Regulation of Innate Lymphocytes, Colitis, and Colon Cancer by Transcription Factor Nfil3

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Abstract: Colon cancer is one of the leading causes of death among cancers that affect both men and women, and patients with inflammatory bowl disease (e.g. Crohn's disease or ulcerative colitis) have an elevated risk of being diagnosed with colon cancer. Thus, a greater understanding of the gastrointestinal immune and microbial mechanisms behind development of colitis and colon cancer is of utmost importance. In recent years, innate lymphoid cells (ILC) have been shown to contribute to the immune response at barrier surfaces such as the gastrointestinal tract. We have new data demonstrating that the transcription factor Nfil3 is critical for the development of all innate lymphocytes (ILCs and natural killer (NK) cells). Using novel mouse models where innate lymphocytes are genetically ablated, but adaptive lymphocyte numbers remain intact, our goal is to investigate how innate lymphocytes impact gut disease processes. In addition, we will investigate the crosstalk between innate lymphocytes and the commensal microbiota in mediating IBD and intestinal tumorigenesis. The aims of our proposal will test the hypothesis that lack of innate lymphocytes will render Nfil3-deficient mice susceptible to development of colitis and colon cancer using both established and novel models of these gut-associated diseases. We hope to uncover new insights into how Nfil3 and the microbiota shape development of colitis and colon cancer, providing a framework and new clinical approaches for manipulating the innate lymphocyte response to tackle these major public health problems.