

Review

The evolutionary functions of cardiac NOS/NO in vertebrates tracked by fish and amphibian paradigms

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ABSTRACT

During early ectotherm vertebrate evolution the heart was redesigned as a high pressure pump adapted to perfuse larger body sizes. To compensate the consequent higher organ complexity and heterogeneity (ventricular myoarchitecture and blood supply), conceivably the three principal cardiac cell components, the endocardium, the contractile myocardium and the epicardium recruited and diversified the cardiac NOS system for functioning not only as a major modulator, but also as a spatio-temporal integrator of heart function. In the context of NOS isoform evolution, we will use fish and amphibian paradigms to illustrate major aspects of cardiac spatial and temporal integration achieved by the NOS/NO systems. This may reveal a primordial cardiac NOS/NO function, allocating it in a wider biological framework than so far envisioned.

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Introduction

In the early 1990s, Edelman and Gally [1] suggested nitric oxide (NO) as a molecule linking space and time in the brain. This concept can be well extended to the heart, in which the nitric oxide synthase (NOS)/NO system is now acknowledged as a major organizer of complex connection–integration processes that span multiple spatial and temporal scales, hence modulating the organ

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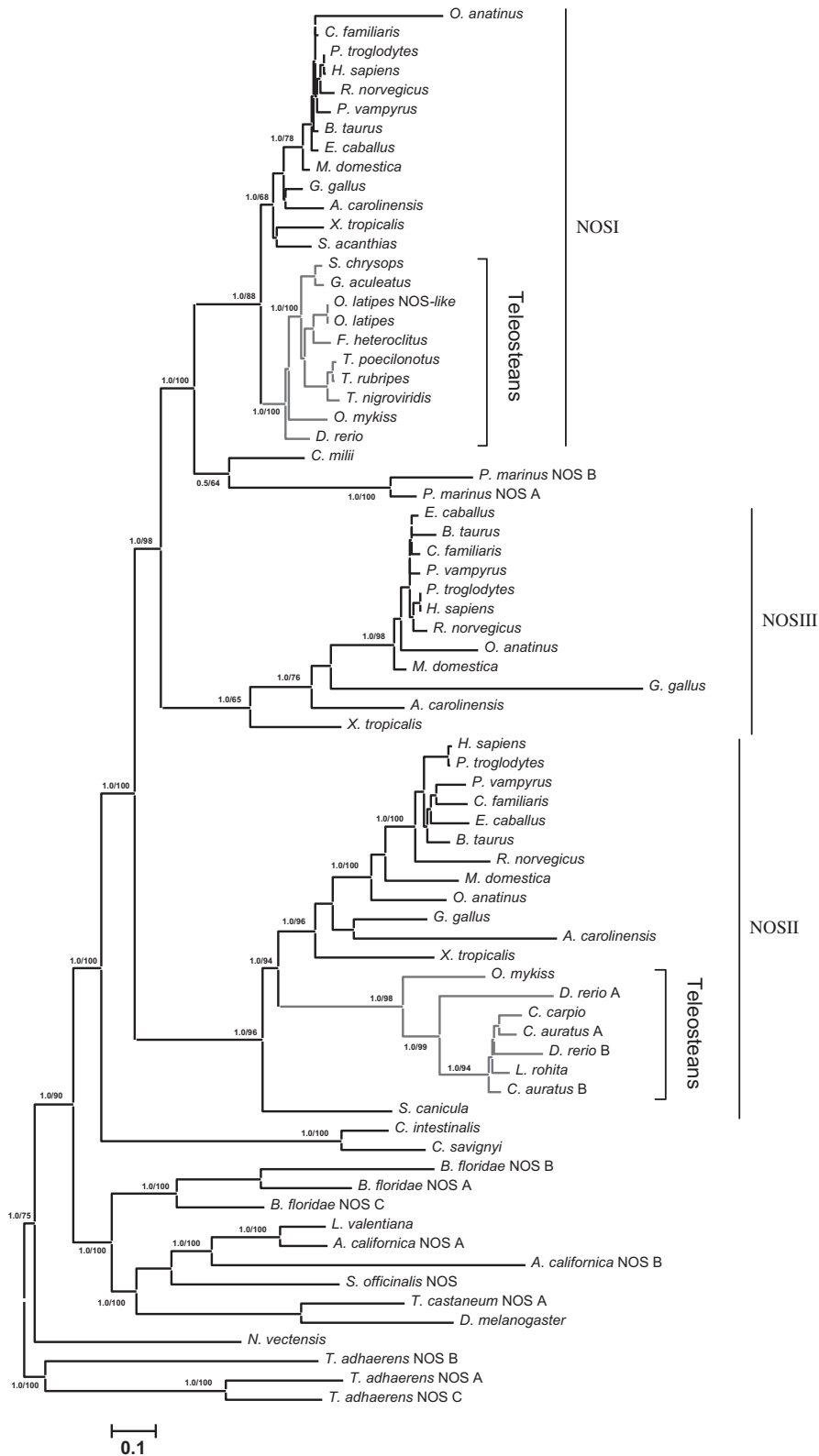


Fig. 1. Genealogical relationships among NOS protein sequences encountered in selected vertebrate and invertebrate taxa. From Andreakis et al. [2]. (The authors thank Andreakis et al. [2] for kind permission to use their data).

physiology both at basal and stimulated conditions. However, since the NO discovery in the 1980s, despite the growing number of data published on this molecule during the last 20 years, about 99% are referred to mammalian models. Consequently, while the essential

role of NO as a pleiotropic regulator of mammalian cardiac biology is well established, the research on the evolutionary aspects of the NOS/NO system remains at an early stage and some basic problems are still controversial.

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