The evolution of vascular nitric oxide signalling

John A. Donald, Sofie Trajanovska, Rachel E. Blake, and Melissa S. Cameron
School of Life and Environmental Sciences, Deakin University, Geelong, Australia, 3217

The role of the endothelium as the primary source of nitric oxide (NO) that mediates vasodilation is well-established in mammals. Endothelial NO is primarily generated by an isoform of NO synthase (NOS) called NOS3. In addition, NO can be generated by two additional NOS isoforms called NOS1 and NOS2, respectively; NOS1 is also called neuronal NOS and is expressed in nitrergic nerves. It is now clear that endothelial NO signalling is not ubiquitous in vertebrates. In fact, comparative genomics and molecular cloning have shown NOS1 and NOS2 are present in all vertebrates, but that NOS3 has arisen in the tetrapod lineage. NOS3 is found in amphibians but is not found in the vascular endothelium. A key question is when did NOS3 become expressed in the endothelium of tetrapods. In the absence of endothelial NO signalling in teleost fish and amphibians, NO control is provided by perivascular, nitrergic nerves. Interestingly, the majority of the perivascular, nitrergic nerves are also adrenergic as NOS1 and tyrosine hydroxylase are colocalised in many nerve terminals. Thus, the same neuron could release vasodilator and vasoconstrictor signalling molecules. However, in amphibians, NO-mediated vasodilation appears to be independent of a functional adrenergic innervation.