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EDITORIAL

Stem cells in the context of evolution and development

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The field of stem cell biology originated and grew around the discovery that it was possible to isolate undifferentiated cells ("stem cells") from various adult organs, as well as from early mammalian embryos. These could then be grown in culture, made to differentiate into various cell types, and put back into host organisms. It gradually became clear that most, if not all, adult tissues possess stem cells, and that neoplastic growth typically takes off from stem cells. Since the implications for the cure of cancer and degenerative diseases are great, research on the biology of stem cells has expanded rapidly over the past two decades. In particular, stem cell research has moved into using genetic model systems, including the invertebrates *Drosophila* and *Caenorhabditis elegans*, and into investigations of stem cell development (in vertebrates and *Drosophila* alike). Both approaches have delivered significant new insights. In small organisms such as *Drosophila*, stem cell pools and their niche environment often consist of only a few cells, and questions concerning the pattern of cell division, niche-stem cell contacts, or differentiation can be addressed at the single cell level (as for example, in the gonadal stem cells and the intestine; Spradling et al. 2011; Eliazer and Buszczak 2011; Papagiannouli and Lohmann 2012; Jiang and Edgar 2012; Takashima and Hartenstein 2012). Studying the development of stem cells offers the opportunity to follow step by step where in the embryo these cells come from, what structures in their environment they interact with, and what signaling pathways are active sequentially as a result of these interactions.

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Stem cells of the adult organism are typically slowly cycling, undifferentiated, and often multipotent cells located in special microenvironments, called "niches" (Martinez-Agosto et al. 2007; Haegebarth and Clevers 2009; Boral and Nie 2012). Embryonic stem cells can be molecularly defined by a small number of transcription factors and signaling pathways (Boyer et al. 2006; Loh et al. 2008; Chambers and Tomlinson 2009) which are crucial for self renewal, and which are even able to induce embryonic stem (ES) cell characteristics when expressed in mature cells. The combination of "ES stemness factors" found in ES cells is not typically expressed in adult stem cells of vertebrates, or other model organisms; instead, adult somatic stem cells typically express markers specific for an individual organ or tissue (e.g., membrane glycoprotein CD34 in hematopoietic stem cells; Lgr5 in intestinal stem cells; Leushacke and Barker 2012). Through their mitotic activity, stem cells generate two types of offspring. First, they renew themselves and thereby maintain a pool of proliferating stem cells. Secondly, they produce offspring that then become postmitotic and differentiate or (more typically) that first undergo a phase of rapid cell division before differentiating. Since these cells have a limited proliferative potential and eventually turn into differentiated progeny, they are referred to as transient amplifying cells.

The great interest in stem cells, whether analyzed in a culture system or in model organisms, has also spawned lines of research that aim at the evolutionary origin and subsequent modifications of this fundamental cell type. Many areas of early research received an infusion of new concepts and new technologies. Hydrozoa and Planaria, to name but two examples, have long been known for their amazing capacity of regeneration, and the existence of multipotent stem cells (i.e., interstitial cells and neoblasts, respectively) play an important role in regeneration and normal development (Gierer 1977; Chandebois 1976). More recently, new technologies have permitted the investigation of refined questions about these stem cells, including questions concerning the signaling pathways controlling their behavior and the batteries of genes that are turned on or off depending on the developmental state (Bosch et al. 2010; Tanaka and Reddien 2011; Baguñà 2012). The quickly expanding field of comparative stem cell biology notably also includes flowering plants, organisms that clearly outdo animals when it comes to vegetative growth (Aichinger et al. 2012). Throughout the ensuing studies, a question that naturally looms in the background is how related, in terms of genetic constitution and developmental potential, are these "primordial stem cell systems" to the stem cells that we observe in highly derived bilaterians? Can one consider multipotent stem cells as fundamentally homologous? Or did they evolve separately from a primitive state that lacked "professional stem cells", where cell renewal occurred by division of differentiated cells, or by dedifferentiation (followed by division) of these cells?

A satisfactory answer to these and many other questions cannot yet be provided, because our knowledge of stem cells outside the few model organisms is far too sketchy. In an effort to bring together information on stem cells by studying multiple different taxa, we collected a set of review articles in this special issue of DGE. In these articles, attention is paid to the questions of developmental origin, lineage potential, and possible homologies of stem cells. The first two articles (Ereskovsky et al. 2013; Funayama 2013) address these issues in sponges. They emphasize the overall conservation in terms of cell movements and morphogenesis that exists between sponges and higher animals and summarize the growing body of evidence for a dual system of stem cells, choanocytes, and archaeocytes as the mechanism underlying growth and regeneration in this animal taxon. The next pair of papers (Galliot 2013; Gold and Jacobs 2013) surveys stem cells of Cnidaria. Hydra, as one member of this taxon, has yielded important insights in the developmental questions of regeneration, organizers, morphogen gradients, and, more recently, specific signaling pathways underlying these phenomena. The article by Galliot summarizes recent research on the interplay between apoptosis, interstitial stem cells, and epithelial stem cells that takes place during injury-induced head regeneration. Gold and Jacobs take a comparative look into the different types of stem cells that have been identified (or affirmed to exist) in Cnidaria outside the hydrozoans. With the paper by Rink (2013) we move into the bilaterian animals, more specifically, the planarians, members of the diverse phylum Platyhelminthes; the review provides an overview of stem cell characteristics that gradually become established for the neoblasts. The last four articles focus on different classes of somatic stem cells, including those of the intestine, blood, heart, and nervous system. Takashima et al. (2013) survey in a comparative manner the developmental mechanisms of producing and maintaining the cell types found in animal guts. Grigorian and Hartenstein (2013) take a look at the process of hematopoiesis in a more restricted set of taxa, the arthropods. The contribution by Pandur et al. (2013) reviews recent data pertaining to the embryonic fields that give rise to tissues, including stem cells, of the vertebrate heart. Finally, Grandel and Brand (2013) focus on the central nervous system of vertebrates, where the fairly restricted distribution and function of neural stem cells found in mammals contrast with the widespread occurrence of these cells in anamniotes; despite this discrepancy, detailed comparisons looking at stem cell development and proliferative mechanisms reveal a number of common themes throughout vertebrates.

We hope the articles of this special issue will be of help as a source of information for researchers in stem cell biology, as well as interested readers who will try to draw together concepts and ideas that are spawned by discoveries in the fields of evolution, development, and stem cells.

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