ANXA3

Annexin A3 is a protein that in humans is encoded by the ANXA3 gene.

It is abnormally expressed in fetuses of both IVF and ICSI, which may contribute to the increase risk of birth defects in these ART.

This gene encodes a member of the annexin family. Members of this calcium-dependent phospholipid-binding protein family play a role in the regulation of cellular growth and in signal transduction pathways. This protein functions in the inhibition of phospholipase A2 and cleavage of inositol 1,2-cyclic phosphate to form inositol 1-phosphate. This protein may also play a role in anti-coagulation.

Annexin A3 (ANXA3) is dysregulated and plays an important role in various cancers.

Wang et al. investigated the role of Annexin A3 (ANXA3) silencing in intracranial aneurysm (IA) with the interaction of the c-Jun N-terminal kinase JNK signaling pathway. In IA and vascular smooth muscle cell (VSMC)s of IA, the relationship between ANXA3 and the JNK signaling pathway was verified. To investigate the specific mechanism of ANXA3 silencing in IA, they transfected VSMCs with the overexpressed or small interfering RNA (siRNA) of ANXA3, or treated them with an inhibitor of the JNK signaling (SP600125). Cell counting kit-8 (CCK-8) assay was conducted to detect cell viability, and flow cytometry was conducted to assess cell cycle and apoptosis so as to evaluate the gain- and loss-of-function of ANXA3 and investigate the involvement of the JNK signaling pathway. The aneurysm wall of IA cells demonstrated an elevated level of ANXA3 expression and an activated JNK signaling pathway. VSMCs treated with siRNA-ANXA3 or SP600125 showed decreased expression of JNK, caspase-3, osteopontin (OPN), Bax, and matrix metalloproteinase-9 (MMP-9), as well as phosphate (p)-JNK, but increased the expression of α smooth muscle actin (α-SMA), β-tubulin, and Bcl-2. ANXA3 silencing or inactivation of the JNK signaling pathway also enhanced proliferation and repressed apoptosis of VSMCs. Collectively, this study shows that the silencing of ANXA3 can rescue VSMC function in IAs by inhibiting the phosphorylation and activation of the JNK signaling pathway. These findings may provide a potential therapy for the molecular treatment of IAs [1)].

The role of ANXA3 in breast cancer is still unclear. Here, we observed that the expression level of ANXA3 was significantly upregulated in breast cancer tissues. ANXA3 knockdown inhibited cell invasion but promoted cell proliferation in both in vitro and in vivo assays. Furthermore, we found that ANXA3 knockdown inhibited the NFκB pathway via upregulating IκBα, resulting in mesenchymal-epithelial transition (MET) and a heterogeneity change of breast cancer stem cells (BCSCs). In addition, we demonstrated that ANXA3 knockdown increased the sensitivity of breast cancer cells to doxorubicin by increasing the drug uptake. The combination of ANXA3 knockdown and doxorubicin treatment simultaneously inhibited tumor growth and metastasis in vivo. This study described the role and mechanisms of ANXA3 in regulating BCSCs and breast cancer growth and metastasis, indicating that downregulating ANXA3 together with chemotherapy might be a novel therapeutic strategy for treating breast cancer [2)].

1)

Wang Y, Wang C, Yang Q, Cheng YL. ANXA3 Silencing Ameliorates Intracranial Aneurysm via Inhibition of the JNK Signaling Pathway. Mol Ther Nucleic Acids. 2019 Jun 19;17:540-550. doi: 10.1016/j.omtn.2019.06.005. [Epub ahead of print] PubMed PMID: 31362241.
2)

Du R, Liu B, Zhou L, Wang D, He X, Xu X, Zhang L, Niu C, Liu S. Downregulation of annexin A3 inhibits tumor metastasis and decreases drug resistance in breast cancer. Cell Death Dis. 2018 Jan 26;9(2):126. doi: 10.1038/s41419-017-0143-z. PubMed PMID: 29374148.