ImmunoTools *special* Award 2015

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Lung epithelial cell response to *Bordetella pertussis*

Bordetella pertussis is a strictly human pathogen and the main causative agent of whooping cough, aka pertussis. Despite a high vaccination cover pertussis remains endemic within the world population. The persistence of pertussis in countries with highly vaccinated populations has been attributed to various causes including suboptimal vaccines, a waning immunity, and pathogen adaptation.

Our laboratory is focused on the study of *B. pertussis* pathogenesis and the mechanisms that allow this bacterium to persist within the population. One of our projects is focused in investigating the interaction of *B. pertussis* with the respiratory tract epithelium. Attachment to epithelial cells in the respiratory tract is a key event in *B. pertussis* colonization. Recently we have shown that *B. pertussis* is also able to invade and survive within human alveolar epithelial cells probably contributing to its persistence (1). The purpose of the present project is to gain a better insight into *B. pertussis* interaction with epithelial cells focusing on host cell response upon infection.

It is well known that the respiratory epithelium plays a critical role in innate immunity. Not only constitutes an anatomical barrier for bacterial invasion but also responds to pathogens by mounting an inflammatory response aimed at controlling the infection. By the recognition of pathogen-associated molecular patterns (PAMPs), the respiratory epithelium activate a multitude of intracellular signaling cascades that culminate in the activation of transcriptional factors and the synthesis of a broad range of molecules, including cytokines, chemokines, immunoreceptors, and cell adhesion molecules; which together orchestrate the early host response to infection and at the same time represent an important link between innate and adaptive immune responses. In addition to epithelial cells, macrophages, another cell type in which Bordetella is capable of survive (2); produce proinflammatory cytokines in response to infection, such as TNF-α or IL-1β, that can in turn induce the production of cytokines by lung epithelial cells (3). Several intracellular pathogens fine-tune this immune response to produce a selective response that favors their persistence (4). In

the case of pertussis, the inflammatory response induced in the airways upon infection is not fully understood. The present study will be performed to examine the cytokine and chemokine responses of lung epithelial cells after infection with *B. pertussis* and after interacting with Bordetella-infected macrophages. To this end, the human alveolar epithelial cell line A549 or the 16HBE14o- human bronchial epithelial cellline will be infected with *B. pertussis* and the expression levels of IL-4, IL-10, IL-8, IL-6, IL-12p40 and TNF-α will be analyzed using flow cytometry and ELISA. The epithelial cell response in the context of macrophage infection will be analyzed by incubating lung epithelial cells with supernatants of macrophages infected with *B. pertussis*. TNF-α or IL-1β will be used as positive controls. An ImmunoTools Award would be a significant contribution to this study, and would permit extended research concerning the role of lung epithelial cells in the innate immunity against *B. pertussis* and evasion mechanisms displayed by this bacterium.

1. Lamberti, Y., J. Gorgojo, C. Massillo, and M. E. Rodriguez. 2013. Bordetella pertussis entry into respiratory epithelial cells and intracellular survival. *Pathog Dis 69:194*.
2. Lamberti, Y. A., J. A. Hayes, M. L. Perez Vidakovics, E. T. Harvill, and M. E. Rodriguez. 2010. Intracellular Trafficking of *Bordetella pertussis* in Human Macrophages. *Infect. Immun. 78:907*.
3. Wickremasinghe, M. I., L. H. Thomas, and J. S. Friedland. 1999 Pulmonary Epithelial Cells are a Source of IL-8 in the Response to Mycobacterium tuberculosis: Essential Role of IL-1 from Infected Monocytes in a NF-kB-Dependent Network. *The Journal of Immunology 163 3936*.
4. Lutay, N., G. Hakansson, N. Alaridah, O. Hallgren, G. Westergren-Thorsson, and G. Godaly. 2014. Mycobacteria Bypass Mucosal NF-kB Signalling to Induce an Epithelial Anti-Inflammatory IL-22 and IL-10 Response. *PLoS ONE 9:e86466 EP*

ImmunoTools *special* AWARD for **Yanina Lamberti** includes 24 reagents

FITC - conjugated anti-human IL-6,

PE - conjugated anti-human IFN-gamma, IL-8, TNFα,

human ELISA-set for 96 wells: human IFN-gamma, human IL-4, human IL-6, human IL-8, human IL-10, human IL-12p40 total (detect IL-23 as well), (each 3 reagents),

recombinant human cytokines: rh IL-1beta, rh TNFα DETAILS more AWARDS