Cancer, Stem cells & Developmental biology

The Master's & The PhD Programme

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The role of distinct populations of muscle stem cells during regeneration and organ growth

Skeletal muscle is an example of a tissue that deploys a self-renewing stem cell, the satellite cell, to effect regeneration. Recent *in vitro* studies have highlighted a role for asymmetric divisions in renewing rare "immortal" stem cells and generating a clonal population of differentiation-competent myoblasts. However, this model has lacked in vivo validation. We have defined a zebrafish muscle stem cell population analogous to the mammalian satellite cell and image the entire process of muscle regeneration from injury to fiber replacement in vivo[1]. This analysis reveals complex interactions between satellite cells and both injured and uninjured fibers and provides in vivo evidence for the asymmetric division of satellite cells driving both self-renewal and regeneration via a clonally restricted progenitor pool.

In contrast to regeneration, organ growth requires a careful balance between cell commitment and stem cell self renewal to maintain tissue growth trajectories. While the processes that regulate resident stem cells during regeneration and disease have received much attention, the basis of stem cell deployment during organ growth remains poorly defined. Using imaging and fate mapping techniques in zebrafish we identify a lifelong stem cell pool that exhibits extensive clonal drift, shifting from the random deployment of a large population of stem cells during larval growth, to the reliance on a small number of dominant stem cell clones to fuel adult muscle growth[2]. We further reveal that self renewal and clonal drift of growth specific muscle stem cells requires the activity of specific genes and cell cycle control. We define a distinct mechanism for the regulation of the stem cells required for organ growth and in the process provides a molecular understanding of the mechanisms underlying clonal drift *in vivo*.