

# The immortal *Hydra*

**Professor Thomas Bosch** explains why he chose the biologically immortal *Hydra* as his organism of study, and how clues from its genes could help unravel the mechanisms behind human ageing



## Can you give us a brief overview of your project and what it entails?

The unlimited lifespan of *Hydra*, due to the indefinite self-renewal capacity of their stem cells, has long attracted attention from biologists as it promises insights into the mechanisms controlling longevity in more advanced animals, including humans.

While in search of transcription factors that are strongly expressed and shared by all three stem cell lineages, we discovered FoxO, a member of the forkhead box (Fox) family of proteins. This finding immediately reminded us of several studies in worms, flies and humans that showed FoxO expression levels and FoxO variants to be associated with longevity. Gain-of-function and loss-of-function approaches have provided clear evidence that *Hydra*'s single FoxO gene plays a key role in controlling stem cell proliferation and terminal differentiation, suggesting an ancient role in maintaining developmental youth.

Our studies have several important implications; they not only reveal FoxO as a molecular factor that has contributed to the early evolution of stem cells, but also highlight intriguing similarities between *Hydra* and other multicellular organisms in the mechanisms that maintain 'stemness' and control lifespan.

## How did you come to choose *Hydra* as your study organism?

As with many important things in life, it happened accidentally! As an undergraduate at the University of Munich, I was granted a one-year scholarship at Swansea University, Wales. While there, I grew increasingly fascinated with biological systems after undertaking lab

research. This exposure to experimental science was unlike my experiences in Germany, where undergraduates sit in large classes and work on readymade school experiments.

When I returned to the University of Munich, they had hired a new professor for Zoology and Developmental Biology, Charles N David from the Albert Einstein College of Medicine in New York. I started working with him and he introduced me to a simple animal model for understanding pattern formation and development: the freshwater polyp *Hydra*.

## What are the mechanisms behind *Hydra*'s supposed 'immortality'?

Experimental evidence in flies, worms, and mice indicates that changes in life span indeed can occur through changes in FoxO expression. Since we have made similar observations using transgenic *Hydra* in our recent study, we have proposed a model in which the high expression of FoxO in all three stem cell lineages is crucial for the continuous self-renewal capacity and potentially unlimited life span, together with the continuous maintenance of the functionality of the innate immune system.

In this model, the ageing process is caused by a progressive reduction of FoxO activity, which might be due to changes in the upstream regulating signalling cascades. In this view, the amount of FoxO present in a given tissue and organism is age-dependent, and falling below a threshold permits ageing to occur.

## Are any other animals immortal?

The freshwater polyp *Hydra* seems one of few organisms that may be considered as potentially immortal, but besides them there are numbers of species that are very long-lived. Examples include deep-sea rockfish, which still produce a normal number of eggs at the age of 100; some incredibly ancient turtles and tortoises; and certain clams and oysters that live for nearly half a millennium.

Long-lived animals tend to have one attribute in common, and that is protection. Clams and turtles have tough outer shells, whereas bowhead whales, which can reach 200 years of age, are protected by their size. On the whole, larger species tend to live longer than smaller species.

## Finally, how have recent technological and computational advances made work like this possible?

Developing a transgenic method for *Hydra* cells allowed for the tracing of GFP-labelled cells. This demonstrated that *Hydra*'s stem cells continuously proliferate and generate eternal lineages. Importantly, with these new advances we are able to uncover not only the molecular signatures of the three stem cell lineages in *Hydra*, but also a new perspective on the molecular mechanisms controlling the unlimited self-renewal capacity of its stem cells.

