To contract or not to contract: Decision controlled by 2 microRNAs

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New research has provided insight into the molecular regulators of the function of muscle cells in the walls of blood vessels, i.e., vascular smooth muscle cells. Specifically, the acquisition and/or maintenance of the ability of VSMCs to contract and relax, thereby modulating blood pressure and distributing blood to the areas of the body that need it most, was found to be controlled in mice by two small RNA molecules known miR-143 and miR-145.

The walls of blood vessels contain muscle cells known as vascular smooth muscle cells (VSMCs). These cells contract and relax to modulate blood pressure and distribute blood to the areas of the body that need it most. However, some environmental signals, many of which are associated with human disease, cause VSMCs to switch from being contractile in nature to being dividing cells that produce large amounts of the proteins that form tissue matrix.

Despite the fact that this switch has been associated with a number of human blood vessel diseases, the mechanisms that control it have not been well defined. However, a team of researchers at the Max-Planck-Institut für Herz- und Lungenforschung, Germany, has now identified two small RNA molecules (microRNAs) known miR-143 and miR-145 that regulate acquisition and/or maintenance of the contractile nature of VSMCs in mice.

The team, led by Thomas Braun and Thomas Boettger, generated mice lacking both miR-143 and miR-145 and found that they had dramatically

reduced numbers of contractile VSMCs and increased numbers of tissue matrix-producing VSMCs in their large arterial blood vessels. Further analysis revealed that these two small RNA molecules were required for normal contractility of arteries in vitro and maintenance of normal blood pressure in vivo. As their absence led to signs of blood vessel disease in mice, the authors suggest that miR-143/145 might provide new therapeutic targets to enhance blood vessel repair and attenuate blood vessel disease.

In an accompanying commentary, Michael Parmacek, at the University of Pennsylvania School of Medicine, Philadelphia, discusses the importance of this study and highlights the fact that miR-143 and miR-145 were found to alter the expression of differing sets of genes, meaning that future studies will need to determine precisely how they alter control of blood pressure and disease development.

More information: Acquisition of the contractile phenotype by murine arterial smooth muscle cells depends on the Mir143/145 gene cluster, *Journal of Clinical Investigation*, www.jci.org/

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