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Alterations of Pericytes in the Bone Marrow Stem Cell Niche of Patients with Type 2 Diabetes Mellitus

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Background: Type 2 Diabetes Mellitus (T2D) endangers vascular cell integrity and remodels the bone marrow (BM) with microangiopathy and hematopoietic dysfunction. Pericytes are mural cells that physically and molecularly support the microvasculature but are lost in diabetic retinopathy. Little is known about pericyte alterations in the T2D BM, where they can be identified as CD146⁺ cells. This study analyses the expressional and functional changes of CD146⁺ BM pericytes in T2D.

Methods: CD34⁻CD45⁻CD146⁺ (CD146⁺) cells from non-T2D and T2D human BM were expanded in vitro. They were characterized for mesenchymal, hematopoietic, and endothelial markers by flow cytometry and immunocytochemistry. Functional assays of proliferation, viability, and apoptosis were performed. Angiogenic factors were assessed by qPCR and ELISA. Phosphorylated Akt (p-Akt) S473 and T308 were measured by western blotting.

Results: CD146⁺ non-T2D and T2D cells were similarly positive for CD146 and mesenchymal markers CD105, CD73, and CD90. They were positive for nestin, leptin receptor (Lep-R), and NG2. They lacked expression of hematopoietic (CD34, CD45) and endothelial markers (vWF). Platelet-derived growth factor receptor- β (PDGFR- β) was less expressed in T2D cells. Both non-T2D and T2D passage 0 cells had a stellate morphology at confluency. T2D CD146⁺ cells had a significantly reduced proliferation, viability, and increased apoptosis. T2D cells had an upregulation of angiopoietin-1 and angiopoietin-2, but a downregulation of most angiogenic factors compared to non-T2D cells, indicating diminished angiogenic potential. P-Akt S473 and T308 were reduced in T2D cells.

Conclusion: BM CD146⁺ pericytes are functionally impaired in T2D and this may be due to compromised Akt signalling. This could relate to the BM microangiopathy and delayed healing that occurs in T2D patients.

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