Annexin A2

Annexin A2 also known as annexin II is a protein that in humans is encoded by the ANXA2 gene.

Annexin 2 is involved in diverse cellular processes such as cell motility (especially that of the epithelial cells), linkage of membrane-associated protein complexes to the actin cytoskeleton, endocytosis, fibrinolysis, ion channel formation, and cell-matrix interactions. It is a calcium-dependent phospholipid-binding protein whose function is to help organize exocytosis of intracellular proteins to the extracellular domain. Annexin II is a pleiotropic protein meaning that its function is dependent on place and time in the body.

Porcù et al. demonstrated that Annexin A2 (ANXA2) is a pivotal mediator of the pro-oncogenic features displayed by glioblastoma (Glioblastoma) tumors, the deadliest adult brain malignancies, being involved in the cell stemness, proliferation, and invasion, thus negatively impacting patient prognosis. Based on these results, they hypothesized that compounds able to revert ANXA2-dependent transcriptional features could be exploited as reliable treatments to inhibit Glioblastoma cell aggressiveness by hampering their proliferative and migratory potential. Transcriptional signatures obtained by the modulation of ANXA2 activity/levels were functionally mapped through the QUADrATiC bioinformatic tool for compound identification. Selected compounds were screened by cell proliferation and migration assays in primary Glioblastoma cells, and we identified Homoharringtonine (HHT) as a potent inhibitor of Glioblastoma cell motility and proliferation, without affecting their viability. Further molecular characterization of the effects displayed by HHT, confirmed its ability to inhibit a transcriptional program involved in cell migration and invasion. Moreover, they demonstrated that the multiple antitumoral effects displayed by HHT are correlated to the inhibition of PDGFRA-dependent intracellular signaling through the impairment of STAT3 and RhoA axes. The results demonstrate that HHT may act as a potent inhibitor of cancer cell proliferation and invasion in glioblastoma, by hampering multiple PDGFRα-dependent oncogenic signals transduced through the STAT3 and RhoA intracellular components, finally suggesting its potential transferability for achieving an effective impairment of peculiar Glioblastoma hallmarks [1)].

In order to set up a reliable prediction system for the tumor grade and glioma outcome, Li et al. clarified the complicated crosstalk of Annexin A2 (ANXA2) with Glypican 1 (GPC1) and demonstrate whether combined indexes of ANXA2 and GPC1 could improve the prognostic evaluation for glioma patients. Li et al. found that ANXA2-induced glioma cell proliferation in a c-Myc-dependent manner. ANXA2 increased the expression of GPC1 via c-Myc and the upregulated GPC1 further promoted the c-Myc level, forming a positive feedback loop, which eventually led to enhanced proliferation of glioma cells. Both mRNA and protein levels of ANXA2 were upregulated in glioma tissues and coincided with the overexpression of GPC1. Besides, they utilized tissue microarrays (TMAs) and immunohistochemistry to demonstrate that glioma patients with both high expressions of ANXA2 and GPC1 tended to have a higher rate of tumor recurrence and shorter overall survival (OS). In conclusion, the overexpression of ANXA2 promotes proliferation of glioma cells by forming a GPC1/c-Myc positive feedback loop, and ANXA2 together with its downstream target GPC1 could be a potential “combination biomarker” for predicting the prognosis of glioma patients [2)].

1)

Porcù E, Maule F, Manfreda L, Mariotto E, Bresolin S, Cani A, Bortolozzi R, Puppa AD, Corallo D, Viola

G, Rampazzo E, Persano L. Identification of Homoharringtonine as a potent inhibitor of glioblastoma cell proliferation and migration. Transl Res. 2022 Jul 1:S1931-5244(22)00151-7. doi: 10.1016/j.trsl.2022.06.017. Epub ahead of print. PMID: 35788055.
2)
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