Mathematical model of adult stem cell regeneration with cross-talk between genetic and epigenetic regulation

With the support by the National Natural Science Foundation of China, Prof. Lei Jinzhi at Zhou Pei-Yuan Center of Applied Mathematics, Tsinghua University, and his collaborators, Prof. Simon Levin from Princeton University and Prof. Qing Nie from the University of California Irvine, outline a general mathematical model that applied tools from optimization theory to understand stem cell dynamics, which was published in *Proc Natl Acad Sci USA* (2014, 111: E880-E887).

Stem cell populations continually regulate cell division, growth, and death to sustain regeneration throughout the lifetime of an organ or tissue. The mechanisms of self-regulation, however, are unclear. Lei *et al*. contribute an original idea to the ongoing discussion. They proposed a general mathematical framework that views regulation of stem cell population activity as an optimization problem, which achieves the best solution when there is cross-talk between genetic and epigenetic feedback mechanisms.

This work provides fresh perspective on some well-known phenomena. For instance, the authors found that heterogeneous proliferation of stem cells, dependent on the epigenetic state of the parent cell, leads to the balanced populations that are able to respond robustly to sudden changes in the stem cell system. Allowing genetic mutation in the model induces the population to evolve apoptosis regulation to maximize cell performance during homeostasis. The results suggest that stem cell regulation processes are active both over a single cell division cycle and over the lifetime of a tissue, and that heterogeneous proliferation, in which cells possess variable probabilities of proliferation, increases the overall robustness of the stem cell population.

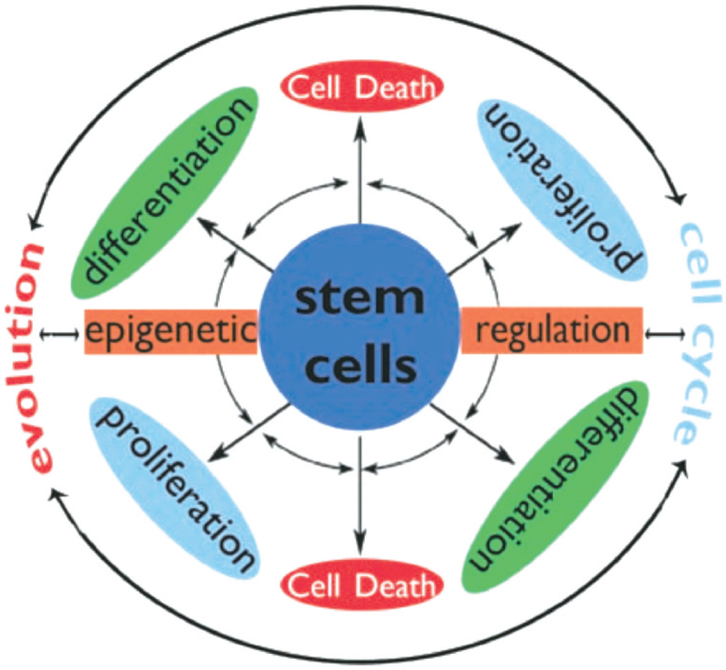

Figure Stem cell regulation processes interact with cell cycle processes to maintain robust populations.