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IMMUNOLOGICAL CHARACTERISATION OF VACCINES BASED ON GENERALISED MODULES FOR MEMBRANE ANTIGENS (GMMA)

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GSK Vaccines Institute for Global Health (GVGH) aims to develop affordable vaccines to fight neglected bacterial diseases prevalently affecting developing countries. GMMA (generalized module for membrane antigens) are outer membrane blebs naturally released from Gram-negative bacteria, genetically modified to induce hyper-blebbing and reduce the endotoxic activity of lipopolysaccharides. We have developed a panel of immuno-assays to assure full characterization of GMMA based vaccines. Such methods have been used in pre-clinical studies and are important to support GMMA clinical testing. Immunogenicity of sera is assessed by ELISA, while functionality of antibodies is characterized through a newly developed high-throughput luminescence-based serum bactericidal assay (L-SBA), able to detect surviving bacteria by measuring their ATP. L-SBA considerably shortens assay time, facilitates data acquisition and analysis, and reduces the operator dependency, avoiding the plating and counting of CFUs. We showed, both in pre-clinical and clinical studies that GMMA based vaccines targeting different pathogens such as *Shigella*, *Salmonella* or *N. meningitidis* are highly immunogenic. In animal studies, GMMA elicited higher functional antibody responses against key vaccine candidate antigens, whether these are polysaccharide or protein moieties, compared with corresponding purified antigens delivered as glycoconjugate vaccines (for polysaccharide antigens, e.g. O-antigen of *Salmonella*) or recombinant formulations (for protein antigens, e.g. factor H binding protein of meningococcus). This could be the result of efficient antigen presentation to the immune system, the adjuvanting effect of GMMA, which changes the IgG profile or a combination of both effects. *S. sonnei* GMMA have been already tested in clinical trials, showing to be well tolerated and immunogenic in European adults and endemic populations. With good immunogenicity, low cost, and ability to induce functional antibodies, GMMA technology is potentially attractive for development of vaccines against bacteria of global health significance.

Biography

Francesca Mancini has completed her PhD from Padova University and Post-doctoral studies from Novartis Vaccines and Florence University. She is a Scientist at Glaxo Vaccines Institute for Global Health (GVGH), an organization that operates in order to develop effective and affordable vaccines against neglected infectious diseases, such as typhoid fever, shigellosis and streptococcal disease (and relevant complications). She has published 10 papers in reputed journals.

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