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Immunostimulatory conjugates for targeted delivery as adjuvants

Novel vaccine adjuvants composed of TLR7/TLR8 stimulating compounds conjugated to Hyaluronic Acid (HA) to achieve limited systemic exposure

IP Status: PCT Patent Application Filed; **Application #:** PCT/US2019/039940

A potent adjuvant with limited systemic exposure

This technology encompasses novel vaccine adjuvants with limited systemic exposure. The development of vaccines based on antigen subunits have been plagued by struggles with inducing the necessary T-cell response to confer protection while maintaining minimal toxicity. This technology overcomes these challenges using a two-pronged approach. First, the use of novel agonists for TLR7 and TLR8 trigger a prominent T-cell response. Second, conjugation of these agonists to a biomolecule that is trafficked to lymph nodes elicits focused immunostimulation. The sum product is a covalent conjugate that is "immune silent" until it travels to the lymph node where it is unmasked, leading to potent adjuvantic effects with negligible systemic exposure.

The right molecule delivered to the right place

Due to their ability to stimulate strong T-cell responses, TLR7 and TLR8 agonists have been prime targets for development as adjuvants. Unfortunately, their propensity to diffuse out of the vaccination site and cause systemic exposure and toxicity has been a major drawback. This technology identified novel TLR7/TLR8 stimulating compounds (C2-phenolic imidazoquinoline derivatives) and conjugated them to Hyaluronic Acid (HA) for targeting to lymph nodes. Other technologies have attempted similar lymph node delivery, but the strategies or compounds employed to do so are often incredibly complex. HA as a natural biopolymer is optimal for this purpose, with ideal biodegradability, biocompatibility and an excellent clinical track record. HA also serves to mask the reactive portions of the agonists and the adjuvant remains unreactive until it is delivered to the target lymphoid tissue and unmasked.

Phase of Development

- In vitro and in vivo pre-clinical data (published). In vitro studies showing the agonists alone trigger a Th1 response but the conjugates are immune-silent. In vivo studies showing the conjugates are trafficked to the lymph nodes and have potent adjuvantic activity.

Features & Benefits

- **Facilitates development of subunit-based vaccines:** Stimulation of TLR7 and TLR8 leads to strong T-cell activation that is notoriously challenging to achieve in subunit-based vaccines
- **Potent adjuvant with limited toxicity:** Conjugation of agonists to the natural biopolymer, HA leads to trafficking to the lymph node and renders the compound immune-inert until it reaches its destination and is unmasked.
- **Amenable to customization:** Novel TLR7/8 agonist structure allows for easy covalent conjugation to a variety of molecules, facilitating customization and optimization.

Technology ID
20180330

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Applications

- Vaccine adjuvant
- Basic research on toll-like receptor activation

Researchers

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Publications

Hyaluronic Acid Conjugates of TLR7/8 Agonists for Targeted Delivery to Secondary Lymphoid Tissue
Bioconjugate Chemistry, 2018, 29, 2741−2754

Ready for Licensing

This technology is now available for license! The university is excited to partner with industry to see this innovation reach its potential. Please contact us to share your business' needs and your licensing interests in this technology. The license is for the sale, manufacture or use of products claimed by the patents.