Public Abstract

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AGAINST PNEUMONIC PLAGUE

Yersinia pestis is the causative agent of bubonic, pneumonic, and septicemic plague and has killed more people than any other bacterial pathogen throughout history. In modern times, naturally occurring cases are rare; however, there is a legitimate concern that the organism could be utilized in a bioterrorist attack. Thus, there is an increased push to better understand how the organism infects the host and to develop novel therapeutics that can be used to treat disease. To this end, we investigated the mechanism of action of antibodies that promote the clearance of plague in order to identify targets that could be exploited to enhance antibody treatment. We found that protective antibodies not only block an essential toxin produced by the bacterium, but also promote sequestration of the organism by a white blood cell known as a macrophage. However, although antibodies promoted uptake by macrophages which served to slow bacterial replication, organisms were not killed. Instead, we found that pathways that stimulate neutrophils, another type of white blood cell, were required to kill the organism and protect the host from plague. These results will provide researches important data which can be used to develop new therapies to more quickly and effectively protect us from plague.