Our laboratory at the Stanford Institute for Stem Cell Biology & Regenerative Medicine and the Department of Developmental Biology aspires to understand how different human cell-types develop from stem cells, and how developing tissues incipiently take shape and form. To this end, we have delineated a comprehensive roadmap that describes how embryonic stem cells can develop into a spectrum of over twenty different human cell types. This roadmap enabled us to generate rather uniform populations of human liver progenitors, bone progenitors and heart progenitors from embryonic stem cells, each of which could regenerate their cognate tissue upon injection into respective mouse models. This platform to produce these engraftable human tissue progenitors provides fundamental building blocks for regenerative medicine and provides an ideal venue to understand human developmental biology. In particular we are interested in questions regarding cellular signaling, developmental competence and tissue organization.

Kyle received his B.A. from Rutgers University, interned with Bing Lim at the Genome Institute of Singapore, and received his Ph.D. from Stanford University (working with Irving Weissman) as a fellow of the Hertz Foundation, the National Science Foundation and the Davidson Institute of Talent Development. He then continued research as the Siebel Investigator at the Stanford Institute for Stem Cell Biology & Regenerative Medicine, and later, as an Assistant Professor of Developmental Biology. His research has been recognized by the NIH Director's Early Independence Award, Donald and Delia Baxter Foundation Faculty Scholar Award, A*STAR Investigatorship, Harold Weintraub Graduate Award and Hertz Foundation Thesis Prize.
CURRENT RESEARCH AND SCHOLARLY INTERESTS

Embryonic stem cells can produce any type of human cell in a dish. Thus they afford an opportunity to recreate, and thus study, basic developmental phenomena (lineage diversification, tissue self-organization and multilineage competence) that are difficult to probe in a developing embryo. However, this opportunity has yet to be fully realized because stem-cell differentiation often yields heterogeneous mixtures of cells that are ill-suited for molecular analysis or cell therapy.

We have developed a reductionist system to define the minimal essential inductive and repressive signals necessary for the developmental induction of a given embryonic lineage from differentiating ESCs. These efforts culminated in systematic roadmaps describing the extrinsic signals that guide human ESCs into a variety of endoderm and mesoderm germ layer derivatives (including liver, intestinal, bone and heart progenitors) through a series of bifurcating intermediate steps. The overarching goal is to exploit the resultant highly-pure populations of human tissue progenitors to explore classic questions in developmental biology, using stem-cell differentiation as a technological platform.

Teaching

STANFORD ADVISEES

Postdoctoral Faculty Sponsor
Phillip Geter

Postdoctoral Research Mentor
Phillip Geter

Publications

PUBLICATIONS

• Generating Cellular Diversity and Spatial Form: Wnt Signaling and the Evolution of Multicellular Animals. Developmental cell
Loh, K. M., van Amerongen, R., Nusse, R.
Mapping the Pairwise Choices Leading from Pluripotency to Human Bone, Heart, and Other Mesoderm Cell Types. *CELL*
2016; 166 (2): 451-467

Ex uno plures: molecular designs for embryonic pluripotency. *Physiological reviews*
Loh, K. M., Lim, B., Ang, L. T.
2015; 95 (1): 245-295

Stem cell signaling. An integral program for tissue renewal and regeneration: Wnt signaling and stem cell control. *Science*
Clevers, H., Loh, K. M., Nusse, R.
2014; 346 (6205)

Efficient endoderm induction from human pluripotent stem cells by logically directing signals controlling lineage bifurcations. *Cell stem cell*
2014; 14 (2): 237-252

A Precarious Balance: Pluripotency Factors as Lineage Specifiers *CELL STEM CELL*
Loh, K. M., Lim, B.
2011; 8 (4): 363-369

Thirst-associated preoptic neurons encode an aversive motivational drive. *Science (New York, N.Y.)*
2017; 357 (6356): 1149–55

An atlas of transcriptional, chromatin accessibility, and surface marker changes in human mesoderm development *SCIENTIFIC DATA*
2016; 3

Reprogramming mouse fibroblasts into engraftable myeloerythroid and lymphoid progenitors *NATURE COMMUNICATIONS*
2016; 7

Inhibition of Apoptosis Overcomes Stage-Related Compatibility Barriers to Chimera Formation in Mouse Embryos. *Cell stem cell*
2016; 19 (5): 587-592

Stem cells: Equilibrium established. *Nature*
Loh, K. M., Lim, B.
2015; 521 (7552): 299-300

Differentiation of trophoblast cells from human embryonic stem cells: to be or not to be? *REPRODUCTION*
2014; 147 (5): D1-D12

Rapid and efficient conversion of integration-free human induced pluripotent stem cells to GMP-grade culture conditions. *PloS one*
2014; 9 (4)

Rapid and Efficient Conversion of Integration-Free Human Induced Pluripotent Stem Cells to GMP-Grade Culture Conditions. *PloS one*
2014; 9 (4)

Clonal precursor of bone, cartilage, and hematopoietic niche stromal cells. *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
2013; 110 (31): 12643-12648
• Rejuvenating tithonus. *EMBO reports*
  Loh, K. M., Lim, B.
  2013; 14 (7): 583-584

• **EPIGENETICS Actors in the cell reprogramming drama** *NATURE*
  Loh, K. M., Lim, B.
  2012; 488 (7413): 599-600

• Investigating the bona fide differentiation capacity of human pluripotent stem cells *CELL RESEARCH*
  Heng, J. D., Loh, K. M., Ng, H.
  2012; 22 (1): 6-8

• **Recreating Pluripotency?** *CELL STEM CELL*
  Loh, K. M., Lim, B.
  2010; 7 (2): 137-139

• A Small-Molecule Inhibitor of Tgf-beta Signaling Replaces Sox2 in Reprogramming by Inducing Nanog *CELL STEM CELL*
  2009; 5 (5): 491-503