Kyle M. Loh

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Research Overview

Our goal is to understand how human tissue progenitors are specified and maintained and then to eventually apply this knowledge to generate pure populations of these cell-types from embryonic stem cells (Loh & Ang et al., 2014; *Cell Stem Cell*; Loh & Chen et al., 2016; *Cell*; Brown & Loh et al., 2017; *Cell Reports*; Ang et al., 2018; *Cell Reports*). This will lend insight into how early human tissues develop and should provide a foundation for regenerative medicine. Other interests include pluripotency (Loh & Lim, 2011; *Cell Stem Cell*; Loh et al., 2015, *Physiol Rev*), expansion of multipotent tissue progenitors (Nichane et al., 2017; *Nature Methods*), signal transduction (Clevers, Loh & Nusse, 2014; *Science*), evolution (Loh & van Amerongen et al., 2016; *Dev Cell*) and cell-fate transitions (Loh & Lim, 2012, 2013, 2015; *Nature*).

Training & Appointments

Assistant Professor and The Anthony DiGenova Endowed Faculty Scholar, Stanford University 2018-Current
Department of Developmental Biology and the Institute for Stem Cell Biology & Regenerative Medicine
Member, Bio-X, ChEM-H, Stanford Cancer Institute, Stanford Cardiovascular Institute, Stanford Diabetes Research Center, Stanford Maternal Child Health Research Institute & Wu Tsai Neurosciences Institute

Siebel Investigator and Instructor, Stanford University 2016-2018
Independent group leader at the Institute for Stem Cell Biology & Regenerative Medicine

Ph.D., Developmental Biology, Stanford University (Advisor: Prof. Irving Weissman) 2011-2016

Intern, Genome Institute of Singapore, A*STAR (Advisor: Prof. Bing Lim) 2010-2011

B.A., Cell Biology & Neuroscience *summa cum laude*, Rutgers University 2007-2010
Advisors: Prof. Dale Woodbury (Rutgers RWJMS) and Prof. Kevin Eggan and Prof. Douglas Melton (Harvard)

Fellowships & Awards

Pew Biomedical Scholar, $300K USD 2019
Recognizes junior faculty in biological research; each institution nominates a single faculty member to a national competition (22 selected from across the U.S. in 2019)

Human Frontier Science Program Young Investigator, $375K USD 2019
Recognizes junior faculty in biological research working "across national and disciplinary boundaries" (9 teams selected from 160 applicants worldwide in 2019)

The Anthony DiGenova Endowed Faculty Scholar at Stanford University 2018

Forbes 30 Under 30 2018
Recognizes individuals under age 30 in the healthcare category (30 selected from across the U.S.)

Donald and Delia Baxter Foundation Faculty Scholar, $100K USD 2018
2 junior faculty selected from across Stanford Medicine in 2018

Fannie and John Hertz Foundation Thesis Prize 2018

Recognizes exceptional Ph.D. thesis work by graduating Hertz Fellows (1 selected from across the U.S. in 2018)

NIH Director's Early Independence Award (**DP5**), $1.25M USD 2017
To establish an independent research program in the U.S., awarded under the NIH High Risk/High Reward Research Program (11 selected from across the U.S. in 2017)

Siebel Investigatorship 2016
To establish an independent research program at the Stanford Inst. for Stem Cell Biology & Regenerative Medicine

A*STAR Investigatorship (**declined**), ~$5M USD 2016
To establish an independent research program in Singapore (2 selected from 120 applicants worldwide in 2016)

Harold M. Weintraub Graduate Award, **Fred Hutchinson Cancer Research Center** 2015
Recognizes thesis work by graduating biology Ph.D. students across the world (13 selected worldwide in 2015)

Fannie and John Hertz Foundation Graduate Fellowship Award, $250K USD 2011-2016
The most selective science Ph.D. fellowship in the U.S. (15 selected from 558 applicants in 2011, top 3%)

U.S. National Science Foundation Graduate Research Fellowship, $121K USD 2011-2014
Science and technology U.S. Ph.D. fellowship (selected from ~20,000 applicants across the U.S. in 2011)

Davidson Laureate Fellowship, $50K USD 2010-2020
Recognizes research by students age 18 or under, from across the U.S.

A*STAR Singapore International Pre-Graduate Award, for 1-year research internship 2010-2011
Rutgers University School of Arts & Sciences Excellence Award 2007-2010
Harvard Stem Cell Institute Internship Program 2008
Research & Development Council of New Jersey Scholarship 2007

Publications (Research Articles)

**Co-first authors; **Co-second authors; †Co-senior/corresponding authors*

1. Ichida JK*, Blanchard J*, Lam K*, Son EY*, Chung JE, Egli D, **Loh KM**, Carter AC, Di Giorgio FP, Koszka K, Huangfu D, Akutsu H, Liu DR, Rubin LL, Eggan K (2009). **A small molecule inhibitor of TGF-β signaling replaces *Sox2* in reprogramming by inducing *Nanog***. ***Cell Stem Cell*** 5: 491-503, PubMed 19818703

2. Chan CK*, Lindau P*, Jiang W*, Chen JY, Zhang LF, Chen CC, Seita J, Sahoo D, Kim JB, Lee A, Park S, Nag D, Gong Y, Kulkarni S, Luppen CA, Theologis AA, Wan DC, DeBoer A, Seo EY, Vincent-Tompkins JD, **Loh K**, Walmsley GG, Kraft DL, Wu JC, Longaker MT, Weissman IL (2013). **Clonal precursor of bone, cartilage, and hematopoietic niche stromal cells**. ***Proc Natl Acad Sci USA*** 110: 12643-8, PubMed 23858471

3. Durruthy-Durruthy J, Briggs SF, Awe J, Ramathal CY, Karumbayaram S, Lee PC, Heidmann JD, Clark A, Karakikes I, **Loh KM**, Wu JC, Hoffman AR, Byrne J, Reijo Pera RA, Sebastiano V (2014). **Rapid and efficient conversion of integration-free human induced pluripotent stem cells to GMP-grade culture conditions**. ***PLoS ONE*** 9: e94231, PubMed 24718618

4. **Loh KM***, Ang LT*, Zhang J**, Kumar V**, Ang J, Auyeong JQ, Lee KL, Choo SH, Lim CYY, Nichane M, Tan J, Noghabi MS, Azzola L, Ng ES, Durruthy-Durruthy J, Sebastiano V, Poellinger L, Elefanty AG, Stanley EG, Chen Q, Prabhakar S, Weissman IL, Lim B (2014). **Efficient endoderm induction from human pluripotent stem cells by logically directing signals controlling lineage bifurcations**. ***Cell Stem Cell*** 14: 237-52 (**co-first author*), PubMed 24412311

Summary: We comprehensively mapped how 7 human endodermal lineages emerge from pluripotent cells.

We identified the pairwise lineage choices through which these cell-types emerge and the positive and negative extracellular signals that specify each lineage. This knowledge enabled the generation of enriched human liver progenitors from ESCs that could engraft the mouse liver for multiple months. Lastly, we revealed stepwise changes in transcriptional and chromatin state at each endodermal lineage transition, delineating a coherent map of human endoderm development.
Featured in *A*STAR Research*

5. **Loh KM***, Chen A*, Koh PW, Deng T, Sinha R, Tsai JM, Barkal AA, Shen KY, Jain R, Morganti RM, Ng SC, Fernhoff NB, George BM, Wernig G, Salomon RAE, Chen Z, Vogel H, Epstein JA, Kundaje A, Talbot WS, Beachy PA, Ang LT†, Weissman IL† (2016). **Mapping the pairwise choices leading from pluripotency to human bone, heart, and other mesoderm cell types**. ***Cell*** 166: 451-67 (**co-first author*), PubMed 27419872

Summary: We comprehensively mapped how 12 human mesodermal lineages emerge from pluripotent cells. We identified the pairwise lineage choices through which these cell-types emerge and the positive and negative extracellular signals that specify each lineage. This knowledge enabled the generation of enriched human mesoderm tissue progenitors from ESCs, including human bone and heart progenitors that could engraft mouse models and regenerate their cognate tissue *in vivo*. Finally, we discovered unique cell-surface markers to purify major mesodermal tissue progenitors.
Featured in the NIH Director's Blog, Stanford Medicine News, the *San Jose Mercury News* and *Fierce Biotech*; with an accompanying Cell Press Video Abstract (only one paper selected per issue) and Preview by Kyba (2016); *Cell Stem Cell* 19: 146-8

6. Hui C, Ang HYK, Farran CAEL, Li P, Fang H, Liu T, Kong SL, Chin ML, Lim EKH, Li H, Huber H, **Loh KM**, Loh YH, Lim B (2016). **Reprogramming mouse fibroblasts into engraftable myeloerythroid and lymphoid progenitors: induction and underlying mechanisms**. ***Nature Communications*** 7: 13396, PubMed 27869129

7. Masaki H, Kato-Itoh M, Umino A, Sato H, Ito K, Yanagida A, Hirabayashi M, Sasaki E, Yamaguchi T, **Loh KM**, Weissman IL, Nakauchi H (2016). **Inhibition of apoptosis overcomes stage-related compatibility barriers to chimera formation in mouse embryos**. ***Cell Stem Cell*** 19: 587-592, PubMed 27814480

8. Koh PW*, Sinha R*, Barkal AA, Morganti RM, Chen A, Weissman IL†, Ang LT†, Kundaje A†, **Loh KM**† (2016). **An atlas of transcriptional, chromatin accessibility, and surface marker changes in human mesoderm development**. ***Scientific Data*** 3: 160109 *(†co-senior author)*, PubMed 27996962

9. Allen WE*, DeNardo LA*, Chen MZ*, Liu CD, **Loh KM**, Fenno LE, Ramakhrishnan C, Deisseroth K†, Luo L† (2017). **Thirst-associated preoptic neurons encode an aversive motivational drive**. ***Science*** 357: 1149-1155, PubMed 28912243

10. Brown K*, **Loh KM***, Nusse R (2017). **Live imaging reveals that the first division of differentiating human embryonic stem cells often yields asymmetric fates**. ***Cell Reports*** 21: 301-307 (**co-first author*), PubMed 29020617

11. Nichane M, Javed A, Sivakamasundari V, Ganesan M, Ang LT, Kraus P, Lufkin T, **Loh KM**†, Lim B† (2017). **Isolation and expansion of Sox9$^+$ mouse embryonic lung progenitors that generate both airway and alveolar lineages**. ***Nature Methods*** 14, 1205-1212 *(†co-senior/co-corresponding author)*, PubMed 29106405
Featured in Stanford Medicine News

12. Ang LT, Tan AKY, Autio MI, Goh SH, Choo S, Lee KL, Tan J, Pan B, Lee JJ, Lum JJ, Lim Y, Yeo K, Wong J, Oh L, Chia P, Chen A, Chen QF, Weissman IL, **Loh KM**†, Lim B† (2018). **A roadmap for human liver differentiation from pluripotent stem cells**. ***Cell Reports*** 22, 2190–2205 *(†co-senior author)*, PubMed 29466743

13. Wilkinson AC, Ishida R, Kikuchi M, Sudo K, Morita M, Crisostomo RV, Yamamoto R, **Loh KM**, Nakamura Y,

Watanabe M, Nakauchi H, Yamazaki S (2019). **Long-term *ex vivo* haematopoietic-stem-cell expansion allows nonconditioned transplantation**. ***Nature***, advance online publication: doi:10.1038/s41586-019-1244-x

14. George BM, Kao KS, Kwon HS, Velasco BJ, Poyser J, Chen A, Le AC, Chhabra A, Burnett C, Cajuste D, Hoover M, **Loh KM**, Shizuru JA, Weissman IL (2019). **Antibody conditioning enables MHC-mismatched hematopoietic stem cell transplants and organ graft tolerance**. ***Cell Stem Cell***, accepted (*bioRxiv*, doi:10.1101/525899)

15. Roodgar M, Suchy F, Bajpai V, Viches-Moure JG, Bhadury J, Oikonomopoulos A, Wu JC, Mankowski JL, **Loh K**, Nakauchi H, VandeVoort C, Snyder M (submitted). **Cross-species blastocyst chimerism between nonhuman primates using iPSCs**. *bioRxiv*: doi:10.1101/635250

Publications (Review or Other Articles)

16. **Loh KM***, Soh BS*, Tam WL, Lim B (2010). **Molecular principles underlying the pluripotency and differentiation of embryonic stem cells**. ***Stem Cells: From Bench to Bedside*** *(**2nd Edition**)* by World Bioscience *(*co-first author)*

17. **Loh KM** and Lim B (2010). **Recreating pluripotency?** ***Cell Stem Cell*** 7: 137-9

18. **Loh KM** and Lim B (2011). **A precarious balance: pluripotency factors as lineage specifiers**. ***Cell Stem Cell*** 8: 363-9

> Summary: We proposed a fundamentally different view of the embryonic stem cell state and the role of stem cell transcription factors (TFs). The prevailing model suggested that undifferentiated state of pluripotent stem cells is maintained by TFs that monolithically suppress differentiation. By contrast, we asserted that pluripotency TFs are lineage specifiers that drive differentiation to downstream lineages. We further suggested that co-expression of multiple competing lineage-specifying pluripotency factors generates an undifferentiated state while maintaining the competence to differentiate into multiple lineages. This changed how the field views how the stem-cell state is maintained.
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> Featured in Editorial "Our top 10 developments in stem cell biology over the last 30 years" by Armstrong et al., 2012; *Stem Cells* 30: 2-9

19. Heng DJC, **Loh KM**, Ng HH (2012). **Investigating the *bona fide* differentiation capacity of human pluripotent stem cells**. ***Cell Research*** 22: 6-8

20. **Loh KM** and Lim B (2012). **Actors in the cell reprogramming drama**. ***Nature*** 488: 599-600

21. **Loh KM** and Lim B (2013). **Rejuvenating Tithonus**. ***EMBO Reports*** 14: 583-4

22. **Loh KM** and Lim B (2013). **Close encounters with full potential**. ***Nature*** 502: 41-42

23. Roberts RM, **Loh KM**, Amita M, Bernardo AS, Adachi K, Alexenko AP, Schust DJ, Schulz LC, Telugu BP, Ezashi T, Pedersen RA (2014). **Differentiation of trophoblast cells from human embryonic stem cells: to be or not to be?** ***Reproduction*** 147: D1-D12

24. Clevers H, **Loh KM**, Nusse R (2014). **An integral program for tissue renewal and regeneration: Wnt signaling and stem cell control**. ***Science*** 346: 1248012

25. **Loh KM**, Lim B, Ang LT (2015). **Stem cell genomics: developmental competence**. ***Principles and Practice of Genomic Medicine*** *(**2nd Edition**)* by Oxford University Press

26. **Loh KM**, Lim B, Ang LT (2015). **Ex uno plures: molecular designs for embryonic pluripotency**. ***Physiological Reviews*** 95: 245-295

27. **Loh KM** and Lim B (2015). **Equilibrium established**. ***Nature*** 521: 299-300

28. **Loh KM***, van Amerongen R*, Nusse R (2016). **Generating spatial form and cellular diversity: Wnt signaling and the evolution of multicellular animals**. ***Developmental Cell***, 38: 643-655 *(*co-first author)*

Summary: We propose that Wnt proteins were primordial symmetry-breaking signals that enabled the speciation of the earliest animals from their unicellular predecessors. Wnt signals can specify cell fate and position by polarizing a cell at the point of contact, inducing it to divide asymmetrically and producing two daughter cells of differing fates in a spatially-choreographed way. Emerging contemporaneously with the first animals, Wnt signals may have polarized aggregates of unicellular organisms, breaking symmetry and leading to lineage diversification and spatial form within the first incipiently-arising animals.

29. Tan AKY, **Loh KM**, Ang LT (2017). **Evaluating the regenerative potential and functionality of human liver cells in mice**. ***Differentiation*** 98: 25-34

30. Nichane M and **Loh KM** (2018). **Obliterating obstacles to an odyssey**. ***Cell Stem Cell*** 23: 313-15.

31. **Loh KM**, Palaria A, Ang LT (2019). **Efficient differentiation of human pluripotent stem cells into liver cells**. ***Journal of Visualized Experiments*** 148: e58975

Patents

1. **Methods of differentiating stem cells into one or more cell lineages** (filed October 19, 2012). International Patent Application PCT/SG2013/000453 (US14437147, EP20130848074, JP2015534805A and CN104995294A).

2. **Methods of differentiating stem cells into liver cell lineages** (filed October 8, 2014). International Patent Application PCT/SG2015/050359.

3. **Producing mesodermal cell types and methods of using the same** (filed March 2, 2015). International Patent Application PCT/US2016/020488.

Professional Activities

- 2010. **Loh KM** and Lim B. **Fears are based on biological myths**. *The Straits Times* newspaper (*Nov 8, 2010*).
- 2011. **Selection Committee**, **L'Oréal Singapore For Women In Science National Fellowship**.
- 2014-Incumbent. ***Ad hoc* reviewer**. ***Nature, Cell Stem Cell, Nature Cell Biology***, ***Proc Natl Acad Sci USA, eLife, Cell Reports, PLoS Biology, Stem Cells, Stem Cell Reports, Stem Cell Research, Genome Biology***, ***FASEB J***, ***iScience***
- 2015. **Helped commercialize** endoderm differentiation technology (Loh & Ang et al., 2014; *Cell Stem Cell*), which was licensed and is now sold worldwide as a cell culture media by Thermo Fisher Scientific, Inc.
- 2015-2018. **Scientific Advisory Board**, **Americans for Cures Foundation**. Advised public outreach efforts to inform the American public about stem cell research.
- 2017-Incumbent. **Admissions Committee, Stanford Stem Cell Biology & Regenerative Medicine Ph.D. Program**.
- 2018-Incumbent. **Retreat Committee, Stanford Institute for Stem Cell Biology & Regenerative Medicine**.
- 2018-Incumbent. **Admissions Committee, Stanford Developmental Biology Ph.D. Program**.
- 2018-Incumbent. **Scientific consultant** for a pharmaceutical company and venture capital firms.

Teaching

All lectures drawn from >20 papers in the primary literature, listed in the Works Cited of each lecture.
STEMREM201A (**Stem Cells and Human Development**) – Autumn 2015-2017 (Lecturer); Autumn 2018 (Director)

Leader of revised course to teach principles of stem cell biology and regenerative medicine to Stanford Ph.D. students, M.D. students and undergraduates; presented 9 out of 26 total lectures and organized curriculum (2018). In previous years, I presented up to 3 lectures in the course (2015-2017).

STEMREM200 (**Stem Cell Intensive**) – Autumn 2018 (Co-Director)
Co-leader of revised course to immerse incoming Stanford Ph.D. students in stem cell research; organized curriculum and laboratory sessions and presented 1 lecture.

STEMREM202 (**Stem Cells and Regenerative Medicine**) – Winter 2017-2018 (Lecturer)
1 lecture on pluripotent stem cell differentiation for Stanford Ph.D. students.

HUMBIO157 (**The Biology of Stem Cells**) – Spring 2017 (Lecturer); Spring 2019 (Co-Director)
Co-leader of course to teach principles of stem cell biology and regenerative medicine to Stanford undergraduates (2019); presented 3 lectures on pluripotency, lineage decisions and blood stem cells (2017, 2019).

Oral Presentations

2020 **Stem Cell Symposium Vienna 2020**, **Austria** (*pending*)

2019 **Stanford Siebel Stem Cell Institute Workshop**
Merck & Co., Inc.
3rd Stanford Center for Definitive and Curative Medicine Symposium
Genentech, Inc.
Erasmus University Medical Center, **Netherlands**
EMBL Barcelona, **Spain**
3D Tissue Culture and Organoids Symposium, **Japan**
Bay Area Stem Cell Conference
3rd Stanford-RIKEN Center for Integrative Medical Sciences Symposium (*organizer*)
VenRock
5AM Ventures Speaker Series
International Society for Stem Cell Research (**ISSCR**) **Meeting 2019** (*pending*)
Stanford University, Urology Research Seminar (*pending*)
Nanyang Technological University, LKC Medical School, Singapore (*pending*)
42nd Molecular Biology Society of Japan Annual Meeting, **Japan** (*pending*)

2018 **Stanford Siebel Stem Cell Institute Workshop**
Stanford University, Vision (**Ophthalmology**) **Seminar Series**
Dutch Society for Stem Cell Research, **Netherlands**
Hubrecht Institute/Princess Máxima Center for Pediatric Oncology, **Netherlands**
2nd Stanford-RIKEN Center for Integrative Medical Sciences Symposium, **Japan**
Kyoto University, **Center for iPS Cell Research and Application, Japan**
Weill Cornell Medicine
Memorial Sloan Kettering Cancer Center, **Developmental Biology Program**
Frontiers in Organoid Medicine Symposium, **Cincinnati Children's Hospital Medical Center**
University of Southern California

2017 **San José State University**
RIKEN Center for Integrative Medical Sciences, **Japan**
Stanford University, **Center for Definitive and Curative Medicine**
UC Los Angeles, **Department of Biological Chemistry**

Fred Hutchinson Cancer Research Center, Clinical Research Division
1st Stanford-RIKEN Center for Integrative Medical Sciences Symposium
Stanford University, Center for Cell Biology
3rd CIRM Annual Stem Cell Genomics Retreat
UC Los Angeles, Broad Stem Cell Research Center
Stanford Institute for Stem Cell Biology & Regenerative Medicine
Duke University, Regeneration Next Initiative
The Rockefeller University
Fred Hutchinson Cancer Research Center, Basic Sciences Division
UC Berkeley Siebel Stem Cell Institute Workshop

2016 **University of Pennsylvania, Institute for Regenerative Medicine**
San José State University, California Institute for Regenerative Medicine Internship Reception
NIH Progenitor Cell Biology Consortium HSC Focused Workshop 2016
Stem Cell Society Singapore Symposium 2016, Singapore
Cincinnati Children's Hospital Medical Center
A*STAR Investigatorship Symposium, Singapore
International Society for Stem Cell Research (ISSCR) Meeting 2016
UC Santa Cruz, Department of Biomolecular Engineering
Carnegie Institute of Washington, Department of Embryology

2015 **Genome Institute of Singapore, A*STAR, Singapore**
Institute of Molecular and Cellular Biology, A*STAR, Singapore
Stanford Institute for Stem Cell Biology & Regenerative Medicine
Stem Cell Research Briefing Session for U.S. Senator Ron Wyden – for U.S. Senator Ron Wyden
UC Berkeley Siebel Stem Cell Institute Workshop

2014 **University of Cambridge Stem Cell Institute, UK**
Cambridge Centre for Trophoblast Research Annual Meeting, UK
Center for Genomic Regulation, Spain
Stanford Reproductive and Stem Cell Biology Symposium 2014

2013 **Stem Cell Society Singapore Symposium 2013**