## modulator of the nuclear response to mitogen-activated protein kinase signaling cascades. Binds to

**ETS homologous factor** 

DNA sequences containing the consensus nucleotide core sequence GGAA. Involved in regulation of TNFRSF10B/DR5 expression through Ets-binding sequences on the TNFRSF10B/DR5 promoter. May contribute to the development and carcinogenesis by acting as a tumor suppressor gene or antioncogene.

ETS homologous factor (EHF) belongs to the epithelium-specific subfamily of the ETS transcription factor family. Currently, little is known about EHF's function in cancer. Sakamoto et al. previously reported that ETS1 induces expression of the ZEB family proteins ZEB1/\deltaEF1 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 <sup>1)</sup>.

## 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.

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Last update: 2024/06/07 02:58

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Transcriptional activator that may play a role in regulating epithelial cell differentiation and proliferation. May act as a repressor for a specific subset of ETS/AP-1-responsive genes and as a