Stem & PRogenitor Cell INterest Group

Wednesday, January 30, 2019

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"Using scRNA-seq analysis to decipher microbiome-host crosstalk in the small intestine"

Inflammatory Bowel Disease (IBD) arises due to a loss of tolerance to environmental antigens in genetically susceptible individuals. Longitudinal analysis of IBD incidence has identified an inverse correlation between rates of communicable disease and autoimmune disorders, particularly in countries endemic for helminth infestation. A case report published by Broadhurst *et al* described the use of helminth eggs to promote mucosal healing and clinical remission in a patient with refractory IBD. Intestinal epithelial tuft cells are responsible for orchestrating the type 2 immune response following helminth colonization and modulation of tuft cell function may prove efficacious in CD treatment. In a well-established mouse model ($TNF^{\Delta ARE}$) of Crohn's-like ileitis, we observed an inverse correlation between inflammation and tuft cell number. We applied p-Creode, a novel trajectory mapping algorithm, to single-cell RNA sequencing datasets in order to demonstrate that epithelial tuft cells are specified outside of the canonical secretory lineage. We then developed a novel, genetically-inducible model of tuft cell hyperplasia ($Lrig1^{CreERT2/+}$; $Atoh1^{fl/fl}$ – AtohKO), where the loss of the master secretory regulator *Atonal Homolog 1* (*Atoh1*) drove increased tuft cell numbers in the *in vivo* small intestine. Using the AtohKO model, we have identified a role for the microbiome and commensal-derived metabolites in induction of tuft cell hyperplasia, independent of helminth infection. Understanding tuft cell specification and function could enable us to better leverage this rare and elusive cell type to modulate inflammatory symptoms in IBD.

9:00 am – 9455 MRB IV

Bagels provided