Ectopic activation of $GABA_B$ receptors inhibits neurogenesis and metamorphosis in the cnidarian *Nematostella vectensis*

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The neurotransmitter GABA regulates the preliminary development of the nervous system in mammals and particularly in humans, acting through receptors called $GABA_B$Rs. Although cnidarians (jellyfish, corals, and sea anemones) have a much simpler nervous system than humans, until now it was not clear what regulates neuronal development in these organisms. Cnidarians are one of the more ancient groups of living species, having evolved more than 700 million years ago. During their life cycle, the fertilized egg develops into a larva that moves freely in the sea, but after several days, it metamorphoses into a polyp that attached to the seabed.

We set out to discover what controls the larva-to-polyp metamorphosis in the sea anemone *Nematostella vectensis*. We were surprised to discover that this process is regulated by a receptor from the $GABA_B$R family, that it is mediated by the *Nematostella*'s nervous system, and that we could influence and even halt the metamorphosis using a drug that was developed to target human $GABA_B$Rs. We further showed that the signal transduction cascade that was characterize in mammals is evolutionary conserved and is found in *Nematostella*, even though its nervous system is extremely simple and does not include a central brain as in mammals. Using computer modeling of the anemone's $GABA_B$R proteins we found that the active site of these receptors, where activating molecules and drugs bind, is conserve between mammals and the anemone. Moreover, we showed that activation of this signaling cascade inhibits the expression of genes that are related to neuronal differentiation in *Nematostella*. Our results reveal a tight connection between the nervous system and metamorphosis in this organism and open new evolutionary and ecological avenues for research, as well as new opportunities for pharmaceutical discoveries – where the sea anemone can be a simple yet accessible model organism for testing new drugs.