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NOD-2-active carboxamide compounds as vaccine adjuvants

Benzimidazole-thiophene carboxamide compounds with NOD-2 agonist activity as potential vaccine adjuvants.

IP Status: Issued US Patent; **Issued Patent No.** 11,465,998

Applications

- Vaccine adjuvants
- Innate immune signaling research tool

Key Benefits & Differentiators

- **Synergistic effect:** Compounds synergistically enhanced responses to TLR7, TLR8, and TLR5 agonists
- **Reduced reactogenicity:** Compounds did not cause a pro-inflammatory response in human blood-based assays

Technology Overview

Vaccines are important and effective preventive tools against infectious diseases. The efficacy of a vaccine depends not only on its antigen components, which are weakened or inactive parts of a particular organism that trigger an immune response but also on adjuvants. Adjuvants are compounds or substances added to a vaccine to stimulate and enhance the magnitude and durability of the immune response to the antigen components. Adjuvants have several benefits, including reducing the antigen amount per vaccine dose, reducing the number of vaccination sessions, and, at times, extending the half-life of the antigen, thereby indirectly improving its immunogenic power potency. Despite their clear benefits, few adjuvants have been included in vaccines due to safety and tolerability concerns. There is an urgent need for novel compounds with adjuvant properties that are safe and tolerable to improve vaccine efficacy against infectious diseases.

Researchers at the University of Minnesota have identified benzimidazole-thiophene carboxamide compounds with human nucleotide-binding oligomerization domain-2 (NOD-2) agonist activity. Structure-activity relationship (SAR) studies led to the discovery of 4-(2-pentyl-1H-benzo[d]imidazol-1-yl)thiophene-2-carboxamide and 4-(2-hexyl-1H-benzo[d]imidazol-1-yl)thiophene-2-carboxamide as lead compounds with significantly enhanced potency. These compounds induced chemokines and cytokines in a murine macrophage cell line and synergistically enhanced responses to TLR7, TLR8, and TLR5 agonists in a human monocytic cell line. In addition, they did not cause a pro-inflammatory response in human blood-based assays. These results render these compounds attractive candidates for evaluation as vaccine adjuvants and tools to explore innate immune signaling.

Phase of Development

TRL: 3-4
SAR studies identified lead compounds that were subsequently tested in vitro using murine and human

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2019-001

Category
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Researchers

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