Sample Abstract

The unique stem cell system of the immortal larva of *Echinococcus multilocularis*

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From classical studies, it is assumed that in cestodes undifferentiated stem cells (so-called "germinative cells") are the only source of cell proliferation, similarly to the neoblasts of free-living flatworms. However, nothing is known about the properties of germinative cells regarding their heterogeneity and gene expression patterns. In this work, we investigated the germinative cells of the metacestode larva of the cestode *Echinococcus multilocularis*. This larva grows continuously like a mass of vesicles, infiltrating the tissues of the intermediate host and generating protoscoleces by asexual budding. We demonstrate that only the germinative cells proliferate by morphological criteria and by developing for the first time molecular markers of differentiated cells in *E. multilocularis*, including markers for previously undescribed nerve cells in the larval vesicles. The germinative cells are heterogeneous at the molecular level, since only specific sub-populations express homologs of the post-transcriptional regulators *nanos* and *argonaute*, suggesting lineages of germinative cells with different potencies. Experiments of recovery after partial germinative cell depletion indicate extensive self-renewal capabilities for individual germinative cells. In spite of the similarity in morphology and function between the *E. multilocularis* germinative cells and the neoblasts of other flatworms, important differences are observed in their gene expression patterns. Furthermore, cestodes and trematodes lack orthologs of *piwi* and *vasa*, classical germ-line markers in many animals with key functions in the somatic neoblasts of free-living flatworms. The lack of *piwi* is particularly striking: although this gene family has a conserved role in the control of transposable elements, very few of these elements are present in cestode genomes, suggesting efficientalternative mechanisms for their control. Finally, we show that a novel family of non-autonomous retrotransposons has escaped repression and is massively expressed in the germinative cells.

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