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Protocols for Recinto et al. "A rewiring of the earliest immune events leading to T-cell mediated disease following intestinal microbial infection in a PINK1 KO mouse model of Parkinson's disease"

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Sherilyn Junelle Recinto[1], adam.macdonald[1], Moein Yaqubi[1], Alexandra Kazanova[2]

[1]Department of Neurology and Neurosurgery, Montreal Neurological Institute-Hospital, McGill University, Montréal, QC, Canada;
[2]Department of Microbiology and Immunology, McGill University, Montréal, QC, Canada

ASAP Collaborative Rese… | Desjardins ASAP team

L Lilia Rodriguez
Université de Montréal

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Abstract

Our group has developed GI-targeted pathogen-induced PD mouse modeling systems (in PINK1 KO mice with gram negative bacterial infections) and found that T cells are a major player in driving PD-like motor symptoms at late stages following infection. Herein, we now map the initiating immune events at the site of infection at the earliest stages with the goal of shedding light on the earliest mechanisms triggering T cell-mediated pathological processes relevant to PD. Using unbiased single cell sequencing, we demonstrate that myeloid cells are the earliest dysregulated immune cell type in PINK1 KO infected mice (at 1-week post-infection) followed by a dysregulated T cell response shortly after (at 2 weeks post-infection). We find that these myeloid cells have an enhanced proinflammatory profile, are more mature, and develop enhanced capacity for antigen presentation. Using unbiased prediction analysis, our data suggests that cytotoxic T cells and myeloid cells are particularly poised for interacting with each other, and we identify possible direct cell-cell interaction pathways that might be implicated.

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