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Aortic stiffness in type 2 diabetes is contributed by endothelial-to-mesenchymal transition

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Background/Introduction: Endothelial-to-mesenchymal transition (EndMT) is a process in which endothelial cells lose their characteristics and gain a myofibroblast-like phenotype. EndMT was originally identified in heart development, but we now know that it contributes to several pathologies such as organ fibrosis, cardiovascular disease and cancer.

Purpose: We hypothesized that EndMT contributes to aortic stiffness in the context of type 2 diabetes. Aortic stiffness is an early contributor and independent predictor of cardiovascular disease and mortality in type 2 diabetes patients.

Methods: To confirm the presence of EndMT, aortic sections of db/db mice (a murine model for diabetes) were co-immunofluorescent stained with the endothelial marker CD31 and the mesenchymal markers α-SMA or S100A4. Moreover, mRNA expression of the EndMT transcription factors SNAIL, SLUG and TWIST was analyzed in aortic tissue from db/db mice as well as in aortic tissue from diabetic patients. To identify how EndMT is initiated, we performed co-immunofluorescent staining of the endothelial marker CD31 in combination with the macrophage marker F4/80 in aortic sections from db/db mice. We also performed co-culture of mouse endothelial cells with macrophages and assessed EndMT.

Results: We demonstrated a robust co-localization of CD31 with either α-SMA or S100A4 in aortas of db/db mice which was almost absent in control mice. We also showed that the mRNA levels of the EndMT transcription factors were significantly upregulated in aortic tissue of both db/db mice and diabetic patients when compared to controls. We demonstrated that the macrophage staining was in close proximity with endothelial cells undergoing EndMT. In line with this, we showed in vitro that macrophaghes induce EndMT in a contact-dependent manner.

Conclusion: We demonstrated that EndMT contributes to aortic stiffness in the context of type 2 diabetes.

Biography

Melanie S. Hulshoff studied a Bachelor program in Biomedical Sciences at the University of Groningen, The Netherlands which she completed with distinction. She was also enrolled in the so-called Honors College, an additional extracurricular program for talented students. She then continued with the selective Topmaster program in Medical and Pharmaceutical Drug Innovation at the University of Groningen, which she completed with distinction as well. After completing her Master studies, she was selected for a joint double degree PhD Scholarship in which she could perform her self-designed research proposal. This PhD work is performed at the University of Groningen and the University of Göttingen, Germany under supervision of Dr. Guido Krenning and Prof. Elisabeth M. Zeisberg respectively. Now, she is in the final year of her PhD in which she has published and prepared several manuscripts on the topic of cardiac fibrosis, epigenetics and endothelial-to-mesenchymal transition.

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