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How mechanical stretching forces impact human vascular cells

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Cardiovascular diseases are globally the main cause of death and vascular tissue integrity is important for the proper functionality and homeostasis of the blood system. Therefore, a profound understanding of vascular cell physiology is beneficial in successfully treating vascular diseases and for improving strategies for regenerative medicine. Blood vessels walls are mainly composed of smooth muscle cells (SMCs) and endothelial cells (ECs). These cells are continuously subjected to a repeated mechanical stretching (cyclic tensile strain) caused by the pulsatile blood flow driven by the heart.

Dr. Ralf Kemkemer and colleagues located at the Max Plank Institute for Intelligent Systems, The Karlsruhe Institute of Technology, the University of Heidelberg and Reutlingen University in Germany assumed that SMCs and ECs might react differently to mechanical perturbation in their in vitro study providing evidence for cell-type specific dynamic mechano-responses.

In a report published in the Oct. 2015 issue of *Experimental Biology and Medicine* they cultured SMCs and ECs separately on elastic membranes and subjected them to a range of uniaxial periodic stretching with frequencies from 0.01 to 1 Hz with constant amplitude of 8 percent. It is know that different cell types adapt their cell body upon exposure to uniaxial cyclic stretching by perpendicular alignment to the direction of stretch. SMCs and ECs show such a morphological adaption response. Dr. Kemkemer said "Due to the novel experimental method of time-lapse microscopy during the stretching experiment we were also able to

quantify the kinetics of that adaptation. Strikingly, we could reveal that the dynamic reorientation response of SMCs and ECs show different levels and speed of reorientation dependent on the stretch frequency. Furthermore, a cell-type dependent minimum threshold frequency is detected below which no responses are detectable." These results were accompanied by matching data for actin cytoskeleton reorientation, cell-matrix adhesion realignment and size, GTPase activities (RhoA and Rac1), and membrane protrusion activity depending on the vascular cell type and the stretching conditions.

Overall, these promising results indicate a cell-type dependent mechano-response of ECs and SMCs and may allow cell-type specific activation of vascular cells by frequency-selective mechanical stretching. In addition, understanding in more detail the reactions of vascular cells to mechanical perturbations can be helpful in elucidating physiological and pathological aspects in vessel biology.

Dr Steven R. Goodman, Editor-in-Chief of *Experimental Biology and Medicine* said "Greiner et al have demonstrated different properties of ECs and SMCs in response to mechanical stretch. These studies provide improved insight into how vascular cells react to mechanical stresses in the normal and pathological cardiovascular system".

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