Myc

Myc (c-Myc) is a oncogene that codes for a transcription factor. The protein encoded by this gene is a multifunctional, nuclear phosphoprotein that plays a role in cell cycle progression, apoptosis and cellular transformation.

A mutated version of Myc is found in many cancers, which causes Myc to be constitutively (persistently) expressed. This leads to the unregulated expression of many genes, some of which are involved in cell proliferation, and results in the formation of cancer.

A common human translocation involving Myc is critical to the development of most cases of Burkitt Lymphoma.

Malfunctions in Myc have also been found in carcinoma of the cervix, colon, breast, lung and stomach.

The super elongation complex (SEC) inhibition downregulates MYC and MYC-dependent transcriptional programs in mammalian cells and delays tumor progression in a mouse xenograft model of MYC-driven cancer, indicating that small-molecule disruptors of SEC could be used for targeted therapy of MYC-induced cancer [1].

Myc is thus viewed as a promising target for anti-cancer drugs.

In the human genome, Myc is located on chromosome 8 and is believed to regulate expression of 15% of all genes through binding on Enhancer Box sequences (E-boxes) and recruiting histone acetyltransferases (HATs). This means that in addition to its role as a classical transcription factor, Myc also functions to regulate global chromatin structure by regulating histone acetylation both in gene-rich regions and at sites far from any known gene.

The Myc oncogene and the Let 7 microRNA precursor, lethal-7a microRNA (let-7a MicroRNA) have been suggested to cooperatively regulate multiple downstream targets leading to changes in chromosome stability, gene mutations, and/or modulation of tumor growth.

Wang et al. review the roles of Myc and let-7a in glucose metabolism and tumor growth and addresses their future potential as prognostic markers and therapeutic tools in glioblastoma (GBM), and focus on the functions of Myc and let-7a in glucose uptake, tumor survival, proliferation, and mobility of glioma cells. In addition, we discuss how regulation of different pathways by Myc or let-7a may be useful for future GBM therapies. A large body of evidence suggests that targeting Myc and let-7amay provide a selective mechanism for the deregulation of glucose metabolic pathways in glioma cells. Indeed, Myc and let-7a are aberrantly expressed in GBM and have been linked to the regulation of cell growth and glucose metabolism in GBM [2]

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Liang K, Smith ER, Aoi Y, Stoltz KL, Katagi H, Woodfin AR, Rendleman EJ, Marshall SA, Murray DC, Wang L, Ozark PA, Mishra RK, Hashizume R, Schiltz GE, Shilatifard A. Targeting Processive Transcription Elongation via SEC Disruption for MYC-Induced Cancer Therapy. Cell. 2018 Oct 18;175(3):766-779.e17. doi: 10.1016/j.cell.2018.09.027. PubMed PMID: 30340042.

2)
Wang G, Wang J, Zhao H, Wang J, To SS. The role of Myc and let-7a in glioblastoma, glucose metabolism and response to therapy. Arch Biochem Biophys. 2015 Jul 4. pii: S0003-9861(15)30009-6. doi: 10.1016/j.abb.2015.07.005. [Epub ahead of print] Review. PubMed PMID: 26151775.