

The Planaria Model System

Guest Editors

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Preface

Planarian regeneration: a classic topic claiming new attention

The term planarian is derived from the Latin *planus* (meaning flat) and refers to worms of the order Tricladida (phylum Platyhelminthes) whose body is flattened along the dorso-ventral axis. Planarians are best known for their ability to regenerate complete animals from tiny fragments of tissue, and for their capacity to continually remodel both the size and form of their body. Both features are dependent on the presence of pluripotent adult stem cells called “neoblasts”. This complex cell population is able to proliferate and give rise to all differentiated cell types. Furthermore, although the mechanisms remain poorly understood, it confers adult planarians with a degree of plasticity similar to that of embryos. Alongside these fascinating properties, freshwater planarians are easy to culture and handle in the laboratory. They are therefore an ideal bilaterian model system in which to study the molecular and cellular mechanisms that control stem-cell proliferation and differentiation, pattern formation, organogenesis, growth, regeneration, senescence, and even rejuvenation.

Interest in regeneration has grown among the general public as a result of advances in regenerative medicine. With the isolation of human ES and iPS cells, even high school students have become aware of the concept of pluripotent stem cells. Planarians are not a recent introduction to regeneration research, however. The first reports of planarian regeneration were published 250 years ago, and in 1828 Dugès asked himself the first sound questions on axial polarity in planarians (see Bronsted, 1969). Charles Darwin even spent time on the west coast of Australia observing planarian regeneration after chopping them by hand. At the beginning of the 20th century, research into planarian regeneration was boosted by the work of T.H. Morgan and C.M. Child, who were responsible for the first classic papers in the field. In the 1930s, however, interest declined both in the USA and elsewhere. There was a resurgence of interest between the late 1940s and the mid-1960s following the establishment of the neoblast theory. This theory, proposed by the so-called French School led by Etienne Wolff and Françoise Dubois, established the basic framework for planarian regeneration research over the next 30 years. After this period, however, planarians fell behind other model systems such as *Drosophila* and *C. elegans*, which were more amenable to genetic and cellular analyses. Nevertheless, planarian research continued in several labs in Japan (Kyoto, Hiroaki), France (Strasbourg, Paris, Nancy, Marseille), Italy (Bologna, Pisa, Roma) and Spain (Barcelona).

The last two decades have seen the introduction of cellular and molecular techniques, including high-throughput genetic and genomic analyses. Whole-mount *in situ* hybridization and immunostaining have been made possible by techniques to remove the copious amounts of mucus produced by planarians (Agata *et al.*, 1998). Fluorescence-activated cell sorting has been used to isolate X-ray-sensitive stem cells (Hayashi *et al.*, 2006). Chimeric analyses have allowed us to trace the fate of transplanted tissues (Kato *et al.*, 1999) and BrdU labeling to trace that of proliferative stem cells (Newmark and Sánchez, 2000). Most recently, the fate of a single transplanted cell has been analyzed to demonstrate pluripotency of planarian adult stem cells after transplantation (Wagner *et al.*, 2011).

The development of a method to carry out RNAi in planarians (Sánchez-Alvarado and Newmark, 1999) had a dramatic impact on research by allowing systematic screens of candidate genes. Thus, EST, genome and proteome databases were constructed (Sánchez-Alvarado *et al.*, 2002; Mineta *et al.*, 2003; Zayas *et al.*, 2005; Ishizuka *et al.*, 2007; Robb *et al.*, 2008; Abril *et al.*, 2010; Blythe *et al.*, 2010; Adamidi *et al.*, 2011; Sandmann *et al.*, 2011; Yun-Fei Qin *et al.*, 2011; Fernandez-Taboada *et al.*, 2011) and these are now being used by researchers to delineate the key pathways involved in planarian regeneration. In other areas, however, challenges still remain. Although it is conceivable, for instance, that whole animals might one day be regenerated from cultured stem cells, efforts to maintain planarian stem cells *in vitro* have so far been unsuccessful. Likewise, transgenesis has only been achieved in some species (González-Estévez *et al.*, 2003), and reproducible transgenic techniques are still required for precise investigation of gene function. As these

methodological advances are made, however, planarians may ultimately become one of the most powerful model animals available for the study of regeneration and organogenesis.

With the resurgence of interest in planarians as a model system, there has been a significant increase in the number of papers published on planarian research in leading journals. Moreover, countries such as Germany, the United Kingdom, India and China, which do not have a tradition of research into planarian regeneration, have now successfully joined the planarian research community. As a result, new collaborations have developed and the growing network of laboratories has formed a critical mass to share news, data, and tools, including web-based tools such as the “EuroPlanNet” (<http://www.europlannet.org>). It is hoped that the efforts of this community will ultimately provide important insights for translational research in regenerative medicine.

In this Special Issue of *The International Journal of Developmental Biology*, we have endeavoured to provide an overview of the most active areas of research into planarian regeneration, as well as historical reviews, general reviews, interviews and original data. We have even offered a historical perspective on aspects of planarian phylogeny and two examples of their potential pharmacological applications.

We are grateful to all the authors who contributed to this Special Issue for taking time out of their busy schedules. We hope we have succeeded in representing the diversity of contemporary planarian research. We also hope this Special Issue will be a stimulus for further contributions. We warmly thank the editorial team of *The International Journal of Developmental Biology* for their diligent and capable editorial assistance. Finally, our special gratitude to Juan Aréchaga for convincing us to produce this Special Issue and for his unfailing encouragement and support.

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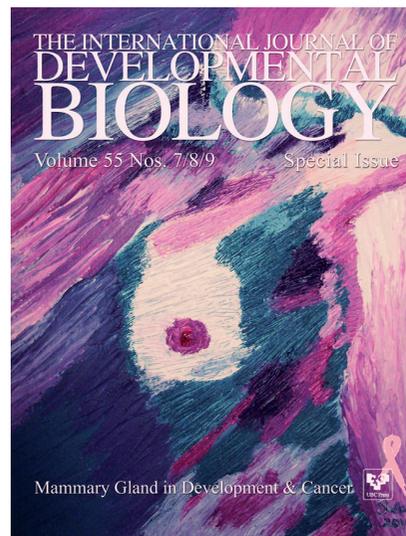
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