Understanding immunity to invasive Salmonella diseases to design new preventive measures

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Bacterial diseases are a grave threat for humankind causing approximately six million deaths per year. Invasive non-typhoidal *Salmonella* (iNTS) are a leading cause of lethal sepsis in young children and immune-compromised individuals, especially in developing countries with an estimated 3.8M illnesses and 680,000 deaths. Antimicrobial resistance is on the increase and no vaccines are currently licensed. iNTS disease has a pathogenesis that is both extracellular and intracellular, with systemic spread in multiple body tissues. iNTS are vulnerable to antibodies and complement that lyse the bacteria and/or target them to phagocytes, increasing the antimicrobial functions of host cells. Development and optimisation of preventive measures against iNTS, including vaccines, requires a clearer understanding of the correlates and mechanism of action of the protective immune response. Using multidisciplinary approaches that include novel gene-targeted animals and human *in vitro* systems, our work has identified phagocyte receptors, intracellular killing mechanisms and bacterial antigens that are involved in phagocyte- and antibody-mediated killing of iNTS. Using recombinant chimeric immunoglobulins, we have determined the relative potency of different IgG subclasses in human preclinical models, thus generating essential information on the requirements of the protective response. This work lays a foundation for the development of vaccines and antibodies in the prevention and therapy of septicaemic iNTS in immune-deficient individuals.

Biography

Dr.Mastroeni is a scientist with a medical background. His research is focused on the interplay between bacterial pathogenesis and the immune system as the foundation for vaccine development. His work has established many key requirements and mechanisms of protective immunity to bacterial infections and has identified and characterized bacterial virulence and/or immune-evasion genes as targets for live attenuated vaccine candidates. His group has pioneered innovative multidisciplinary approaches, which combine immunology, microscopy, molecularly tagged microbial subpopulations and mathematical modeling, to study bacterial infection dynamics in vivo. This has allowed to unravel the impact of immunity, vaccination and antibiotics on pathogen behaviour at the single cell level and to gather a global understanding of infection biology.

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