TCF7L2 is a transcription factor influencing the transcription of several genes thereby exerting a large variety of functions within the cell. It is a member of the TCF family that can form a bipartite transcription factor (β-catenin/TCF) alongside β-catenin.

A previous study showed LCN2 promotes migration and invasion of Esophageal squamous cell carcinoma cells through a novel positive feedback loop. However, the key transcription activation protein (KTAP) in the loop had not yet been identified. In this study, Zhao et al., first predicted the most probable KTAPs by bioinformatic analysis. They then assessed the transcription regulatory regions in the human LCN2 gene by fusing deletions of its 5'-flanking region to a dual-luciferase reporter. They found that the region -720/-200 containing transcription factor 7-like 2 (TCF7L2) (-273/-209) and early growth response 1 (EGR1) (-710/-616) binding sites is crucial for LCN2 promoter activity. Chromatin immunoprecipitation (ChIP) experiments demonstrated that TCF7L2 and EGR1 bound directly to their binding sites within the LCN2 promoter as KTAPs. Mechanistically, overexpression of TCF7L2 and EGR1 increased endogenous LCN2 expression via the ERK signaling pathway. Treatment with recombinant human LCN2 protein enhanced activation of the ERK pathway to facilitate endogenous LCN2 expression, as well as increase the expression level of TCF7L2 and EGR1. Treatment with the MEK inhibitor U0126 inhibited the activation by TCF7L2 or EGR1 overexpression. Moreover, overexpression of TCF7L2 or EGR1 accelerated the migration and invasion of ESCC cells. A synergistic effect was observed between TCF7L2 and EGR1 in amplifying the induction of LCN2 and enhancing migration and invasion. Taken together, our study indicates that TCF7L2 and EGR1 are the KTAPs of LCN2, within a positive “LCN2→MEK/ERK→LCN2” path, to promote the migration and invasion of ESCC cells. Based on their clinicopathological significance, LCN2 and its two expression regulators TCF7L2 and ERG1 might be therapeutic targets for ESCC [1].

1)
Zhao Y, Xia Q, Liu Y, Bai W, Yao Y, Ding J, Lin L, Xu Z, Cai Z, Wang S, Li E, Xu H, Wu B, Xu L, Du Z. TCF7L2 and EGR1 synergistic activation of transcription of LCN2 via an ERK1/2-dependent pathway in esophageal squamous cell carcinoma cells. Cell Signal. 2018 Dec 14. pii: S0898-6568(18)30309-7. doi: 10.1016/j.cellsig.2018.12.007. [Epub ahead of print] PubMed PMID: 30557604.