Regulatory heterogeneity of neuroendocrine tumors

Ester Davis, Shahd Abu Kamel, Merav Hecht, Shani Avniel-Polak, Dana Rimini, Simona Grozinsky-Glasberg, Yotam Drier

Treating patients with neuroendocrine tumors is challenging. The two main challenges are the lack of effective drug treatments and the lack of reliable biomarkers to guide management, since patients with the same tumor grade/stage often have different clinical courses. The genetic, epigenetic and developmental programs that drive neuroendocrine tumors remain obscure, limiting our abilities to suggest new biomarkers and drug targets. We have recently successfully identified regulatory and developmental subtypes of pancreatic neuroendocrine tumors, and matching biomarkers that demonstrated clear clinical prognostic value. These discoveries were enabled by a genome-wide characterization of cis-regulatory elements (known as enhancers) and transcriptional regulatory networks. We now apply these methods to lung neuroendocrine tumors, to identify new subtypes, new biomarkers and drug targets, for this disease as well. We have characterized the transcriptomes and enhancer maps of 9 lung neuroendocrine tumors, and already begin to see potentially new sub-classifications.