The surprises of suppressors in cancer development

Madelon Maurice, Center for Molecular Medicine, University Medical Center Utrecht, The Netherlands

The overall aim of my lab is to gain a fundamental understanding of the dual nature of signals that guide tissue renewal and cancer cell growth, with a key focus on Wnt signaling. Over the past years, we contributed to the understanding of adult stem cell regulation in complex tissues, and we uncovered novel ways by which cancer cells exploit deregulated signaling for their self-renewal and proliferation.
A key focus of our work is to acquire a deep molecular understanding of how patient-derived cancer mutations impact on cellular signaling and tissue organization to promote cancer growth. I will present our recent insights in how mutations that affect two major signaling pathways, Wnt and EGF, cooperate to drive colorectal cancer (CRC) subtypes with distinct clinical manifestations. We discovered a class of Wnt pathway mutations that directly drives formation of a non-proliferative secretory tumor cell population to supply essential niche factors for sustained tumor growth and metastasis. Thus, these CRC subtypes misuse differentiation pathways to self-organize their niche, enabling them to populate distant organs. Furthermore, our work implies that mutations in components of a single pathway may support divergent routes towards cancer development.