Small Molecule, TLR-4 Ligands as Immunomodulators

Tech ID: 23140 / UC Case 2013-065-0

BACKGROUND

As part of a comprehensive campaign to screen for effective vaccine adjuvants, 180,000 compounds were tested in a cell-based HTS screen to assess ability to activate NF-kB. Several classes of scaffolds bearing appropriate substitutions were found to stimulate innate immune responses and some of these scaffolds were structurally different from all other known ligands. More interestingly, the structure of one class of scaffolds challenges current dogma regarding what is necessary for efficacy.

TECHNOLOGY DESCRIPTION

UC researchers have validated means of using TLR-4-specific small molecules as immunomodulatory compositions. Strong ligands are useful as vaccine adjuvants, anticancer agents and immune-stimulants; more weakly binding compositions have been substantially validated, in vivo, for inducing tolerance.

APPLICATIONS

Compositions may be useful for the treatment of cancer and infectious diseases. Tolerance inducers may be useful for inflammatory and autoimmune disorders, including but not limited to as toxic shock, multiple sclerosis or diabetes. Those that are not inflammatory of cytokines appear to be useful for inducing tolerant.

ADVANTAGES

• Small molecules are more readily scaled and controlled in drug development (vs. proteins and peptides)

• TLR-4 specificity allows one to modulate the immune response in a more cell-specific manner

• Small molecules easily modified to enable linking to other TLR-agonists for combined drugs

STATE OF DEVELOPMENT

Inventors have confirmed the molecular target in mouse and human models and have generated structure-activity relationships around hits. For some compositions, activity has been confirmed in vivo. Tolerance induction has been tested in nine distinct murine models of autoimmunity and/or inflammation. Additional animal studies and lead optimization are in process.

INTELLECTUAL PROPERTY INFO

Worldwide rights available; Pending patents available under confidentiality.

RELATED MATERIALS

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- Wu CC, et al., Innate immune protection against infectious diseases by pulmonary administration of a phospholipid-conjugated TLR7 ligand. J Innate Immun. 2014;6(3):315-24.
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OTHER INFORMATION

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PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,505,768	11/29/2016	2013-065

OTHER INFORMATION

KEYWORDS

vaccine, vaccination, adjuvant, innate immunity, TLR, Toll-like, cancer, immunomodulation, immomodulatory, immunotherapy, immunotherapeutic, small molecule, Tolerance Inducers

CATEGORIZED AS

- **Medical**
  - Disease: Autoimmune and Inflammation
  - Disease: Cancer
  - Disease: Infectious Diseases
  - New Chemical Entities, Drug Leads
  - Vaccines

RELATED CASES

2013-065-0, 2014-123-0

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