

# Study reveals potential biomarkers of cerebral aneurysm risk

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Expansive arterial remodeling (EAR) comprises a genetically programmed biological response designed to restore homeostatic levels of arterial wall stress after an increase in vessel flow load occurs. The magnitude and rate of EAR reactions relative to local hemodynamic stress fields and the tensile strength of vascular tissue determines whether the process will result in a stable mural structure (adaptive

remodeling) or an unstable mural structure that progresses to form an aneurysm (maladaptive remodeling). A recent study published in *Current Neurovascular Research* reveals the molecular mechanisms underlying adaptive and maladaptive remodeling of cerebral arteries for the first time.

In this study, investigators flow loaded the basilar artery in [rats](#) by performing bilateral carotid artery ligation. Flow induced changes in basilar artery morphometry and histology were correlated with changes in mRNA expression and protein expression. Flow induced alterations in mural structure and biology were revealed by comparison of flow loaded basilar [arteries](#) with basilar arteries from rats that underwent sham surgery. The adaptive and maladaptive remodeling responses were differentiated by comparing the results from an aneurysm prone inbred strain of rats to an aneurysm resistant inbred strain of rats. The study revealed 24 genes that were differentially expressed between strains in the absence of flow loading (resting state). More than half of these genes have previously been associated with pathological vascular phenotypes, and more than a third have specifically been associated with aneurysmal pathology.

Numerous flow-induced genes were revealed by this study, including a group of 8 genes that showed very strong flow induced expression conserved in both inbred strains. A group of 9 genes showed very strong flow induced expression with major differences between aneurysm prone inbred rats and the aneurysm resistant inbred rats. These genes are considered to play major roles in maladaptive cerebrovascular remodeling responses that lead to mural destabilization and cerebral aneurysm formation. Three of these genes including the *Tgfb3*, *Ldha* and *Rgs16* genes have specifically been associated with aneurysmal pathology in prior studies.

The newly discovered maladaptive cerebrovascular remodeling genes

revealed by this research may enable the development of new diagnostic biomarker tests for patients at increased risk of cerebral aneurysm formation. Such tests may be used to identify patients at risk for cerebral aneurysm formation at a very early stage. In such cases, it may be possible to stabilize or reverse the aneurysm forming process with targeted therapies before clinical complications occur. The products of maladaptive cerebrovascular remodeling [genes](#) may eventually prove to be high yield drug targets for targeted arterial wall stabilizing therapies. Such therapies may be particularly beneficial for individuals at high risk of [aneurysm](#) formation, including patients with severe hypertension, unilateral carotid artery occlusions, cerebral arteriovenous malformations and aneurysmal cerebral arteriopathies such as Tuberous Sclerosis, Alagille syndrome and Sickle cell disease.

**More information:** Todd A. Abruzzo et al, Genetic determinants of cerebral arterial adaptation to flow-loading., *Current Neurovascular Research* (2018). [DOI: 10.2174/1567202615666180712150143](https://doi.org/10.2174/1567202615666180712150143)

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