Research Presented by Pauline Hamon, PhD, Postdoctoral Fellow in the Merad Lab
February 27 Post-Doctoral Scientific Symposium, a joint effort of TCI and the Herbert Irving Comprehensive Cancer Center at Columbia

Hepatocellular carcinoma (HCC) has a dismal prognosis, and though checkpoint blockade has significantly improved patient outcomes, many are left without clinical benefit, highlighting the need to identify additional immune targets to enhance therapeutic immunity. Macrophages (macs) are an abundant and heterogeneous population in the tumor microenvironment (TME), associated with poor prognosis in multiple tumor types, including HCC. In this study, Pauline Hamon, PhD, and team analyzed the molecular and spatial organization patterns of immune cells within the TME and adjacent tissue of 35 resected HCC lesions of treatment-naïve patients, as well as responders and non-responders to neoadjuvant anti-PD-1 therapy. Using unbiased model of scRNAseq, they identified that the TME was highly enriched in monocyte-derived macrophages, among which macs expressing high levels of *TREM2*, *GPNMB* and *CD9* (TREM2 macs) formed a significant population. Strikingly, Dr. Hamon and team found that TREM2 macs were significantly enriched in responder patients compared to non-responders; they also accumulated in immune aggregates, in which they were found to interact with T cells. These results are in contrast to recent results from the Merad Lab and others showing that TREM2 macs dampen anti-tumor immunity in pre-clinical sarcoma and lung cancer models prompting the researchers to explore the causal role of TREM2 macs in the modulation of liver using experimental cancer models. Importantly, TREM2 macs accumulated in a pre-clinical model of HCC (developed by Amaia Lujambio, PhD) and TREM2 deficiency significantly reduced the survival of HCC-bearing mice compared to controls. Altogether, these data strongly suggest that the role of TREM2 macs on tumor immunity is tissue specific, highlighting the need to explore the role of tumor-associated macrophages in a cancer specific manner.