Abstract

Nuclear receptors constitute a large family of transcription factors that are powerful regulators of animal tissue metabolism, homeostasis, tissue maintenance and development. They are particularly attractive for their ability to respond to the binding of hormones, metabolites, xenobiotics and artificially prepared molecules and transmit the interaction with these small lipophylic molecules to specific regulatory potential.

In search for nuclear receptors that are likely to be critical for neural tissues in invertebrates and conserved during the evolution of animals, we have identified a close homologue of vertebrate TLX in a planarian *Schmidtea mediterranea*. Planaria represent very promising biological model systems for studies on tissue maintenance and regeneration. Planaria are able to resorb their tissues and use them as sources of energy during fasting and they re-build their bodies from neoblasts when food is plentiful.

Our search in *Schmidtea mediterranea's* publicly accessible genome sequencing data indicated that planarian genome contains at least one gene with a high degree of similarity to vertebrate TLX. We cloned full length CDS (coding DNA sequence of cDNA) and characterized the gene functionally. This showed that the planarian and vertebrate NR2E1 are highly similar in their entire coding sequence and the derived protein molecule. We found that the planarian TLX, that we name *Smed-tlx-1* is expressed in heads, as well as in tails of animals. *Smed-tlx-1* expression is at least 10times bigger in heads than in tails of animals and in both body parts increases approximately twice during the feeding phases. Inhibition of Smed-tlx-1 by RNA interference revealed that *Smed-tlx-1* is critical for sustaining the body plan during fasting – feeding cycles and for integrity of brain areas and eyes.

In the second part of the study, we studied the expression and intracellular distribution of TLX in glioblastoma cell lines. We have found that TLX is detected in multiple protein forms suggesting that they may be posttranslationally modified. Using immunofluorescence and collocalization studies, we show that TLX is localized in the nuclei as well as in the cytoplasm and we have found indications that TLX intracellular distribution may be regulated.

The results indicate that NR2E1 function in regulation of maintenance and development of neural tissues is evolutionarily conserved and its mechanism of function may include its regulated intracellular distribution.