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Lysibodies – A New Class of Chimeric Antibodies for The Treatment of Bacterial Infections

RU 1322

Technology Summary

Antibiotic-resistant bacterial infections are common in both hospital and immunocompromised patients, frequently causing life-threatening problems such as pneumonia and sepsis. These infections are notoriously difficult to treat because existing therapeutic antibodies that target bacterial virulence factors and carbohydrate cell wall have mixed efficacy and poor binding affinity respectively.

Unlike protein-based virulence factors that can rapidly mutate and result in treatment resistance, bacterial cell wall carbohydrates are highly conserved, invariant, ubiquitous and surface exposed, making carbohydrates an attractive antigen for immunotherapy. Bacteriophage lysins and bacterial autolysins are hydrolases that bind to bacterial cell wall carbohydrates with high affinity, an affinity that is similar to that of the Fab domain in IgGs. Lysin and autolysin binding domains are therefore ideal binding partners to these bacterial cell wall carbohydrate antigens.

By fusing the binding domain of a staphylococcal autolysin or phage lysin with the Fc portion of human immunoglobulin IgG, our scientists have engineered and produced fully functional therapeutic opsonic chimeric antibodies ("lysibodies"). These lysibodies have been shown to fix complement and subsequent active phagocytosis of several pathogenic MRSA strains which were able to protect mice in kidney abscess and bacteremia models of MRSA disease. Lysibodies represent a new class of anti-infectives that resolve the long-standing problem of effectively targeting bacterial surface carbohydrates with antibodies. Since phage lysins and autolysins are present in most bacteria, lysibodies may be universally developed for bacterial pathogens.

Application

- Therapeutic antibodies that provide protection from MRSA infections

Advantages

- Bacterial resistance to lysibodies is unlikely since mutations within the binding target necessarily prevent endogenous autolysin function, leading to cell death
- Construction and production methods are broadly applicable to creating lysibodies to treat various opportunistic Gram-positive pathogens, since autolysins bind to carbohydrates with high affinity

Stage of Development

- Lysibodies have been developed and validated in mice model.

Lead Inventors

- Dr. Vincent Fischetti and Assaf Raz

Patent Information

- Patent pending

Reference

- Raz *et al.* 2017. Lysibodies are IgG Fc fusions with lysin binding domains targeting *Staphylococcus aureus* wall carbohydrates for effective phagocytosis. *PNAS* 114(18):4781-4786 DOI: 10.1073/pnas.1619249114
- https://www.rockefeller.edu/news/19180-scientists-engineer-human-germ-hybrid-molecules-attack-drug-resistant-bacteria/

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