Abnormal transcriptomes are a hallmark of cancer and several RNA binding proteins have been identified in tumors to contain hotspot mutations. Dr. Dominguez and his team evaluated the consequences of colorectal adenocarcinoma-associated hotspot mutations in poly C binding protein 1 (PCBP1), a ubiquitous and highly expressed RBP, on RNA processing. Using a variety of biochemical, structural, and cell-based approaches, the lab found that hotspot mutations in PCBP1 led to a hyperactivated state that enhanced RNA binding and regulation. Overall, the lab’s work establishes molecular mechanisms and regulatory consequences of PCBP1 hyperactivation in colon cancer and is likely to have implications for other mutant RBPs.