



BMC-GPMLS: Distinguished lecture series



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Metastatic colonization by circulating cancer cells

Abstract

Metastasis typically occurs long after the removal of a primary tumor. It emerges from disseminated cancer cells that remain latent until conditions allow their outgrowth. Eradication of disseminated cancer cells would prevent metastasis in high-risk patients. We developed mouse models of latent metastasis using cancer cells from early-stage lung and breast tumors. These models allow us to define mechanisms that suppress the outgrowth, support the long-term survival, and enable the eventual outbreak of latent metastatic cells. These cells have stem cell-like properties imparted by SOX2 and SOX9 lineage-determining transcription factors. These metastatic stem cells (MetSCs), reside in perivascular niches. By avoiding WNT growth stimuli and responding to TGF- β in this context, MetSCs can self-impose a slow-cycling state that evades immune surveillance. Latent MetSCs frequently enter the cell cycle, but are cleared by natural killer (NK) cells unless the proliferating MetSCs gain additional immune evasive capacities. Outbreaks have additional organ-specific as well as general requirements. Spreading of MetSCs on capillaries via the cell adhesion molecule L1CAM is required for metastatic outgrowth in lung, bone, brain and liver. An understanding of latent metastasis should yield therapeutic strategies for the prevention of overt metastasis.

Dr. Massagué is director of the Sloan Kettering Institute in New York City. He is a world leader in signaling pathways that determine cell behavior and cancer metastasis. He identified the TGF- β receptors, elucidated the TGF- β signal transduction pathway, and he provided a direct explanation for how these external signals control cell proliferation through cell cycle inhibitors and tumor suppression through cancer cell death. Disruption of these mechanisms causes cancer. Building on this work, Dr. Massagué identified molecular mechanisms for metastatic latency and metastatic colonization of distant organs, thus illuminating the basis for metastasis as the overwhelming cause of cancer mortality, and opening new avenues for treatment.

Time: Tuesday, August 22nd, 15.00-16.00

Location: Fróði auditorium, Sturlugata 8