Epithelial-mesenchymal plasticity in cancer progression: mechanisms and clinical significance

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Epithelial-mesenchymal transition (EMT) has been recognized for its essential role in cancer progression. Increasing evidence suggests the existence of an intermediate status between epithelial and mesenchymal phenotypes, and the appearance of hybrid epithelial-mesenchymal (E/M) phenotype offers a more plastic status for cancer cells to adapt the stressful environment for metastasis. Cancer cells in the hybrid E/M state are easier to switch between epithelial and mesenchymal states and migrate collectively with retained intercellular junctions. However, the understanding of the control of the hybrid E/M state is limited. We previously demonstrated that acetylation of the EMT transcriptional factor Snail switches it from a transcriptional repressor to an activator through recruiting different co-factors. Acetylated Snail induces the expression of the junctional protein claudin-11 to engender collective migration and formation of circulating tumor clusters. We recently also noted the importance of GATA3 as the gatekeeper for hybrid E/M state. Our results highlight a mechanism for controlling the hybrid E/M state of cancer cells for facilitating metastasis.