John F. Ouyang

PERSONAL INFORMATION

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RESEARCH INTEREST

I transitioned from a computational chemistry background into bioinformatics when I started my first post-doctoral stint with Assistant Professor Owen Rackham in Duke-NUS Medical School. Since then, I have taken an interest in reprogramming between cell states and understanding the molecular drivers governing cell fate transitions. In particular, the emergence of single-cell transcriptomics (scRNA-seq) has enabled us to study cell fate transitions at an unprecedented resolution. Leveraging on this technology, my co-workers and I mapped the molecular trajectories during a timeseries reprogramming of human fibroblast into induced pluripotent stem cells. In the same study, we found a novel trophoblast-like cell population, leading to the derivation of induced trophoblast stem cells (Liu, Ouyang, Rossello et al. Nature, 2020). Apart from reprogramming, scRNA-seq has also been applied to disease where we dissected cell type specific transcriptomic changes in the brains of healthy and Alzheimer's Disease individuals (Grubman, Chew, Ouyang et al. Nature Neuroscience, 2019). To harness the rich information in scRNA-seq, I am currently developing new computational tools that can identify cell state specific regulators and their associated surface receptors, and also predict gene perturbations *in silico* from single-cell data. These new tools will then be used to tackle important biological problems, for example, understanding the influence of tumour microenvironment on cancer progression and how certain gene perturbations can reverse such progression. Eventually, I intend to leverage on my chemistry knowledge to identify small molecules that can target the predicted regulators / receptors, which will accelerate the development of new therapies to treat diseases.

I am a firm believer that both experimental and computational expertise are required to solve increasingly complex biological problems. Thus, I enjoy collaborating with wetlab co-workers who generate large volumes of next-generation sequencing data to enable data-driven research. My computational expertise has facilitated the interpretation of such large-scale datasets, enabling the generation of hypotheses that can be readily tested experimentally, resulting in high-impact studies. Furthermore, by working with wetlab co-workers, I can better understand the unmet needs in the field, allowing me to develop more tailored computational tools. One such example is the development of ShinyCell, a tool which generates sharable interactive web interfaces for visualising complex single-cell datasets. I also believe in the importance of mentoring and teaching, which helps to further reinforce one's own knowledge. Within Duke-NUS and internationally, I have conducted several workshops, focusing on data manipulation/ visualisation and the analysis of scRNA-seq data. In addition, I am currently mentoring a PhD student with my PI, who is focusing on the development of new single-cell computational tools.

ACADEMIC QUALIFICATIONS

2012–2016   **National University of Singapore**
                          - Doctor of Philosophy (Ph.D.), Computational Chemistry

2008–2012   **National University of Singapore**
                          - Bachelor of Science, 1st class honours, Chemistry, CAP: 4.92/5.00

2010   **University of British Columbia**
                          - Student Exchange Program

EMPLOYMENT

2022–Present   Principal Research Scientist, CCB, Duke-NUS Medical School
- Research-track PI based at Centre for Computational Biology (CCB)
- Developing new tools to predict cellular dynamics and effects of drug perturbations using scRNA-seq and machine learning

2021–2021   Senior Research Fellow, CVMD, Duke-NUS Medical School
2017–2020   Research Fellow, CVMD, Duke-NUS Medical School
- Working under Asst. Prof. Owen J. L. Rackham (DDNB lab)
- Develop new tools to predict master regulators using scRNA-seq and gene regulatory networks
- Computational analysis and experimental design of single-cell combinatorial CRISPR screening
- Analysis of scRNA-seq and bulk RNA-seq datasets involving somatic cell reprogramming, stem cell differentiation and Alzheimer Disease progression
- Mentor PhD students in developing new scRNA-seq analysis tools

2012–2016   Research Assistant, Department of Chemistry, NUS
- Worked under A/P Ryan P. A. Bettens
- Research on inexpensive ways to calculate the energetics of large molecular clusters
- Developed an algorithm to identify significant intermolecular interactions using graph theory
- Wrote an MOE academic research grant with supervisor to fund the project
- Supervised undergraduate research projects

2010–2016   Graduate Mentor, Special Program in Science, NUS
- Mentored groups of students in scientific inquiry and facilitated seminar-styled tutorials
- Graded and gave timely feedback to students on their reports, presentations and viva
- Headmentor in 11/12: liaison between staff, mentors and students, performed grades moderation

2010–2011   Data Manager, Module-Review.com
- Module-Review is a community-driven review website for choosing undergraduate modules
- Identified quantitative metrics to rate the content and lecturers of modules

SOCIETY / CONSORTIUM MEMBERSHIPS

2018–Present   Stem Cell Society Singapore (SCSS)
2018–Present   International Society for Stem Cell Research (ISSCR)
2017–Present   Functional Annotation of the Mammalian Genome (FANTOM)

HONOURS AND AWARDS

2019   SCSS Overseas Travel Fellowship 2019 - Travel fellowship for overseas conference
2018   SCSS-EMBO 2018 Fellowship - Fellowship for attending the EMBO Workshop 2018
2018   ISSCR 2018 Abstract Merit Awards - Outstanding abstract
2017   Valedictorian for NUS Commencement - Chemistry class of 2017
2012–2016   President's Graduate Fellowship - Ph.D. scholarship
2012   Singapore National Institute of Chemistry Gold Medal - Top honours student in Chemistry
2012   Valedictorian for NUS Commencement - Chemistry class of 2012
2011   GlaxoSmithKline Gold Medal - Top 3rd year Chemistry undergrad
2010   Singapore National Institute of Chemistry Book Prize - Top 2nd year Chemistry undergrad
2009   Singapore National Institute of Chemistry Book Prize - Top 1st year Chemistry undergrad

SCIENTIFIC PUBLICATIONS / PATENTS

Summary Statistics

18 scientific publications, 1 patent

- 15 peer-reviewed research
    - 13 (87%) papers with Journal IF > 5
    - 6 (40%) papers with Journal IF > 10, including
        - Nature (2×), Nat. Neurosci.
- 3 book chapters / invited reviews / meeting reports

Number of citations

Source: Google Scholar	All	Since 2016
Citations	915	855
h-index	12	12
I10-index	13	13

Complete List of Publications

#	Year	Citation (* joint author contribution; † corresponding author) *First / second / corresponding author contributions highlighted in blue*	JIF	PMID
18	2021	GP Risbridger†, AK Clark, LH Porter, R Toivanen, A Bakshi, NL Lister, D Pook, CJ Pezaro, S Sandhu, S Keerthikumar, RQ Urban, M Papargiris, J Kraska, HB Madsen, H Wang, MG Richards, B Niranjan, S O'Dea, L Teng, W Wheelahan, Z Li, N Choo, **JF Ouyang**, H Thorne, L Devereux, RJ Hicks, S Sengupta, L Harewood, M Iddawala, AA Azad, J Goad, J Grummet, J Kourambas, EM Kwan, D Moon, DG Murphy, J Pedersen, D Clouston, S Norden, A Ryan, L Furic, DL Goode, M Frydenberg, MG Lawrence, RA Taylor†. The MURAL collection of prostate cancer patient-derived xenografts enables discovery through preclinical models of uro-oncology. *Nature Communications* 12, 5049 (2021)	12.1	34413304
17	2021	A Grubman*, XY Choo*, G Chew*, **JF Ouyang**, G Sun, NP Croft, FJ Rossello, R Simmons, S Buckberry, DV Landin, J Pflueger, TH Vandekolk, Z Abay, X Liu, JM Haynes, C McLean, S Williams, SY Chai, T Wilson, R Lister, CW Pouton, AW Purcell, OJL Rackham, E Petretto†, JM Polo†. Transcriptional signature in microglia associated with Aβ plaque phagocytosis. *Nature Communications* 12, 3015 (2021) - **2nd author**: Analysed bulk RNA-seq data and assisted in scRNA-seq analysis	12.1	34021136
16	2021	**JF Ouyang**, US Kamaraj, EY Cao, OJL Rackham†. ShinyCell: Simple and sharable visualisation of single-cell gene expression data. *Bioinformatics* 19, 3374 (2021) - **1st author**: Created a tool that makes interactive web apps from single-cell data - Allows for visualisation of complex single-cell data e.g. UMAP plots, coexpression plots, violin / box plots, proportion plots and bubbleplots / heatmaps - Compatible with common single-cell objects (Seurat/SCE/h5ad/loom)	5.6	33774659
15	2021	X Liu*, JP Tan*, J Schröder, A Aberkane, **JF Ouyang**, M Mohenska, SM Lim, YBY Sun, J Chen, G Sun, Y Zhou, D Poppe, R Lister, AT Clark, OJL Rackham, J Zenker, JM Polo†. Modelling human blastocysts by reprogramming fibroblasts into iBlastoids. *Nature* 591, 627–632 (2021)	42.8	33731926
14	2021	XY Choo, YM Lim, K Katwadi, L Yap, K Tryggvason, AX Sun, S Li, L Handoko, **JF Ouyang**†, OJL Rackham†. Evaluating Capture Sequence Performance for Single-cell CRISPR-activation Experiments. *ACS Synthetic Biology* 10, 640–645 (2021) - **Co-corresponding author**: Supervised study and guided experimental design - Designed single-cell CRISPR-activation experiments with wet lab postdocs - Planned and implemented computational analysis quantifying the extent of gRNA capture and CRISPRa efficiency from single-cell readouts	4.4	33625849
13	2021	OJL Rackham†, P Cahan, N Mah, S Morris, **JF Ouyang**, AL Plant, Y Tanaka, CA Wells†. Challenges for Computational Stem Cell Biology: A discussion for the Field. *Stem Cell Reports* 16, 3–9 (2021) - Meeting report for discussions on comp. stem cell biology during ISSCR 2020	6.0	33440181
12	2020	US Kamaraj*, J Chen*, K. Katwadi, **JF Ouyang**, YBY Sun, YM Lim, X Liu, L Handoko, JM Polo†, E Petretto†, OJL Rackham†. EpiMogrify Models H3K4me3 Data to Identify Signalling Molecules that Improve Cell Fate Control and Maintenance. *Cell Systems* 11, 509–522 (2020)	8.7	33038298

11	2020	X Liu*, **JF Ouyang***, FJ Rossello*, JP Tan, KC Davidson, DS Valdes, J Schröder, YBY Sun, J Chen, AS Knaupp, G Sun, HS Chy, Z Huang, J Pflueger, J Firas, V Tano, S Buckberry, JM Paynter, MR Larcombe, D Poppe, XY Choo, CM O'Brien, WA Pastor, D Chen, AL Leichter, H Naeem, P Tripathi, PP Das, A Grubman, DR Powell, AL Laslett, L David, SK Nilsson, AT Clark, R Lister, CM Nefzger, LG Martelotto, OJL Rackham†, JM Polo†. Reprogramming roadmap reveals route to human induced trophoblast stem cells. *Nature* 586, 101–107 (2020)	42.8	32939092

    - **Co-1st author**: Analysed scRNA-, RNA-seq and designed single-cell experiments
    - Uncovered trajectories during reprogramming of fibroblast into primed/naïve iPSC
    - Identified genes associated with primed and naïve pluripotency
    - Found a novel cell population, leading to the derivation of iTSCs
    - Integrated transcriptomic data of iTSCs, embryonic TSCs and in vivo placenta data

10	2020	JA Ramilowski*, CW Yip*, S Agrawal, J-C Chang, Y Ciani, IV Kulakovskiy, M Mendez, JLC Ooi, **JF Ouyang**, …, MJL de Hoon†, JW Shin†, P Carninci†. Functional annotation of human long noncoding RNAs via molecular phenotyping. *Genome Research* 30, 1060–1072 (2020)	11.1	32718982

    - Assisted in analysis of CAGE RNA-seq data as part of FANTOM consortium

9	2020	EY Cao, **JF Ouyang**, OJL Rackham†. GeneSwitches: Ordering gene expression and functional events in single-cell experiments. *Bioinformatics* 36, 3273–3275 (2020)	5.6	32058565

    - **2nd author**: Supervised PhD student (1st author) and helped in code optimisation

8	2019	A Grubman*, G Chew*, **JF Ouyang***, G Sun, XY Choo, C McLean, RK Simmons, S Buckberry, DB Vargas-Landin, D Poppe, J Pflueger, R Lister, OJL Rackham†, E Petretto†, JM Polo†. A single-cell atlas of entorhinal cortex from individuals with Alzheimer's disease reveals cell-type-specific gene expression regulation. *Nature Neuroscience* 22, 2087–2097 (2019)	20.1	31768052

    - **Co-1st author**: Analysed the scRNA-seq data from AD and healthy individuals
    - Identified major cell types and AD-associated cell populations in each cell type
    - Found genes upregulated in each cell populations and linked them to GWAS hits
    - Implemented the web interface to encourage the sharing of this resource

7	2019	S Chothani, E Adami, **JF Ouyang**, S Viswanathan, N Hubner, SA Cook, S Schafer, OJL Rackham†. deltaTE: Detection of Translationally Regulated Genes by Integrative Analysis of Ribo-seq and RNA-seq Data. *Current Protocols in Molecular Biology* 129, e108 (2019)	1.2	31763789

6	2019	**JF Ouyang**, US Kamaraj, JM Polo, J Gough, OJL Rackham†. Molecular Interaction Networks to Select Factors for Cell Conversion. *Book chapter in Methods in Molecular Biology: Computational Stem Cell Biology.* 333–361 (2019)	n/a	31062318

    - **1st author**: Book chapter describing the principles of the Mogrify algorithm which predicts regulator TFs driving cell fate transitions from RNA-seq data

5	2016	**JF Ouyang**, RPA Bettens†. When are Many-Body Effects Significant? *Journal of Chemical Theory and Computation* 12, 5860–5867 (2016)	5.5	27779845

4	2015	**JF Ouyang**, RPA Bettens†. Many-Body Basis Set Superposition Effect. *Journal of Chemical Theory and Computation* 11, 5132–5143 (2015)	5.8	26574311

3	2015	**JF Ouyang**, RPA Bettens†. Modelling Water: A Lifetime Enigma. *Chimia* 69, 104–111 (2015)	1.0	26507212

2	2014	**JF Ouyang**, MW Cvitkovic, RPA Bettens†. Trouble with the Many-Body Expansion. *Journal of Chemical Theory and Computation* 10, 3699–3707 (2014)	5.7	26588515

1	2012	HA Le, HJ Tan, **JF Ouyang**, RPA Bettens†. Combined Fragmentation Method: A Simple Method for Fragmentation of Large Molecules. *Journal of Chemical Theory and Computation* 8, 469–478 (2012)	5.7	26596597

Patents

#	Year	Patent
1	2020	JM Polo, K Davidson, OJL Rackham, X Liu, **JF Ouyang**, L David, G Castel. Generation of induced Trophoblast Stem Cells from human somatic cells by reprogramming. PCT Application: PCT/AU2020/051235

MENTORING AND TEACHING

Mentoring

Year	Student	Description
2018–Present	Cao Yiqun	PhD Student in Integrated Biostatistics and Bioinformatics (IBB) - Co-supervised student with postdoc supervisor on single-cell algorithm development - Developed an algorithm that uses single-cell pseudotime to identify the order of gene activation events (Published as item #9 in "Complete List of Publications") - Developing another tool to explore the activation of gene networks across pseudotime
2020	Hilary Toh	PhD Rotation (6 weeks) - Co-supervised student on single-cell analysis of human neuronal subtypes

Teaching Conducted

#	Year	Description
6	2022	Guest lecture "Single-cell technologies and network biology", Duke-NUS, Singapore, 21 Mar 2022 - Guest lecturer for Duke-NUS College module, GMS6850 Core Concepts in Bioinformatics - Taught >25 students in a seminar-style class, discussing the basics of single-cell technologies and how network biology can be applied to single-cell data
5	2021	Guest lecture "Single-cell omics & its application in biology", Yale-NUS, Singapore, 12 Apr 2021 - Guest lecturer for Yale-NUS College module, YSC3241 Computational and Systems Biology - Taught >10 students in a seminar-style class, discussing the basics of single-cell technologies and its applications in biomedical applications
4	2020	Fundamentals of data visualisation with R, Zoom Workshop, 16 Sep 2020 - Main lecturer, invited by Career Development Program, Duke-NUS Medical School - Taught >20 participants on data wrangling and visualisation using dplyr and ggplot2 - Led a team of three to facilitate interactive breakout sessions
3	2020	Duke-NUS Basic scRNA-seq analysis Zoom Workshop 2020, Webinar, 8 Apr 2020 - Main lecturer, part of lab's initiative to teach bioinformatics to wetlab colleagues - Taught >40 participants on experimental design and computational analysis of single-cell RNA-seq
2	2020	RIKEN-KI joint doctoral course 2020, Karolinska Institutet, Stockholm, 5–11 Mar 2020 - Overseas lecturer, invited by Karolinska Institutet - Taught >25 PhD students / postdocs from RIKEN, Japan and KI, Sweden on single-cell analysis - Mentored a group of students for hands-on analysis
1	2019	Duke-NUS Advanced Single Cell RNA-seq Workshop, Singapore, 14–16 May 2019 - Main lecturer, co-organised workshop with postdoc supervisor and planned topics to be covered - Taught 10 participants on experimental design and computational analysis of single-cell RNA-seq - Led a team of four to facilitate hands-on analysis from pre-processing to biological interpretations

ACADEMIC PRESENTATIONS

#	Year	Description
9	2021	*Speaker* on "Computational Methods in Stem Cell Research", ASSCR Stem Cell Conversations, Virtual, 3 Nov 2021
8	2021	*Poster presentation* on "Evaluating gRNA Scaffold Design for scRNA-seq of CRISPRa HESC Differentiation", ISSCR Annual Meeting, Virtual, 2021
7	2020	*Q&A Panellist* on "Investigating functional microglial diversity in Alzheimer's disease by Single-cell RNA Sequencing", Illumina Webinar, 24 July 2020
6	2019	*Poster presentation* on "Computational Analysis of Timeseries Single-cell RNA-seq Datasets to Unravel Reprogramming Dynamics", ISSCR Annual Meeting, Los Angeles, 2019
5	2019	*Poster presentation* on "Prediction of Transcriptional Regulators during Reprogramming via Timeseries Single-cell RNA-seq Datasets", EMBO Workshop on Single Cell Biology, Tokyo, 2019
4	2019	*Oral presentation* on "Single-Cell Transcriptomics Unravel Differences in Human Reprogramming into Primed and Naïve Pluripotency", Cell Symposia Single Cells: Technology to Biology, Singapore, 2019
3	2018	*Poster presentation* on "An Improved Mogrify Algorithm for Lineage Conversion", EMBO Workshop Molecular mechanisms of developmental and regenerative biology, Singapore, 2018
2	2018	*Poster presentation* on "An Improved Mogrify Algorithm for Lineage Conversion", ISSCR Annual Meeting, Melbourne, 2018
1	2016	*Oral presentation* on "When are Many-Body Effects Significant?", 99th Canadian Chemistry Conference and Exhibition, Halifax, 2016

TECHNICAL EXPERTISE

Programming languages:	• R / Python / Perl / SQL / Fortran
Computer software:	• Matlab / Mathematica • Adobe Illustrator / Photoshop • LaTeX / Microsoft Office
Next-generation sequencing analysis:	• RNA-seq (including CAGE) • Single-cell RNA-seq (including antibody capture and CRISPR) • ATAC-seq • Ribo-seq • Integration of data across different platforms
Computational biology expertise:	• Machine learning applied to biology • Network biology • Computational stem cell biology • Drug-gene interactions • Algorithmic development