Presenter: Sonali Sharma

Authors: Benjamin J Rodems, Sonali Sharma, Erika Davidson, Jeevisha Bajaj

Title: THE ROLE OF SLC6A6 IN ACUTE MYELOID LEUKEMIA

Abstract:
Cancers often hijack developmental signals for their progression. It is thus likely that niche-driven signals that sustain normal Hematopoietic Stem Cells (HSCs) also influence the growth of leukemias arising from mutations in these normal HSCs. Despite recent advances in treatment, ~75% of acute myeloid leukemia (AML) patients still succumb to the disease, highlighting the need to better understand the mechanisms of disease progression. While much work has focused on leukemia cell-intrinsic regulators, the role of the microenvironment in disease establishment and propagation is poorly understood. To determine the molecular effectors of leukemia growth and proliferation in vivo, we carried out a genome-wide CRISPR/CAS9 screen in a primary myeloid leukemia murine model. This identified ~140 cell surface genes including those previously shown to promote growth (e.g., CD98, CD47, and CD157), as well as novel regulators of leukemia progression. To identify cancer specific signals, we focused on a subset of novel cell surface regulators with a 2-fold higher expression in human leukemia stem cells (LSCs) compared to normal HSCs. Of these, we focused on the taurine transporter (TauT) SLC6A6, since its high expression is associated with poor prognosis in AML patients (TCGA). Our data demonstrates that TauT loss significantly impairs AML growth compared to the controls both in vitro and in vivo, suggesting that TauT is essential for AML initiation and progression. We also show that the enzymes synthesizing taurine are upregulated during early osteogenic differentiation in the bone marrow, and taurine is secreted in the microenvironment. Thus, our work identifies a novel role for bone marrow osteoprogenitors in sustaining LSCs and supporting leukemia growth by secreting taurine. These data indicate that targeting TauT may be of therapeutic relevance for AML.