Polymeric Delivery Platform for Therapeutics

Summary (1024-character limit)
The National Cancer Institute (NCI) seeks licensing and/or co-development research collaborations for a polymeric drug delivery platform that targets scavenger receptor A1 (SR-A1), a receptor highly expressed in macrophages, monocytes, mast cells, dendritic cells (myeloid lineages), and endothelial cells. The platform delivers various immunomodulatory therapeutic cargo including small molecule drugs, therapeutic peptides, and vaccines, to the lymphatic system and myeloid/antigen presenting cell (APC) sub-populations.

NIH Reference Number
E-097-2017

Product Type
• Therapeutics

Keywords
• Drug Delivery, Scavenger Receptor A1, SR-A1, Immunotherapy

Collaboration Opportunity
This invention is available for licensing and co-development.

Contact
• John D. Hewes
  NCI - National Cancer Institute
  240-276-5515
  John.Hewes@nih.gov

Description of Technology
Drug delivery technologies have long claimed the ability to selectively deliver therapeutic cargo to target cells. Despite advances in nanomedicine and drug delivery systems, there are no targeted nanoscale drug delivery technologies on the market. Thus, there is still tremendous potential in improved therapeutic efficacy when targeted drug delivery is achieved.

Investigators at the Nanotechnology Characterization Laboratory at the National Cancer Institute (NCI) developed a drug delivery platform that targets scavenger receptor A1 (SR-A1), a receptor highly expressed in macrophages, monocytes, mast cells, dendritic cells (myeloid lineages), and endothelial cells. The platform is based on the anionic polymer poly (L-lysine succinylated), which contains side chains with pendant carboxylic acids that allow conjugation of small molecule drugs through hydrolysable ester linkages.
bonds and have demonstrated drug release half-lives greater than 10 hours. Peptide therapeutics and vaccine antigens can also be conjugated to the polymer platform. Through such conjugation, improved delivery of peptide vaccines to target macrophages and dendritic cells (antigen presenting cells [APCs]) can be achieved for better vaccine efficacy.

Through this approach, high levels of prodrug will be preferentially distributed to SR-A1 expressing cells, such as myeloid/APC, but also to the entire lymphatic system as a result of SR-A1-mediated endothelial transcytosis. Furthermore, active drug is released in a controlled manner – a milestone not yet achieved with current nanomedicine platforms. There is the potential for numerous applications and products as detailed below.

Recent similar technologies are emtricitabine (HIV nucleoside analog reverse transcriptase inhibitor) and PI-103 (pan-class I PI3K/mTOR inhibitor) prodrug versions of the delivery platform. In support of the platform’s ability to target latent lymphatic HIV reservoirs, the emtricitabine prodrug demonstrated increased active drug concentrations in lymphatic tissues 10-fold over the unformulated drug in a rat model. Several PI3K-Akt-mTOR pathway inhibitors are currently in clinical stage development for treatment of diverse cancers, despite autoimmunity and glucose-insulin axis derangement as common side effects of this drug class. Such adverse events are thought to be due to PI3K-Akt-mTOR pathway inhibition effects on non-target-tissues. In a syngeneic mouse B16 melanoma model, the PI-103 prodrug significantly reduced tumor growth at doses as low as 0.1 mg/kg and increased the targeted-tumor associated macrophage M1 (anti-tumor):M2 (pro-tumor) ratio by ~4 fold. Even 100-fold higher doses (10 mg/kg) were without clinically apparent toxicity! As supported by these various in vitro and in vivo studies, the highly selective SR-A1 targeted macromolecular platform has tremendous potential for both cancer and anti-viral immunotherapies.

Potential Commercial Applications
- Targeted drug delivery of immunomodulatory small molecule drugs, peptide therapeutics, and vaccine antigens
- Cancer therapeutic
- Immunotherapies
- Immunomodulatory therapies
- Vaccines
- Anti-viral therapeutic; anti-viral approaches against infectious diseases (e.g., HIV)
- CNS therapeutic; e.g., brain delivery for neurodegenerative conditions and glioma

Competitive Advantages
- High levels of prodrug preferentially distributed to SR-A1-expressing cells, including myeloid/APC
- Active drug is released slowly in a controlled manner, without burst release, which has not yet been achieved with current nanomedicine platforms
- The prodrug preferentially accumulates in the lymphatic system because of SR-A1-mediated
transcytosis
• Application in a wide range of therapeutics requiring crossing the blood-brain barrier

Inventor(s)
David Michael Stevens (NCI), Stephan Stern (NCI), Scott McNeil (NCI), Marina A. Dobrovolskaia (NCI)

Development Stage
• Pre-clinical (in vivo)

Patent Status

Therapeutic Area
• Cancer/Neoplasm
• Infectious Diseases
• Immune System and Inflammation
• Central Nervous System