“In Cystic Fibrosis, lung function declines because of airway inflammation and bacterial infections. *Pseudomonas aeruginosa* is the most frequent bacteria infecting adult CF lungs. It can take different phenotypes that have a direct impact upon disease severity and response to treatment. Moreover, multiple modes of interaction in a CF lung may occur between epithelial cells and bacteria: 1) direct interaction of live bacteria with host epithelial cells; 2) internalization of bacteria inside epithelial cells and 3) diffusion of bacterial-derived exoproducts from intraluminal colonies. However, not all forms of interactions between *P. aeruginosa* and host epithelial cells in CF disease are equal when it comes to pathogenesis. In the last few months, we observed in human CF lungs, the intracellular presence of *P. aeruginosa* resident and living within some epithelial cells, an extraordinary finding that challenges our current conception of CF lung infections. The contribution of intracellular persistence to the inflammatory response of epithelial cells and bacterial clearance is not fully understood. In this seminar, our most recent findings on the complex relationship between *P. aeruginosa* and human bronchial cells will be presented”.