Olig2

Oligodendrocyte transcriptional factor-2 (Olig2) is an essential marker for oligodendrocytes expression. Olig2 marker cannot be used as an alternative diagnostic method for 1p 19q co-deletion to distinguish oligodendrogliomas from other glial neoplasms. Although some glial tumors showed diffuse Olig2 expression, 1p19q co-deletion testing is the best diagnostic method [1].

Wu et al. identified and independently validated two reproducible subtypes associated with distinct molecular characteristics and clinical outcomes. The proliferative subtype, named Oligo1, was characterized by more tumors of CNS WHO grade 3, as well as worse prognosis compared to the Oligo2 subtype. Besides the clinicopathologic features, Oligo1 exhibited enrichment of cell proliferation, regulation of cell cycle and Wnt signaling pathways, and significantly altered genes, such as EGFR, NOTCH1 and MET. In contrast, Oligo2, with favorable outcome, presented increased activation of immune response and metabolic process. Higher T cell/APC co-inhibition and inhibitory checkpoint levels were observed in Oligo2 tumors. Finally, multivariable analysis revealed this classification was an independent prognostic factor in oligodendrogliomas, and the robustness of these molecular subgroups was verified in the validation cohorts [2].

Distinct neural stem cells (NSCs) reside in different regions of the subventricular zone (SVZ) and generate multiple olfactory bulb (OB) interneuron subtypes in the adult brain. The molecular mechanisms underlying such NSC heterogeneity, however, remain largely unknown. Del Águila et al. showed that the basic helix-loop-helix transcription factor Olig2 defines a subset of NSCs in the early postnatal and adult SVZ. Olig2-expressing NSCs exist broadly but are most enriched in the ventral SVZ along the dorsoventral axis complementary to dorsally enriched Gsx2-expressing NSCs. Comparisons of Olig2-expressing NSCs from early embryonic to adult stages using single-cell transcriptomics reveal stepwise developmental changes in their cell cycle and metabolic properties. Genetic studies further show that cross-repression contributes to the mutually exclusive expression of Olig2 and Gsx2 in NSCs/progenitors during embryogenesis, but their expression is regulated independently from each other in adult NSCs. Finally, lineage tracing and conditional inactivation studies demonstrate that Olig2 plays an important role in the specification of OB interneuron subtypes. Altogether the study demonstrates that Olig2 defines a unique subset of adult NSCs enriched in the ventral aspect of the adult SVZ [3].

Among the evaluated markers MAP - 2, OLIG - 2 and WT - 1 showed the best potential to separate between glioma entities and can be recommended for a standardized immunohistochemical panel [4].

The basic helix-loop-helix transcription factor OLIG2, which is universally expressed in gliomas, has emerged as an important player in Glioblastoma cell reprogramming, genotoxic resistance, and tumor phenotype plasticity. In an animal model of proneural Glioblastoma, elimination of mitotic OLIG2+ progenitors blocks tumor growth, suggesting that these progenitors are a seeding source for glioma propagation. OLIG2 deletion reduces tumor growth and causes an oligodendrocytic to astrocytic phenotype shift, with PDGFRα down-regulation and reciprocal EGFR signaling up-regulation, underlying alternative pathways in tumor recurrence. In patient-derived glioma stem cells (GSC),

knockdown of OLIG2 leads to down-regulation of PDGFRα, while OLIG2 silencing results in a shift from proneural-to-classical gene expression pattern or a proneural-to-mesenchymal transition in distinct GSC cell lines, where OLIG2 appears to regulate EGFR expression in a context-dependent manner. In addition, post-translational modifications such as phosphorylation by a series of protein kinases regulates OLIG2 activity in glioma cell growth and invasive behaviors [5].

Several studies have hypothesized that gliomagenesis occurs in perivascular niches with highly invasive peripheral proliferating zones. The purpose of a study was to investigate the pathological and clinical significance of Olig2 and YKL40 immunoexpression in 152 GBs in relationship to the SVZ II and III. Olig2 expressions were successfully detected in 12 (15.58%) of 77 SVZ type II GBs and 16 (21.3%) of 75 SVZ type III GBs, respectively. YKL-40 expression was observed in 45 (58.4%) of 77 SVZ type II GBs and in 17 (22.6%) of 75 SVZ type III GBs, respectively. Stepwise multivariate Cox proportional hazards models were used, and the prognostic factors to significantly impact OS were: PFS < 54 weeks (HR: 5.86; CI: 3.02-11.33; p = 0.00); radiotherapy (HR: 0.34; CI: 0.18-0.60; p = 0.00); radio- and chemotherapy (HR: 0.05; CI: 0.03-0.10; p = 0.0), and YKL-40+ GBs (HR: 1.61; CI: 1.28-2.31; p = 0.01) [6].

1)
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