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The RNA binding protein quaking is a key regulator of endothelial cell differentiation, neovascularization and angiogenesis through direct binding of the 3'UTR of stat3

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The capability to derive endothelial cell (ECs) from induced Pluripotent Stem (iPS) cells holds huge therapeutic potential for diabetes. This study elucidates the precise role of the RNA-binding protein Quaking Isoform 5 (QKI-5) during EC differentiation from both mouse and human iPS cells and dissects how RNA-binding proteins can improve differentiation efficiency towards cell therapy for important vascular diseases such as diabetes. iPS cells represent an attractive cellular approach for regenerative medicine today since they can be used to generate patient-specific therapeutic cells towards autologous cell therapy. In this study, using the model of iPS cells differentiation towards ECs, the QKI-5 was found to be an important regulator of STAT3 stabilisation and VEGFR2 activation during the EC differentiation process. QKI-5 was induced during EC differentiation, resulting in stabilisation of STAT3 expression and modulation of VEGFR2 transcriptional activation as well as VEGF secretion through direct binding to the 3' UTR of STAT3. Importantly, iPS-ECs overexpressing QKI-5 significantly improved angiogenesis and neovascularization and blood flow recovery in experimental hind limb ischemia. Notably, human iPS cells overexpressing QKI-5, induced angiogenesis on Matrigel plug assays *in vivo* only seven days after subcutaneous injection in SCID mice. These results highlight a clear functional benefit of QKI-5 in neovascularization, blood flow recovery and angiogenesis. They, thus, provide support to the growing consensus that elucidation of the molecular mechanisms underlying EC differentiation will ultimately advance stem cell regenerative therapy and eventually make the treatment of vascular diseases such as diabetes a reality.

Biography

Andriana Margariti has developed significant expertise in stem cell biology, with particular emphasis on cell reprogramming, chromatin remodelling, cell signalling and endothelial cell biology. Her research program is based on the remarkable idea of direct reprogramming which will allow her to realize fundamental principles of cell reprogramming and establish homogeneous populations of endothelial cells. Development of fast and robust new methodologies that produce well-characterized, homogenous, clinical-grade cells suitable for tissue repair/re-modelling would have great utility. Her research team has generated patient-specific iPS cells and PiPS cells and they now have exciting novel data and they are working towards to develop a remarkable new highly efficient strategy of cell reprogramming. Importantly, the potential of the reprogrammed endothelial cells to enhance angiogenesis and neovascularisation and to promote perfusion of ischemic tissue will be established. Her research is demonstrating the therapeutic potential of "re-born" reprogrammed endothelial cells which would have transforming consequences for regenerative and personalized medicine.

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