ZEB

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 [1].

1)
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.