NRP1

Medulloblastoma (MB) is the most common type of malignant pediatric brain tumor. Neuropilin-1 (NRP1), encoded by the NRP1 gene, is a transmembrane glycoprotein overexpressed in several types of cancer. Previous studies indicate that NRP1 inhibition displays antitumor effects in MB models and higher NRP1 levels are associated with poorer prognosis in MB patients. Here, we used a large MB tumor dataset to examine NRP1 gene expression in different molecular subgroups and subtypes of MB. We found overall widespread NRP1 expression across MB samples. Tumors in the sonic hedgehog (SHH) subgroup showed significantly higher NRP1 transcript levels in comparison with Group 3 and Group 4 tumors, with SHH samples belonging to the α, β, Δ, and γ subtypes. When all MB subgroups were combined, lower NRP1 expression was associated with significantly shorter patient overall survival (OS). Further analysis showed that low NRP1 was related to poorer OS, specifically in MB subgroups SHH and Group 3 MB. Our findings indicate that patients with SHH and Group 3 tumors that show lower expression of NRP1 in MB have a worse prognosis, which highlights the need for subgroup-specific investigation of the NRP1 role in MB [1].

Neuropilin-1 is an agonist of angiogenesis through complex-binding of VEGF-A, but it can also work as an inhibitor through competitive binding of semaphorin-3A. The complex binding of semaphorin-3A to neuropilin-1 can also induce endothelial cell apoptosis, thus working as an antagonist of angiogenesis [2].

Zhang et al. found that NRP-1 and its downstream NRP-1/GIPC1 pathway played an important role in GBM.

They further investigated the upstream signaling of NRP-1 to understand how it is regulated. Firstly, they identified that hsa-miR-124-3p was miRNA differentially expressed in GBM and in normal brain tissues by high-throughput sequencing. Then, by dual luciferase reporter gene, we found miR-124-3p can specially bind to the 3'UTR region of the NRP-1 thus suppresses its expression. Moreover, miR-124-3p overexpression significantly inhibited GBM cell proliferation, migration and tumor angiogenesis which resulted in GBM apoptosis and cell cycle arrest, putatively via NRP-1 mediated PI3K/Akt/NFκB pathways activation in GBM cells. Meanwhile, miR-124-3p overexpression also suppressed tumor growth and reduced tumor angiogenesis when targeted by NRP-1 in a PDX model. Furthermore, NRP-1 mAb exerted synergistic inhibitory effects with miR-124-3p overexpression in GBM. Thus, we discovered that miR-124-3p acts as the upstream suppressor of NRP-1 which promotes GBM cell development and growth by PI3K/Akt/NFκB pathway. The miR-124-3p/NRP-1/GIPC1 pathway as a new pathway has a vital role in GBM, and it could be considered as the potential target for malignant gliomas in future [3].

1)
de Araújo MA, Malafaia O, Ribas Filho JM, Fratini L, Roesler R, Isolan GR. Low Expression of the NRP1 Gene Is Associated with Shorter Overall Survival in Patients with Sonic Hedgehog and Group 3 Medulloblastoma. Int J Mol Sci. 2023 Jul 18;24(14):11601. doi: 10.3390/ijms241411601. PMID: 37511358; PMCID: PMC10380701.
2)
Nassehi D. Intracranial meningiomas, the VEGF-A pathway, and peritumoral brain oedema. Dan Med J. 2013 Apr;60(4):B4626. Review. PubMed PMID: 23651727.

3)

Zhang G, Chen L, Khan AA, Li B, Gu B, Lin F, Su X, Yan J. miRNA-124-3p/neuropilin-1(NRP-1) axis plays an important role in mediating glioblastoma growth and angiogenesis. Int J Cancer. 2018 Feb 19. doi: 10.1002/ijc.31329. [Epub ahead of print] PubMed PMID: 29457830.