BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Tan, Aaron Tze Kai

eRA COMMONS USER NAME (credential, e.g., agency login): tan.tzekai

POSITION TITLE: PhD Graduate Student

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Singapore Polytechnic, SG	Dip.	04/2013	Biotechnology
The University of Edinburgh, UK	BSc (Hons.)	07/2018	Development, Regeneration and Stem Cell Biology

A. Personal Statement

I am a PhD Graduate Student in the Stem Cell Biology and Regenerative PhD Program at Stanford University, School of Medicine. My ultimate research goal is to advance and leverage our understanding of the biology of stem cells to exert control over them for therapeutic applications in regenerative medicine. To understand and advance the use of stem cells for regenerative medicine, I am motivated to learn the biology of stem cell self-renewal in order to expand and scale-up numbers of *bona fide* stem cells in a dish. Fascinated by the 2012 Noble-prized work of Shinya Yamanaka, John Gurdon, and colleagues on cell-fate reversal and induced pluripotent stem cells (iPSCs) and their potential regenerative medicine therapeutics, I began research at age seventeen as a high school diploma student in the lab of Dr Loh Yuin Han Jonathan at A*STAR. Excited by the thrill of research in stem cell biology, I dedicated most of my waking hours in the lab learning from graduate students and post-docs. I was lucky to have supportive mentors as a young scientist that inspired me and provided me research opportunities. Balancing coursework with lab for two years, I focused on studying reprogramming of human somatic peripheral blood mononuclear derived from a finger-prick drop of blood to human iPSCs which led to my first publication as a co-author in *Stem Cells Translational Medicine*. With recommendations from Dr Loh my mentors, I was fortunate to have competed in Singapore's top scientific talent to secure the A*STAR National Science Scholarship program that fully funds my undergraduate to graduate studies worldwide. Such an opportunity has allowed me to commit and dedicate my time into research at the age of twenty. After two years of compulsory national military service at a rank of Sergeant, I chose to pursued my undergraduate studies at The University of Edinburgh, having been inspired by the creation of the first cloned mammal, Dolly, the sheep. Besides the University's rich history pioneering the stem cell field, they offered the Development, Regeneration, and Stem Cell Biology (DRSC) honors program. The DRSC curriculum honed my undergraduate training in three major area of focus: developmental biology, biology of regeneration, and stem cell biology. I had the privilege to work under the tutelage of world-renowned stem cell biologist, Professor Ian Chambers, for my honors thesis where I utilized a functional cloning approach, as Professor Chambers landmark work, to screen for NANOG mutants that confers cytokine independent self-renewal in embryonic stem cells for my honors thesis. I then spent the following year as a graduate research assistant in the lab of Dr Tee Wee Wei at A*STAR to cumulate experience and skills for graduate school. I focused on epigenetic reprogramming of somatic cells to a totipotent two cell-like stage at Dr Tee's lab. My undergraduate background and research assistantships prepared me exceptionally for my graduate work in stem cell biology research, and my cumulative research experience, and my graduate coursework have strengthen this ability. Coming from a first-generation college graduate family and being first in my family to pursue a PhD graduate education, my humble background made me appreciate and cherish every available learning opportunity where they used to be limited. As such, I

proactively seized and pursue research opportunities worldwide and attended international conferences outside my coursework and curriculum every summer to increase exposure of the breath of research and network with scientists worldwide. For my graduate training at Stanford, I am working in the labs of Professor Garry Nolan, a pioneer and world-renowned leader in the field of multiplexed spatial proteomics technologies and Professor Hiromitsu Nakauchi, an internationally recognized hematopoietic stem cell (HSC) expert, both of which have trained numerous graduate students and postdoctoral fellows that become successful scientific leaders. In my proposed thesis, I will bridge the key gap in knowledge for *ex vivo* expansion of rare and limited population of human HSCs by applying multiplexed spatial proteomics technologies developed in the Nolan lab to understand *in vivo* expansion of HSC in their native niche during early development. By leveraging on the knowledge gained of novel cell-cell interactions between HSCs and niche cells and their cellular neighborhoods, I aim to re-create a synthetic HSC niche for *ex vivo* expansion of human HSCs. Having a robust method to produce ample supply of *bona fide* HSCs in a dish will fulfil the clinical demand for hematopoietic stem cell (bone marrow) transplant in immunocompromised patients post-chemotherapy, conditioning, and avoid graft-versus-host disease from an allogenic organ transplants. Furthermore, scientists will be able to model Clonal Hematopoiesis, the pre-malignant hematological state of leukemia, in a dish. This will advance the development of novel curative therapies, such as drug screens, for various blood diseases/hematopathologies including leukemias, anemias, and bone marrow failures.

B. Positions and Honors

Positions

Sep 2019 - Present	PhD. Student, Stanford University, Garry Nolan and Hiromitsu Nakauchi Laboratories (*Building synthetic niches for Long-Term Ex vivo Expansion of Hematopoietic Stem Cells using Multiplexed Spatial Proteomics Technologies)*
Aug 2018 – Sep 2019	Research Officer, A*STAR Institute of Molecular and Cell Biology, Tee Wee Wei Laboratory (*Epigenetic Reprogramming towards Totipotency)*
Jan 2018 – July 2018	Honors Thesis Student, University of Edinburgh, Ian Chambers (*Investigation of NANOG Homeodomain DNA-binding residues in Embryonic Stem Cell Self-Renewal*)
Jun 2017 – Aug 2017	Undergraduate Research Assistant, A*STAR Genome Institute of Singapore, Ng Huck Hui (*Modeling of Parkinson's Disease using Human Pluripotent Stem Cells Derived Midbrain-like Organoids)*
Jul 2016 – Sep 2016	Undergraduate Research Assistant, University of Cambridge, Helle Jørgensen Laboratory (*Epigenetic Regulation in Cardiovascular Development and Disease*)
Jan 2012 - Apr 2013	Diploma Thesis Research Student, A*STAR Institute of Molecular and Cell Biology, Jonathan Loh Yuin Han Laboratory (*Somatic Reprogramming of Human Blood Cells to Induced Pluripotent Stem Cells*)

Honors

Jun 2019	A*STAR National Science Scholarship (PhD)
Sep 2018	EMBO - Stem Cell Society Singapore Conference Travel Fellowship
Nov 2017	Stem Cell Biology Class Prize
Oct 2014	Duke of Edinburgh's International Award – Singapore National Youth Achievement Award (Gold)
Jul 2013	A*STAR National Scholarship (BS)

Apr 2013	Academic Award for Outstanding Performance by Singapore Polytechnic
Mar 2013	Young Scientists Symposium - Merit Award
Nov 2012	A*STAR Science Award (Polytechnic)

C. Contributions to Science

1. **Early Mammalian Development and Somatic Reprogramming**: My early research relates to molecular mechanisms governing cell fate reprogramming of somatic cells to pluripotency, the cell fate resembling the epiblast cells of the preimplantation embryo, that possess both properties of self-renewal (carry out symmetric cell division) and differentiation to form all cells of the body.
   (a) Endogenous Retrovirus Elements. I assayed for the role of transcription factors: YY1, ESET, TRIM28 and ZFP809 roles in silencing Endogenous Retroviral Elements (ERVs) during pluripotency and somatic cellular reprogramming. Using single and combinatorial shRNA knockdowns of these factors, I have demonstrated that: ESET was a crucial retroviral silencing factor in pluripotent cells; YY1 was crucial in pluripotency genes interaction; and that matured iPSCs downregulated Class I to III ERVs than early iPSCs[(i)]
   (b) Blood Reprogramming. My team and I at A*STAR, Singapore, were the first to demonstrate the efficient derivation of transgene-free human induced pluripotent stem cells (hiPSCs) using a simple "do-it-yourself" finger-prick kit for donor to collect a drop of blood sample, as little as 2uL, to be sent to a hiPSC facility for cellular reprogramming to generate hiPSCs, DNA sequencing, and blood serotyping simultaneously. This strategy has facilitated the development of large-scale hiPSCs banking worldwide, and has led to my first co-author paper in *Stem Cells Translational Medicine*[(ii)]
   (c) Embryonic Stem Cell Self-Renewal. I led an independent project demonstrating that loss-of-function mutation of Y137A and K138A residues in NANOG leads to reduced NANOG function in DNA binding affinity and abolishment of cytokine-independent ESC self-renewal when overexpressed. Furthermore, I utilized an unbiased DNA library screen to screen for residues that can replace Y137 and K138 to confer cytokine-independent ESC self-renewal. Interestingly, I have identified and isolated gain-of-function NANOG mutant that is able to confer 4-fold increase in cytokine-independent ESC self-renewal. In this study, I have highlighted the important roles of NANOG DNA-binding residues involved in mediating ESC self-renewal and possible biochemical interactions, previously unidentified[(iii)]
   (d) Totipotency. I led an independent project to decipher the role of the maternal factor, NELF-A (Negative Elongation Factor A), in contribution to somatic cellular reprogramming as compared to the four classical Yamanaka factors. Through my results, I have uncovered a novel mechanism by which transient overexpression of the maternal factor facilitates direct/indirect expression of endogenous OCT4 and NANOG in somatic cells by means of fluorescence-based reporter assay systems. My data exemplifies the principle in Gurdon and Wilmut's pioneering Somatic Nuclear Cell Transfer experiments by which oocyte-enriched maternal factor confers the capacity to reprogram and propel the somatic nuclei towards acquiring early developmental cell fate and possibility extended fate potential in embryonic stem cells.

   i. **Tze-Kai Tan**, Adeline Koh Mei Choo, Yuin Han Loh: *Molecular Mechanisms in Murine Pluripotent Stem Cells.* Singapore Young Scientist Symposium 2013.
   ii. Hong-Kee Tan, Cheng-Xu Delon Toh, Dongrui Ma, Binxia Yang, Tong Ming Liu, Jun Lu, Chee-Wai Wong, **Tze-Kai Tan**, Hu Li, Christopher Syn, Eng-Lee Tan, Bing Lim, Yoon-Pin Lim, Stuart A Cook, Yuin-Han Loh: *Human Finger-Prick Induced Pluripotent Stem Cells Facilitate the Development of Stem Cell Banking*. STEM CELLS TRANSLATIONAL MEDICINE 03/2014; 3(5)., DOI:10.5966/sctm.2013-0195.
   iii. **Aaron Tze-Kai Tan**, Nicholas Mullin, Ian Chambers: *Investigation of NANOG Homeodomain DNA Binding Residues in Embryonic Stem Cells*. 11th Guangzhou International Conference on Stem Cell and Regenerative Medicine 2018.

2. **Hematopoietic Stem Cell Niche.** Hematopoietic stem cells (HSCs) are the rare and limited population of blood-forming stem cells that reside in the bone marrow. HSCs are clinically important because they carry out long-term hematopoiesis to regenerate and form all blood and immune cells of the body. My ongoing doctoral research focuses on developing the synthetic niche for long-term *ex vivo* expansion of HSCs. I aim to bridge and apply cutting-edge multiplexed spatial proteomics technologies to understand

cellular neighborhoods and cell-to-cell interactions between HSCs with niche cells at key sites of HSCs expansion *in vivo* during early development that has never been done before. By leveraging the knowledge gained from the study, I will be able to develop the synthetic niche that will allow recapitulation of key signals and cellular interactions to simulate HSCs for long-term *ex vivo* expansion. Having a robust method to produce ample supply of *bona fide* HSCs in a dish will fulfil the clinical demand for HSC bone marrow transplant in immunocompromised patients post-chemotherapy, conditioning, and avoid graft-versus-host disease from an allogenic organ transplants. Furthermore, this will advance the leukemia field in understanding and modeling Clonal Hematopoiesis, the pre-malignant hematological state of leukemia, in a dish. This will advance the development of novel curative therapies, such as drug screens, for various blood diseases/hematopathologies including leukemias, anemias, and bone marrow failures.

D. Additional Information: Research Support and/or Scholastic Performance

YEAR	COURSE TITLE	GRADE
	GRADUATE SCHOOL (STANFORD UNIVERSITY)	
2020	DENDRITIC CELLS AND OTHER MYELOID CELLS: FUNCTIONS AND ANALYTICAL TOOLS	A
2020	PRINCIPLES OF PHARMACOGENOMICS	A
2020	DEVELOPMENTAL BIOLOGY	A
2020	COVID-19 ELECTIVE	A
2020	INTRO TO R FOR DATA ANALYSIS	A
2020	STEM CELLS AND HUMAN DEVELOPMENT: LABORATORY	A-
2020	STEM CELLS AND HUMAN DEVELOPMENT: FROM EMBRYO TO CELL LINEAGE	A
2020	STEM CELL INTENSIVE	A
2020	FOUNDATIONS IN EXPERIMENTAL BIOLOGY	A+
2020	ADVANCED GENETICS	A-
2020	THE RESPONSIBLE CONDUCT OF RESEARCH	A+
2020	STEM CELLS AND TRANSLATIONAL MEDICINE	A
2020	REGENERATIVE MEDICINE SEMINAR SERIES	A
2020	STEM CELL BIOLOGY AND REGENERATIVE MEDICINE JOURNAL CLUB	A
	UNDERGRADUATE (EDINBURGH UNIVERSITY)	
2018/2017	DEVELOPMENTAL, REGENERATION AND STEM CELLS RESEARCH PROJECT	A
2018/2017	STEM CELL BIOLOGY	A+
2018/2017	BIOLOGY OF REGENERATION	A
2018/2017	SEGMENTATION: EVOLUTION AND DEVELOPMENT	A
2018/2017	MAMMALIAN TRANSGENIC TECHNOLOGY AND REGENERATIVE MEDICINE	A
2018/2017	PATTERNING IN DEVELOPMENT	A
2017/2016	BIOTECHNOLOGY 3	A
2017/2016	DEVELOPMENTAL BIOLOGY 3	A
2017/2016	IMMUNOLOGY 3	A
2017/2016	GENOME AND GENOMICS 3	A
2016/2015	CELLS TO ORGANISMS 2	A
2016/2015	MICROORGANISMS, INFECTION AND IMMUNITY 2	A
2016/2015	BIOLOGY, ECOLOGY AND ENVIRONMENT 1	A