

## HYPERTENSION

## Nogo-B regulates BP homeostasis

Nogo-B regulates sphingolipid biosynthesis within the endothelium to modulate blood pressure (BP) and could open up new avenues for pharmacologic intervention in hypertension, according to new findings by Annarita Di Lorenzo and colleagues. “The importance of sphingolipid signalling in cardiovascular diseases, including hypertension, has been recognized,” says Di Lorenzo, “but the molecular connection between the sphingolipid pathway and Nogo-B was previously unknown.”

Nogo-B is one of three *RTN4* isoforms, and is highly expressed in endothelial cells, whereas Nogo-A and Nogo-C are abundantly expressed in the central nervous system. In their study, the researchers found that Nogo-B might have a specific role in BP homeostasis after observing that mice deficient in Nogo-A and Nogo-B isoforms (Nogo-A/B), both systemically and specifically in endothelial cells, were hypotensive and had elevated sphingolipid levels in endothelial cells compared to controls.

The contractility of resistance vessels was maintained.

The Nogo-A/B mice were resistant to the effects of chronic infusion of angiotensin II (Ang-II) to induce hypertension. However, their BP did rise to that of Ang-II-treated controls after administering an inhibitor of serine palmitoyltransferase—the rate-limiting enzyme of *de novo* sphingolipid synthesis. Nogo-B was also shown to bind and inhibit the activity of serine palmitoyltransferase *in vitro* and *in vivo*, thus implicating it as a direct regulator of sphingolipid production. The researchers hope to further their understanding of how Nogo-B regulates sphingolipid signalling, and identify ways by which this pathway can be therapeutically manipulated.

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