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Sommario/riassunto

Francisella tularensis, the causative agent of tularemia, is a paradigm among human pathogens. This Gram-negative bacterium has an intracellular lifestyle, which probably reflects an adaptation to its natural animal and protozoa reservoirs. This is one of the most infectious agents in humans and animals; only a few bacteria are needed to induce a severe infection in both types of hosts. The clinical presentation and severity of human tularemia varies according to the portal of entry of bacteria, the bacterial inoculum, the virulence of the infecting strain, and the immune response of the host. Although most infections occur after direct inoculation of bacteria through the skin (through skin wounds or bites of arthropods), pneumonia due to inhalation of infected aerosols is the most feared of the clinical forms of the disease, particularly in the context of biological threat. Two subspecies are responsible for tularemia (subsp. tularensis and subsp. holarctica), and several clades have been described for each, which might be associated with changes in disease severity in humans. Tularemia is also more severe in people with an impaired immune response. No safe vaccine is currently available for prophylaxis of tularemia in humans. On the other hand, control of proliferation of F. tularensis in wildlife is not feasible. Thus, only the anti-infective agents are used for treatment and prophylaxis of human tularemia. The standard options include aminoglycosides (gentamicin), tetracyclines (eg, doxycycline) and fluoroquinolones (eg, ciprofloxacin). The

selection of acquired resistance to these antibiotics in F. tularensis, especially in the context of a biological threat, may quickly limit the therapeutic options. New prophylactic and therapeutic alternatives must be developed rapidly. The present Research Topic focuses on potential new strategies for treatment of tularemia, including the development and evaluation of new compounds having proper antibacterial activity, reducing the virulence of F. tularensis or enhancing the immune host response.