MedicalXpress

Small vessels with big impact on cardiovascular disease

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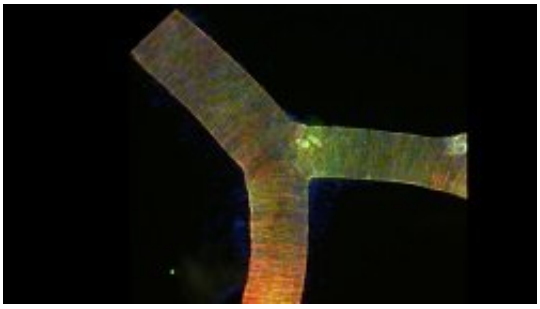

Credit: Ed van Bavel

Cardiovascular diseases are commonly associated with large vessel atherosclerosis. However, accumulating evidence demonstrates disturbances in the small arteries that control tissue perfusion. In particular, under specific conditions such as hypertension, aging, diabetes and obesity, these vessels undergo alteration in size and function, a process known as small artery remodelling. Such changes limit the capacity of these vessels to deliver oxygen to the various organs in our body, resulting in poor oxygenation and loss of organ function. Moreover, remodelling causes hypertension, creating a vicious circle of high blood pressure and remodelling that requires interruption.

Despite the importance of small artery remodelling in the pathogenesis of cardiovascular disease, little is known about this part of the vascular system. As a result, scientists of the EU-funded SMARTER project have

shed light on the molecular mechanisms of remodelling and how it can be diagnosed at an early stage and efficiently treated. "The objective of the study was to unravel the molecular and physiological events that drive small artery remodelling and identify ways to reverse it," explains project coordinator Prof. Ed van Bavel.

Researchers focused on novel and marketable technology aimed at studying these vessels in vitro under the right biomechanical conditions. "The ultimate goal was to use this information to develop novel therapies against cardiovascular disease based on targeting the small artery remodelling process," continues Prof. van Bavel.

Methodology for studying small artery remodelling

SMARTER research encompassed a vast array of small artery biology aspects including molecular pathways, cell-matrix interaction and the role of pluripotent cells in the arterial wall. Scientists employed progenitor cell isolation and culture, microarray and proteomics technology as well as atomic force microscopy to detect actin dynamics.

Particular emphasis was given to differential vascular gene and microRNA expression in hypertension. Researchers were able to identify new candidate genes and obtain insight into the role of the vasculature in brain interstitial homeostasis, unravelling the role of ion channel physiology in remodelling.

In addition, they developed an innovative method known as pressure myograph for studying small vessels. In this assay, small arteries were mounted on glass chambers. This allowed scientists to investigate the vasoactive responses to physiological agonists, providing a possible mechanism for the functional and structural control of arterial networks. Maintaining small arteries under organoid culture provided information on the vascular remodelling process in vitro while in vivo imaging of the

microcirculation improved understanding of endothelial and smooth muscle cell function.

Toward novel therapies for cardiovascular disease

From a therapeutic perspective, the consortium provided novel insight into the role of several factors and signalling pathways in small artery remodelling. Prof. van Bavel is confident that "valorisation of the SMARTER in vitro small artery technology will improve services in the cardiovascular domain in the long-term."

New treatment possibilities have appeared on the horizon, including inducible progenitor cell therapy, interference with micro-RNAs and personalised medicine. A better appreciation of the role of small arteries in cardiovascular health will not only provide fundamental knowledge but will help identify new therapeutic targets.

SMARTER, through a network of well-trained young scientists, hopes to sustain and expand research in the field. Considering that cardiovascular diseases and their associated complications like stroke and heart failure currently account for 40 percent of deaths in Europe, the deliverables of the SMARTER project provide hope for reducing these dismal statistics.

Provided by CORDIS