Medicine, Nursing and Health Sciences

Biomedicine Discovery Seminar

Monash Biomedicine Discovery Institute

Stem cell self-renewal and lineage aging determine clone size fluctuations in granulopoiesis

Wednesday 9 November 2016

11:00 – 12:00pm

H4 Lecture Theatre
20 Chancellors Walk Walk
Clayton campus

Presenter

Professor Tom Chou

MD, PhD

Department of Biomathematics and Mathematics, UCLA

About the presenter

I am a Professor in the Departments of Biomathematics and Mathematics. I am also an affiliate faculty in the Department of Bioengineering, the Physiology interdepartmental program (IDP), the Bioinformatics IDP, and the Statistical and Biomathematical Consulting Center. As such, I look forward to mentoring quantitatively well-trained PhD students across these departments and IDPs.

I have broad research interests, especially in biophysics, cell biology, physiological modeling, virology, and in more fundamental applied/statistical/computational mathematics. I like to combine advanced physics approaches with statistical/stochastic/optimization techniques to formulate and analyze predictive models that not only help us understand mechanisms, but guide the posing of new questions in physics, biology, biomedicine, and engineering..

Abstract

In recent experiments, virally tagged hematopoietic stem cells (HSCs) were autologously transplanted into rhesus macaques and peripheral blood cells were sampled over fourteen years. Peripheral blood samples were then sequenced and the abundances of cells with different tags were quantified. Through mathematical modeling and statistical analysis on data, we find that random HSC self-renewal events in the bone marrow is consistent with the observed clonal size heterogeneity in the sampled peripheral blood. The dynamic variability in the sizes of individual clones, including the occasional extinctions and resurrections of certain clones, is naturally explained by a proliferation model that incorporates lineage aging by imposing a maximum number of divisions on progenitor cells. After constraining specific parameters via a mechanistic model, we find that the level of clone size fluctuations are controlled by the product of the steady-state HSC numbers and the per-HSC differentiation rate. Our analysis quantifies the multi-stage stochastic dynamics of HSCs, progenitor cells, and peripheral blood, and shows that they can arise from an initial self-renewal stage followed by generation-limited progenitor cell bursting. Within this mechanistic picture, we use the data to infer estimates for the total HSC differentiation rate and a consistent maximum number of progenitor cell divisions.

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