

Modulating MD-2-Integrin Interaction for Sepsis Treatment

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ABSTRACT

Researchers at the University of California, Davis have developed a potential therapeutic treatment for sepsis by modulating the interaction between integrins and Myeloid Differentiation factor 2 (MD-2).

FULL DESCRIPTION

Sepsis is responsible for 1 in 5 deaths worldwide and has a mortality rate of around 30% depending on its severity. It occurs when the body suffers a severe chain reaction to an infection which damages major organ groups. The typical treatment for sepsis is nonspecific and may include general antibiotics, administering fluids, and blood pressure medication, all of which treat the symptoms of the disease rather than the biomechanism that is directly responsible. Myeloid Differentiation factor 2 (MD-2) binds to Lipopolysaccharides (LPS) and toll-like receptor 4 (TLR4) to form the LPS-MD-2-TLR4 complex. This complex is involved in TLR4 and MD-2 signaling, which play a role in generating inflammatory responses as well as general immune responses. In addition, the binding between MD-2 and integrins is also crucial for signaling to occur. Despite its clear role in the immune system and inflammation, MD2 has not been studied as a target in drug discovery. There is still an unmet need for novel drugs to treat inflammatory and infectious diseases, particularly in the developing world where they are the most widespread.

Researchers at the University of California Davis have developed a method of modulating the activity of MD-2-integrin interactions as a possible treatment for sepsis. Using molecular docking simulations, several MD-2 mutants were identified that don't interact with integrins and can disrupt the signaling of TLR4 and MD-2, effectively altering the immune response and reducing inflammation throughout the body. This slows the effects of sepsis and is an effective therapeutic treatment. It is possible to administer these mutated MD-2 proteins to modulate MD-2 signaling and inflammation. In addition to sepsis, MD-2 mutants can potentially be used to treat several other inflammatory diseases. This research may influence drug discovery and can be used as a target for drug delivery in the future.

APPLICATIONS

- Treatment for sepsis and other inflammatory diseases
- Modulation of inflammatory response

FEATURES/BENEFITS

- First use of MD-2 targeting for drug discovery

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	2022035611	11/10/2022	2021-678

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OTHER INFORMATION

KEYWORDS

myeloid Differentiation
factor 2 (MD-2), toll-like
receptor 4 (TLR4), sepsis,
inflammation, infectious
disease, new drug lead,
mutagenesis

CATEGORIZED AS

- **Biotechnology**
 - Health
 - Proteomics
- **Medical**
 - Disease: Autoimmune and Inflammation
 - Disease: Infectious Diseases
 - New Chemical Entities, Drug Leads
 - Therapeutics

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