Scientists discover the proteins that control development of varicose veins

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A new discovery published in the October 2011 print issue of The *FASEB Journal* explains for the first time what kicks off the process that causes varicose veins. In the article, researchers from Germany describe a single protein that binds to DNA to control gene function (called "transcription factor AP-1") and the subsequent production of a newly discovered set of proteins that significantly affect the development of varicose veins.

"We very much hope that our findings spur further studies focusing on the mechanisms underlying this widespread and precarious but still largely neglected venous disease," said Thomas Korff, Ph.D., study author from the Institute of Physiology and Pathophysiology at the University of Heidelberg in Heidelberg, Germany. "In the long run, such approaches will result in the development of a drug therapy that improves the quality of life for all people suffering from varicose veins."

To make this discovery, Korff and colleagues increased the blood pressure in a single vein of the ears of white mice, and followed the resulting changes in the size and architecture of the adjacent veins for several days. These changes were further analyzed in the abundance and activity of specific proteins in the veins connected to the one with increased blood pressure, and results were compared to those obtained from human varicose veins. By inhibiting the transcription factor AP-1 in the mouse ear model, synthesis of proteins associated with varicose remodeling and the proliferation of blood vessel smooth muscle cells were significantly reduced, and the varicose remodeling process was

virtually abolished. AP-1 was inhibited by decoy oligonucleotides (decoy ODN), a well-studied class of nucleic acid-based drugs.

"Most people know varicose veins as an unsightly reminder of aging," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal, "but for some, varicose veins cause significant pain that affects the quality and in some cases, length of life. While surgery may be beneficial in some cases, it's not the ideal solution. This research really opens the doors for an entirely new approach to treatment and prevention."

More information: Anja Feldner, Hannes Otto, Stephan Rewerk, Markus Hecker, and Thomas Korff. Experimental hypertension triggers varicosis-like maladaptive venous remodeling through activator protein-1. FASEB J. 2011 25:3613-3621; doi: 10.1096/fj.11-185975

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