

The epigenetic landscape and 3D chromatin architecture of epithelial-mesenchymal transition (EMT) spectrum

Speaker: **Ruby Huang, M.D., Ph.D.**

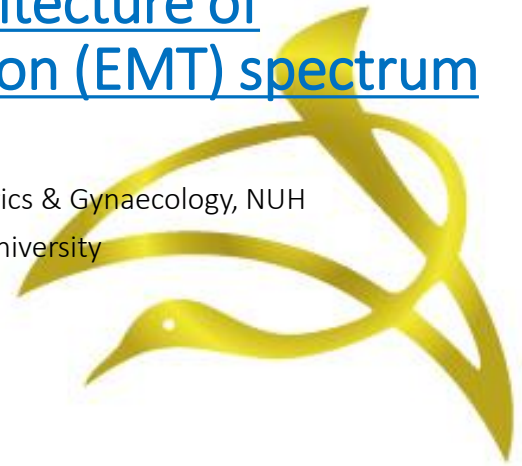
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Time: **5:30 pm**

Venue: **IRCMS 1F Meeting Lounge**



Epithelial-mesenchymal transition (EMT) is a reversible and dynamic process proposed to be co-opted by carcinoma during disease progression and therapeutic refractoriness. The concept of EMT has evolved from a binary phenomenon of epithelial (E) and mesenchymal (M) states to a continuous spectrum, which includes intermediate hybrid E/M states. This continuous spectrum reflects the transition through multiple energy barriers which is similar to the concept of metastability in physics. The control of metastability could be demonstrated by a gradient of complex regulatory networks among several transcription factors (TFs) such as SNAI1, SNAI2, ZEB1, ZEB1, TWIST1, and the epithelial transcriptional gatekeeper, grainyhead-like 2 (GRHL2). Grainyhead-like 2 (GRHL2) is an evolutionarily conserved transcription factor that regulates a repertoire of epithelial-specific genes during EMT. Previously, we reported GRHL2 regulates its target genes such as E-cadherin and miR-200b via transcriptional control and histone modifications. In this talk, I will further illustrate the genome-wide transcriptional and epigenetic landscapes including the CpG methylation and histone modifications regulated by GRHL2. These epigenetic changes along the EMT spectrum are also accompanied by the alterations of 3D chromatin architectures such as the switching of A (active)/B (inactive) compartments, topologically associated domain (TAD) boundaries, and short- and long-range chromatin loopings.

References:

- *EMT: 2016. Nieto et al, Cell 2016 166 (1), 21-45*
- *An EMT spectrum defines an anoikis-resistant and spheroidogenic intermediate mesenchymal state that is sensitive to e-cadherin restoration by a src-kinase inhibitor AZD0530. Huang et al, Cell death & disease 2013 4 (11), e915*
- *GRHL2-miR-200-ZEB1 maintains the epithelial status of ovarian cancer through transcriptional regulation and histone modification. Chung et al, Scientific reports 2016 6, 19943*
- *The transcription factor Grainy head primes epithelial enhancers for spatiotemporal activation by displacing nucleosomes. Jacobs et al, J, Nat Genet. 2018 Jul;50(7):1011-1020.*

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