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Role of FRZB in proliferative vascular diseases

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Proliferative vascular diseases result from excessive cell proliferation, leading to plaque formation in blood vessels and various vascular health issues. Vascular Smooth Muscle Cells (VSMCs) play a critical role as a key cell type present throughout every stage of proliferative vascular disease plaque development. FRZB (Frizzled-related protein) plays a central role in Wnt signaling, impacting cell growth, differentiation, and tissue development. Previous research has shown the significance of FRZB in maintaining blood vessel integrity within Abdominal Aortic Aneurysm (AAA). However, the role of FRZB in overall proliferative vascular disease remains unclear. The purpose of this study is to examine the role of FRZB in proliferative vascular diseases. We conducted experiments using AAA (induced Hypertension) and Wire-injury mouse models, which revealed decreased FRZB expression in these diseases. Experiments on FRZB knockdown VSMC were conducted to confirm the function of FRZB in human cells, and cell migration and proliferation were observed to increase. Using single-cell RNA sequencing based on GSE155512 (n=3) data from the National Center for Biotechnology Information (NCBI), we conducted an evaluation to assess the presence of consistent results in atherosclerosis, a representative proliferative vascular disease. As expected, FRZB was highly expressed in the VSMC region, and FRZB was significantly reduced in the Synthetic Type among the two types of VSMC. Synthetic regions could be divided into FRZB Low, Middle, and High according to the difference in FRZB expression. Synthetic type genes were highly expressed in FRZB Low, and the cell type was changed from FRZB knock-down to Synthetic Type in cell experiments. Gene set enrichment analysis revealed a reduction in ECM-receptor interaction, focal adhesion, and the PI3-AKT signaling pathway in the FRZB Low group. Cell experiments also confirmed these reductions. Thus, we presume that decreased FRZB expression leads to a shift in VSMCs towards a Synthetic phenotype, potentially worsening vascular diseases. This suggests that FRZB could serve as a potential therapeutic target for proliferative vascular disease.