SESSION II

IMMUNITY AND INFLAMMATION

New Cell Pathways for Understanding IBD

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Inflammatory bowel disease (IBD) is a chronic relapsing, remitting disorder of the gastrointestinal tract. The aetiology of IBD remains unclear, but it is driven by a range of genetic and environmental factors that disrupt the delicate symbiotic relationship that exists between the intestinal immune system and the microbiome. Regulatory T cells (Treg) are a population of immunomodulatory cells that play a fundamental role in dampening undesired immune responses, particularly in the intestine. Tregs employ a variety of cell contact-dependent and -independent mechanisms to suppress the action of both innate and adaptive immune cells. To elicit their suppressive function, Tregs need to be stimulated via recognition of a cognate MHC-peptide complex, but once activated, they suppress cells in their local vicinity in an antigen-independent manner. This phenomenon, referred to as bystander or linked suppression, is key for the maintenance of intestinal homeostasis. In addition to their suppressive function, Tregs also act in the local environment to promote tissue repair and regeneration via a range of mechanisms. Quantitative and qualitative deficiencies in Tregs are correlated with IBD development and progression in mice and humans. As such, Treg therapy is a promising strategy to restore intestinal immune homeostasis. Evidence supporting its therapeutic potential in IBD will be discussed, including potential antigens they could target and cell engineering strategies that could be used to enhance their function.

Key references

Alexander KL, Zhao Q, Reif M, et al. Human Microbiota Flagellins Drive Adaptive Immune Responses in Crohn's Disease. *Gastroenterology*. 2021;161(2):522–35.e6.

Clough JN, Omer OS, Tasker S, et al. Regulatory T-cell therapy in Crohn's disease: challenges and advances. *Gut*. 2020;69(5):942–52.

Cook L, Stahl M, Han X, et al. Suppressive and Gut-Reparative Functions of Human Type 1 T Regulatory Cells. *Gastroenterology*. 2019;157(6):1584–98.