Universität Basel

Research Project

A CRISPR/Cas9-screening platform to decipher conserved cell fate specification networks in vivo

Third-party funded project

Project title A CRISPR/Cas9-screening platform to decipher conserved cell fate specification networks in vivo
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The adult human body consists of hundreds, if not thousands, of distinct cell types. Examples include different neurons in the brain, epithelial cells lining the gut, or the cells that produce the bone or cartilage in our skeletons. During embryogenesis, all of these diverse cell types develop from a single progenitor cell - the fertilized egg. Understanding the different molecular mechanisms that orchestrate this diversification can help us re-create a particular cell type in a cell culture dish. Having access to such 'in vitro'-generated cells would then enable their use in tissue repair and replacement strategies in human patients.

What are the potential difficulties in achieving these goals? Many cell type specification processes require complex interactions with the surrounding tissue. Hence, only in the context of a developing embryo can these processes be fully understood, making the use of non-human 'model organisms' indispensable. This, however, raises additional questions: how can we minimize the number of experimental animals used in these studies, and how can we ensure that findings in such model organisms also translate to us humans?

To address these challenges, here I propose to integrate comparative genomics data to define conserved 'core regulatory switches' that specify a given cell type across species. We will then functionally test the relevance of these candidate 'switches' using genetic perturbations in chicken embryos. Our experimental approach will prevent the euthanasia of any pregnant female animal while at the same time maximize its relevance for the subsequent in vitro specification of human cell types.

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