NATIONAL CANCER INSTITUTE
Technology Transfer Center

Peptide Hydrogels for Rate-Controlled Delivery of Therapeutics

Summary

Scientists at the National Cancer Institute (NCI) have developed a novel delivery platform in which the scaffold of an anionic hydrogel (AcVES3) can be attenuated to deliver therapeutic small molecules, peptides, proteins, nanoparticles, or whole cells. The NCI seeks collaborators and licensees for the development of this technology in various clinical and laboratory applications.

NIH Reference Number

E-188-2017

Product Type

- Therapeutics

Keywords

- Peptide-based Hydrogel, Small Molecule, Peptide, Protein, Nanoparticle, Whole Cell Delivery System, T Cell Enhancer, IL-7, Device, Schneider

Collaboration Opportunity

This invention is available for licensing and co-development.

Contact

- Lauren Nguyen-Antczak
  NCI TTC

  lauren.nguyen-antczak@nih.gov (link sends e-mail)

Description of Technology

Hydrogels represent an attractive controlled drug-delivery system that have been used in various clinical applications, such as: tissue engineering for wound healing, surgical procedures, pain management, cardiology, and oncology. High-water content of hydrogels confers tissue-like physical properties and the crosslinked fibrillar network enables encapsulation of labile small molecule drugs, peptides, proteins, nucleic acids, proteins, nanoparticles, or cells. The porosity of the mesh-like network contributes to enhanced protection and controlled release of therapeutics compared with the rapid clearance and degradation of some proteins observed using conventional drug-delivery methods. Although all hydrogel platforms provide spatial and temporal control over the release of therapeutics, the current standard requires designing a unique hydrogel for a select

therapeutic agent for a specific application. This one therapeutic agent-one gel model adds significant research and regulatory burden.

To address this, researchers at the National Cancer Institute (NCI) developed a novel syringe-injectable/sprayable hydrogel platform that can deliver a variety of different therapeutic agents. This hydrogel can be used to deliver small molecules, peptides, proteins, nucleic acids, nanoparticles, or cells. Further, this hydrogel has been engineered to be compatible with a protein delivery platform invented at the NCI. This tunable combination system enables the release of different kinds of proteins based on the electrostatic interaction between the fusion sequence engineered directly at the amino- or carboxy-terminus of proteins and the anionic fibrillar network of the hydrogel AcVES3. In a proof-of-concept study, NCI researchers have delivered a cytokine protein, IL-7, a therapeutic agent critical for improving T cell development for immunotherapy in cancer, sepsis, and HIV-infected patients. Administration of a single dose of IL-7 encapsulated within AcVES3 was shown to exhibit comparable development of T cell populations compared to soluble IL-7 added every 3 days in vitro and to daily subcutaneous IL-7 injections for greater than 30 days in vivo. Thus, this hydrogel platform can reduce the amount of protein needed to attain desired endpoints and potentially reduce patient burden for targeted therapies.

Furthermore, the AcVES3 platform can be used to culture cells in 2D and 3D environments and deliver these cells as potential therapeutic agents. NCI researchers conducted murine studies to culture and deliver fluorescently labeled human dermal fibroblasts encapsulated in AcVES3-RGDV hydrogel at high cellular concentrations. Stem and cancer cells can be also be grown within the 3D AcVES3 hydrogel environment; instead of the commonly used murine-derived Matrigel reagent and subsequently these cells may be injected in vivo, even into larger scale animal models such as non-human primates. These proof-of-concept studies suggest that the AcVES3 platform can be used to encapsulate an appropriate number of cells of interest over time in vivo for therapeutic applications. Overall, the AcVES3 platform is a promising hydrogel system that is applicable for numerous non-clinical and clinical applications.

Potential Commercial Applications

- Cancer – especially those involving therapeutic whole cells – such as stem cells, T cells, CAR T cells for cancer therapy and/or fibroblasts
- Sepsis – especially when boosting T cell levels is effective
- HIV
- Autoimmune disorders – especially to modulate T cell populations
- Transplantation
- Delivering viruses for gene therapy or oncolytic viruses for cancer therapy

Competitive Advantages

- Rate-controlled release of therapeutic drugs including small molecules, nucleic acids, peptides, proteins, or nanoparticles: therapeutic drugs encapsulated in the anionic hydrogel platform
- Rate-controlled release of therapeutic whole cells: such as stem cells, T cells, CAR T

cells for cancer therapy and/or fibroblasts
- T cell enhancer for in vitro and in clinical setting: stimulating T cells in cultures, essential in adoptive T cell therapy, cancer and HIV-immunotherapy, boosting T cell levels in sepsis patients, and modulating T cell populations in autoimmune diseases
- Delivers locally or systemically a variety of different therapeutic drugs including small molecule, peptides, proteins, nucleic acids, nanoparticles, or cells
- Reduces the amount of drugs or cells needed to attain desirable clinical results
- Reduces the patient burden from multiple injections and travel time to the clinic
- Offers targeted syringe or catheter injectable delivery or sprayable delivery
- Is a tunable delivery platform that can attenuate peptide or protein release rate within hydrogel

Inventor(s)

Joel P. Schneider Ph.D. (NCI), Scott T. Walsh Ph.D. (NCI), Stephen E. Miller Ph.D. (NCI), Yuji Yamada Ph.D. (NCI), Scott K. Durum Ph.D. (NCI), Caroline Andrews DVM, Ph.D. (NCI), Wenqing Li Ph.D. (NCI), Julie Hixon M.S. (NCI), Steven Tau (NCI)

Development Stage
- Pre-clinical (in vivo)

Publications

Yamada Y, et al. Design of a peptide-based electronegative hydrogel for the direct encapsulation, 3D culturing, in vivo syringe-based delivery, and long-term tissue engraftment of cells. [PMID 31448901]

Miller SE, et al. Electrostatically driven guanidinium interaction domains that control hydrogel-mediated protein delivery in vivo. [PMID 31807676]

Patent Status
- **PCT:** PCT Application Number PCT/US2017/066893, Filed 17 Dec 2017

Therapeutic Area
- Cancer/Neoplasm
- Infectious Diseases
- Immune System and Inflammation

Updated
Sunday, September 11, 2022