Epithelial-Mesenchymal Transition

The epithelial-mesenchymal transition (EMT) is a process by which epithelial cells lose their cell polarity and cell-cell adhesion, and gain migratory and invasive properties to become mesenchymal stem cells; these are multipotent stromal cells that can differentiate into a variety of cell types.

The epithelial-Mesenchymal transition (EMT) of the Basement Membrane (BM) allows cells of epithelial phenotype to transform into a mesenchymal-like (quasi-mesenchymal) phenotype and metastasize via the lymphovascular system through a metastatic cascade by intravasation and extravasation. This helps in the progression of carcinoma from the primary site to distant organs. Collagen, laminin, and integrin are the prime components of BM and help in tumor cell metastasis, which makes them ideal cancer drug targets. Further, recent studies have shown that collagen, laminin, and integrin can be used as a biomarker for metastatic cells. In a review, Banerjee et al. summarized the current knowledge of such therapeutics, which are either currently in preclinical or clinical stages and could be promising cancer therapeutics [1)].

Sakamoto et al. previously reported that ETS1 induces expression of the ZEB family proteins ZEB1/δEF1 and ZEB2/SIP1, which are key regulators of the epithelial-mesenchymal transition (EMT), by activating the ZEB1 promoters. They have found that the EHF gene produces two transcript variants, namely a long-form variant that includes exon 1 (EHF-LF) and a short form variant that excludes exon 1 (EHF-SF). Only EHF-SF abrogates ETS1-mediated activation of the ZEB1 promoter by promoting the degradation of ETS1 proteins, thereby inhibiting the EMT phenotypes of cancer cells. Most importantly, we identified a novel point mutation within the conserved ETS domain of EHF and found that EHF mutations abolish its original function while causing the EHF protein to act as a potential dominant-negative, thereby enhancing metastases in vivo. Therefore, they suggest that EHF acts as an anti-EMT factor by inhibiting the expression of ZEBs and that EHF mutations exacerbate cancer progression [2)].

1)
Banerjee S, Lo WC, Majumder P, Roy D, Ghorai M, Shaikh NK, Kant N, Shekhawat MS, Gadekar VS, Ghosh S, Bursal E, Alrumaihi F, Dubey NK, Kumar S, Iqbal D, Alturaiki W, Upadhye VJ, Jha NK, Dey A, Gundamaraju R. Multiple roles for basement membrane proteins in cancer progression and EMT. Eur J Cell Biol. 2022 Mar 30;101(2):151220. doi: 10.1016/j.ejcb.2022.151220. Epub ahead of print. PMID: 35366585.

2)
Sakamoto K, Endo K, Sakamoto K, Kayamori K, Ehata S, Ichikawa J, Ando T, Nakamura R, Kimura Y, Yoshizawa K, Masuyama K, Kawataki T, Miyake K, Ishii H, Kawasaki T, Miyazawa K, Saitoh M. EHF suppresses cancer progression by inhibiting ETS1-mediated ZEB expression. Oncogenesis. 2021 Mar 12;10(3):26. doi: 10.1038/s41389-021-00313-2. PMID: 33712555.