Speaker: Dr. Roger Geiger, Institute for Research in Biomedicine, Bellinzona, (CH)

Title: Towards Immunotherapies for Liver Cancer

Abstract:
T cells play a crucial role in the host defense against pathogens and cancer cells. Using systems approaches, we studied the dynamics in protein translation and metabolic activity in resting and activated T cells from healthy donors. Our results revealed that T cells fundamentally remodel the arginine metabolism following activation, and that the amino acid L-arginine globally regulates metabolism, survival and anti-tumor functionality of T cells. More recently, we extended our analysis to tumor-infiltrating T cells from patients with liver cancer. Tumor-infiltrating T cells are often dysfunctional and cannot control tumors. Aiming at identifying new targets to revitalize dysfunctional T cells, we analyzed proteomes of tumor-infiltrating T cells and found novel dysfunction-associated proteins that may serve as targets for drug-based immunotherapies. Another option for cancer immunotherapy is the infusion of tumor-reactive T cells. To identify tumor antigen-specific T cell receptors (TCRs), we cultured tumor-infiltrating T cells in vitro but they hardly proliferated and were not suitable for cell culture-based assays. To overcome this limitation we started developing a method to graft the entire TCR repertoire from dysfunctional onto functional T cells. The resulting T cell cultures can be interrogated for tumor specificity and used for cellular immunotherapy.