***DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO (38° Ciclo)***

**Title:** Analysis of the effect of CFTR modulators on the innate immune response of people with cystic fibrosis.

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**Summary** The pulmonary disease represents the main cause of morbidity and mortality in people with Cystic fibrosis (pwCF). In the CF airways the loss of CFTR mediated anion transport in epithelial cells causes air-liquid dehydration and defective mucociliary clearance leading to chronic bacterial infections and inflammation (1). In addition, an impairment in the antimicrobial activity of monocytes/macrophages further contribute to CF chronic infection and inflammation (2). Recently the development of small molecule drugs termed CFTR modulators targeting CFTR itself has revolutionized the treatment of Cystic fibrosis (3). However, at present, the effects of modulator therapy have been mainly evaluated in clinical trials demonstrating improvement in lung function, respiratory symptoms, reduced risk of acute pulmonary exacerbation and weight gain while *in vitro* studies were mainly focused on epithelial cells. Thus, the aim of this project is to analyse *ex vivo* and *in vitro* the effects of CFTR modulators on the innate immune responses of pwCF.

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