

Epithelial-mesenchymal transition (EMT): a spectrum beyond binary.

Ruby Yun-Ju Huang

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, such as GRHL2 and OVOL2. In this lecture, I will introduce the concept of EMT spectrum and how it is defined. I will summarize the transcriptional regulatory networks and how it controls the plasticity along the EMT spectrum.

References:

1. EMT: 2016. MA Nieto, RYJ Huang, RA Jackson, JP Thiery. *Cell* 2016 166 (1), 21-45
2. 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. R YJ Huang, MK Wong, TZ Tan, KT Kuay, AHC Ng, VY Chung, YS Chu, N Matsumura, HC Lai, YF Lee, WJ Sim, C Chai, E Pietschmann, S Mori, JJH Low, M Choolani, JP Thiery. *Cell death & disease* 2013 4 (11), e915
3. EMT Transition States during Tumor Progression and Metastasis. Pastushenko I, Blanpain C. *Trends Cell Biol.* 2019 Mar;29(3):212-226.
4. Identification of the tumour transition states occurring during EMT. Pastushenko I, Brisebarre A, Sifrim A, Fioramonti M, Revenco T, Boumahdi S, Van Keymeulen A, Brown D, Moers V, Lemaire S, De Clercq S, Minguijón E, Balsat C, Sokolow Y, Dubois C, De Cock F, Scozzaro S, Sopena F, Lanas A, D'Haene N, Salmon I, Marine JC, Voet T, Sotiropoulou PA, Blanpain C. *Nature.* 2018 Apr;556(7702):463-468.