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Adaptive Immune Response Stimulated with TLR8 and Dual TLR7/TLR8 Agonists

Technology No. 20170196

Augments Innate Immune Response

Highly potent and selective TLR8 and dual TLR7/TLR8 agonists can stimulate human adaptive immune response.

- **TLR8 agonist:** 5-(4-Aminobutyl)-N4-butyl-6-methylpyrimidine-2,4-diamine dihydrochloride is a novel potent and highly selective TLR8 agonist.
- **TLR7/TLR8 agonist:** N4-butyl-6-methyl-5-(3-morpholinopropyl) pyrimidine-2,4-diamine is a very potent dual TLR7/TLR8 agonist.

These compounds hold potential as vaccine adjuvants that could augment innate immune response against inflammatory, microbial and/or viral diseases as well as cancer.

Superior Adjuvant Properties

Toll-like receptors (TLRs) play a crucial role in host defense, inflammation, and immune response, and significant efforts have gone into development of potent TLR agonists. Adjuvants help antigens elicit an early, high and long-lasting immune response, allowing more robust responses to vaccines and reducing vaccine production costs. In these newly discovered agonists, potency at TLR7 correlates with IFN-alpha/beta production in human blood, whereas IFN-gamma and TNF-α induction are largely TLR8-dependent. Dual TLR7/TLR8 agonists markedly upregulate CD80 expression in multiple dendritic cell subsets, providing insight into the immunological basis for the superior adjuvantic properties of such innate immune stimuli. This lead compound induces Th1-biasing interferon gamma and IL-12 in human blood cells but does not induce significant levels of IL-1beta, IL-6 or IL-8 (proinflammatory cytokines).

BENEFITS AND FEATURES:

- Stimulate human adaptive immune response
- Vaccine adjuvants could augment innate immune response against inflammatory, microbial and/or viral diseases as well as cancer

- Pure TLR-8 agonists are especially important as vaccines adjuvants for newborns as well as the elderly as their bodies do not mount adequate immune response

APPLICATIONS:

- Vaccine adjuvants against allergic, viral and microbial diseases
- Immunostimulant/immunotherapy against cancer
- Scientific study of how TLR-8 receptors augment immune response; may lead to more efficient therapeutics
- Immunoassays
- Ex vivo experiments

Phase of Development:
In vitro data.
20170196: Compounds generated and tested in vitro for inducing various cytokines
20160410: Lead compound generated and tested *in vitro* for inducing various cytokines

Researchers

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Publications

Identification of High-Potency Human TLR8 and Dual TLR7/TLR8 Agonists in Pyrimidine-2,4-diamines
Journal of Medicinal Chemistry, 2017, 60 (5), pp 2084–2098

Interested in Licensing?

The University relies on industry partners to scale up technologies to large enough production capacity for commercial purposes. The license is available for this technology and would be for the sale, manufacture or use of products claimed by the issued patents. Please contact Kevin Anderson to share your business needs and technical interest in this immune response technology and if you are interested in licensing the technology for further research and development.

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