Transcriptional repressor

Transcriptional repressors are usually viewed as proteins that bind to promoters in a way that impedes subsequent binding of RNA polymerase. Although this repression mechanism is found at several promoters, there is a growing list of repressors that inhibit transcription initiation in other ways.

Transcriptional repressors can be classified based on mechanism of action, molecular structure, or biological function. Here's a comprehensive classification:

 By Mechanism of Action Direct DNA-binding repressors Bind directly to DNA sequences (usually at promoters or enhancers) to block transcription factor binding or RNA polymerase recruitment.

Example: REST (RE1-Silencing Transcription factor)

Corepressor-dependent repressors Do not block transcription on their own but recruit corepressors that modify chromatin or inhibit transcription machinery.

Example: NCoR (Nuclear receptor corepressor)

Quenching repressors Bind to and inactivate transcriptional activators, preventing them from activating gene expression.

Example: Some Groucho/TLE family members

Chromatin-modifying repressors Recruit enzymes (e.g., histone deacetylases, methyltransferases) that compact chromatin, making DNA inaccessible.

Example: Polycomb group proteins (e.g., EZH2)

Transcriptional interference repressors Inhibit transcription by transcriptional collision or occlusion, often in bidirectional or overlapping gene regions.

 By Molecular Type or Family Zinc finger repressors Contain zinc finger motifs for DNA binding.

Example: Krüppel-like repressors

Homeodomain repressors Involved in development; often repress genes that specify alternate cell fates.

Example: Engrailed, Hox proteins

Basic helix-loop-helix (bHLH) repressors Compete with activators or form inactive heterodimers.

Example: Id proteins

Nuclear hormone receptor repressors Bind to hormone response elements in the absence of ligand and recruit corepressors.

Example: Thyroid hormone receptor (TR) in absence of T3

Polycomb group proteins Maintain transcriptional repression via chromatin modification over many cell divisions.

Example: PRC1 and PRC2 complexes

 By Biological Role or Context Developmental repressors Temporally and spatially regulate gene expression during embryogenesis.

Example: Snail (in epithelial-mesenchymal transition)

Tumor suppressor repressors Repress genes that promote cell cycle progression or inhibit apoptosis.

Example: Rb protein (retinoblastoma protein)

Epigenetic repressors Establish heritable transcriptional silencing via DNA methylation and histone modification.

Example: MeCP2

Zhang et al crucially identified that KIF4A drives glioma growth by Rac1/Cdc42 transcriptional repressors to induce cytoskeletal remodeling in glioma cells. Knockdown of KIF4A decreased RohA, Rac1, Cdc42, Pak1 and Pak2 expression level. The study provided a prospect that KIF4A functions as an oncogene in glioma [1)].

1)
Zhang H, Meng S, Chu K, Chu S, Fan YC, Bai J, Yu ZQ. KIF4A drives glioma growth by transcriptional repression of Rac1/Cdc42 to induce cytoskeletal remodeling in glioma cells. J Cancer. 2022 Nov 21;13(15):3640-3651. doi: 10.7150/jca.77238. PMID: 36606197; PMCID: PMC9809311.