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Upgrading the 100 year-old BCG vaccine

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The increasing spread of drug-resistant *M. tuberculosis* (Mtb) strains is dramatically impacting upon tuberculosis (TB) control programmes. Therefore many health authorities came to the conclusion that efficient preventive vaccination would be the best cost-effective strategy to stop the spread of all form of TB, especially in developing countries. The current vaccine *M. bovis* BCG (developed in early 1900's) is proven to protect efficiently newborns unfortunately, its efficacy wanes as kids age. Therefore, many investigators are focusing their efforts towards upgrading the 100 year-old BCG. We have been investigating the underlying mechanisms behind the inefficacy of BCG for the last five years. We found that BCG, although safe and non pathogenic for human, mimics many pathogenic features of Mtb. In particular we found that BCG blocks macrophage (MØ) apoptosis and phagolysosome fusion, which are essential innate responses that restrict bacterial persistence and also initiate adaptive immune response. We recently developed a strategy to convert BCG into a strong proapoptotic strain that induces MØ apoptosis and accelerate phagolysosome fusion. The reshaped BCG also induces the shedding of apoptotic blebs, which cross-prime dendritic cells for antigen presentation to T cell, a novel mode of antigen presentation called the "detour pathway". Current research efforts in this lab are focusing on upgrading further proapoptotic BCG to express TB10.4 and VAPB47, which are major protective Mtb antigens not expressed in conventional BCG. We strongly believe that this novel approach will generate a novel TB vaccine highly competitive to those currently under evaluation in clinical trials.

Biography

Zakaria Hmama received a PhD degree from the University Claude Bernard (Lyon, France) in 1993. He is currently Associate Professor at the University of British Columbia (Department of Medicine) and holds a Scholarship Award from the Michael Smith Foundation of Health Research. Ongoing research in her lab focuses on developing novel gene manipulation technologies to upgrade the current BCG vaccine in order to maximize the induction of protective TB immunity. Of equal importance to the vaccine project, a biology-based study of Mtb persistence has revealed important virulence factors that represent attractive drug targets that could be used for TB treatment.

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