Chromosome 7

Asparagine synthetase (ASNS) is a gene on the long arm of chromosome 7 that is a copy number amplified in the majority of glioblastomas. ASNS copy number amplification is associated with a significantly decreased survival. Using patient-derived glioma stem cells (GSCs), Thomas et al. showed significant metabolic alterations occur in gliomas when perturbing the expression of asparagine synthetase, which is not merely restricted to amino acid homeostasis. ASNS-high GSCs maintained a slower basal metabolic profile yet readily shifted to a greatly increased capacity for glycolysis and oxidative phosphorylation when needed. This led ASNS-high cells to a greater ability to proliferate and spread into brain tissue. Finally, we demonstrate that these changes confer resistance to cellular stress, notably oxidative stress, through adaptive redox homeostasis which led to radiation resistance. Furthermore, ASNS overexpression led to modifications of the one-carbon metabolism to promote a more antioxidant tumor environment revealing a metabolic vulnerability that may be therapeutically exploited. Implications: This study reveals a new role for ASNS in metabolic control and redox homeostasis in glioma stem cells and proposes a new treatment strategy that attempts to exploit one vulnerable metabolic node within the larger multilayered tumor network [1)].

The current WHO classification on and its emphasis on molecular characteristics has made the distiction on between tumor grades less clear. The revised classification on now emphasizes molecular similarities, with only minimal morphologic and subjective differences between grades 2 and 3. This is reflected in the decreased difference in survival between grades 2 and 3 IDH-mutant (IDHmt) astrocytoma, and, taken together, this suggests more of a continuum between grades. Instead, the WHO appropriately now distinguishes between types of IDHmt glioma (astrocytoma for those 1p/19q intact and oligodendroglioma if 1p/19q is codeleted). There is now compelling evidence that patients with grade 2 or 3 IDH-wildtype glioma with TERT mutations and polysomy of chromosome 7 plus loss of heterozygosity of chromosome 10q have similar outcomes compared with those with Glioblastoma.

1)

Thomas TM, Miyaguchi K, Edwards LA, Wang H, Wollebo H, Aiguo L, Murali R, Wang Y, Braas D, Michael JS, Andres A, Zhang M, Khalili K, Gottlieb RA, Perez JM, Yu JS. Elevated Asparagine Biosynthesis Drives Brain Tumor Stem Cell Metabolic Plasticity and Resistance to Oxidative Stress. Mol Cancer Res. 2021 Apr 16:molcanres.0086.2020. doi: 10.1158/1541-7786.MCR-20-0086. Epub ahead of print. PMID: 33863814.

From:
https://neurosurgerywiki.com/wiki/ - **Neurosurgery Wiki**

Permanent link:
https://neurosurgerywiki.com/wiki/doku.php?id=chromosome_7

Last update: **2024/06/07 02:57**