

CF Innovation Grant 2020 – Final Report

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Proposal Title: Enhancing the innate ability of CF macrophages to kill and clear MABS Background.

Due to COVID-19, our research facility was shut down, patient recruitment was stopped for a significant period in 2020-2021.

Project Annual Report.

Macrophages are the professional bacteria killer cells in the tissues. In the lungs, macrophages first uptake the bacteria (MABS in this research study) inside them and then utilize several mechanisms to kill the bacteria, such as, lysosomal acidification, mitochondrial reactive oxygen species (mitoROS), zinc toxicity.

The general project aim was to investigate whether the resolution of MABS infection by CF macrophages is defective and can be improved by enhancing anti-microbial responses of macrophages using novel anti-inflammatory agents or by Zn supplementation. We had significant progress in understanding the defects of CF macrophages in killing of MABS.

Using high-resolution microscope, we observed a reduced number of MABS inside CF macrophages than macrophages obtained from health controls (HCs), indicating that CF macrophages are unable to uptake MABS inside them. We observed high levels of mitoROS production by macrophages from HCs, however, the level of mitoROS produced by CF macrophages was substantially low. Macrophages from patients with CF have less zinc level inside them compared to macrophages from HCs. Together this means, CF macrophages are not only impaired in MABS uptake, but also they are inefficient in killing MABS.

Together our study identified, why CF macrophages are less efficient to kill and clear MABS. Daily zinc supplementation will increase the zinc level inside CF macrophages and will be helpful to kill and clear MABS from the lungs of the patients with CF.