Complex Traits Group

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Crohn's and Colitis Canada
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Workshop Series: **Inflammation at Barrier Surfaces: From Bench to Bedside**

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"Imaging Immunity: Creating a Spatiotemporal Picture of Inflammation and Host Defense"

Immune responses involve cell-cell interactions within lymphoid tissues, trafficking of activated cells to sites of effector function, and the migration of effector cells within peripheral tissues. To gain a more detailed appreciation of the relationships among cell movement, tissue architecture, and immune function, we have used intravital multiphoton microscopy and a novel multiplex immunohistochemical method to analyze immune cell dynamics and tissue micro-anatomy.

Migrating T cells follow stromal pathways in lymph nodes, which together with chemokine cues, enhances interactions with dendritic cells. The strength of these interactions as assessed by motility assessment and Ca2+ imaging dictates the polarization of the ensuing effector T cell response. In tissue sites, neutrophil migration is integrin independent until a tight swarm firms to isolate the wounded region or site of infection, with migration largely guided by a signal relay involving neutrophil production of and response to the leukotriene LTB4.

Effector T cells stop when they perceive antigen and undergo transient activation, followed by tuning of their response to existing antigen levels. The role of cell localization in both innate and adaptive immunity has also been addressed using a new method called histo-cytometry that reveals at high resolution the spatial positioning and activation state of cells with complex phenotypes in tissues.

These observations show the power of in situ imaging in the acquisition of a more accurate picture of the molecular, cellular, spatial, and temporal aspects of cell function and signaling events in host inflammatory and immune responses.

This work was supported in part by the Intramural Research Program of the NIH, NIAID.

"Non-alcoholic Fatty Liver Disease-Chronic Inflammation"

Steatosis (fat accumulation) in the liver is widespread and when classified as non-alcoholic fatty liver disease (NAFLD), is often viewed as the hepatic manifestation of the metabolic syndrome. Depending on region, up to one in two have NAFLD. Hepatic steatosis is by itself not correlated with increased morbidity rate but when coupled with non-alcoholic steatohepatitis (inflammation, NASH), increases the risk for terminal liver disease including cirrhosis, hepatocellular carcinoma (HCC) and/or hepatic decompensation. About one in five have NASH and about one in three of NAFLD patients have NASH.

Of these and over the course of 15 years on average, 11% will develop NASH with cirrhosis with about one third ending up with hepatic decompensation after 8 years. About 7% of those afflicted by NASH with cirrhosis go on to develop HCC after 6.5 years. Chronic hepatic inflammation (NASH) therefore presents a significant risk and indeed, correlates with increased morbidity rates. NASH is most often seen together with varying degrees of fibrosis that can easiest be likened with a form of wound healing yet is largely asymptomatic.

Very little is known at the mechanistic level as to what triggers NASH and how this contributes to terminal liver disease. To study this more closely, we have assembled a translational team to undertake a proteomics-based study using human liver tissue derived from donors as well as patients. A biobank framework has been established that enables liver tissue to be processed within 20-30 minutes after resection for subsequent subcellular fractionation, liquid chromatography-based tandem mass spectrometry and bioinformatics analysis. Proteins correlating with disease state are then elucidated for functional context. In this, we are in the process of mapping novel pathways, some of which will be presented and discussed.

Wednesday, February 11, 2015 at 4:00 PM

Palmer Amphitheatre, Room 522
McIntyre Medical Sciences Bldg | 3655 Promenade Sir William Osler

Followed by a *Wine and Cheese* mixer | Bellini Atrium - 5:30 PM

Hosted by the Complex Traits Group

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