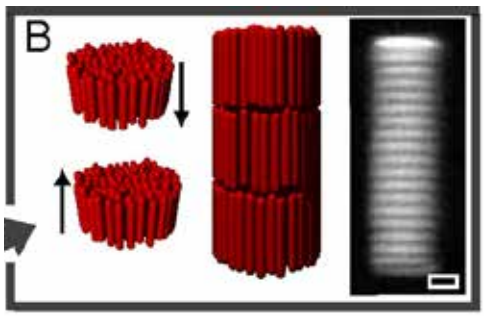
Key Benefits

- 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

Innovation

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. This invention 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. In one such example, the porous polymer membrane was used to remove rod-shaped virus particles with a biomineralization agent.

Technical Summary



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. This invention specifically targets the issue of generalizing such methods 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. Important prerequisites to realization of electronic or semi-conductor devices, filtration systems, and biosensors devices include the ability to assemble and align nanorods over large length scales (>1 mm2) and tune physical properties of the final assemblages, including the density of rods and the inter-particle spacing between rods.

Publications

1. ”Entropy driven self-assembly of nonamphiphilic colloidal membranes (Barry & Dogic, 2010). PNAS, PMID: 20498095.

Intellectual Property

- US 11,421,046

Tech ID: Brandeis #1019

Lead Inventors: Zvonimir Dogic, Michael Hagan, Daniel Perlman, Department of Physics, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/5446a888-7909-497c-b4fe-bf2a6f38fb5e

A Novel Method to Produce Chlorine Dioxide On-Site from Dry Precursors

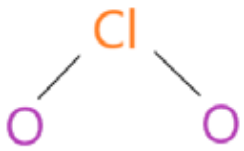
Application

Versatile commercial, enterprise, and academic production/generation and use of chlorine dioxide, such as to prevent mold/ microbial growth on textiles for clothing, uniforms, or interior of cars

Key Benefits

- Improved, convenient, portable method for decontaminating microbiologically contaminated surfaces of textiles
- Can be used in humid environments
- Can be used in contained environments
- Chlorine dioxide can be produced for use in an enclosed container where it previously could no be
- Chlorine dioxide can be made cheaper and more easily, and can also be transported more simply
- Chloride dioxide generation can occur in various mediums, such as polymers and super absorbent hydrogels

Innovation



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 in polymers, superabsorbent hydrogels, stimuli-responsive hydrogels, smart materials, and polymeric packaging films.

Technical Overview

A new method has been developed to produce chlorine dioxide on-site using a dry chemical composition. The composition contains hydroxymethanesulfinic acid monosodium salt dihydrate (HMS) and a chlorine dioxide precursor. When water is added to the composition, it activates the HMS and the chlorine dioxide precursor, which then react to produce chlorine dioxide. This method can be used to prevent mold, mildew, and pathogen growth on textiles or other surfaces. It is an alternative to bio-decontaminating Bacillus anthracis Sterne spores on individual protective fabrics using chemicals in the liquid or gaseous state. The method uses a novel chemical composition and method to produce chlorine dioxide from dry precursors embedded in media that absorbs water in humid environments. This reaction produces a disinfectant that kills mold, mildews, and other contaminating microorganisms on textiles. The method is convenient, has simplified logistics, and offers technological advantages over existing methods.

Intellectual Property

- US 10,626,016
- US 11,358,863

Tech ID: Brandeis # 2017-059

Inventors: Christopher J. Doona, Irving R. Epstein, Department of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/d4f8cf29-7c2f-4ceb-849a-a5fc92e553a8

Self-Decontaminating Clothing That Kills Germs and Neutralizes Odors

Application

Antiviral and antimicrobial coatings for surfaces including fabric (mask, gloves, doctor coats, curtains, bed sheet)

Key Benefits

- Novel chemical method of creating self-decontaminating and self-disinfecting fabrics that are effective, practical and economical
- Can satisfy unmet needs for self-clean textiles during a global pandemic
- Improved, convenient, portable method for decontaminating microbiologically contaminated surfaces of textiles
- This antimicrobial 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

Technology

There is a critical need for self-decontaminating, self-deodorizing, self-disinfecting, and/or self- cleaning textiles to protect healthcare professionals, patients, military personnels and others from exposure to harmful chemicals and biological agents. A new method has been developed to make substrates self-decontaminating by incorporating disinfectant into a stimuli-responsive hydrogel polymer. The polymer can take up, store, and controllably release chlorine dioxide, which can be used to neutralize odors, inactivate microorganisms, or prevent cross-reactions with container surfaces. The polymer-functionalized or polymer-associated surfaces are re-chargeable and can be used for single-use or for multiple cycles of use.

Technical Overview

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 (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 release 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 (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 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 **Clostridiodes difficile**, the notorious pathogen in hospitals and nursing care settings), yeasts, molds, mildews, fungal spores, and viruses.

Intellectual Property

- US 2022-0307194

Tech ID: Brandeis # 2020-002

Inventors: Christopher J. Doona, Irving R. Epstein, Department of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/6cfa9de2-3c5f-4bdc-84a3-c62c5a3e9d66

Modular Phase Chip for Determining Optimal Protein Structure for Drug Design

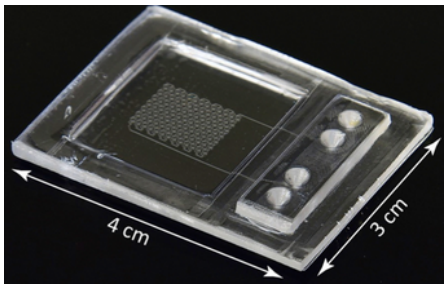
Application

Commercial & academic use in protein crystallization condition optimization and protein structure determination

Key Benefits

- High-throughput screening
- Cryo-conditions avoided
- Defect-free crystal growth
- In-situ diffraction
- Minimal fluid volume (nL) and protein amount required for structure determination
- High data quality

Innovation



Determining the structure of a protein with a small molecular weight ligand bound is important for many pharmaceutical applications. In the measurement of a stable protein structure, three main challenges include: (i) screening chemical conditions for stable protein crystals, (ii) producing large, defect-free crystals, (iii) cryo-protecting and then freezing the sample to avoid radiation damage. A few companies have developed robotic systems to simultaneously screen multiple crystallization conditions to expedite the process. However, a skilled person is required to extract the crystals and protect them against radiation damage by cryo-cooling crystals before X-ray diffraction, and a large amount of protein is required in such systems. Our invention is a set of microfluidics chips which can be used for optimizing the crystallization conditions, generate several tiny crystals and get x-ray diffraction data without moving them from the chips.

Technical Summary

The devices can be categorized into the consumables segment including injection module, PhaseChip, and in-situ X-ray diffraction module. They greatly improve and simplify current protein crystallization and X-ray diffraction protocols. They collect sufficient data for structure determination by merging the diffraction patterns produced one at a time from hundreds of individual crystals prepared on the same chip. The 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. Using X-ray transparent Chip, the diffraction is done in-situ with multiple individual small crystals and then massive data is merged, avoiding handling and cryo-protection of the crystals entirely. This reduces labor and improves crystal quality.

Publications

1. Room-temperature serial crystallography using a kinetically optimized microfluidic device for protein crystallization and on-chip X-ray diffraction (Heymann et al., 2014). IUCrJ, PMID: 25295176.
2. Cross polarization compatible dialysis chip (Kornreich et al, 2014). Lab Chip., PMID: 25105977.

Intellectual property

- US 10,365,188 | US 10,942,095 | US 11,366,042 | US 11,148,140 | US 2021/0394186

Tech ID: Brandeis #1113; 1238; 2019-005

Inventors: Seth Fraden, Professor of Physics, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/8dcdb6ac-4350-4a6c-907a-55f1976ba105

Glass-Bottom Microscopy Chamber Designs For Imaging Biological Materials

Application

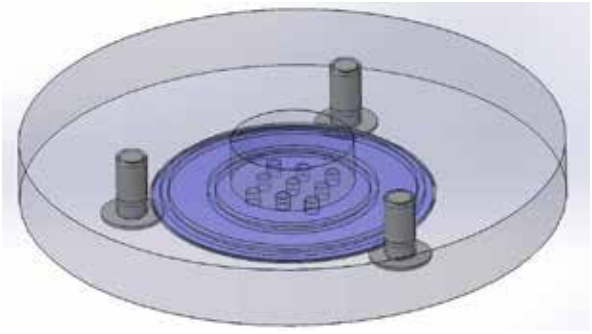
Accessory devices for microscopy imaging applications involving biological materials such as embryos

Key Benefits

- Increased safety and biocompatibility for sensitive biological materials like embryos
- Near limitless customizability of the frame
- The ability to incorporate additional functionalities into the frame

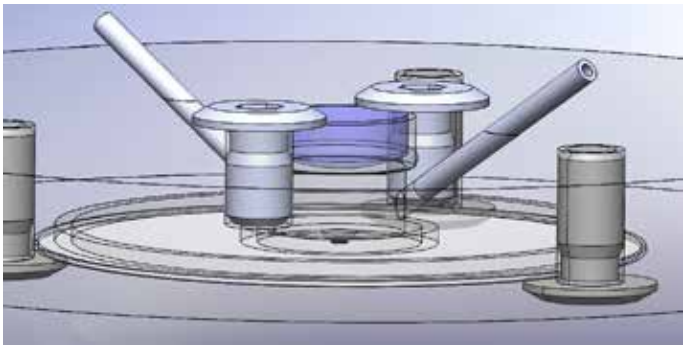
Innovation

Imaging sensitive biological samples is often limited by the use of plastic dishes, which can degrade imaging quality. The present invention overcomes this limitation by combining treated glass coverslips with a plastic rim. This adhesive-free design maximizes biological compatibility and provides far superior resolution and fluorescence excitation efficiency than traditional plastic dishes.



Technical Overview

This invention uses siliconized glass coverslips, which are safe for embryos and produce blastocyst development rates that are equivalent to standard plastic Petri dishes. To avoid the use of adhesive, we designed a mechanical attachment system that uses screws to secure the coverslip to the bottom of a plastic mask. A thin layer of mineral oil is applied between the coverslip and the plastic mask to prevent leaking. The oil spreads to make a continuous seal, and media and biosamples can be pipetted directly into the microwells and the main cavity. The oil also prevents evaporation. Mineral oil of this kind is commonly used in IVF clinics with human embryos, where safety and biocompatibility standards are of the utmost concern.



The decoupling of the glass bottom from the plastic frame allows for near-limitless customizability of the frame. One could implement arbitrary geometries for custom experiments (e.g., varying well sizes, channels, large open cavities). Furthermore, additional functionalities can be designed into the frame.

Publications

1. Combined noninvasive metabolic and spindle imaging as potential tools for embryo and oocyte assessment (Sanchez et al, 2019). Hum Reprod. PMID: 31812992

Intellectual Property

- US 20220382036

Tech ID: Brandeis # 2020-006

Inventors: Seth Fraden, Professor of Physics, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/1777a396-99b0-481b-bd11-4dee6b8ef834

Devices for Simultaneous Generation and Storage of Isolated Droplets

Application

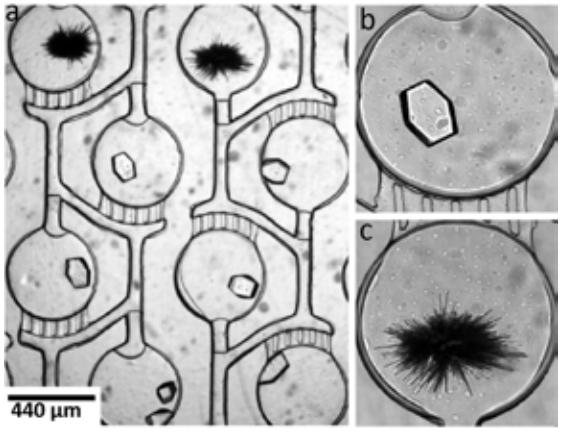
For protein crystallization or other applications requiring formulation and storage of many small samples of nanoliter volumes like high-performance immunoassays and other in vitro diagnostics

Key Benefits

- Eliminates cross-contamination between samples
- low-cost, high yield rapid fabrication method for casting cyclic olefin copolymer (COC) microfluidic chips

Innovation

This invention describes a microfluidic device that uses a sequence of capillary valves and storage chambers to generate and store isolated droplets in chambers that are isolated from one another by oil. The droplets are generated serially, and different chemicals can be added without mixing, or mixed in pre-determined quantities set by the geometry of the device. The device also consists of an injection system that allows for a predetermined amount of each of the at least two different aqueous solutions to be delivered to the droplet isolation device sequentially.



Technical Overview

Our microfluidic device uses multiple sequences of capillary valves and storage chambers to efficiently generate and store aqueous solutions in chambers that are isolated from one another by oil. The device can serially generate drops, and different chemicals can be added without mixing, or chemicals can be added to mix in pre-determined quantities set by the geometry of the device. The device is built from inexpensive biocompatible material via a rapid fabrication procedure, and it can be altered as needed to meet the specific requirements of the customer. In addition to crystallography, the device can be used to perform rapid and low-cost immunoassays with an enhanced range of detection.

Publications

1. Rapid prototyping of cyclic olefin copolymer (COC) microfluidic devices (Aghvami et al, 2016). Sensors & Actuators B: Chemicals.
2. Room-temperature serial crystallography using a kinetically optimized microfluidic device for protein crystallization and on-chip X-ray diffraction (Heymann et al., 2014). PMID: 25295176

Intellectual Property

- US 11,148,140
- US 2021/0394186

Tech ID: Brandeis # 1238, 2019-005

Inventors: Seth Fraden, Professor of Chemistry, Brandeis University

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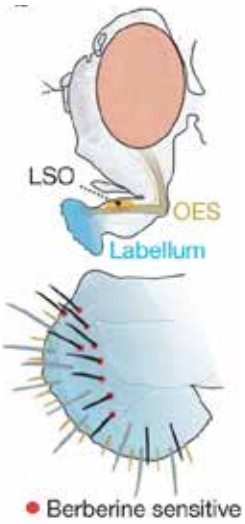
Link: https://brandeis.flintbox.com/technologies/87a22b81-db19-44f4-b713-b5a0016d132c

TRPA1 Modulators for Insect Control

Application

Commercial, industrial, residential, agricultural, horticultural, for parasitic pest or disease vector control and potential use in insect and homeostasis research



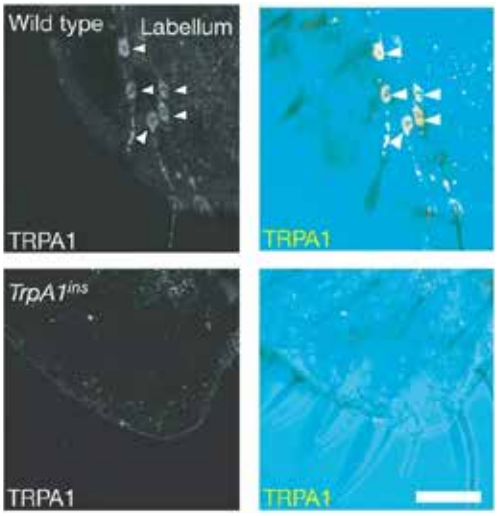
Key Benefits

- TRPA1 isoforms are conserved in malaria-causing mosquitos and other insects suggesting that all utilize similar mechanisms for discriminating host-derived warmth from chemical repellents.
- 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.

Innovation

Insects pose significant threats to agriculture, food supply, storage, horticulture, animal and public health, resulting in substantial losses. Despite progress in control measures, insects have proven resilient by adapting and evading control methods. Our invention offers a novel approach to identify insect-specific TRPA1 modulators, enabling effective insect control. By using compounds like allyl isothiocyanate (AITC) or N-methyl-maleimide (NMM), we can modulate the sensory abilities of insects, providing a targeted solution.

Technical Overview



The invention leverages the discovery of two distinct TRPA1 isoforms, TRPA1(A) and TRPA1(B), in Drosophila. While these isoforms have different amino termini, they share the same carboxy-terminal ankyrin and transmembrane domains. Similar patterns have been observed in other insects, including disease vectors like Aedes aegypti and Culex quinquefasciatus mosquitoes, as well as Pediculus humanus corporis lice, which transmit diseases such as dengue, West Nile fever, and typhus. This functional differentiation between TRPA1 isoforms presents two separate molecular targets, TRPA1(A) and TRPA1(B), for disrupting the behavior of disease vectors, agricultural and horticultural pests, and parasitic pests. Potential applications encompass aerial crop dusting, environmental sprays, topical lotions, and sprays. The invention introduces methods to identify novel compounds that modulate the activity of the TRPA1(A) cation channel, providing a means to control pests by inhibiting feeding behavior in larvae, pupae, or adults.

Publications

1. Modulation of TRPA1 thermal sensitivity enables sensory discrimination in *Drosophila* (Kang et al. 2012). Nature. PMID: 22139422
2. The Drosophila ortholog of vertebrate TRPA1 regulates thermotaxis (Rosenzweig et al. 2005). Genes & Development. PMID: 15681611

Intellectual Property

- US 9,488,640 | US 9,986,740

Tech ID: Brandeis # 1054

Lead Inventor: Paul Garrity, Professor of Biology, Brandeis University

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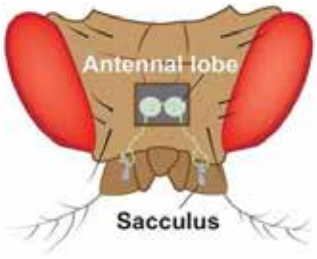
Link: https://brandeis.flintbox.com/technologies/9692cdd7-3b8e-4277-962e-572b911255f4

Ending Mosquito-Borne Diseases, One Receptor at a Time

Application

A novel target platform for the development of broad-spectrum pest control via IR modulation.



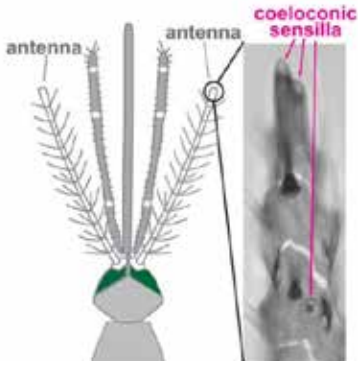
Key Benefits

- New species-specific pesticides without strong resistance selection pressures
- Assays targeting 2 highly conserved environment sensing pathways essential for survival
- Innovative approach to exploit moisture and temperature for pest control

Innovation

Water is a vital and necessary chemical for all life on earth and water balance is a key component of hydro-homeostasis. Humidity plays a role in the rate of water evaporating and also functions as a cue for locating water sources thus making humidity awareness crucial for survival. Inserts have evolved to have highly tuned hygrosensation and possess ionotropic receptors (IRs) on the surface of their hair-like sensilla in their antennae, legs, and head to sense environmental changes. However, insects like mosquitoes pose a threat due to their host-seeking behavior spreading disease like malaria, chikungunya, and dengue fever. Here, we present a novel method to study hygrosentation and host-seeking behaviors in invertebrates via modulations of their IR receptors. By modulating their ability to sense their environment, we can disrupt disease-carrying invertebrates from spreading viruses addressing the need for insert control.

Technical Overview



Signaling through ionotropic receptors (IRs) allow insects, like flies and mosquitoes, to sense changes in their environment's temperature and moisture. IRs are found on hair-like sensilla, small fibers located on the surface of their antennae, legs, and heads; by detecting changes in ambient moisture and temperature, inserts can avoid dessication, improve reproduction rate by locating mates, and locate both hosts and prey. ITs are a large family of highly conserved cation channels located in the dendrites of sensory neurons and are related to ionotropic glutamate receptors (iGluRs) that are conserved in both plants and animals. We have shown that IR-heteromeric complexes consisting of IR25a/IR93a/IR40a and IR25a/IR93a/IR68a located in the sacculas of antennae are critical in mediating hygro preferences and those flies expressing mutant loss- of-function forms of IR25a, IR93a or IR40a will lack normal hygro sensory 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. 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 hygro-sensory 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.

Publications

1. Distinct combinations of variant ionotropic receptors mediate thermosensation and hygrosensation in *Drosophila* (Knecht et al. 2016). eLife. PMID: 27656904
2. Ionotropic Receptor-dependent moist and dry cells control hygrosensation in *Drosophila* (Knecht et al. 2017). eLife. PMID: 28621663
3. Mosquito heat seeking is driven by an ancestral cooling receptor. (Greppi et al. 2020). Science. PMID: 32029627

Intellectual Property US 11,198,875

Tech ID: Brandeis # 1276

Lead Inventor: Paul Garrity, Professor of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/719d1789-5d04-4b0d-9da4-2d9ae46543cb

How CRISPR/Cas9 is Revolutionizing SIT: A New Method to Produce Sterile Male Insects

Application

Commercial, enterprise, residential, agricultural, disease vector and monsoon season pest control, mitigation, and elimination

Key Benefits

- Enables the production of large numbers of healthy sterile animals
- Generates stable heterozygous individuals that can be used to produce more sterile animals in the next generation
- Labeling protein increases sorting efficiency of sterilized males
- Can be used for a range of insect and non-insect species
- Sterilization process is cheaper than current SIT methods
- Will not promote resistance to sterilization treatment in insect populations

Innovation

Sterile Insect Technology" (SIT) is a powerful and environmentally friendly strategy for controlling and even eradicating insect pests and vectors of disease. In SIT, sterile male insects of a given species are released into the environment to compete with their wild male counterparts for mating to wild females. Mating to sterile males leads to species-specific reductions in the levels of reproduction followed by declines in population size, in some cases driving the population to zero. The sterile insect technique (SIT) has been applied against plant and animal pests and vectors of animal and human disease for over 50 years. Sterile males can be generated in a variety of ways, from irradiation to the introduction of a sterilizing pathogen or transgene. A major bottleneck in implementing SIT against many species is the difficulty and expense in generating large numbers of males that reliably fail to produce viable offspring but are otherwise fit and effective at mating. This method maintains sterile males, thereby reducing cost as less males are lost in the SIT process.

Technical Overview

Brandeis inventors have developed a simple and versatile molecular genetic strategy for producing sterile male insects. One approach to creating sterile males that can still mate effectively involves using animals that carry a stable, knock-out mutation in a gene crucial for fertility. The inventors employ CRISPR/Cas9 technology to introduce two-color knock-ins in the key reproductive gene, replacing it with RFP, GFP, and following Mendelian genetics. Specifically, a pair of marked disruption alleles is generated by inserting selectable markers into identical sites in fertility genes, inducing recessive sterile mutations. These mutant alleles are then propagated within populations that contain both fertile heterozygous and sterile homozygous animals; the latter are readily and easily collected by screening for both markers. High-throughput sorting of insects can be accomplished using existing automated fluorescence sorting machines or chemical selection, resulting in a high yield of sterile insects as well as fertile heterozygous ones. Researchers have successfully demonstrated sterilizing mutations in laboratory fruit flies, invasive spotted-wing fruit flies, and dengue fever mosquitoes.

Publications

1. DMKPs provide a generalizable strategy for studying genes required for reproduction or viability in nontraditional model organisms (Laursen *et al*. 2023). Genetics, PMID: 37036394

Intellectual Property

- WO 2022/072334A1

Tech ID: Brandeis # 2020-046

Inventors: Paul Garrity, Professor of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/c491182e-9bd8-4ab5-8405-49b2049f154b

Releasable Adhesive Device with Light-Responsive Properties

Application

Commercial use in semiconductor manufacturing and residential use for home decorations

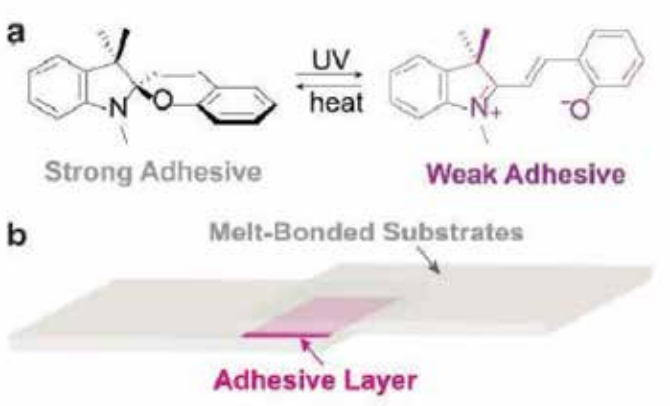
Key Benefits

- One-step removal of light-responsive adhesives from various substrates
- Variable time frame (hours, days, weeks) energy storage capability
- Attractive opportunities in solar energy harvesting with triggered release of stored energy

Innovation

Adhesives are commonly used in daily life, and in specialty circumstances such as between silicon components in electronic devices. Various strategies and formulae have been developed to achieve high adhesive strengths suitable for a wide range of uses, but the selective and controlled removal of adhesives has remained a significant challenge especially in the fabrication of electronics devices. A new type of light-responsive molecules has been synthesized that exhibit adhesive properties that can be controlled through exposure to UV light. Initial testing of this temporary adhesive will be focused on its potential use in processing silicon wafers. However, the technology could also have broader applications in packaging tapes and hanging strips that need to be easily removable without causing damage to the substrate, such as walls or packages. The specific light-activated debonding process and lack of residue upon removal make this technology favorable for both recycling and home decoration purposes.

Technical Overview



The pre-adhesive powders are first melted to bond substrates, and the debonding process is triggered by the irradiation with UV. Our light-responsive adhesives offer several advantages, including the ability to selectively remove glue from the desired substrate (such as a silicon wafer) using a one-step, specific triggering procedure. This more gentle process results in lower rates of substrate damage, leading to a higher yield of finer quality industrial products. Since the debonding process is triggered by light, it can be operated locally and controlled with a high degree of precision using a narrow beam of light. This enables meticulous work, such as the detachment of micron-scale components in electronics, which can optimize multi-step assembly and customization of intricate devices.

Publications

1. Phase transition of spiropyrans: impact of isomerization dynamics at high temperatures (Gerkman et al. 2019). *Chem. Commun.* PMID: 31041949

Intellectual Property

- US2022/0228035

Tech ID: Brandeis # 2019-041

Inventors: Grace Han, Assistant Professor of Chemistry, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/aaed00f9-142c-40ad-96aa-ebe247bb442a

Functional Heat Storage Materials for Heating Engine Oil

Application

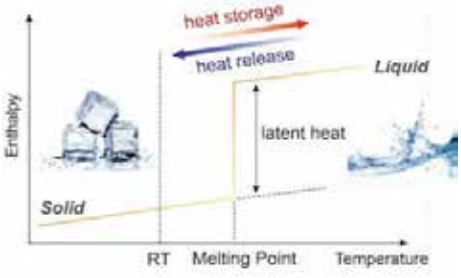
Gas or diesel powered vehicles and corporations that operate oil-lubricated machinery that are impacted by cold weather. May also be used in commercial oil pan heaters and domestic water heating systems

Key Benefits

- 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
- 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 ~300 kWh of electricity per winter

Innovation

The majority of damage in engine components occurs during a cold start, due to the frozen/viscous oil in the engine at low temperatures. Oil heating devices are used to warm up the oil pan in an engine using electricity. These devices have several drawbacks, including the need to plug in the car for hours to fully heat the oil pan, and the high energy consumption. There is currently no commercial device that can quickly heat up engine oil in an energy-efficient way. We have developed 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 (~300 J/g) to cold oil when triggered. 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.



Technical Overview

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 the electricity bill of car owners, CO2 emission associated with the electricity generation, and the everyday life of car owners residing in cold climates. 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.

Publications

1. Arylazopyrazoles for Long-Term Thermal Energy Storage and Optically Triggered Heat Release below 0 °C (Gerkman et al. 2020). J. Am. Chem. Soc. PMID: 32319773

Intellectual Property

- US 2022-0220871
- EP3963185

Tech ID: Brandeis # 2019-042

Inventors: Grace Han, Assistant Professor of Chemistry, Brandeis Univerity

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Link: https://brandeis.flintbox.com/technologies/f8926f24-805d-4ed9-9001-c005be40a314

Molecular Solar Thermal (MOST) Systems for Thermal Energy Storage

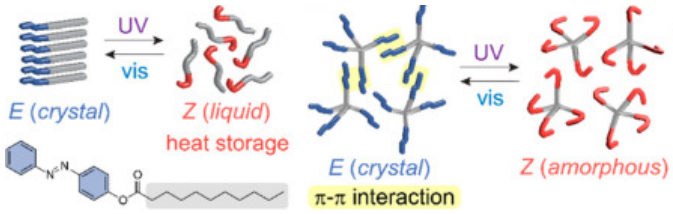
Application

Commercial and residential heat storage, thermal battery, space heating, and domestic water heating systems

Key Benefits

- Low- cost solution
- Absorption spectrum adjustable
- Controlled heat release
- Instant heating
- Solar energy based—eco friendly
- Electricity saving in cold climate
- CO_2 emission reduction, engine preservation, sustainability

Innovation



Traditional phase-change materials (PCMs), both inorganic and organic, with high latent heat densities are valuable means for harnessing waste heat from industrial processes and solar irradiation. However, the active control of thermal energy storage and release remains a challenge. Han's group has developed a collection of MOST which consists of various PCMs and methods that enable control of the kinetics of thermal energy dissipation. These novel state-of-the-art light-responsive phase change materials (PCMs) are capable of controllably storing solar energy and releasing it in the form of heat through their chemical and physical changes.

Technical Overview

Photoisomerization of molecular switches and the corresponding energy level changes enable the storage of photon energy in metastable-state isomers. This optically controllable energy storage-release cycle in a closed system has emerged as a viable model for heat storage. In one of the examples, 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. The PCMs can store energy for months (or even years) 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. Harnessing solar energy and storing heat in a controllable fashion can significantly reduce the use of fossil-fuel based energy. The group has developed various classes of PCMs (azopyrazole-based, azobenzene-based among few) that have various capacities for the energy storage density, energy, conversion efficiency, and energy storage time.

Publications

1. Arylazopyrazoles for Long-Term Thermal Energy Storage and Optically Triggered Heat Release below 0 °C (Gerkman et al, 2020). PMID: 32319773.
2. Light-Responsive Solid-Solid Phase Change Materials for Photon and Thermal Energy Storage (Li et al, 2023). PMID: 36647455.
3. Sunlight-activated phase change materials for controlled heat storage and triggered release (Shi et al, 2021). https://doi.org/10.1039/D1TA01007G.

Intellectual Property

- US 2023/0053197, WO 2022/169879, additional provisional applications

Tech ID: Brandeis # 2020-033; 2021-007, 2023-006

Inventors: Grace Han, Assistant Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/7adf6ad8-7d48-4dc5-bcfb-598916b85c05

Light-Activated Catalyst Recycling: A Green and Sustainable Solution

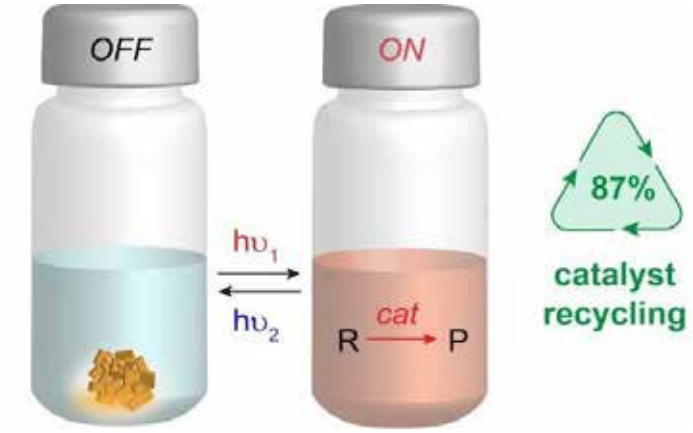
Application

- In biomanufacturing and drug/API synthesis for pharmaceuticals
- In chemical synthesis

Key Benefits

- Recovery and recycling
- Reduces environmental impact & cost
- Homogeneous catalyst
- Temperature insensitive
- High spatiotemporal resolution
- Large scope of reactions
- Light trigger
- Non-invasive

Innovation



The concept of recovering and recycling homogenous catalyst has been widely explored. The traditional methods, such as distillation, chromatography, and extraction are destructive, energy-intensive, and costly, often leading to catalyst decomposition and loss. Heterogenization of homogeneous catalysts, which involves placing them on a solid support, is limited due to catalyst leaching and loss of activity. A series of organocatalysts that display a reversible solubility change in response to light has been developed. The initially-insoluble catalysts (stable state) are UV-switched to a soluble isomeric state (metastable state), which catalyzes the reaction in higher activity, then back-isomerizes to their insoluble state upon completion of the reaction to be filtered and recycled.

Technical Overview

In the stable state, the organocatalysts appear as orange solids aggregated via strong intermolecular interactions that result in compact packing. Upon the irradiation of UV light, the stable-state azobenzene moieties isomerize to their metastable state. Consequently, the ordered packing collapses because of the weakened intermolecular interactions and the increased polarity of the catalysts. This results in a significant increase in solubility and catalytic activity of metastable organocatalysts compared to that of a stable state. Upon the completion of reactions, the metastable organocatalysts isomerize to their stable state through exposure to visible light, then precipitate from the reaction mixture. The formed precipitate is easily recovered by filtration to be re-used in reactions.

Publications

1. Optically Controlled Recovery and Recycling of Homogeneous Organocatalysts Enabled by Photoswitches (Qiu et al, 2023) Angew. Chem. Int. Ed. PMID: 36688731

Intellectual Property

- Provisional application filed

Tech ID: Brandeis #2023-031

Inventors: Grace Han, Assistant Professor of Chemistry, Brandeis University

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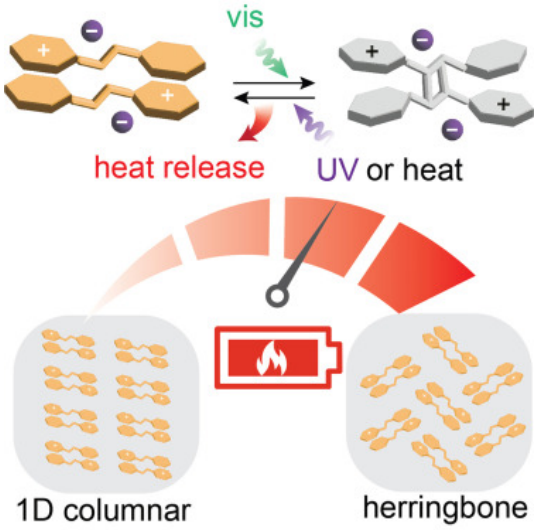
Link: https://brandeis.flintbox.com/#technologies/e8395ae6-19c0-4fa2-b2c0-b7864b8b1d7f

Molecular Solar Thermal (MOST) Systems for Thermal Energy Storage Only with Solid Phase

Application

Commercial and residential Solar energy storage, thermal battery, space heating, and domestic water heating systems



Key Benefits

- Broad absorption spectrum for maximum conversion
- Environmental-friendly heat storage
- Tunable period for energy storage
- On-demand heat energy release

Innovation

Previous Brandeis inventions have reported a series of molecular solar thermal (MOST) energy storage materials that can store photon/solar energy in chemical bonds upon light irradiation and release the stored energy as heat on demand. This energy-storing process is through the development of photoswitches. The ground state (storage-OFF state) undergoes a reversible structural change to the metastable state (storage-ON state), and the storage-ON state will keep the energy long enough (days-years) until it is triggered by UV irradiation. Upon triggering, the stored energy is released as heat and transferred to another object. The energy released from the storage ON-state consists of the isomerization energy released from the metastable state to the ground state.

Technical Overview

This invention describes a new type of photoswitch that can absorb visible light and store energy. The photoswitch is a solid-state compound, which makes it safer and more stable than other photoswitches that need to be dissolved in a liquid or phase changed to work. The solid-state photoswitch can also absorb a wider range of wavelengths, which means that it can collect more energy from the sun. The photoswitch is made up of a series of styrylpyrylium compounds that undergo a chemical reaction called [2+2] photocycloaddition when exposed to light. This reaction forms a new compound with a cyclobutane ring moiety, which has a significant ring strain. When the compound reverts to its original state, the ring strain is released, which releases energy in the form of heat. The solid-state photoswitch is a yellow solid in its storage OFF-state and a white solid in its storage ON-state. The solid form of both states makes them suitable for practical applications, such as thermal battery devices, without the risk of liquid leakage. This new type of photoswitch has the potential to revolutionize solar energy storage. It is a safer, more stable, and more efficient way to store solar energy than existing technologies.

Publications

1. Solid-state photon energy storage via reversible [2+2] cycloaddition of donor-acceptor styrylpyrylium system (Cho et al, 2023). Chemistry. https://doi.org/10.1016/j.chempr.2023.06.007

Intellectual Property

- Provisional application filed

Tech ID: Brandeis # 2023-033

Inventors: Grace Han, Assistant Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/6ad85236-0c01-4426-abc5-1bcc3898dde0

The D-Hasp: New Tamper-Resistant Hasp

Application

The ideal hasp for securing access control systems, storage compartments (medical, filing, drawers, containers, lockers), retail and museum displays, and cash boxes

Key Benefits

- Quick and easy installation
- Sleek, compact design for a smaller profile
- Mountable on ulta-narrow frames
- Enhanced security with innovative shackle and aperture system

Innovation

Introducing our innovative steel tamper-resistant hasp for securing cabinet drawers and more! The D-Hasp features two pivotable components with a shackle aperture accessible only in a specific configuration, ensuring maximum security. The unique overlay of a separate aperture blocks access to the fastenings, further deterring tampering. With easy installation using self-tapping screws on horizontal and vertical lips, our hasp offers efficient manufacturing and heightened security. Easy to scale depending on your specific applications**:** Protect your cabinet contents with our space-saving and installation-friendly solution!

Technical Overview

This invention discloses a tamper-resistant hasp for securing a file cabinet drawer. The D-hasp has a design that makes it difficult to pry open. The hasp also has a shackle aperture that provides additional security. The tamper-resistant hasp is an improvement over traditional hasps, which can be easily pried open. The tamper-resistant hasp provides an additional layer of security for file cabinet drawers and access panels, making it more difficult for unauthorized individuals to access the contents. The D-Hasp is made up of two hinges. Each hinge has two parts: a mounting component and a shackling component. The mounting component has three holes, with the outer two holes secured with screws. The shackling component has two holes, one of which is on a rectangular plate. When the two hinges are pivoted together, the security hole on the rectangular plate aligns with the middle hole on the mounting component. A screw can then be inserted through both holes, making the mounting screws inaccessible. The other hole on the shackling component can be used to connect the two hinges with a padlock or pin. This design makes the D-Hasp more secure and easier to use.

Intellectual Property

- WO 2023/133088

Tech ID: Brandeis # 2021-034

Inventors: Donald Hodge, Locksmith, Brandeis University

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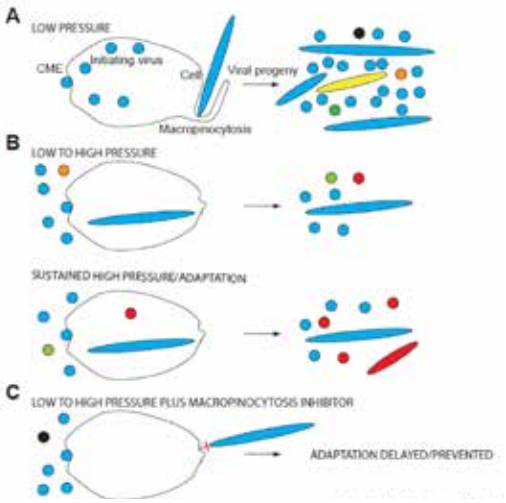
Link: https://brandeis.flintbox.com/technologies/57b3355e-a8db-4018-a4d9-187eaf2b9493

High-Throughput, Quantitative Assay for Measuring Pleomorphic Virus Particle Size and Composition

Application

Drug discovery and characterization



Key Benefits

- High throughput (automated, up to a 96-well plate format)
- high sensitivity (requires low particle concentrations)
- Quantitative (derives particle-size distributions and counts particles)

Innovation

Pleomorphic particle shape is a largely overlooked feature of viruses due to difficulties in assessing and quantifying shape distributions. Pleomorphic virus particles have a broad size range and an unusual shape distribution that falls through the cracks of most standard analytical techniques. They are too large for processes typically used to analyze proteins, such as liquid chromatography (FPLC or HPLC) or electrophoresis. Studies have shown that the filamentous particles resist the effects of neutralizing antibodies and inhibitors of cell entry, which could enable established infections to persist or emerging viruses to adapt to human-cell entry. Inhibitors of filamentous-particle assembly are urgently needed to delay and prevent viral resistance. This invention overcomes all limitations of the above-listed technologies. It enables high-throughput, automated counting of particles and quantification of the relative fraction of spherical vs. filamentous particles in a population.

Technical Overview

A new high-throughput, quantitative assay has been developed for measuring the size distributions of pleomorphic virus particles. The assay is based on flow cytometry and is very sensitive, requiring only a simple dilution of infected-cell supernatants. The basic principle of the assay is that larger particles or longer filamentous particles cause greater scattering of the 405nm laser light (Violet Side Scatter, or VSSC) than the spherical particles. The assay is very sensitive, requiring virus concentrations in the order of 1^{e7}-1^{e8} particles/ml. It is also very sensitive, requiring only ~0.5-2µl of unprocessed/unmanipulated infectious cell supernatant, avoiding processing artifacts and enabling scale-up needed for inhibitor screens that test many compounds for their effects on particle shape and/or numbers in parallel. The screens can be performed in cell culture (screens for cellular/viral modulators of budding) or on purified viruses (screens for compounds that alter the particle shape of assembled virions). The assay can also be used to quantify virus particle composition by including antibodies specific for viral surface proteins. The assay has broad utility for studying the cellular and viral determinants of budding and pleomorphic-particle shape and for screening for inhibitors of filamentous particle budding and modulators of virus morphology.

Publications

1. The shape of pleomorphic virions determines resistance to cell-entry pressure (2021). Nat Microbiol. PMID: 33737748.

Intellectual Property

- WO 2023/034362

Tech ID: Brandeis # 2022-001

Inventors: Tijana Ivanovic, Biochemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/1686a8fe-0ef2-4980-8e0a-f84de41c50ed

Drug Development Platform Leveraging Protein Energy Landscape

Application

A drug development platform that uses biophysical analysis of proteins' unique energy landscape intended to be licensed for commercial, enterprise, academic and research applications for drug discovery, design, and development

Key Benefits

- Assesses energy landscape of free and boun protein interactions
- Insights on transition rate conversion betwe initial binding and induced fit conformations
- Ability to screen for strong and specific inhibitory binding
- Identifiable agents include small molecules, polypeptides, peptides, or peptide mimetics

Innovation

The drug development pipeline is a time and resource intensive process that faces many roadblocks on the path specifically in the identification and selection of potential candidates. A fundamental pitfall in the current drug development process is the lack of understanding around what makes inhibitors successful, specifically the underlying biophysical mechanisms. Protein kinases are an attractive therapeutic drug target candidate as kinase activity has been correlated with various disease states, like cancer, and function by regulating different signaling cascades. However, there are more than 500 human kinases who share an extremely high-level of structural similarity, particularly in their active sites. This degree of similarity makes it difficult to effectively design potential drug inhibitors that are specific enough to target a particular kinase that can function as an anticancer therapeutic. Our drug discovery platform allows for a novel approach to develop high-affinity, specific drug inhibitors through the biophysical analysis of the kinase energy landscape highlighting inhibitor-target interactions, conformational changes and binding affinity. This novel approach to drug development will better identify drug inhibitory compounds by exploiting the dynamic nature of protein-target interactions to design effective inhibitors.

Technical Overview

Our drug development platform focuses on the analysis of the dynamic nature of proteins allowing for the design of agents with better affinity and binding to target sites. Our approach is a result of examining the energy landscapes of Gleevec-Alb and Danusertib-Aurora A kinase pairs during drug inhibitor-target protein interactions. Our platform employs modern techniques including NMR spectroscopy dynamics, fast fluorescence binding kinetics, crystallography structures, enzyme kinetics, ancestral sequence reconstruction and/or molecular dynamics simulation. Using our platform, we were able to predict the transition conversion rate between two confirmation states, "initial binding" and "induced fit", after an agent contacts the target's active site. By analyzing the pairs' binding kinetics, the stability of the induced fit confirmation for the active site can be assessed and compared to physiologic reference binding agents. Using this approach, the design and screening of inhibitors to their target can be predicted along with their binding stability quantified allowing for the selection of only those strong candidates that exhibit the desired specific binding. Candidates identified in screening assays can include small molecules, polypeptides, peptides or peptide mimetics. Our novel drug design approach solves the problem for how to design new inhibitor drugs with high affinity, long on-target residence times and high specificity.

Publications

1. Energetic dissection of Gleevec's selectivity toward human tyrosine kinases (Agafonov et al 2014). Nature Structural & Molecular Biology. PMID: 25218445
2. Using ancient protein kinases to unravel a modern cancer drug's mechanism (Wilson et al. 2015). Science. PMID: 25700521
3. Dynamics of human protein kinase Aurora A linked to drug selectivity (Pitsawong et al. 2018). eLife. PMID: 29901437

Intellectual Property

- US 2017-0356024

Tech ID: Brandeis # 1175

Lead Inventor: Dorothee Kern, Professor of Biochemistry, HHMI Investigator, Brandeis University

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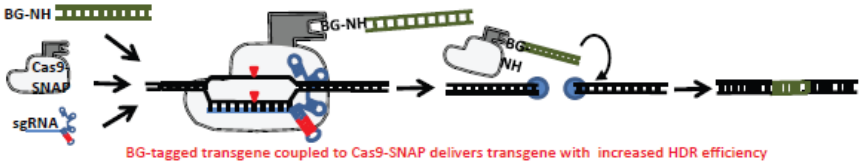
Link: https://brandeis.flintbox.com/technologies/1c16e5c5-8999-42ed-ba72-086e471c5faa

Next Gen. CRISPR-Based Genome Modification System using Tethered Target Transgene

Application

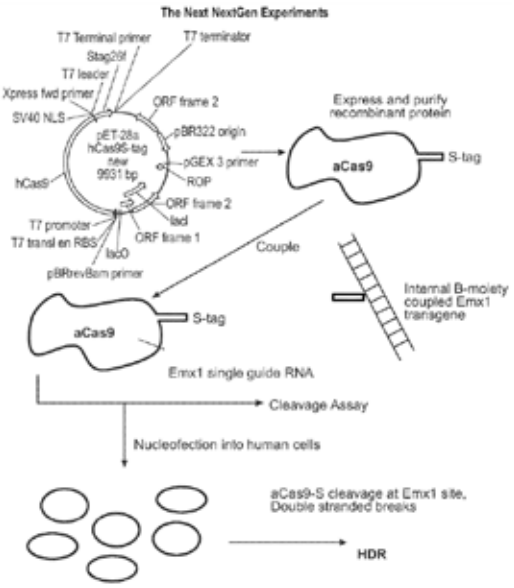
An innovative Cas9-SNAP toolkit catering to commercial enterprise, and academic applications.



BG-tagged transgene coupled to Cas9-SNAP delivers transgene with increased HDR efficiency

Key Benefits

- Cas9-SNAP tag fusion nuclease doubles integration efficiency compared to wild-type Cas9
- Enables seamless insertion of long DNA sequences into constitutive and inducible endogenous loci



Innovation

The advent of the CRISPR/Cas9 revolution has empowered researchers to surgically disable or repair individual genes in cells and animals. By leveraging the Cas9 enzyme, specific gene locations are targeted and selectively cut, while a supplied repair template precisely matches the gene site of interest to facilitate successful repair. Presently, this event is random, resulting in notably low efficiency rates. While the CRISPR/Cas9 system excels in disabling genes with an impressive efficiency rate of over 80%, the gene repair function remains lackluster. Repair events range from approximately 1% - 10% efficiency depending on the specific CRISPR/Cas9 system utilized. Our invention represents significant advancements in CRISPR technology, specifically enhancing Homologous DNA Recombination (HDR) by directly linking a transgene to the Cas9 enzyme. While the standard CRISPR approach has shown improvements in HDR from its initial very inefficient step (>0.01 to now ~5%), it still falls short of being a robust platform. By tethering the transgene, efficiency rates of at least 10%, 15%, 20% or higher are achievable. Our invention is an enhancement in the next generation of CRISPR/Cas9 technology.

Technical Overview

Our invention presents a groundbreaking method to improve the rate of HDR repair through the implementation of a recombinant Cas9 protein fused to SNAP-tag, a 20kDA mutant of the DNA repair protein O6-alkylguanine DNA alkyltransferase. This innovative fusion protein serves as a powerful tool by physically associating the repair transgene DNA template with the target gene location, where the CRISPR/Cas9 system creates a double-stranded break. The strategic delivery of the repair template greatly enhances the efficiency of HDR. The successful development and in vivo proof-of-concept testing of the Cas9-SNAP tag fusion polypeptide have been accomplished in mammalian human embryonic kidney cell systems (HEK293T cells). The results are truly promising, demonstrating a substantial approximately two-fold increase in transgene integration efficiency compared to the conventional wild-type (WT) Cas9.

Publications

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. 2021). G3. PMID: 33989385.

Intellectual Property

- US 11,111,508

Tech ID: Brandeis # 1166

Lead Inventor: Nelson Lau, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/f16839d7-09aa-4abe-88c9-9188f488549b

Novel and Optimized Cryo-EM Sample Preparation with PicoCell™

Application

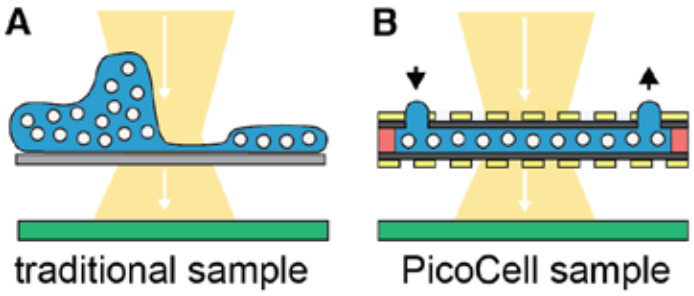
Commercial, enterprise, and academic research and use of Cryo-electron microscopy (cryo-EM)

Key Benefits

- 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

Innovation

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. Previous methods for imaging cryo-EM samples used robotic blotting methods that resulted in frozen samples with variable ice thicknesses and concentration gradients. This made it difficult to find suitable regions for imaging and complicated data post-processing. These problems have made the sample preparation stage of cryo-EM a bottleneck in structure determination and an obstacle to automation. 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.



Technical Overview

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.

Intellectual Property

- US 11,402,308 | CA 3,046,200 | EP 3552223A4 | CN 110337706A | KR 102484315B1 | US 20230034150

Tech ID: Brandeis # 1307

Inventors: Joel R Meyerson, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/ada53e27-bb13-402b-8032-afc182ceb85d

Improved Gene Silencing using Organic Small Hairpin RNAs (OshR)

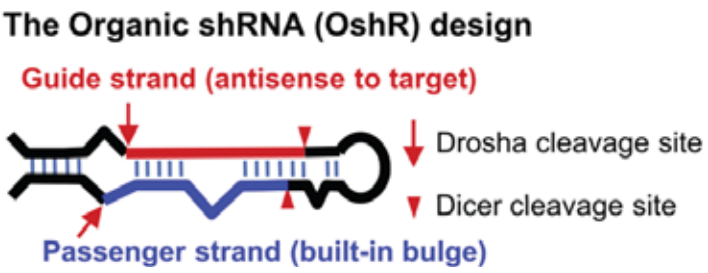
Application

An innovative gene suppression platform providing efficient and cost-effective solutions for targeting RNAi-refractory genes

Key Benefits

- Cas9-SNAP tag fusion nuclease doubles integration efficiency compared to wild-type Cas9
- Enables seamless insertion of long DNA sequences into constitutive and inducible endogenous loci

Innovation



RNA interference (RNAi) is a potent gene silencing process that enables targeted suppression of any gene in animal cells. It relies on small RNAs incorporating into the RNA Induced Silencing Complex (RISC) as Guide strands to direct RISC to specific transcripts, causing translation inhibition or degradation. MicroRNAs (miRNAs) regulate the transcriptome in vertebrate cells through RNAi. Researchers use chemically synthesized small interfering RNAs (siRNA) or vector-driven short hairpin RNAs (shRNA) as triggers to program RISC. However, challenges arise due to unpredictable efficacy, off-targeting, and competition with endogenous miRNA pathways, making improved shRNAs essential for more reliable and effective gene silencing applications. The unpredictable silencing efficacy and potential off-targeting effects of individual shRNAs necessitate researchers to acquire multiple shRNA constructs when targeting specific genes, and even then, failure may occur. Our invention overcomes these deficiencies by incorporating distinct elements of endogenous inhibitory miRNAs to more closely mimic their natural structure resulting in improved shRNA performance.

Technical Overview

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. The flexible OshR design for use in silencing any target gene of interest contains, in 5' to 3' order: a 5' constant stem sequence, a 22 base guide strand that is reverse complement of the target sequence, a constant stem loop, a 20 base passenger strand that is 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. Additionally, bases 11 and 12 are deleted. This design ensures precise cleavages of the hairpin by the Drosha and Dicer enzymes 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.

Publications

1. Organic small hairpin RNAs (OshR): a Do-It-Yourself platform for transgene-based gene silencing (Zeng et al. 2014). Methods. PMID: 23707624.

Intellectual Property

- US 9,777,277

Tech ID: Brandeis # 1137

Lead Inventor: Suzanne Paradis, Professor of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/ce320f7c-d8d1-4fb7-b269-a8a64268fb8f

High-Throughput Video Drosophila Behavior Monitoring System

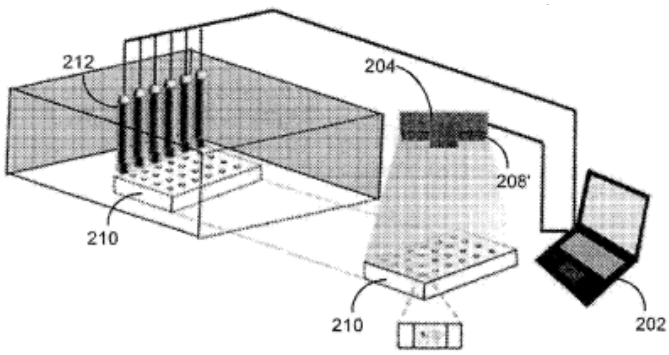
Application

A novel behavior apparatus for the study and monitoring of drosophila and other similar small invertebrates

Key Benefits

- Increased survival and longevity of flies due to increased food availability
- Increased recording capability by a factor of three (3x)
- Ability to pair with bioluminescence plate reader for paired real-time readout of neuronal activity or transcriptional activity

Innovation



Drosophila melanogaster - the fruit fly - continues to be one of the most commonly used animal models for biomedical research due to their low cost, rapid generation time, and the ample array of genetic tools available. To capture changes in *Drosophila* activity, researchers rely on a *Drosophila* activity monitor (DAM). Our innovative DAM revolutionizes fly research. Unlike the current DAM options, it eliminates blind spots, capturing even tiny movements with precise timing over an extended period of time. Remarkably affordable, our option employs a standard 96-well plate for effortless fly loading, saving time and labor. In contrast to standard use DAM tubes that quickly dry out and compromise fly health, our 96-well plate approach sustains flies for weeks with generous food supply (300ul per well). Step into the future of fly research with our cutting-edge system, unlocking new insights and discoveries in *Drosophila* studies.

Technical Overview

Our new and improved DAM system introduces a cutting-edge high-throughput video recording system with optogenetic stimulation capabilities allowing for both visualization and modulation of *Drosophila* activity. Flies are loaded into standard 96-well plates containing food, while their locomotor behavior is meticulously tracked. A symmetrical pair of LEDs emitting a specific wavelength enables precise optogenetic stimulation, offering control over timing, frequency and intensity via an Arduino Uno Board or Raspberry Pi. The system seamlessly integrates with a bioluminescence plate reader utilizing luciferase as a reporter, facilitating measurements of neuronal or transcriptional activity. This versatile invention allows stimulation and recording of neuronal activity within distinct neurons while correlating manipulations with changes in behavior. With long-lasting operational capacity, it enables comprehensive measurements of sleep-wake cycles and circadian rhythms. Ideal for neuroscience labs, researchers can efficiently screen genes and neuronal circuits implicated in various behaviors including sleep, courtship and aggression. Moreover, the system serves as a powerful tool for drug screening for disease models, advancing the study of behavior disorders.

Publications

1. Clk post-transcriptional control denoises circadian transcription both temporally and spatially (Lerner et al. 2015). Nature Communications. PMID: 25952406.

Intellectual Property

- US 11,058,093

Tech ID: Brandeis # 1231

Lead Inventor: Michael Rosbash, Nobel Laureate in Physiology or Medicine, Professor of Biology, Howard Hughes Medical Institute Investigator, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/6ad78154-a1bc-4134-a654-396ffac4b624

TRIBE: A Novel Tool for the Analysis of RNA-Binding Proteins (RBP)

Application

Targets of RNA-Binding Proteins Identified by Editing (TRIBE) is intended to be licensed for commercial, enterprise, academic and research use in drug discovery and RNA-protein research

Key Benefits

- No additional reagents necessary requiring 10,000-fold fewer materials; cost-effective
- Streamlined experimental timeline (3 days v. traditional 8 days)
- Low false-positive rate
- Facilitates identification of cell-specific targets from tiny amounts of RNA

Innovation

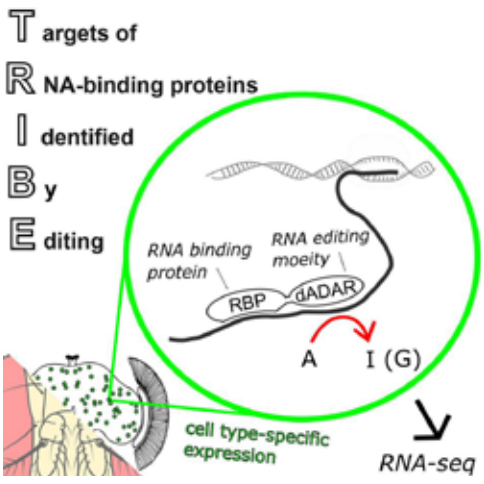
The accurate identification of novel potential drug targets for neurological disorders is a critical focal point for the development of treatments and therapies; however, identifying targets can be laborious resulting in a longer time-to-market. Abnormalities in RNA-Binding proteins (RBP) have been associated with numerous human pathologies: Parkinson's disease (PD), autism spectrum disorders (ASD), and amyotrophic lateral sclerosis (ALS); 10% of human protein-coding genes are RBPs, yet the pathological mechanism and targets for RBPs remain uncharacterized. TRIBE is a genetic tool that identifies *in vivo* targets of RBPs via the fusion of an RBP of interest with the RNA-editing enzyme, ADAR, at the catalytic domain. Targets are marked by novel RNA editing events and easily identifiable via standard sequencing techniques. Requiring significantly less material and not limited to high-affinity antibodies, TRIBE allows researchers to effectively and efficiently analyze targets in a cell-specific manner with greater accuracy and low cost. TRIBE is available for licensing and will help in identifying cell-specific RBP targets via fusion polypeptides.

Technical Overview

The traditional methods to identify RBP targets include immunoprecipitation and its more sophisticated variant, CLIP. However, both techniques have their limitations including the lack of specificity in tissue targets due to post-lysis *in vitro* association with spurious targets, dramatic changes in results with seemingly subtle differences in experimental conditions, and the requirement for a high-affinity specific antibody, respectively. By fusing the RBP of interest to the catalytic domain of ADAR, an RNA-editing enzyme, TRIBE creates novel *in vivo* RNA-edited events that can be easily identifiable via sequencing. TRIBE is positioned to reduce time investment by reducing the amount of biomaterials required and offering more specificity without the cost of a high-affinity antibody. Identification of targets and understanding the mechanisms underlying RBP-RNA interactions will undercover and lead to effective treatments for a variety of neurological diseases.

Publications

- TRIBE: Hijacking an RNA-Editing Enzyme to Identify Cell-Specific Targets of RNA-Binding Proteins (McMahon et al. 2016.) Cell. PMID: 27040499
- Mechanistic implications of enhanced editing by a HyperTRIBE RNA-binding protein (Xu et al. 2018). RNA. PMID: 29127211
- Identification of RNA-binding protein targets with HyperTRIBE (Rahman et al. 2018). Nature Protoc. PMID: 30013039
- Targeted RNA editing: novel tools to study post-transcriptional regulation (Xu et al. 2022). Mol Cell. PMID: 34739873



Intellectual Property:

- US 2023-0045462 | US 11,401,514 | EP 348799

Tech ID: Brandeis # 1306

Lead Inventor: Michael Rosbash, Nobel Laureate in Physiology or Medicine, Professor of Biology, Howard Hughes Medical Institute Investigator, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/6b42fca7-52df-4e32-a11d-8dcbb61cd47d

EZ Amp- Simple DIY Current Measuring Tool

Application

Commercial use in electrical engineering, electrical repair, and installation in commercial, industrial, and residential properties

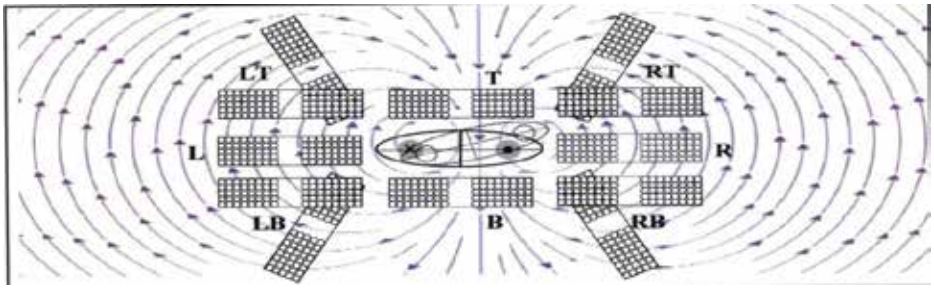
Key Benefits

- Allows for non-intrusive accurate measurement of multi-conductor cables without separating each cable
- Cost effective utilization of a small number of coils with a large number of turns in each coil
- Optimized coil geometry and placement with respect to certain parameters

Innovation

In electrical engineering, a clamp or current-probe device is used for non-intrusive current measurement. It consists of two jaws that clamp around an electrical conductor, enabling current measurement without physical contact or disconnection. An integrated current clamp in an electrical meter is referred to as a clamp meter, clamp-on ammeter, or tong tester. However, conventional clamp meters have limitations, such as the requirement to separate conductors in multi-conductor cables to measure individual currents. This violates electrical installation codes that prohibit cable opening or wire separation. The present invention addresses these limitations by utilizing the magnetic field pattern around a multi-conductor cable to accurately measure AC current using simple and cost-effective components.

Technical Overview



Our innovative technology offers a solution for measuring current in multi-core cables without the need to separate the individual cores. By utilizing an array of magnetic sensors, we can determine the magnetic field pattern surrounding the cable with two, three, or four cores. From this field profile, we compute the current flowing in each conductor. Our current meter design incorporates a small number of coils (one or two) with a high number of turns in each coil, ensuring a robust and reliable signal output. The coil geometry and placement in our current meter can be optimized to achieve a strong, accurately proportional output signal that remains insensitive to small displacements between the cable and the meter. This device and procedure offer an effective means of measuring alternating electric current in multi-conductor cables.

Intellectual Property

- US 8,922,193

Tech ID: Brandeis # 1050

Inventors: Hermann F. Wellenstein, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/878076f3-4d2b-4d79-a3f2-0ad4e022b938

Active Crosslinkers for Chemomechanical Polymers

Application

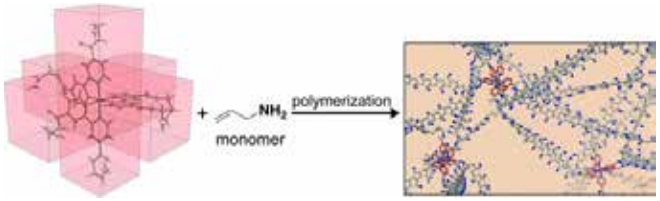
To create shape changing soft materials for tissue engineering

Key Benefits

- Presents a new way to control molecular architecture of polymer with active cross-linkers
- Shape change ability for the stimuli-responsive polymer networks

Innovation

Cross-linking is essential for creating a 3D network in a polymer, either through physical or covalent means. While conventional bifunctional cross-linkers become inactive once covalent crosslinks are formed during polymerization, the cross-linkers in biopolymer networks remain active. For instance, myosin motors in muscle cell cytoskeletons serve as active cross-linkers, binding actin filaments together. Although supramolecular gels incorporating active or functional molecules are increasingly employed, such as in self-healing soft materials, the generation of synthetic polymeric gels with active cross-linkers has yet to be achieved. This technology relates to the design and synthesis of active cross-linkers for creating a novel type of active soft material, in which the material properties are controlled by the active cross-linkers of the polymer network.



Technical Overview

This invention provides 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 changes of the polymer networks that act as the component of soft materials. By successfully designing and synthesizing the first octahedral ruthenium bipyridine complex with six polymerizable vinyl groups as active cross-linkers, the inventors have introduced a novel approach to controlling molecular architecture in active materials. In this approach, the active hyper-cross-linkers within the polymer network dictate the material's properties. This breakthrough suggests that utilizing an active catalyst as the hyper-cross-linker in a polymer network could revolutionize the production of active soft materials. Furthermore, this expands the range of active materials, establishing a foundation for constructing intricate chemomechanical systems or materials by combining opposing components.

Publications

1. Active Crosslinkers that Lead to Active Gels (Zhang, Y et al. 2013). Angewandte. PMID: 24030921.

Intellectual Property

- US 9,920,147 | US 10,519,265

Tech ID: Brandeis # 1140

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/341cffa3-00f8-43e1-ad6e-bfd158402854

Novel Magnetic Nanoparticles Selectively Target Cancer Cells

Application

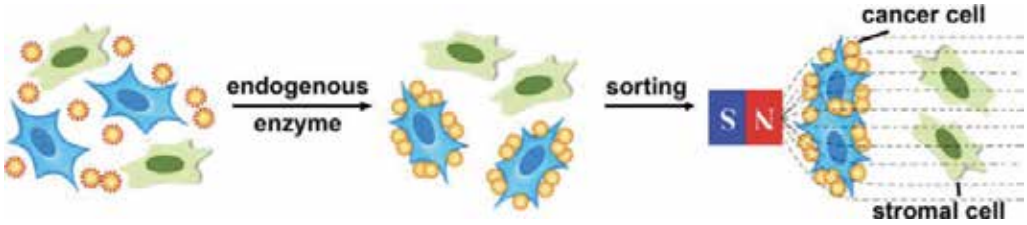
Cell sorting, cell separation, cell imaging, and disease diagnostics and treatment

Key Benefits

- Enzymatically-triggered adhesion of magnetic nanoparticles (MNps) selectively to cancer cells can be utilized in various biomedical applications
- MNps perform better than nanoparticles loaded with cisplatin1 as cancer therapeutics
- Unlike FACS, this invention eliminates the need of labeling cells with fluorescent proteins
- Reducing the cost, increasing product stability and improving cell sorting efficacy
- Does not require expensive set-up or antibodies
- The high selectivity of adherence can generate better cell imaging by enhancing contrast
- Selective adherence of the hydrolyzed MNp is also sufficient to inhibit cancer cell survival

Innovation

Cell sorting has become an important sampling method for isolating specific cells from a mixed population, contributing to many biomedical advances. Unfortunately, sorting mammalian cells requires complicated and expensive instruments and reagents, 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.



Technical Overview

The current invention is a new approach that eliminates both the high cost of FACS and involvement of specific ligand receptor interactions. Designed around the inherent difference between cancer and normal cells, overexpression of ectophosphatases, this method employs magnetic nanoparticles (MNp) that are modified to selectively sort and/or 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. More specifically, 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 the magnetic field.

Publications

1. Enzymatic Transformation of Phosphate Decorated Magnetic Nanoparticles for Selectively Sorting and Inhibiting Cancer Cells (Du et al., 2014). Bioconjugate Chem., PMID: 25431967.

Intellectual Property

- US 10,857,243

Tech ID: Brandeis # 1162

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/09953c8c-7fba-4982-9d1a-c3ab51b68299

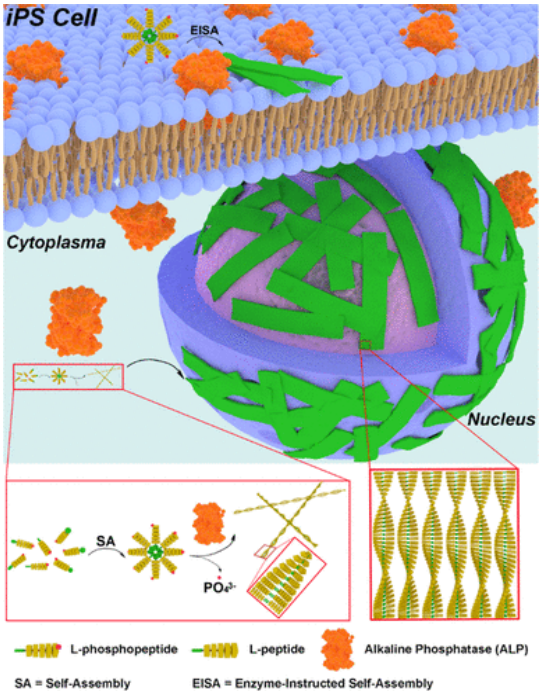
New Biocompatible Small Molecule to Eliminate Undifferentiated Residual iPSCs

Application

In Biopharma and academic labs for selectively eliminating undifferentiated PSCs in cell therapy

Key Benefits

- Selectively targets undifferentiated iPSCs
- One round of treatment emliminates >90% of undifferentiated iPS cells



Innovation

Pluripotent stem cells (PSCs) have the potential to revolutionize personalized medicine by generating a variety of cell types for cell therapy. One major safety concern of iPSCs is their tumorigenicity, or their potential to form tumors. Several studies have shown that even a small number of residual iPSCs can produce teratomas in animals. Considerable efforts have been spent on developing approaches to eliminate residual undifferentiated iPSCs. These approaches include selective ablation, cytotoxic antibodies, lectin-toxin fusion proteins, and magnetic-activated cell sorting. This invention describes a biocompatible small molecule which can kill undifferentiated iPSCs within 2 hours. With further research, the aforementioned technology can be used as a manufacturing tool for processing pure batches of differentiated cell cultures.

Technical Overview

Pluripotent stem cells (PSCs) express much higher levels of alkaline phosphatase (ALP) than normal cells. The designed peptide-conjugated agent used for this purpose is an L-phosphopentapeptide. This peptide can be dephosphorylated by ALP and rapidly form α-helix intranuclear peptide assemblies that selectively kill PSCs. When incubated with human iPSCs, the L-phosphopentapeptide rapidly kills the cells (within 2 hours). The peptide is innocuous to normal cells, such as HS-5 and HEK293, which showed no significant cytotoxicity after 3 hours of incubation. Treating the L-phosphopentapeptide with cell lysate confirmed the proteolysis of the L-peptides.

Publications

1. Enzymatically Forming Intranuclear Peptide Assemblies for Selectively Killing Human Induced Pluripotent Stem Cells (Liu et al. 2021). J. Am. Chem. Soc., PMID: 34528792

Intellectual Property

- WO 2022 271798

Tech ID: Brandeis # 2021-036

Inventors: Bing Xu, Professor of Chemistry, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/214769a1-e23e-44ba-9c8e-df156981e17d

Devices and adaptive technologies that improve accessibility and enable patients to live fuller lives.

Medical Device and Adaptive Technology

Contents

Better Back Brace Design for Treatment of Scoliosis Patients

Application

Commercial medical device manufacturers, practices, hospitals, in the medical industry seeking treatment for young patients with scoliosis

Key Benefits

- Eliminates the long production wait time for obtaining a new, larger device
- Avoids potential damage caused from the use ill-fitted braces or their lack of use
- Adjustable nature reduces overall cost of treatment

Innovation

Scoliosis is a spinal disorder that affects 2-3% of the population, or about 9 million people in the United States. It is more common in young girls than boys, at a rate of 7:1. If left untreated, scoliosis can cause progressive spinal curvature, which can lead to physical deformities and health risks, such as heart and lung problems.

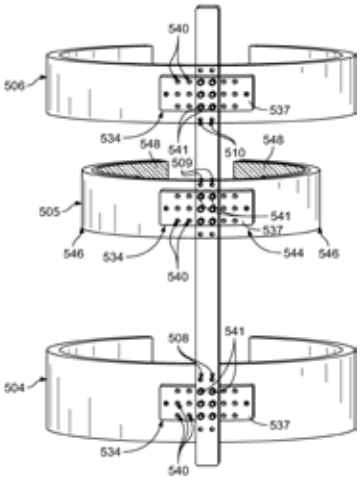
Children with early diagnoses or less severe cases of scoliosis are often recommended to wear back braces. Back braces are designed to stop the progression of curvature and are usually custom-fitted to each patient's body. However, traditional back braces are not adjustable, which can lead to problems as the child grows. If the brace is not properly fitted, it can put unnecessary stress on the spine and worsen the curvature.

The present invention consists of two improved, adjustable back brace designs that can be adjusted throughout the 5-10+ year treatment period. This ensures that the brace remains properly fitted as the child grows, which can help to prevent the progression of scoliosis and improve the patient's overall outcome.

Technical Overview

Our invention is a novel back brace design for scoliosis patients. It consists of two main components: an upper component that tightly conforms to the body around the chest, and a lower component that tightly conforms to the body around the hips. These two components are connected along the back using an adjustable rod. The rod can be adjusted laterally and vertically on both the upper and lower components, 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. In this design, 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 the positioning of these one or two rods. This allows for a better fit during growth over a 5-10+ year period.



Intellectual Property

- US 11,540,934

Tech ID: Brandeis #1349

Inventors: Ingrid Marko

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/22651009-99b9-4a63-bb57-261fc3a77114

WorkingWell: A Support App for Neurodivergent Employees

Application

Commercial and non-commercial businesses looking for support for the employment of neurodivergent employees

Key Benefits

- Enhance job tenure and employee retention, especially among individuals with mental health conditions
- Helps in inducting a portion of the workforce who is currently sitting on the sidelines

Innovation

People with mental health conditions like schizophrenia, bipolar disorder, and major depressive disorder often face employment disparities. However, work can be beneficial by providing routine, social support, and improving self-esteem, independence, and community involvement. Supported employment services have helped these individuals find competitive jobs, but they still face challenges in maintaining employment due to various factors. Unfortunately, on-the-job support is not commonly provided, leaving a gap in support for those who are employed. To address this issue, WorkingWell has been developed for use by autistic individuals with autistic individuals, with relevance for a broader group of neurodivergent users.

Technical Overview

WorkingWell is the result of years of collaborative research with mental health agencies and stakeholders, and was improved based on user feedback. The development process involved researchers, providers, individuals with mental health conditions, and an Expert Advisory Panel of supported employment trainers and providers, along with experienced app designers. The app's design was informed by user experience and underwent iterative usability testing through individual, side-by-side, and focus group methods. The app's principles were based on evidence-based supported employment. Overall, WorkingWell offers accessible and as-needed employment support for neurodivergent individuals and those with mental illnesses. It can be used as a standalone app or integrated into existing employment support frameworks.

Publications

1. Nicholson J et al. “The WorkingWell Mobile Phone App for Individuals With Serious Mental Illnesses: Proof-of-Concept, Mixed-Methods Feasibility Study”. JMIR Mental Health 2018;5(4):e11383. PMID: 30361199

Intellectual Property

- Copyright, software

Tech ID: Brandeis # 2020-008

Inventors: Joanne Nicholson, Professor in the Institute for Behavioral Health, Heller School.

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Link: https://brandeis.flintbox.com/technologies/1387f337-7005-4e6c-8490-02540a7ef1d0

SNAPCAP: Special Needs and Arthritic Practical Swim Cap

Application

Seeking commercialization partners in sports and swimwear equipment or adaptive technologies for individuals with special needs, arthritis, and dexterity issues

Key Benefits

- Able to put on, keep on, and take off a swim cap with minimal musculoskeletal maneuvering.
- Alleviates 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.

Innovation

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 needs 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 as it is put on and taken off. Nevertheless, swim caps are necessary in the sport of swimming and need to be frequently replaced. This is often costly and frustrating.

Technical Overview

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 suggests that they end up constantly ripping and struggling with swim caps because of the process by which they are geared. Given this problem, the inventor has created and developed SNAPCAP, a swim cap that is beneficial and unique in providing a better solution to the existing, costly, and frustrating swim cap. The current SNAPCAP 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 finders 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 prototype has been produced and successfully water tested.

Intellectual Property

- US 10,869,516

Tech ID: Brandeis # 2020-039

Inventors: Rebecka Lauren Sokoloff, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/802f67ad-32ff-4b5d-8220-888e79e63e78

Sclervey: The Non-Invasive, 3D Mapping System for Clear Lens Treatment

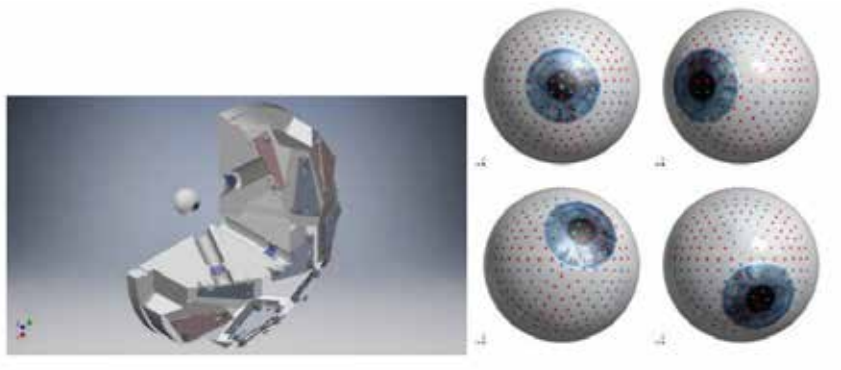
Application

Healthcare/Ophthalmology; Potential application in 3D mapping, vision therapies, prosthetics development, and robotics; Commercial licensing is available for improved scleral lens fitting process used in PROSE treatment

Key Benefits

- Makes PROSE treatment more efficient and cost effective.
- Improves patient experience by reducing the number of fitting sessions

Innovation



Numerous individuals experience intricate corneal disorders that result in severe vision impairment or complete loss of sight. Standard eyeglasses or contact lenses are ineffective in correcting the vision of many affected individuals, as the cornea's surface is no longer smooth. Ophthalmologists have innovated a scleral lens to address the vision challenges faced by patients. However, the fitting process for such lenses currently involves multiple sessions and trial lenses, making it a trial-and-error process. The invention of Sclervey has made the process quicker and more precise. Sclervey surveys the sclera without any contact and maps it to tens of micron precision, providing clinicians and technicians with the necessary data to design custom-fitted lenses that can seal the sclera with high precision.

Technical Overview

Sclervey uses a block containing six LED arrays positioned with the eye at the center of projection to generate a uniform grid of 163 light spots on the surface of the eye. To capture the light spots, six CCD cameras (plus one in the center) are mounted inside a plastic spherical shell. Each dot is visible to two or more cameras, and stereo geometry is utilized to create a 3D surface. The sclera is surveyed in sections where the patient is prompted to look in four directions: straight ahead, right, up left, and down left. At each position, a little over one-third of the sclera is exposed to the projected spots and mapped. The surveyed sections overlap, and neighboring sections are stitched together using image stitching software.

Sclervey's use of stereo imaging and advanced mapping techniques makes the clear lens treatment more efficient, cost-effective, and improves the patient's experience by reducing the number of fitting sessions required. Additionally, Sclervey's non-invasive method eliminates the need for contact with the eye, making the process more comfortable for patients.

Intellectual Property

- US 10,881,293

Tech ID: Brandeis # 1250

Inventors: Hermann Wellenstein, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/0b7b0c6c-cf59-4e58-98cc-30c3525a847a

Functional foods and supplements for heart health, wellness and longevity.

Functional Foods/Dietary Supplements

Contents

Edible Fat Blends for Lowering LDL Cholesterol Levels in Blood

Application

Commercial uses in food manufacturing including margarines, table spreads, cooking oil/fat, shortenings, baked goods, dairy products, fat-containing confectionary goods, mayonnaise and dressings.

Key Benefits

- 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

Innovation

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" cholesterols 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.

Technical Overview

This novel blended dietary fat compositions for food processing contain palm mid-fraction hardstock fat combined with sufficient levels of linoleic acid to enhance lipoprotein metabolism. 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 total cholesterol 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.

Intellectual Property

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

Tech ID: Brandeis # 1017

Inventors: Daniel Perlman, Kenneth C. Hayes, Brandeis University

Contact: Rajnish Kaushik, Director, OTL, 781-736-4220, Rajnish@brandeis.edu

Link: https://brandeis.flintbox.com/technologies/4f326365-dac7-4873-a0ed-500f67ef737c

Palm Fruit Juice Helps Protect DNA Against Drug Damage and Age-related Diseases

Application

Ideal additive for functional foods and beverages, or as a nutraceutical or therapeutic oral supplement, intending to treat or prevent mitochondrial dysfunction, genomic DNA damage, and mtDNA mutations.

Key Benefits

- PFJ can be delivered as a nutraceutical, alone or in conjugation with drug therapies.
- 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)

Innovation

Mitochondrial dysfunction and mitochondrial DNA (mtDNA) damage can occur naturally over time, or be induced by drugs used to treat serious diseases. 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. This permanent side-effect can have a significant impact on the long-term health of patients. Palm fruit juice (PFJ) contains natural polyphenols that can help to treat or prevent mtDNA damage, mitochondrial dysfunction, and genomic DNA mutations caused by aging, disease, and drugs. PFJ is a novel natural product that has the potential to improve the long-term health of patients who are at risk of mitochondrial dysfunction.

Technical Overview

Palm fruit juice (PFJ) is a nutrient-rich by-product of oil extraction from the fruit of the oil palm (Elaeis guineensis), containing antioxidant phenolics and other phytochemicals. Studies have shown that PFJ exhibits a high scavenging activity for hydrogen peroxide, the main reactive oxygen species (ROS) produced by defective mitochondria, resulting in reduced intracellular ROS levels and lower oxidative stress. This, in turn, decreases the number of DNA-associated breaks and mutational events that accumulate during the repair process. Our in vitro experiments, using the human liver carcinoma cell line HepG2, demonstrated that AZT exposure for 30 days resulted in up to a 9-fold increase in mutations compared to normal culture media. However, when PFJ was added in combination with AZT exposure, the number of mutations significantly decreased by 35% compared to AZT alone. Furthermore, PFJ was found to mitigate the cytotoxic effects of AZT after exposure to increasing concentrations over a 6-day period. Similar benefits were observed in reducing drug-induced mtDNA mutational loads by comparing the effects of PFJ on HepG2 cells after exposure to the tuberculosis drug isoniazid (INH).

Publications

1. Osborne et al. (2014) Palm Fruit Juice Mitigates AZT Mitochondrial Genotoxicity and Dose-Dependent Cytotoxicity. J AIDS Clin Res 5: 400.

Intellectual Property

- US 10,813,972
- EP 2953639

Tech ID: Brandeis # 1121

Inventors: Lawrence Wangh, KC Hayes, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/a47512b4-fdb3-4b09-8b97-064a4759587d

Carrot Fiber Pomace: The High-Fiber, Low-Sugar Solution for Diabetes and Weight Loss

Application

In functional food and beverage manufacturing including health and wellness products intended for dieting, weight loss, gut health, blood sugar control and lowering cholesterol levels

Key Benefits

- Abundant and cost-effective ingredient with easy and scalable manufacturing
- All natural, non-GMO, sustainable fiber source that is gluten-free, and digestive well tolerated
- Novel dietary ingredient for reducing blood glucose, cholesterol and triglyceride levels
- Superior blood glucose control and lower incidence of diabetes compared to other dietary fibers
- Supports a healthy gastrointestinal microflora profile
- Promotes a protective gut flora profile relative to controls for developing Type 2 Diabetes

Innovation

Carrot pomace powder (CPP), currently considered a “waste product” of carrot juice production, is an ideal fiber source for use in human and companion animal diets. 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. 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.

Technical Overview

Using our proprietary process, we have found isolated CPP 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. Thus, CPP is a higher balanced fiber source over other options. 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. CPP exerts its effects by beneficially altering carbohydrate uptake and the cecal microflora composition within the gastrointestinal tract.

Intellectual Property

- US 10,596,213
- US 11,464,820

Tech ID: Brandeis # 1186

Inventors: Daniel Perlman, Kenneth C. Hayes, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/c493e1ea-f441-43cb-a1c6-3cbb7fe606a3

PFJ: The New Functional Ingredient for Improved Blood Sugar and Lipid Control

Application

In food, beverage, pharmaceutical, and nutraceutical forms and can be used to treat diabetes mellitus, gestational diabetes, pre-diabetes, and metabolic syndromes

Key Benefits

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

Innovation

Palm Fruit Juice (PFJ) is a cost-effective source of dietary oil palm phenolics (OPP) that are proven to effectively reduce blood glucose and lipid levels when tested in the Nile rat model. This reduced glucose absorption leads to improved insulin sensitivity and enhanced insulin secretion (in vivo). These phenolics were tested in a Phase I clinical trial by the Malaysian Palm Oil Board and showed no ill effects. In terms of taste, OPP has a dark brown color with a sweet yet slightly bitter taste that can be easily masked by a sweetening agent. Thus, it can easily be incorporated as a functional ingredient into foods for humans, pets, and farm animals.

Technical Overview

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. OPP possess anti-hyperglycemic and anti-hyperlipemic properties when provided in the regular diets of animals genetically-prone to developing type II diabetes. Following 12-weeks of consumption, diets supplemented with PFJ lowered fasting blood glucose levels ~5.4 fold in older diabetic animals and resulted in overall levels near those of their non-diabetic controls fed either water or PFJ. 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. 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.

Publications

1. Bolsinger, Julia et al. Anti-diabetic effects of PFJ in the Nile rat (Arvicanthis Niloticus). PMID: 25191613

Intellectual Property

- US 8,071,143
- US 9,326,957
- EP 2288364

Tech ID: Brandeis # 20060802

Inventors: Kenneth Hayes, Professor Emiritus, Department of Biology, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/df6c2155-e36f-407e-9f28-e6e68b8b2f3e

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

Application

Ideal for botanical or nutraceutical dietary supplement use in food, beverage, baked goods, edible goods, capsules, tablets, gels, and personal care (face, hair, skin, bath) products. Also offers a caffeine-alternative to coffee (4g flour ≈ 1 cup of coffee).

Key Benefits

- Milder flavor and odor compared to the strong profile of green coffee beans.
- Mild tan color allows addition to food products without altering the appearance.
- Controlled residual moisture enables rapid flour dispersal of CGA into aqueous mediums
- Benefits over Coffee Cherry flour competitor product:
    - Generally Recognized As Safe (GRAS) ingredient
    - High CGA antioxidant and caffeine content (compared to traditional roasted beans)

Innovation

Green coffee extract, derived from unroasted coffee beans, has gained worldwide attention as a dietary supplement due to its clinically proven health benefits. The antioxidant Chlorogenic acid (CGA) found in green coffee beans can beneficially modulate sugar metabolism and insulin response, lower the risk of cardiovascular disease, cancer, and certain neurodegenerative conditions. However, green coffee beans have an unpleasant flavor and are difficult to mill, necessitating packaging in capsules. Roasting improves the flavor, aroma, and color of coffee beans but unfortunately degrades CGA. Our new method involves partially baking ("par-baking") green coffee beans and milling them into a fine flour that not only preserves CGA and other nutrients but also retains caffeine.

Technical Overview

Our technology offers a new method for processing green coffee beans through partial baking. This method requires lower operational temperatures than conventional roasting, which helps to preserve nutrient levels, including CGA and caffeine, up to 4 times more than conventional roasting (around 8.6-11% w/w CGA). The par-baked beans are also easier to mill, allowing for the production of fine flours with improved chemical stability, limited moisture content, and prolonged shelf life without the need for desiccant. Additionally, the resulting flour has an enhanced flavor and aroma profile and can be easily modified with sugar, high-intensity sweeteners, flavor extracts, and other ingredients.

Intellectual Property

- US 9,210,948
- US 9,936,717
- US 10,278,405
- EP3021684

Tech ID: Brandeis # 1134

Inventors: Daniel Perlam, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/8a85af48-3507-4e13-8fb4-971061dac680

Novel Phytosterol-Glycerine Microparticles for Promoting Heart Health

Application

Versatile food supplement to promote cardiovascular health in a variety of consumer products and dietary consumables such as supplements, processed food and beverages, dairy products, condiments, and health and wellness products

Key Benefits

- Decreased dosage requirement of phytosterols
- Cost-Effective and Shelf-Stable Phytosterol Incorporation
- A fat-free complex of natural (non-esterified) phytosterols and natural glycerine
- Regular consumption reduces risk of developing heart disease by lowering plasma LDL cholesterol levels

Innovation

Phytosterols are naturally occurring water-insoluble molecules commercially isolated from vegetable and tree oils. The use of an edible liquid-crystalline phytosterol complex increases dispersibility and bioavailability of phytosterols whilst reducing dose requirements. This approach is a cost-effective and shelf-stable method for incorporating phytosterols into a variety of products, including dietary supplements, processed foods, and beverages. Both human and animal studies using soft chew dietary supplement formulations demonstrated in vivo efficacy of this complex in lowering LDL cholesterol levels. For aqueous systems, an emulsifier such as monoglyceride can be optionally added during heating to even greater dispersibility. Overall, the edible liquid-crystalline phytosterol complex is a valuable tool for improving the nutritional content and health benefits of a wide range of products.

Technical Overview

Natural phytosterols are plant-based compounds that have been shown to lower cholesterol levels. They are typically extracted from vegetable oils and are hydrophobic, meaning they do not dissolve in water. This makes them difficult to incorporate into foods and beverages.

A new method has been developed to create a more water-soluble form of phytosterols. This method involves mixing phytosterols with glycerine, a natural and edible liquid. The glycerine acts as a spacer between the phytosterol molecules, which prevents them from crystallizing. This results in a more dispersible form of phytosterols that can be easily incorporated into foods and beverages.

The new phytosterol complex has been shown to be effective in lowering cholesterol levels in both human and animal studies. It is a promising new approach for improving the health benefits of foods and beverages.

Patent Information

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

Tech ID: Brandeis # 1138

Inventors: Daniel Perlman, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/760633c6-8eef-45b7-a518-d4849bf24a82

Novel Glass Wine Bottle Having a Dripless Lip Design

Application

Commercial and manufacturing use in glass bottle production for consumer products such as wine, condiments, sodas, liquor, cosmetics, and preservatives

Key Benefits

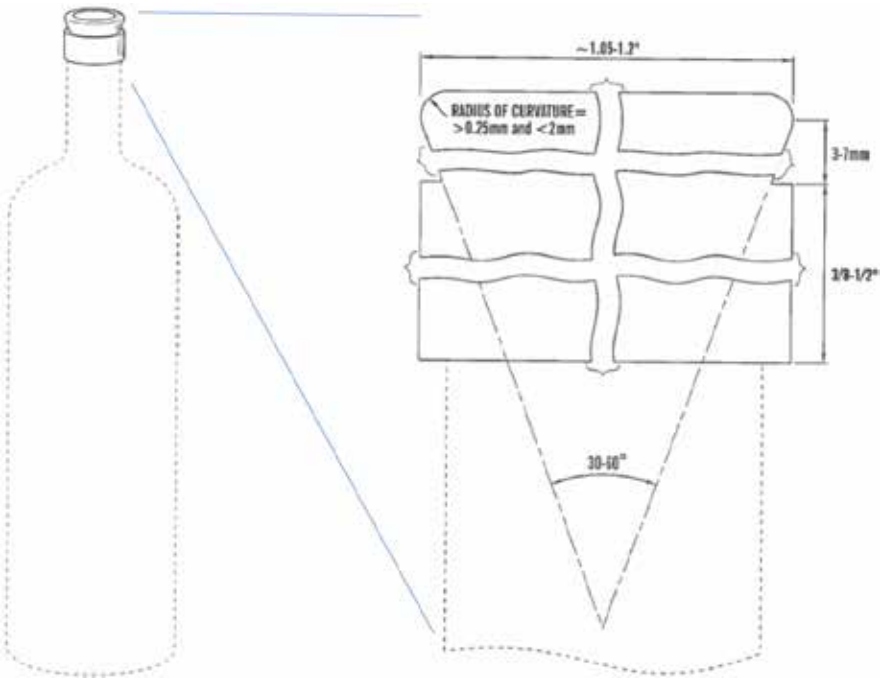
- Significantly decreases droplet formation and allows for drip-free pouring without use of additional extraneous devices.

Innovation

Introducing the revolutionary Drip-Free Pour Glass Bottle! We've taken liquid pouring to the next level with an innovative design that guarantees a seamless and mess-free experience. The glass bottle has been configured to optimize the mechanics of liquid flow, eliminating the hassle of drip initiation. It's engineered to prevent dripping at any pouring angle, ensuring a flawless pour every time, regardless of the amount of liquid held in the bottle.

Technical Overview

In this design, the glass bottle has a lip with a small opening at the end of the bottle. The lip also has an acute included angle that creates a seal around the opening of the bottle. The drip-free pouring method described above has several benefits. First, it prevents messes and makes it easier to pour liquids without dripping. Second, it can help to improve the appearance of the bottle and make it more aesthetically pleasing. Third, it can help to extend the life of the bottle by preventing the liquid from dripping onto the neck of the bottle and causing damage.



Patent Information

- US D947030S1

Tech ID: Brandeis # 1170

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Link: https://brandeis.flintbox.com/technologies/3adc61d2-15f5-41df-95c1-f98bcbf3e4e1

Beneficially Stabilized Probiotics in Fat-Containing Spreads

Application

Functional food supplement for delivering probiotics in a non-dairy alternative

Key Benefits

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

Innovation

Probiotics are increasingly sought after by health-conscious consumers, providing a range of benefits such as reducing bloating, improving bowel regularity, and enhancing nutrient absorption, among others. However, limited shelf life due to the viability of health-promoting bacteria in most food products is a major impediment to industry growth. Despite this, increased awareness and consumer preferences have led to the growth of the probiotic food industry.

To address this challenge, we have developed a technology that enables faster and cheaper manufacturing of low water activity fat-containing probiotic spreads and butters made from nuts, seeds, and beans. Our technology significantly improves the long-term survival of microorganisms over a 12-month period, extending the shelf life of these products without refrigeration. Additionally, our technology ensures long-term uniform physical distribution of probiotic particles throughout the product, which has been demonstrated to remain stable during room temperature storage, eliminating the need for refrigeration during shipping, storage, and sale.

Technical Overview

Our innovative manufacturing methods produce healthy spreads using anhydrous probiotic bacterial blends and low water activity fat-containing foods made from nuts, seeds, or beans, such as peanuts, hazelnuts, almonds, chia seeds, soybeans, and sesame seeds. We blend an anhydrous probiotic bacterial slurry in vegetable oil into a warm nut/seed/bean spread just before adding the structuring fat and packaging. This step ensures bacterial survival of 75-100% for products stored at room temperature for up to 12 months. Eliminating cold storage throughout the value chain benefits both consumers and sales, reducing costs for retailers and manufacturers and improving convenience for consumers who may find it difficult to spread cold butters.

To demonstrate the long-term viability of probiotic bacteria, we measured 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. Our tests showed that the probiotic bacteria remained viable over a 12-month period, providing approx. 109 CFU per serving of a 16 oz. jar of peanut butter containing 14 servings.

Intellectual Property

- US 10,532,076

Tech ID: Brandeis # 1176

Inventors: Daniel Perlman

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Link: https://brandeis.flintbox.com/technologies/e3d8a7e3-17ab-4a30-8d30-37ef837214cf

The Dripless Wine Bottle: The End of Wine Stains

Application

Glass storage bottles for which drip-free pouring of valuable liquids is desirable, such as wine, scotches, whiskeys, vinegars, olive oils, liquid pharmaceuticals, strong acids/bases, and other caustic liquids

Key Benefits

- 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

Innovation

The longstanding problem of wine dripping down the bottle's side after being poured is a common annoyance among connoisseurs, restaurateurs, and the common consumer. 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. The overall result is a novel design that holds onto the last droplet of wine, providing a more controlled and precise pouring experience.

Technical Overview

Our license details the use of an innovative design for the neck of wine bottles that solves the dripping problem. By exploiting capillary adhesion against capillary flow (of a liquid droplet), 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 flow guide is positioned to retain that last droplet directly above an abutting ~2mm wide and ~1mm deep circumferential channel, i.e., groove, that blocks the droplet of wine 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. These modifications can be made towards conventional wine glass bottles without compromising their strength or internal architecture. This offers simple, easy implementation within current manufacturing processes.

Publications

1. Video of pouring from drip-free bottles

Intellectual Property

- US 10,239,672 B2 | EP 3458372

Tech ID: Brandeis # 1300

Inventors: Daniel Perlman, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/4293723e-d051-410d-b462-c2b3d1a8d245

Anti-Rolling Glass Bottle

Application

Glass mold design bottles that feature anti-rolling feature to prevent movement allow for easy storage of bottles.

Key Benefits

- Facilitates the storage and stacking of glass bottles.
- Easy-to-implement design for existing bottle mold tooling.
- Minimal work required to incorporate in the manufacturing process.

Innovation

The body portion of a typical glass wine bottle is generally cylindrical in shape. For wine bottle stability on the shelf, space efficient storage, and for maintaining maximum moisture in cork closures, wine bottles are often stored on their sides. Unfortunately, unless confined by physical barriers, horizontally stored bottles are susceptible to accidentally rolling from a shelf and breaking. Additionally, if bottles are allowed to roll, stacking and storage in multiple layers becomes challenging. The present invention features a molded glass wine bottle that appears remarkably similar to a conventional bottle but additionally, it features a series of small regularly spaced protrusions or bumpers around the bottle's circumference on an otherwise smooth wall surface.

Technical Overview

A typical 750 ml capacity wine bottle may include, for example, nine bumpers spaced apart at about 1-inch intervals. These bumpers can be positioned on the body of the bottle at a similar distance (e.g. 1.0 - 1.5 inches) from the base of the wine bottle and/or from the shoulder of the wine bottle. The anti-rolling feature of this invention is conveniently integrated by molding directly into the wine bottle's structure. By comparison, most of the prior art devices that prevent bottle rolling are accessory devices that are less convenient, requiring separate purchase and/or addition to the bottle after the manufacturing process. Additionally, this invention leaves the essential shape of the original wine bottle intact with an addition of only about 1% to the amount of glass used to form the bottle.

Patent Information: US 18/224,858

Tech ID: Brandeis # 2022-046

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Link: https://brandeis.flintbox.com/technologies/eed8ab2b-52e8-402c-a02e-0ceda5f0925b

Data science and machine learning tools for use in business, IT management, education, food science and more.

Data Analytics

Contents

Predictive Model for Food Safety

Application

Predicting the evolution of microbial populations over time, offering valuable benefits for improving food shelf life safety analysis

Key Benefits

- Analyzes microbial population changes linked to biochemical factors.
- Forecasts food shelf life and microbial growth cycles on surfaces or foods.
- Predicts the temporal evolution of specific microbial populations.

Innovation

This invention offers a predictive modeling approach to enhance food safety and extend shelf life. The method involves a quasi-chemical mathematical model to predict microorganism population dynamics, enabling safer food product formulation and processing conditions. The model takes into account intrinsic factors like pH, water activity, salinity, and anti-microbial constituents, as well as extrinsic factors such as storage temperature, relative humidity, ambient pressure, and processing conditions that influence bacterial growth and decline in food products. Existing prediction models for analyzing bacterial population dynamics rely on equations derived from theories used to study human and animal population dynamics. However, these models utilize parameters like per capita birth rate and sustainable population, which are unsuitable for describing the growth and death of unicellular microorganisms. Consequently, the current prediction models lack criteria that appropriately assess microbial growth and death based on the underlying biochemical and biological principles. This invention addresses the biochemical reasons underlying changes in microbial population dynamics.

Technical Overview

In our pursuit of predicting optimal modeling conditions, we conducted a comprehensive analysis of how bacteria populations respond to various factors affecting food products. The study considered both intrinsic factors, such as pH, water activity, salinity, and the presence of anti-microbial constituents within the food, and extrinsic factors encompassing environmental properties like storage temperature, relative humidity, ambient pressure, and applied processing conditions. These factors collectively influence the survivability of microorganisms.

This technology addresses the biochemical foundations underlying changes in microbial population dynamics. The Quasi-chemical model is a mechanistic-based mathematical approach that employs sequences of chemical reactions and biochemical processes to accurately and meaningfully represent the molecular mechanisms governing bacterial anabolism, catabolism, cellular signaling (e.g., quorum sensing), and lethality, resulting in growth-death behavior. This model offers significant advantages over anthropomorphic models employed by earlier investigators or other empirical models currently in use. In the realm of predictive microbiology, these models serve as invaluable tools for food technologists and non-mathematical experts, enabling the assessment of microorganism survivability concerning food formulations designed to control growth or process conditions intended to limit or eradicate pathogenic bacterial populations at their origin. The data characteristic of bacterial population dynamics are collected, characterized, and quantitatively represented through mathematical models or equations.

Publications

1. Chemical Kinetics for Microbial Safety of Foods Treated with High Pressure Processing or Hurdles (Doona et al. 2016). Food Engineering Reviews. DOI: 10.1007/s12393-015-9138-7

Intellectual Property:

- US 10,437,909

Tech ID: Brandeis # 1239

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Link: https://brandeis.flintbox.com/technologies/56c4f1e7-9044-4b47-8e95-c8b6470d7185

Relational Coordination Survey: A Tool to Enhance Work Productivity

Application

Assessing the interrelationship within the group and among different groups for quality improvement

Key Benefits

- The survey's 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.
- The tool can be customized to any work process, from small co-located teams to large complex multi-level systems, and administered via a web link and generally takes 10 to 20 minutes to complete.

Innovation

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. Relational coordination is communicating and relating for the purpose of task integration. The RC Survey 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.

Technical Overview

The RC Survey tool is a highly effective and extensively validated network measurement tool, specifically designed to enhance coordination within organizations. It incorporates a comprehensive set of seven carefully crafted questions, strategically aligned with the theory of relational coordination. This tool has demonstrated remarkable success across diverse industries and sectors on a global scale.

Moreover, the Relational Model of Organizational Change provides invaluable insights into fostering improved coordination by empowering stakeholders to design targeted interventions. This model emphasizes the importance of addressing structural, relational, and work process factors, enabling organizations to optimize their collaborative efforts and achieve enhanced effectiveness in their work.

Publications

1. Gittell, J. H. et al., (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.
2. Gittell, J.H., Ali, H.N. (2021). Relational Analytics: Guidelines for Analysis and Action. Routledge.

Intellectual Property

- Copyright

Tech ID: Brandeis # 1141

Inventors: Jody Hoffer Gittell, Professor at Heller School, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/b9e4b2ac-fa05-4219-97e8-0f6679f2d523

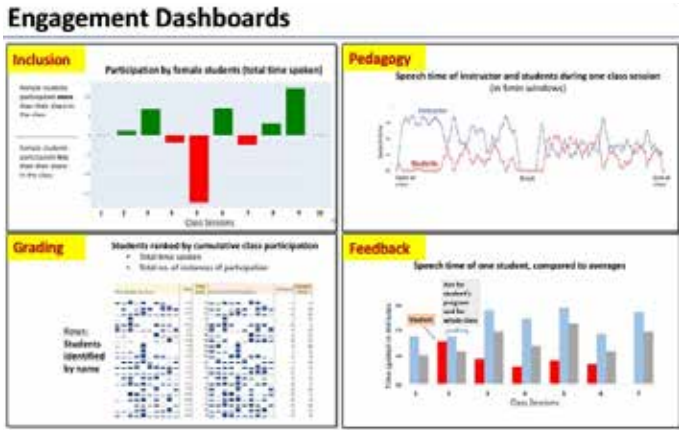
BOCA: A Novel Method for Analyzing Human Interaction in Online Meetings

Application

- Suitable for use in virtual and distributed meeting environments across multiple industries
- Can be used for a range of educational and corporate processes, including meetings, training sessions, and presentations

Key Benefits

- Enhancing Engagement in Virtual Meetings and Courses
- Customized Assessments and Reports for Individuals and Groups
- Comprehensive Overview of Participation, including Time Allocation by Participant Type
- Detailed Demographic Analysis of Participation



Innovation

The COVID-19 pandemic has led to a surge in virtual meeting platform usage, creating challenges in effectively managing participant engagement. This invention provides a solution by utilizing recordings and measurements to automatically and comprehensively evaluate participant engagement. With informative outputs and feedback, this technology empowers management to improve engagement, evaluate performance, and manage participation patterns. Ultimately, this supports both educational and corporate goals by enhancing virtual meeting management.

Technical Overview

The system generates detailed reports on individuals and groups by combining extracted information with past meeting data. These reports cover engagement trends, demographic participation rates, and average speech and interaction times for both individuals and groups. Participant effectiveness indicators, such as audio and video communications, are also included in the reports.

The system also utilizes demographic databases, such as those from an educational institution registration database, to provide a deeper understanding of participation patterns. Ultimately, this invention provides a valuable tool for managing virtual meetings, allowing for more effective monitoring and evaluation of participant engagement and overall meeting effectiveness.

Publications

1. Gomes-Casseres, B et al. You May Think Your Online Class Discussions Are Lively and Balanced—But Are They, Really? Harvard Business Publishing, Apr 2023.

Intellectual Property

- WO 2022/192720

Tech ID: Brandeis #2021-004

Inventors: Professors Benjamin Gomes-Casseres (*Business*) & Pito Salas (*Computer Science*)

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Link: https://brandeis.flintbox.com/technologies/20e6c759-dfd5-460d-91d1-26649dea5a26

Composite-Cut: The Machine Learning Approach to FDR Control

Application

Perform multi-comparison correction when analyzing high-dimensional datasets across various fields: biotech, healthcare, pharmaceuticals, finance, and retail

Key Benefits

- Applicable in biotech, healthcare, pharmaceutical, and finance fields.
- Improves analysis of high-dimensional data and detection of subtle yet meaningful changes.

Innovation

The invention introduces a novel approach for controlling the false discovery rate (FDR) when identifying significant features in high-dimensional datasets, such as genome-wide datasets. Unlike conventional methods that use a single type of statistical hypothesis test, this approach combines multiple statistical tests into a composite index. By formulating FDR control as a machine learning problem, it maximizes the benefits of different statistical tests. The algorithm, Composite-Cut, is developed based on this concept, providing a practical implementation of the approach. Composite-Cut is an innovative method that maximizes the utilization of differential information by integrating multiple base statistics into a composite index. This enhanced approach excels at detecting differential features, especially those with subtle signals. By delving deeper into the data and being more sensitive to subtle yet statistically significant evidence while mitigating the effects of noise, Composite-Cut offers valuable insights, discoveries, and knowledge in practical applications.

Technical Overview

Composite-Cut incorporates multiple base statistics into its Composite-Index, maximizing the utilization of differential information and significantly enhancing its ability to detect differential features, especially those with subtle signals. Comprehensive comparisons on various datasets, including simulated datasets, DNA Microarray datasets, and RNA-seq gene expression datasets, demonstrate that Composite-Cut outperforms a range of existing approaches, such as the Benjamin-Hochberg approach, the Storey approach, Significance Analysis of Microarrays, voom, limma, DSeq/DSeq2, PossionSeq, edgeR, NBPSeq, EBSeq, baySeq, ShrinkSeq, and others. Supplementary analyses, including literature search, gene ontology enrichment analysis, gene set enrichment analysis, survival analysis, dependency analysis, and classification analysis, further validate the results.

Literary evidence confirms the relevance of genes identified as significant exclusively by Composite-Cut to the underlying biology. Additionally, Composite-Cut exhibits the capability to delve deeper into data, displaying increased sensitivity to subtle yet statistically significant evidence while mitigating noise effects. Experimental results also support Composite-Cut's ability to identify relatively more subtle changes, such as features with small fold-changes, which can have significant downstream effects due to systematic aggregation and propagation in complex systems.

Publications

1. Robust differential expression analysis by learning discriminant boundary in multi-dimensional space of statistical attributes. (Bei & Hong 2016). BMC Bioinformatics. PMID: 27993137.

Intellectual Property

- US 11,055,304

Tech ID: Brandeis # 1159

Lead Inventor: Pengyu Hong, Professor of Computer Science, Brandeis University

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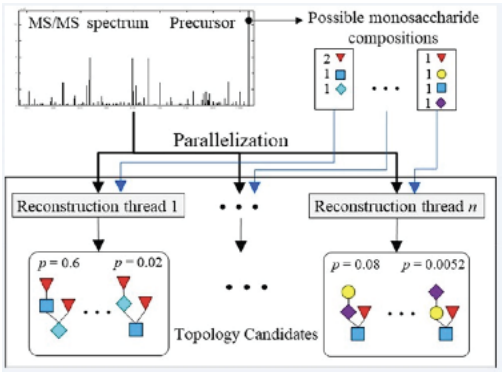
Link: https://brandeis.flintbox.com/technologies/7037bf9e-af96-4c42-ae3c-43d75ae368bd

GlycodeNovo: The Machine Learning Solution for Glycosylation Topologies

Application

A modeling method for the design of glycan structures de novo



Key Benefits

- Uses machine learning to learn fragmentation rules/patterns and distinguish different fragmentation ions in mass spec data, improving topology candidate ranking.
- Significantly lower computational complexity compared to existing methods, resulting in faster and more efficient computation.
- Cost-effective method for indexing long-lived snapshots in parallel with their creation.
- Utilizes append-only index data structures for efficient writes and low-latency snapshot lookup.

Innovation

Glycosylation is a common modification involving the covalent attachment of glycans (or oligosaccharides) to biomolecules like proteins and lipids. It plays vital roles in various biological processes, including protein folding, cell adhesion, and immunological responses. Moreover, glycosylation significantly affects the solubility, stability, and efficacy of biopharmaceuticals. Identifying glycan structures is crucial to understanding their biological functions, but it's challenging due to the vast number of possible topologies, even for moderately sized glycans. Existing tools for topology determination, like mass spectrometry-based catalog-library approaches and brute-force search methods, have limitations that restrict their application to only a few glycans. Currently, there is a need for a reconstruction method with reduced computational complexity that doesn't rely solely on a database of known glycans.

Technical Overview

This invention addresses the limitations by introducing systems and methods for a de novo approach to reconstruct glycan topologies from experimental MS data. The de novo method builds an interpretation-graph in a bottom-up manner, considering non-precursor peaks as B or C ions and specifying their interpretations by appending preceding B and/or C ions to monosaccharides. Additionally, it incorporates machine learning to learn fragmentation patterns and aid in selecting the correct glycan topology from a set of proposed structures. The method has been enhanced in GlycodeNovo.v2, offering further improvements. Firstly, precursor mass measurements for glycan-related peaks help determine potential compositions, narrowing the search space and expediting topology reconstruction. Secondly, a procedure to calculate the empirical p-value of a reconstructed topology candidate has been developed.

Publications

1. GlycoDeNovo2: An Improved MS/MS-Based *De Novo* Glycan Topology Reconstruction Algorithm (Chen et al. 2022). Journal of the American Society for Mass Spectrometry. PMID: 35157458
2. Toward Automatic and Comprehensive Glycan Characterization by Online PGC-LC-EED MS/MS (Wei et al. 2020). Analytical Chemistry. PMID: 31829560
3. De Novo Glycan Sequencing by Electronic Excitation Dissociation and Fixed-Charge Derivatization (Tang et al. 2018). Analytical Chemistry. PMID: 29443510
4. GlycoDeNovo - an Efficient Algorithm for Accurate *de novo* Glycan Topology Reconstruction from Tandem Mass Spectra (Hong et al. 2017). Journal of the American Society for Mass Spectrometry. PMID: 28786094

Intellectual Property

- US 11,402,387 I WO 2023/130045

Tech ID: Brandeis # 2017-051 & 2022-003

Lead Inventor: Pengyu Hong, Professor of Computer Science, Brandeis University; Cheng Lin, Boston University

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Link: https://brandeis.flintbox.com/technologies/cc6a3938-b5ea-4a42-8609-b5360f02c348

OptMark - A Tool for Assessing Query Optimizers

Application

Evaluation of the quality of query optimizers, ensuring database systems are using the most efficient query optimizer

Key Benefits

- First toolkit to separate system component assessment for easy comparison of different optimizers.
- Enables comparison of various optimizer versions within the same data management system and across different systems.
- Minimally invasive to the utilized database management system.

Innovation

Query optimizers, as complex components of a database management system, are tasked with efficiently processing user queries. However, current performance assessment methods for database engines only evaluate the query run-time system rather than the query optimizer itself, lacking tools for optimizer quality evaluation. To overcome this challenge, Brandeis University researchers have introduced OptMark, a system designed to profile and assess the query optimizer's quality.

Technical Overview

OptMark is an advanced toolkit designed to assess the quality of a query optimizer in a comprehensive manner, completely independent of other components within the database management system. This unique toolkit employs two main strategies to achieve its goal:

1. Decoupling Optimizer Quality: OptMark skillfully separates the quality assessment of a query optimizer from the quality evaluation of its underlying execution engine. By doing so, it ensures that the focus remains solely on the optimizer's performance, enabling accurate and unbiased measurements.
2. Evaluating Effectiveness and Efficacy: OptMark performs two independent evaluations to gauge the effectiveness and efficacy of the query optimizer.
    a. Effectiveness Evaluation: OptMark calculates the relative performance factor by generating alternative plans, measuring their execution times, and comparing them to the chosen optimizer plan. This factor gauges how well the optimizer's selected plan compares to alternatives..
    b. Efficacy Evaluation: OptMark reports three essential metrics - the absolute performance factor, the relative performance factor (mentioned earlier), and the optimality frequency. The absolute performance factor measures the optimizer's performance compared to the best possible plan for a given query, while the optimality frequency indicates how often the optimizer selects an identical plan to the best possible one.

OptMark utilizes query hints for the query optimizer's plan selection, but verifying the executed plan against the hint-based query before execution is challenging, especially with large workloads. OptMark aims to develop a general approach to independently verify execution plans against query hints for any database management system. By generating and executing sample plans, OptMark reports both relative and absolute performance factors for a given query, enhancing understanding and improving query optimization in various data management systems.

Publications

1. OptMark: A Toolkit for Benchmarking Query Optimizers (Li et al. 2016). Association for Computing Machinery (ACM) 25th International Conference on Information and Knowledge Management (CIKM). DOI: 10.1145/2983323.2983658

Intellectual Property:

- US 11,327,967

Tech ID: Brandeis # 1346

Lead Inventor: Olga Papaemmanouil, Professor of Computer Science, Brandeis University

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Link: https://brandeis.flintbox.com/technologies/dcf4fa4c-8561-44e7-afa1-895ab1ef485d

Skippy: Enabled Long-Lived Snapshots of the Long-Lived Past

Application

Broad indexing method for long-lived snapshots not limited to specific types of storage systems

Key Benefits

- Cost-effective method for indexing long-lived snapshots concurrently with their creation.
- Utilizes append-only index data structures for efficient writes and low-latency snapshot lookup.
- Performance evaluations demonstrate the effectiveness and efficiency of Skippy.
- Allows nearly optimal access with minimal impact on the current-state storage system.

Innovation

Decreasing disk costs make it possible to take frequent snapshots of past storage system states and retain them for a long duration. Long-lived snapshots are important because, if the past is any predictor of the future, a longer-time prediction needs a longer-lived past. 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. As disk costs decrease, frequent snapshots of past storage system states can now be taken and retained for an extended period. However, efficiently accessing long-lived split snapshots without burdening the storage system remains an unsolved problem. Existing techniques for versioned past data rely on a "no-overwrite" update approach, but they mainly support short-lived snapshots. Therefore, a new access method is required for split snapshot systems that also accommodates 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.

Technical Overview

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.

Publications

1. Skippy: a New Indexing Method for Long-Lived Snapshots in the Storage Manager (Shaull et al. 2008). Association for Computing Machinery (ACM) Special Interest Group on Management of Data (SIGMOD) Conference. Vancouver, Canada. DOI: 10.1145/1376616

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