BREATHE
the lung association

# Research Summary

## Boosting host immunity against Pseudomonas aeruginosa lung infection

Cystic fibrosis (CF) is the most common fatal genetic disease affecting Canadian children and adolescents. It is caused by mutations in the gene for the cystic fibrosis transmembrane conductance regulator (CFTR) protein. Cystic fibrosis is a complex disease with a diverse range of symptoms, which mainly affect the lungs. It is estimated that one in every 3,600 children born in Canada has cystic fibrosis. In Nova Scotia, the IWK Health Centre Pediatric CF Clinic follows approximately 105 patients with CF in the Maritime Provinces. The Capital Health Adult Cystic Fibrosis Program provide health service for similar number of adult patients. In spite of significant progress in treating this disease, there is still no cure for CF and currently available CFTR modulator drugs can only be used to alleviate the symptoms of a small subset of patients with specific mutations in the CFTR gene. Moreover, these drugs cost $300,000/year, which limits access and challenges the publically-funded health care system in Nova Scotia. Pseudomonas aeruginosa is a ubiquitous Gram-negative opportunistic bacterial pathogen that causes infections when normal immune defenses are disrupted. One of the main problems faced by CF patients is inflammation in the lung caused by persistent P. aeruginosa infections. This causes destruction of lung tissue and loss of lung function, eventually leading to death in the majority of CF patients. No vaccine is available for this bacterium and treatment is difficult due to multidrug resistance. Therefore, there is an urgent need to develop a novel therapeutic strategy. Our proof-of-concept experiments identified a novel therapeutic strategy for treating P. aeruginosa infections by enhancing human immunity. The use of host target for antibacterial therapy has the advantage of avoiding selection pressure on bacterial pathogen, therefore limiting the emergence of drug resistance. The objective of the proposed research is to characterize the underlying mechanism by which host immune signaling is clustered efficiently to fend against bacterial infection. This study will shed new light on the organization of host immune signaling networks. This knowledge, in turn, will facilitate the practical application in fighting P. aeruginosa infection. Going forward, this research program will lead to the development of an innovative approach to eradicate chronic P. aeruginosa infection in CF patients. More importantly, this project will both contribute positively to the health outcomes of Nova Scotians with CF, and identify low-cost alternative treatments that could alleviate financial burden on the publically-funded Nova Scotian health care system