

The regeneration of lost body parts is an ever fascinating problem with great importance to both basic research and medicine. There is a need for deuterostome invertebrate models of regeneration. These models need to be practical and interconnected with molecular tools and resources making genetic questions readily answerable. We have primarily studied 2 clades of deuterostomes, the echinoderms and the tunicates. The echinoderm brittle stars regenerate their arms after autotomy and many tunicates can regenerate their entire central nervous system (CNS) following ablation.

We have developed these models of arm regeneration and neural regeneration further and evaluated their value by asking questions relevant to regeneration: 1) Which cells form the blastema in the regenerating arm of ophiuroids? 2) What is the sequence of events leading to CNS regeneration in *Ciona*? 3) Is *Ciona* regeneration functional?

We have shown that dedifferentiated muscle cells take part in regeneration of the ophiuroid arm. Other proliferative centres in the arm are the nerve cord and the coelomic epithelium. We found indication of a subset of the proliferative cells in the nerve cord expressing the neuropeptide SALMFamide 1.

We have described the temporal and spatial events of CNS regeneration in the tunicate *Ciona intestinalis*. Regeneration was divided into stages and a negative correlation between size and rate of regeneration has been found. We have developed and used transgenic animals to follow the regenerating nerves with resolution at the cellular level, thereby laying the framework for numerous future studies of genetic functions.

Furthermore we established that CNS regeneration is functional by following the return of physiological reflexes.

Genes and cells important for regeneration are discussed. We also characterised the three Insulin related genes in *Ciona intestinalis*.

We conclude that *Ciona intestinalis* has the potential to become a valuable model of central nervous system regeneration because of its physiology and the development of genetic tools. The *Amphiura* model is also of great interest because of its ecological importance. The disadvantage of this system is the present lack of genetic resources.

Apart from establishing this biotechnological framework, we here give the first account of using transgenic animals to study CNS regeneration in urochordates. This will provide a great opportunity for further CNS regeneration studies in *Ciona* and open up this field to the research community. The joint findings and knowledge in the whole field of regeneration research will undoubtedly help solve medical problems in the 21<sup>st</sup> century.

**Keywords:** *Amphiura filiformis*, *Ciona intestinalis*, *Ophioderma longicaudum*, tunicate, echinoderm, brittle star, regeneration, CNS regeneration, neural complex, arm regeneration, insulin, relaxin, IGF, SALMFamide, transgenic, live imaging, reflexes, stages of regeneration, blastema, dedifferentia-