

Investigation of biased DNA segregation in mice

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Internship proposal for : Master 2

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Stem cells; asymmetric cell divisions; biased DNA segregation; epigenetic regulation

Summary of project

Stem cells are present in all tissues and organs, and are crucial for normal regulated growth and regeneration. In spite of many advances in the field of stem cell biology, our understanding of stem cells properties and the regulation of their fate remains limited. In this project skeletal muscle stem/progenitor cells will be investigated using mouse genetics, cell and molecular biology and imaging approaches.

A major regenerative cell type in adult skeletal muscle is the satellite cell. Reports that some satellite cells may be more 'stem-like' has highlighted the heterogeneity of this population. The paired/homeobox genes Pax3 and Pax7, as well as the myogenic factors Myf5, MyoD, Mrf4 and Myogenin play important roles in regulating the establishment of skeletal muscle from stem and progenitor cells in the embryo. During adult myogenesis, Pax7 and the myogenic regulators Myf5 and MyoD play important roles in self-renewal and lineage progression. In the laboratory, we have developed unique genetic tools, in particular a transgenic Tg: Pax7-nGFP mouse to investigate how cell relationships in the lineage are established and how this tissue is built. We can isolate highly pure populations of satellite cells for detailed investigations using multiple approaches.

Our previous studies showed that satellite cells can perform asymmetric cell divisions. Notably, co-segregation of template DNA strands (TDSS) ("immortal DNA") takes place to one daughter cell in vivo and in vitro. We have extended these studies and identified a subpopulation of satellite cells that performs biased DNA segregation. Notably, higher resolution techniques including videomicroscopy, FACS analysis and CO-FISH, which permits single chromosome resolution, are being used. In addition, studies on the biological properties of satellite cells using different parameters is being employed including RT-qPCR and in vivo labelling of the population. The characterisation of satellite cells will provide valuable information about stem cells in general and their genetic and epigenetic regulation.

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