Notch3 Is a Major Regulator of Vascular Tone in Cerebral and Tail Resistance Arteries

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Mots-clés	flow-mediated dilation [13], local blood flow regulation [14], myogenic tone [15], Notch receptors [16], resistance arteries [17]
Résumé en anglais	Objective— Notch3, a member of the evolutionary conserved Notch receptor family, is primarily expressed in vascular smooth muscle cells. Genetic studies in human and mice revealed a critical role for Notch3 in the structural integrity of distal resistance arteries by regulating arterial differentiation and postnatal maturation.Methods and Results— We investigated the role of Notch3 in vascular tone in small resistance vessels (tail and cerebral arteries) and large (carotid) arteries isolated from Notch3-deficient mice using arteriography. Passive diameter and compliance were unaltered in mutant arteries. Similarly, contractions to phenylephrine, KCl, angiotensin II, and thromboxane A2 as well as dilation to acetylcholine or sodium nitroprusside were unaffected. However, Notch3 deficiency induced a dramatic reduction in pressure-induced myogenic tone associated with a higher flow (shear stress)-mediated dilation in tail and cerebral resistance arteries only. Furthermore, RhoA activity and myosin light chain phosphorylation, measured in pressurized tail arteries, were significantly reduced in Notch3KO mice. Additionally, myogenic tone inhibition by the Rho kinase inhibitor Y27632 was attenuated in mutant tail arteries. Conclusions— Notch3 plays an important role in the control of vascular mechano-transduction, by modulating the RhoA/Rho kinase pathway, with opposite effects on myogenic tone and flow-mediated dilation in the resistance circulation.
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