MYCN

N-myc proto-oncogene protein also known as N-Myc or basic helix-loop-helix protein 37 (bHLHe37), is a protein that in humans is encoded by the MYCN gene.

MYCN amplification is tightly associated with the poor prognosis of pediatric neuroblastoma (NB). The regulation of NB cell death by MYCN represents an important aspect, as it directly contributes to tumor progression and therapeutic resistance. However, the relationship between MYCN and cell death remains elusive. Ferroptosis is a newly identified cell death mode featured by lipid peroxide accumulation that can be attenuated by GPX4, yet whether and how MYCN regulates Ferroptosis are not fully understood.

Lu et al. reported MYCN-amplified NB cells are sensitive to GPX4-targeting Ferroptosis inducers. Mechanically, MYCN expression reprograms the cellular iron metabolism by upregulating the expression of TFRC, which encodes transferrin receptor 1 as a key iron transporter on the cell membrane. Further, the increased iron uptake promotes the accumulation of labile iron pool, leading to enhanced lipid peroxide production. Consistently, TFRC overexpression in NB cells also induces selective sensitivity to GPX4 inhibition and Ferroptosis. Moreover, they found that MYCN fails to alter the general lipid metabolism and the amount of cystine imported by System Xc(-) for glutathione synthesis, both of which contribute to Ferroptosis in alternative contexts. In conclusion, NB cells harboring MYCN amplification are prone to undergo Ferroptosis conferred by TFRC upregulation, suggesting that GPX4-targeting Ferroptosis inducers or TFRC agonists can be potential strategies in treating MYCN-amplified NB [1)].

Glioblastoma with primitive neuronal components was added as a pattern in glioblastoma. This pattern previously referred to in the literature as glioblastoma with PNET-like component, is usually comprised of a diffuse astrocytoma of any grade (or oligodendroglioma in rare cases) that has well-demarcated nodules containing primitive cells that display neuronal differentiation (e.g., Homer Wright rosettes, a gain of synaptophysin positivity and loss of GFAP expression) and that sometimes has MYC or MYCN amplification; these tumors have a tendency for craniospinal fluid dissemination.

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