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Biosketch

My scientific focus is studying the pathways of cell death in drug induced liver injury and hepatotoxicity models. My initial work has uncovered a significant role for RIPK1 independent of RIPK3, MLKL and necroptosis in Acetaminophen (APAP) induced hepatotoxicity. Interestingly, although hepatocytes do not express RIPK3, the protein is abundant in the non-parenchymal fraction especially the sinusoidal endothelial cells of the liver. RIPK1 knockdown abrogates JNK activation and translocation to mitochondria in response to APAP. However the signaling events between RIPK1 and JNK are unclear. RIPK1 is a multifaceted protein that depending on cell type and context can promote cell survival, apoptosis, or necroptosis. My interest lies in understanding these cell death pathways in hepatocytes. I have worked under the mentorship of Neil Kaplowitz on hepatocyte death pathways in the APAP model for the past 4 years. My entry into experimental work has been non-traditional. I started lab work as a GI fellow back in 2011. For the past three years I have been working particularly on the RIP kinases and studying their contribution to liver injury and cell death.

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Abstract: New Data on Adaptive Processes

In the past decade our understanding of idiosyncratic drug induced liver injury (IDILI) and the contribution of genetic susceptibility and the adaptive immune system to the pathogenesis of this disease process has grown tremendously. One of the characteristics of IDILI is that it occurs rarely and only in a subset of individuals with a presumed susceptibility to the drug. Despite a clear association between single nucleotide polymorphisms in human leukocyte antigen (HLA) genes and certain drugs that cause IDILI, not all individuals with susceptible HLA genotypes develop clinically significant liver injury when exposed to drugs. The adaptation hypothesis has been put forth as an explanation for why only small percentage of susceptible individuals develop overt IDILI and severe injury, while the majority with susceptible genotypes develop only mild abnormalities that resolve spontaneously upon continuation of the drug. This spontaneous resolution is referred to as clinical adaptation. Failure to adapt or defective adaptation leads to clinically significant liver injury. In this review we explore the immuno-tolerant microenvironment of the liver and explore mechanisms of clinical adaptation with a focus on idiosyncratic drug induced liver injury.