Inhibition of endosomal TLR-activation with nucleic acid binding polymers

Value Proposition

Inflammatory and autoimmune diseases are the result of improper activation of the immune system, and can have chronic debilitating effects on quality of life. This inflammation is mediated by pattern recognition receptors (PRRs) that recognize a variety of ligands including bacterial membrane molecules and nucleic-acids. One type of extensively studied PRRs are Toll-like Receptors (TLRs). TLRs are an attractive drug target because the improper activation of TLRs leads to a variety of diseases including systemic lupus erythematosus, bacterial sepsis, multiple sclerosis and rheumatoid arthritis. However, due to redundancy and crosstalk, effective mitigation of a pathogenic inflammatory response is likely to require inactivation of multiple TLRs simultaneously. While many TLR antagonists have been developed, very few are available for clinical use, and most have adverse side effects and limited success in treating inflammatory diseases. Therefore, there is a pressing need for the development of both safe and efficacious TLR inhibitors.

Technology

This technology uses cationic polymers to bind nucleic acids, neutralize nucleic acid-induced endosomal TLRs, and prevent TLR activation. It has been shown that these cationic polymers are capable of simultaneously preventing TLR3 and TLR9 activation in a macrophage cell line. Additionally, the polymers were well tolerated both in-vitro and in-vivo, showing little toxicity. Finally, these polymers were shown to dramatically reduce acute TLR-mediated liver damage in mice sensitized with TLR agonists. As such, this technology has tremendous potential for the treatment of nucleic acid-induced autoimmune and inflammatory responses in a variety of diseases.

Other Applications

- Treatment of thrombic disorders

Advantages

- Specific for nucleic acid-induced TLRs
- Prevents activation of multiple TLRs simultaneously
- Prevents nucleic acid-induced TLR activation without compromising the ability to combat viral infections
- Low toxicity
Publications


Patents

Patent Number: 9,468,650
Title: Inhibition of endosomal TLR-activation with nucleic acid binding polymers
Country: United States of America

Patent Number: 2,774,46010817556.3
Title: INHIBITION OF ENOSOMAL TOLL-LIKE RECEPTOR ACTIVATION INHIBITION OF ENOSOMAL TOLL-LIKE RECEPTOR ACTIVATION
Country: CanadaEurope

Patent Number: 15/291,849
Title: INHIBITION OF ENOSOMAL TOLL-LIKE RECEPTOR ACTIVATION
Country: United States of America