Taurine Boosts Intracellular Delivery of Functional Molecules

**Patent Title:** Synthetic peptides and enzymatic formation of intracellular hydrogels

**Inventor(s):** Xuewen Du, Jie Zhou, Bing Xu

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**Contact:** Sadie E. Knight  
Technology Licensing Associate  
Office of Technology Licensing  
Brandeis University  
415 South Street  
Waltham, MA 02453  
knightse@brandeis.edu  
+1 781.736.2172

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**Summary:**

- The hydrogel precursors are comprised of D-peptides, covalently bound to taurine via an enzymatically cleavable linking moiety.
- Taurine-promoted cellular uptake of the hydrogel precursor leads to intracellular enzyme instructed self-assembly and accumulation of nanofibril assemblies via hydrolysis of the linking moiety by endoenzymes.
- The intracellular self-assembly occurs selectively in cancer cells overexpressing endoenzymes and is contemplated for cancer treatment.
- A fluorophore may also be conjugated to allow for intracellular imaging studies.

**Advantages:**

- Covalent conjugation of taurine is a broadly applicable approach to boost the intracellular delivery of bioactive molecular and therapeutic agents.
- The taurine motif ensures transportation and the subsequent intracellular nanofibril formation under enzymatic catalysis can efficiently reduce the molecular diffusion outside of cells, providing a new mechanism that eradicates drug resistance.
- This method avoids the possibility of immune response and toxicity caused by CPPs.
- The natural and non-proteinogenic amino acid, taurine, is widely available, accessible, and its molecular modification facile.

**Background:**

Internalization of functional molecules is the basis for intracellular delivery of therapeutic agents for the treatment and diagnosis of diseases. Unfortunately, the delivery of biologically active molecules into cells is prevented by the non-permeable plasma cell membrane. Cell penetrating proteins (CPPs) are traditionally used to facilitate the cellular uptake of various cargo, but CPPs are limited by their susceptibility to metabolic degradation, dependency on cell lines, and poor cellular compatibility.

The present invention relies on the covalent conjugation of taurine to a D-peptidic hydrogel precursor to overcome the limitations of non-permeable cell membranes and CPPs. Taurine-promoted cellular uptake boosts intracellular delivery by 10X and eliminates immune response, poor stability, and toxicity caused by CPPs. This is a novel strategy for targeted intracellular enzyme instructed self-assembly of hydrogels for cancer treatment and may serve as an effective method to deliver therapeutic agents, genes, proteins, and siRNA through otherwise impervious cellular membranes into targeted cells.

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**Taurine modified D-peptide conjugates significantly enhances cellular uptake of therapeutic molecules for disease diagnosis and treatment**