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Novel vaccine candidates for an improved a cellular vaccine of *B. pertussis*

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Bordetella pertussis is the etiologic agent of whooping cough. Despite the high coverage of vaccination the disease is still a major public health problem worldwide which is a reflect of the low efficiency of current vaccines. The difference between the phenotype of the infecting bacteria and the vaccine phenotype seems to contribute to this lack of protection. Antigenic proteins whose expression is induced under iron starvation, an environmental condition that bacterial pathogens have to face during colonization, might be potential candidates for improved vaccines. By mean of immune proteomics we identified novel antigens of *B. pertussis* maximally expressed under iron starvation. Among the proteins differentially recognized by human sera from infected individuals, two proteins showed highly protective in cellular formulations against pertussis infection, namely AfuA (Bp1605) and IRP1-3 (Bp1152). IRP1-3 and AfuA were identified as putative iron binding proteins using matrix-assisted laser desorption ionization–time of flight (MALDITOF/TOF) mass spectrometry. In this study, we cloned, expressed and purified the two recombinant proteins from Escherichia coli. The protective activity of these antigens was evaluated in BALB/c mice using the intranasal infection model. Our results demonstrated that although vaccination with either AfuA or IRP1-3 significantly ($p<0.01$) protected the mice against intranasal infection of *B. pertussis*, AfuA vaccination rendered a higher level of protection. The divalent formulation reduced bacterial burden to a degree that suggests a synergistic effect of both antigens. Analysis of antibody biological activity in protected mice revealed that both AfuA and IRP1-3 led to the generation of specific antibodies able to recognize the respective native proteins on bacterial surface and to induce efficient bacterial phagocytosis, one of the main antibody protective activities against this pathogen. Analysis of cytokines in protected mice revealed the induction of a balanced Th1/Th2 type of response by IRP1-3. AfuA, however, promoted an immune response with a remarkable cellular immunity contribution which might explain the higher protection induced by this protein. Given the recent discovery that B. pertussis has an intracellular phase that might represent the niche of persistence, this kind of antigens are particularly interesting for an effective vaccine formulation. Immunoblot analysis demonstrated that the two proteins are expressed by clinical isolates under iron starvation. This observation, together with the presence of antibodies against these proteins in sera from infected individuals, confirmed their expression during human pertussis infection. Altogether our results point at these two antigens as promising new candidates to improve current pertussis vaccines.

Biography

Prof. Rodriguez completed her Ph.D at the National University of La Plata (Argentina) and postdoctoral studies at the Laboratory for Vaccine Research Development and Research on Immune mechanisms (LVM). National Institute of Public Health and the Environment (RIVM). (Netherlands), and Laboratory of Immune Therapy and Experimental Immunology. Department of Immunology, Utrecht University (the Netherlands). She is presently a Professor at the National University of La Plata and Scientific Researcher of the National Research Council at the Applied Biotechnology Center (CONICET- UNLP) in Argentine. He has published more than 30 papers in reputed journals on infectious diseases and immunity, and serving as a reviewer of many repute scientific journals.