J Clin Epigenet 2017, 3:4
DOI: 10.21767/2472-1158-C1-003

SOX18 transcription factor interactome: Protein-protein interaction a new road for anti-cancer drug discovery SOX18 transcription factor interactome: Protein-protein interaction a new road for anti-cancer drug discovery

Mehdi Moustaqil
[1]EMBL, Australia
[2]Single Molecule Science-UNSW, Australia

Pharmacological targeting of transcription factors holds great promise for the development of new therapeutics, but the strategies based on blockading DNA binding, nuclear shuttling, or individual protein partner recruitment have had limited success to date. A single transcription factor has multiple transcriptional effects that are context-dependent. This versatility of activity is thought to be mediated by different protein-protein interactions (PPIs). Therefore, these PPIs offer a new avenue for the selective pharmacological modulation of transcription factor activity, which will lead to develop novel therapeutics. Transcription factors typically engage in complex interaction networks, likely masking the effects of specifically inhibiting single protein-protein interactions. Here, we used a combination of genomic, proteomic and biophysical methods to discover a suite of protein-protein interactions involving the SOX18 transcription factor, a known regulator of vascular development and thus cancer metastasis. We describe a small-molecule that is able to disrupt a discrete subset of SOX18-dependent interactions. This compound selectively suppressed SOX18 transcriptional outputs *in vitro* and interfered with vascular development in zebrafish larvae. In a mouse pre-clinical model of breast cancer, treatment with this inhibitor significantly improved survival by reducing tumor vascular density and metastatic spread.