The cnidarian antiviral immune system reflects ancestral complexity

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The fast co-evolution of viruses and host antiviral systems can result in blurry homology or even in shifts of whole defense mechanisms between species. In vertebrates, the antiviral immunity is heavily based on the interferon pathway whereas in the case of invertebrates, which lack interferons, the antiviral immunity is believed to be based mostly on an RNA interference (RNAi). Until now, the recognition mechanism and mode of action of such systems were studied mostly in vertebrates, insects and nematodes. From this limited phyletic sampling, it is impossible to deduce what was the original mode of action of these systems in their last common ancestor and how antiviral immunity was triggered in early animals. To attain novel insights into the early evolution of this crucial system, we study this system in an outgroup: the sea anemone *Nematostella vectensis*, a representative model species of Cnidaria, a phylum that diverged approximately 600 million years ago from the rest of animals. Beyond its key phyletic position, *Nematostella* is a tractable lab model with available advanced molecular and gene manipulation tools making it an excellent comparative model. We harness these tools to decipher the cnidarian system for battling RNA viruses and answer the outstanding questions regarding the evolution of antiviral immunity and its ancestral state in animals. We show that like bilaterian animals *Nematostella* reacts transcriptionally to the viral hallmark of long (700-7000 bp) double-stranded RNA (dsRNA). However, unlike vertebrates, *Nematostella* is not differentially-responsive to short and long dsRNA carrying or lacking the viral hallmark of 5′-triphosphate group. Our transcriptomic results for long dsRNA put in question the textbook dichotomy between the antiviral immune systems of vertebrates and invertebrates as we find upregulated components of both systems in *Nematostella*. These findings support the intriguing scenario that the ancient antiviral innate immunity system that was present in the last common ancestor of Cnidaria and Bilateria was in several aspects more complex than the systems found in extant vertebrates and protostomes such as arthropods and nematodes. We are also functionally characterizing the roles of the two RIG-I-like Receptors (RLRs) of *Nematostella* and show that one of them is responsible for long dsRNA sensing. As we move forward we aim to continue to decipher the antiviral system of *Nematostella*, test its relationship with environmental stress and assay the generality of our findings in other cnidarian species.

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