Cis-regulatory element

Cis-regulatory elements (CREs) are regions of noncoding DNA which regulate the transcription of neighboring genes. CREs are vital components of Gene regulatory networks, which in turn control morphogenesis, the development of anatomy, and other aspects of embryonic development, studied in evolutionary developmental biology.

CREs are found in the vicinity of the genes that they regulate. CREs typically regulate gene transcription by binding to transcription factors. A single transcription factor may bind to many CREs, and hence control the expression of many genes (pleiotropy). The Latin prefix cis means “on this side”, i.e. on the same molecule of DNA as the gene(s) to be transcribed. CREs are often but not always upstream of the transcription site.

CREs contrast with trans-regulatory elements (TREs). TREs code for transcription factors.

RET finger protein (RFP) forms a complex with histone deacetylase 1, resulting in aberrant deacetylation of H3K27ac and dysregulation of cis-regulatory elements.

Ranjit et al., evaluated the modulatory effects of RFP knockdown on cis-regulatory elements, gene expression, and chemosensitivity to temozolomide both in glioblastoma cells and in an intracranial glioblastoma model. The combination of RFP knockdown and temozolomide treatment markedly suppressed the glioblastoma cell growth due to oxidative stress and aberrant cell cycle and increased survival time in mice with glioblastoma. ChIP-seq and RNA-seq revealed that RFP knockdown increased or decreased activity of numerous cis-regulatory elements that lie adjacent to genes that control functions such as apoptosis, mitosis, DNA replication, and cell cycle: FOXO1, TBP2, and PARPBP. This study suggests that RFP contributes to chemoresistance via aberrant deacetylation of histone H3 at K27, whereas dysregulation of RFP-associated cis-regulatory elements in glioma and RFP knockdown combined with temozolomide is an effective treatment strategy for lethal glioma [1].

1)
Ranjit M, Hirano M, Aoki K, Okuno Y, Ohka F, Yamamichi A, Kato A, Maeda S, Motomura K, Matsuo K, Enomoto A, Ino Y, Todo T, Takahashi M, Wakabayashi T, Kato T, Natsume A. Aberrant Active cis-Regulatory Elements Associated with Downregulation of RET Finger Protein Overcome Chemoresistance in Glioblastoma. Cell Rep. 2019 Feb 26;26(9):2274-2281.e5. doi: 10.1016/j.celrep.2019.01.109. PubMed PMID: 30811978.