Reconstruction of Nitric Oxide Signaling networks during the embryonic development of Amphioxus (NOSA)

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Abstract

This proposal aims to elucidate the regulatory mechanisms governing Nitric Oxide (NO) signaling pathways throughout the embryonic and larval development of the iconic marine invertebrate, amphioxus *Branchiostoma lanceolatum*. NO plays a pivotal role in regulating several critical physiological processes in animals, including neurotransmission, cardiovascular homeostasis, immunity, and development. Notably, it is also implicated in the physiopathology of numerous human diseases. Consequently, a comprehensive understanding of the intricate mechanisms by which NO can exert control over diverse aspects of animal physiology is imperative.

The PhD student will join a **long-term project** of the lab, and in particular will investigate in detail the consequences arising from the chronic endogenous absence of Nitric Oxide during the development of amphioxus, examining both morphological and molecular aspects. Amphioxus, a cephalochordate, is regarded as a proxy for vertebrates due to its analogous body plan, central nervous system, and genome organization. Despite its simplicity compared to vertebrates, amphioxus serves as a valuable experimental system to unravel the mechanisms of NO signaling in chordates, providing insights that can significantly contribute to our understanding of human physiology.

This project builds upon **robust preliminary findings** that have uncovered a functional link between Nitric Oxide (NO) and Retinoic Acid (RA) during the embryonic body patterning of amphioxus. RA, a morphogen with pivotal roles in cell growth, differentiation, and organogenesis, is functionally connected to NO in ensuring normal development through reciprocal signaling modulation. However, the details of the intermediate actors involved in this finely-tuned co-regulation during the early stages of development remain inadequately documented, constituting a primary objective of the current project.

Furthermore, we aim to provide insights into the role of NO in neurogenesis during development. Despite the established role of NO as a neurotransmitter, the specific mechanisms through which NO contributes to the determination of neural differentiation fate from stem cells remain poorly elucidated.

The experimental design involves pharmacological treatments applied from neurula to larva stages to eliminate endogenous NO during the development of amphioxus. The molecular and physiological status of NO-null embryos and larvae will be examined and compared to control siblings using advanced next-generation sequencing techniques, including **RNA-seq, ATAC-seq, proteomics, and computational systems biology approaches**. The already acquired NGS data will be a valuable resource for the student, offering an opportunity to conduct in-depth analyses. The student will play a crucial role in deciphering the functions of genes enriched through one or more approaches and will have the chance to validate these findings *in vivo*.