Background

Anthrax is an acute infectious disease caused by the spore-forming bacterium *Bacillus anthracis*. *B. anthracis* can cause human disease via the gastrointestinal, cutaneous or inhalational routes. There is still a considerably high rate of mortality from inhalational anthrax of up to 75 percent, even though fluoroquinolone class antibiotics (e.g., ciprofloxacin) are being administered as a first-line therapy. This strategy, in addition, is being threatened by the spread of plasmid-mediated resistance to quinolones (1).

The threat of misusing *B. anthracis* as a biological weapon has led to the assessment of novel pre- and post-infection vaccination strategies. Currently available vaccines provide only weak protection. The US administration once cancelled the most advanced contract for the development of a next-generation vaccine within the BioShield program, obviously due to continuing development difficulties (2). While antibiotics are capable of interfering with the lifecycle of *B. anthracis*, they cannot directly influence its most dangerous aspect: lethal toxin (LeTx). LeTx is a combination of lethal factor (LF) and protective antigen (PA), plays a central role in anthrax pathogenesis, and is a major cause of mortality from anthrax infection.

Technology

Scientists from the Max Planck Institute for Infection Biology in Berlin revealed that human neutrophil alpha-defensins (HNP-1/2/3) are potent inhibitors of LF. They showed that human neutrophil protein HNP-1 protected murine macrophages from *B. anthracis*-induced cytotoxicity in vitro. Even more encouraging, they also found that in vivo treatment with HNPs protected mice against the fatal consequences of anthrax LeTx (3). Alpha-defensins are natural peptides of human origin. Hence, they have a higher potential to be more useful than any known synthetic anthrax therapeutic.

Development and Commercialization Opportunities

A large scale solid-phase synthesis manufacturing protocol has been described for HNPs (4). In the US Biotech companies can receive funds upfront when doing R&D on priority-one pathogens, like anthrax is still listed (2009). Reimbursement of costs is no longer dependent on previous licensure of a product by the FDA. Therefore HNPs provide an compelling opportunity from a scientific, technical as well as from an economic perspective to launch a novel therapeutic, possibly in combination with antibiotics or vaccines to effectively inhibit anthrax-related toxemia.
Patent Information


Literature


Mechanism of action — Taken from nature:

A neutrophile granulocyte phagocytes anthrax bacteria, thereby exposing them to alpha defensins stored in its granuloma that can neutralize B. anthracis's most deadly weapon: lethal toxin.

It seems that in the lung neutrophile granulocytes are present in amounts too low to control B. anthracis infection. However, mice control anthrax infection after administration of alpha-defensins.

Figure: MPI for Infection Biology / Volker Brinkmarin

Contact:

Dr. Dieter Link
Patent and Licensing Manager
Tel.: +49-(0)89 / 290919-28
dieter.link@max-planck-innovation.de