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## Stem Cell Research in Platyhelminth

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### COMMENTARY

Acoel and platyhelminth worms are particularly attractive invertebrate models for biological research because their bodies are continually renewed from large pools of somatic stem cells. In particular, these studies ultimately led to the discovery that planarians possess a very unusual stem-cell system the body of a planarian is continually rebuilt from a large pool of somatic stem cells, called neoblasts, that are distributed throughout the animal. Neoblasts are the sole mitotically active cells within the body and constantly proliferate to renew all cell types. Neoblasts are thus required for whole-body homeostasis and are likewise liable for forming new tissues by growth and regeneration in these animals. Other platyhelminths also possess an identical stem-cell system, including one among the foremost basal lineages within the phylum, the macrostomids. Thus, it's likely that possession of neoblasts is ancestral for the Platyhelminthes.

Acoels have historically been placed within the Platyhelminthes, but recent molecular phylogenetic analyses now suggest that they probably represent a definite phylum, the Acoela, that falls well outside of the Platyhelminthes. Specifically, acoels are now thought to represent the foremost basal lineage within the Bilateria, being the sister group to all or any other bilaterian animals. That an identical neoblast system is found in both Platyhelminthes and Acoela has important implications for the evolution of this unusual mode of homeostasis. If acoels are indeed the outgroup to all other bilaterians, the

neoblast stem-cell system may have evolved convergently in acoels and platyhelminths or, alternatively, may even be ancestral for all bilaterian animals.

Because of their unusual neoblast system, platyhelminths and acoels are particularly attractive invertebrate models for biological research. They present variety of benefits, including the very fact that an outsized pool of stem cells is out there throughout the lifetime of every individual; the stem-cell pool is collectively totipotent, not just pluripotent (neoblasts can even produce to the germ line), these stem cells exhibit high rates of turnover, undergoing continual self-renewal and production of differentiated progeny, and neoblasts are the sole proliferative cells within the body while the remainder of the body is post-mitotic, making it possible to selectively disrupt large pools of stem cells in vivo through whole-body irradiation or other techniques.

Because neoblasts are the sole proliferative cells within the body, irradiation that kills proliferating cells selectively destroys neoblasts. Studies administered decades ago showed that in planarians, destroying the neoblast population of adults by whole-body irradiation leads to gradual malformation of the body (as tissues fail to be renewed) and eventually death. Destruction of the neoblast pool in planarians also abrogates the typically extensive regenerative ability of those animals demonstrates that in acoels irradiation dramatically reduces cell proliferation, abolishes the expression of a somatic cell marker, and ultimately results in death, indicating that neoblasts are required for homeostasis in acoels, as

they're platyhelminths. The selective destruction of neoblasts by irradiation is a powerful tool in these animals. For example, a key aspect of the microarray study described above was the comparison of irradiated and unirradiated planarian tissue to reveal neoblast specific genes.