Colorectal cancer (CRC) is one of a cadre of GI tumors that has an increasing incidence at earlier ages. There are now over 18,000 cases in the U.S. each year in persons under 50. Although the etiologic mechanisms underlying this increase are undetermined, there is broad agreement that the increase is driven by exposures in our environment. We approached this problem from the perspective of carcinogenesis. Finding in early-onset CRCs a higher frequency that lacked somatic APC mutations, we have focused on understanding dysregulation of the WNT pathway and the genesis of WNT-dependent tumors.