Jason Chung Lim Tong

Wolfson College, Linton Road, Oxford OX2 6UD, United Kingdom jason.tong@rdm.ox.ac.uk

EMPLOYMENT

Postdoctoral research associate

Radcliffe Department of Medicine, University of Oxford

2025-

EDUCATION

D.Phil in Medical Sciences

2020-

University of Oxford, Wolfson College

Thesis title: Cellular and molecular mechanisms underlying α -cell regulation of β -cell function in health and disease

Project details: Pancreatic cells modulate β-cell function in a paracrine manner through the release of glucagon. Failure of α -cell \rightarrow β -cell communication leads to impaired insulin secretion and hyperglycaemia. However, the detailed molecular architecture underlying regulation of β -cells by α -cells remains poorly characterised. In this work, glucagon-like peptide-1 receptor (GLP1R) was shown to be enriched as nanodomains on β -cell membranes in close contact with α -cells, in keeping with increased single-molecule transcript expression. β -cells located next to α -cells directly sense glucagon release at low glucose by pre-internalising GLP1R. Pre-internalised GLP1R primes β-cells to respond to high glucose with early rises in cytosolic Ca²⁺ signals, which are propagated across the islet. β -cells adjacent to α -cells are more secretory than β-cells next to other β-cells. Localised GLP1R signalling occurs in vitro and in vivo, is operative in the postprandial state, and GLP1R contacts decrease between β -cells and α -cells with advancing age and high fat diet. Thus, a regulated pathway through which glucagon modulates insulin release was detailed, and more broadly, a framework for how G protein-coupled receptors and promiscuous signalling may fine-tune intercellular communication in complex tissue.

Supervisors: Professor David Hodson, Professor Jeremy Tomlinson, Dr. Daniela Nasteska

M.Phil in Medicine 2017–2019

The University of Sydney

Thesis title: Biofunctionalisation enhances cell-based type 1 diabetes therapies via recreation of the native β -cell micro-environment

Project details: Contemporary implantation techniques for pancreatic beta-cells in the treatment of type 1 diabetes currently faces several challenges, notably those of survival and function. To address these issues, novel plasma physics techniques were used to biologically activate synthetic substrates with extracellular matrix proteins, with the aim of recreating a microenvironment for islet β -cells *in vitro* resembling their native niche. β -cells were functionally characterised in these conditions using techniques such as flow cytometry, insulin secretion assays and live-cell imaging,

including Fura-2 and GCaMP6 calcium imaging techniques. The findings of this project revealed a restoration in native β -cell function *in vitro* through interactions with extracellular matrix proteins, via integrin-mediated mechanisms.

Supervisors: Professor Peter Thorn, Dr. Melkam Kebede

B.Sc (Honours) in Physiology

2013-2016

The University of Sydney

Grade: First Class Honours

Majors: Physiology, Anatomy & Histology, Neuroscience

Thesis title: An Arp2/3 complex-mediated contractile actin coat on granules facilitates

insulin secretion in beta cells

Project details: Exocytosis has been studied within various secretory systems, and a myriad of biomechanical actors have been identified in this process. However, while insulin secretion is the principal function of pancreatic β-cells, technological limitations have until now impeded the study of the exocytic processes of insulin. To this end, advanced live-cell super-resolution microscopy techniques were used to characterise insulin granules, which are sub-diffraction limit and cannot be closely observed using conventional techniques. Multiphoton live-cell microscopy was also used to track the temporal and spatial localisation of cytoskeletal regulators. A contractile actin coat was found to localise to fused insulin granules, with evidence that it is essential to efficient secretion. Molecular and pharmacological techniques were used to further elucidate this process through manipulation of actin nucleating proteins, and it was discovered that this contractile actin coating is nucleated by the recruitment of an Arp2/3 complex on granules. The findings highlight new targets for the study of the insulin secretory deficit, characteristic of diabetes.

Supervisor: Professor Peter Thorn

PUBLICATIONS

Journal articles:

Germanos M., Yau B., Taper M., Yeoman C., Wilson A., An Y., Cattlin-Ortolá J., Masler D.,

<u>Tong J.</u>, Naghiloo S., Needham EJ., van der Kraan AG., Sun K., Loudovaris T., Diaz-Vegas A., Larance M., Thomas H., von Blume H., Thorn P., Ailion M., Asensio C., Kebede MA. (2025). Cab45G trafficking through the insulin secretory pathway is altered in human type 2 diabetes. *iScience*, 28, 2, 111719. doi: 10.1016/j.isci.2024.111719

Cuozzo F., Viloria K., Shilleh AH., Nasteska D., Frazer-Morris C., <u>Tong J.</u>, Jiao Z., Boufersaoui A., Marzullo B., Rossoff DB., Smith HR., Bonner C., Kerr-Conte J., Pattou F., Nano R., Piemonti L., Johnson PRV., Spiers R., Roberts J., Lavery GG., Clark A., Ceresa CDL., Ray DW., Hodson L., Davies AP., Rutter GA., Oshima M., Scharfmann R., Merrins MJ., Akerman I., Tennant DA., Ludwig C., Hodson DJ. (2024). LDHB contributes to the regulation of lactate levels and basal insulin secretion in human pancreatic β cells. *Cell Rep.*, 43, 4, 114047. doi: 10.1016/j.celrep.2024.114047

- Jevon D., Deng K., Hallahan N., Kumar K., <u>Tong J</u>., Gan WJ., Tran C., Bilek M., Thorn P. (2022). Local activation of focal adhesion kinase orchestrates the positioning of presynaptic scaffold proteins and Ca²⁺ signalling to control glucose-dependent insulin secretion. *eLife*, 11, e76262. doi: <u>10.7554/eLife.76262</u>
- Koneshamoorthy A., Seniveratne-Epa D., Calder G., Sawyer M., Kay TWH., Farrell S., Loudovaris T., Mariana L., McCarthy D., Lyu R., Liu X., Thorn P., **Tong J**., Chin LK., Zacharin M., Trainer A., Taylor S., MacIsaac RJ., Sachithanandan N., Thomas HE., Krishnamurthy B. (2022). Case Report: Hypoglycemia Due to a Novel Activating Glucokinase Variant in an Adult a Molecular Approach. *Front. Endocrinol.*, 13, 842937. doi: 10.3389/fendo.2022.842937
- Tran C., Hallahan N., Kosobrodova E., <u>Tong J</u>., Thorn P., Bilek M. (2021). Plasma Surface Engineering to Biofunctionalise Polymers for β-Cell Adhesion. *Coatings.*, 11, 9, 1085. doi: 10.3390/coatings11091085
- Ma W., Chang J., <u>Tong J</u>., Ho U., Yau B., Kebede MA., Thorn P. (2020). Arp2/3 nucleates F-actin coating of fusing insulin granules in pancreatic β cells to control insulin secretion. *J. Cell Sci*, 133, 6, jcs236794. doi: 10.1242/jcs.236794

Journal articles in press:

- <u>Tong JCL.</u>, Frazer-Morris C., Shilleh AH., Viloria K., de Bray A., Nair AM., Johnson PRV., Spiers R., Kobitta A., Olaniru OE., Persaud S., Hauffe R., Kleinridders A., Schultz C., Bruce Verchere, C., Cui C., Campbell JE., Cyranka M., Epanchintsev A., Ämmälä C., Broichhagen J., Hodson DJ. Localized GLP-1 receptor pre-internalization directs pancreatic alpha cell to beta cell communication. (In Press). *Cell Metab*.
- de Bray A., <u>Tong JCL</u>., Huhn C., Roßmann K., Shilleh AH., Jiang W., Roberts A., Viloria K., Nasteska D., Pearce A., Miyazaki S., Tomlinson J., Owen D., Nieves D., Ast J., Cyranka M., Epanchintsev A., Ämmälä C., Reimann F., Ladds G., Adriaenssens A., Trapp S., Jones B., Broichhagen J., Hodson DJ. Fluorescent GLP1R/GIPR dual agonist probes reveal cell targets in the pancreas and brain. (In Press). *Nat. Metab*. doi: <u>10.21203/rs.3.rs-4835197/v1</u>
- Capozzi ME., Bouslov D., Sargsyan A., Chan M., Gray SM., Viloria K., Bareja A., Lewandowski SL., <u>Tong JCL</u>., Hasib A., Cuozzo F., Ross EC., Foster MW., Weinstein LS., Hussain MA., Merrins MJ., Willard FS., Sloop KW., Huising MO., Hodson DJ., D'Alessio DA., Campbell JE. β-cell Gαs signaling is critical for physiological and pharmacological enhancement of insulin secretion. (In Revision).

Conference papers:

de Bray A., <u>Tong J.</u>, Huhn C., Roßmann K., Shilleh AH., Jiang W., Roberts A., Viloria K., Nasteska D., Pearce A., Miyazaki S., Tomlinson J., Owen D., Nieves D., Ast J., Cyranka M., Epanchintsev A., Ämmälä C., Reimann F., Ladds G., Adriaenssens A., Trapp S., Jones B., Broichhagen J., Hodson DJ. (2025). daLUXendins reveal dual GLP1R/GIPR agonist targets in the pancreas and brain. *Endocrine Abstracts*, 109, P98. Society for Endocrinology BES 2025, Harrogate United Kingdom, Mar 10-12, 2025. doi: <u>10.1530/endoabs.109.P98</u>

Ma W., <u>Tong J.</u>, Chang J., Thorn P. (2018). Endocytosis occurs right after fusion pore open and plays crucial roles in granule collapse. *Diabetologia*, 61, S235-S235. 54th Annual Meeting of the European-Association-for-the-Study-of-Diabetes (EASD), Berlin Germany, Oct 01-05, 2018. NEW YORK: SPRINGER.

CONFERENCE PRESENTATIONS

2025

Radcliffe Department of Medicine Day

<u>Tong J</u>*, Frazer-Morris C, Shilleh AH, Viloria K, Nair AM, Broichhagen J, Hodson DJ. Localised GLP-1 receptor pre-internalization directs pancreatic alpha cell to beta cell communication. Poster presentation delivered at: Radcliffe Department of Medicine Day; 2025, Mar 17; Oxford, United Kingdom.

Winner of the Poster Presentation Prize

2024

European Incretin Study Group Meeting

<u>Tong J</u>*, Frazer-Morris C, Nair AM, Nasteska D, Viloria K, Broichhagen J, Hodson DJ. Locally pre-internalized glucagon-like peptide-1 receptor (GLP1R) mediates α cell regulation of β cell function. Oral presentation delivered at: European Incretin Study Group Meeting; 2023, Apr 4-6; Cambridge, United Kingdom.

2019

Australasian Diabetes Congress

<u>Tong J</u>*, Gan WJ, Cottle, L, Thorn P. Re-introduction of native extracellular matrix proteins recapitulates the native oscillatory Ca²⁺ phenotype in primary mouse beta-cells. Poster presentation delivered at: Australasian Diabetes Congress 2019, Australian Diabetes Society; 2019 Aug 21-23; Sydney, Australia.

Finalist and 1st prize winner of Basic Science Poster Award

Germanos M*, Yau B, <u>Tong J</u>, Havula E. A Cab for Insulin: The Role of Cab45 in Pancreatic β-cells. Oral presentation delivered at: Australasian Diabetes Congress 2019, Australian Diabetes Society; 2019 Aug 21-23; Sydney, Australia.

2018

Australian Islet Study Group Meeting

Tong J*, Kosobrodova E, Bilek M, Thorn P. Polymer biofunctionalisation to enhance a microenvironment for β-cell encapsulation. Oral presentation delivered at: Australian Islet Study Group Meeting; 2018 Nov 30; Canberra, Australia.

Winner of the JDRF Travel Award (Type 1 Diabetes)

Annual Meeting of the European Association for the Study of Diabetes

Ma W*, <u>Tong J</u>, Chang J, Thorn P. Endocytosis occurs right after fusion pore opening and plays crucial roles in granule collapse. Poster presentation delivered at: 54th Annual Meeting of the European Association for the Study of Diabetes, European Association for the Study of Diabetes; 2018 Oct 1-5; Berlin, Germany.

2017

Annual Scientific Meeting of the Australian Diabetes Society

<u>Tong J</u>*, Gan WJ, Kosobrodova E, Weiss AS, Wise SG, Bilek M, Thorn P. Bioengineering a biofunctionalised synthetic capsule for in vivo implantation of MIN6 beta-cells. Poster presentation delivered at Annual Scientific Meeting of the Australian Diabetes Society; 2017 30 Aug-1 Sep; Perth, Australia.

Australian Islet Study Group Meeting

Tong J*, Gan WJ, Kosobrodova E, Yeo GC, Weiss AS, Wise SG, Bilek M, Thorn P. A biocompatibility screen of polymers for synthetic encapsulation of beta-cells in type 1 diabetes. Poster presentation delivered at Australian Islet Study Group Meeting; 2017 Sep 1-2; Perth, Australia.

Winner of the Best Poster Award

2016

Australian Islet Study Group Meeting

<u>Tong J</u>*, Ma W, Thorn P. An Arp2/3 complex-mediated contractile actin coat on insulin granules facilitates secretion in beta-cells. Oral presentation delivered at: Australian Islet Study Group Meeting; 2016 Nov 18; Melbourne, Australia.

AWARDS AND PRIZES

2025

• Poster Presentation Prize, Radcliffe Department of Medicine Day 2025

2020

- The Eleanor Sophia Wood Postgraduate Research Travelling Scholarship
- The Boulton Postgraduate Scholarship

2019

- Basic Science Poster Award, Australasian Diabetes Congress
- Shortlisted as "Poster Discussion session" finalist, Australasian Diabetes Congress
- Invited to present one of three <u>1 hour research seminars</u> for 2019 (compared to standard 15 minute student talks), due to scoring within the top 3 best research student presentations at the Charles Perkins Centre in 2018

2018

JDRF Young Investigator Travel Award, Australian Islet Study Group Meeting

2017

- University of Sydney Postgraduate Research Support Scheme travel grant
- Australian Islet Study Group Meeting Poster Award
- Bosch Institute Micrograph of the Month, March 2017

2016

- The University of Sydney Honour Roll 2016, Honours Class I
- Honours Summer Scholarship, Physiology 2016
- Bosch Institute Micrograph of the Year finalist

2015

 Invited to participate in the Discipline of Anatomy's Special Studies Program unit for human cranial and cervical dissection

2014

• Top of the cohort, neuroscience research paper project, used as an exemplar in subsequent years.

RESEARCH SKILLS AND TECHNIQUES

Key strength and interest in *imaging and microscopy*, particularly novel and emerging techniques including super-resolution microscopy and live-cell imaging.

- Extensive microscopy experience including super-resolution techniques (dSTORM, TIRF, STED), multiple modalities of live-cell imaging (multiphoton, calcium [Fura-2, Fluo-8, GCaMP6], spinning disc, FRAP, timelapse), confocal, widefield, imagestitching, bioluminescence
- Immunofluorescence,
 Immunohistochemistry techniques
 (suspension and adherent samples),
 tissue preparation and sectioning
 (formalin-fixed paraffin-embedded,
 cryosectioning), fluorescent marker
 and probe validation
- Molecular biology techniques (quantitative RT-PCR, PCR, DNA and RNA extraction and purification, gel electrophoresis, Western blotting, bacterial culture, plasmid assembly,

- cloning, gene silencing, CRISPR genome-editing), spatial transcriptomics (smFISH)
- Cell culture (primary cells and cell lines, co-culture, 3D culture, extracellular matrix, transfection, viral transduction)
- Viral culture, production, and amplification (lentivirus, adenovirus)
- Immunoassays, ELISA, BCA, FRET-HTRF
- Mouse handling and husbandry (primary islet isolations, genetics and genotyping, post-mortem dissection, primary tissue harvest, perfused pancreas)
- Flow cytometry (FACS)
- Human dissection (cranial and cervical)

TEACHING AND SUPERVISION EXPERIENCE

University of Oxford

DPhil student 2023, 2024-

Radcliffe Department of Medicine

Principal supervision and co-supervision of Final Honours Scheme (FHS) students, leading and guiding an undergraduate research project, including teaching techniques such as imaging, immunohistochemistry, data analysis, and reviewing dissertation drafts and practice viva voce examinations. Experience of teaching advanced microscopy techniques and imaging analysis (e.g. iterative deconvolution) to colleagues.

The University of Sydney

2017-2020

Casual academic

Sydney Medical School;

Faculty of Science

- MEDS1X01 Human Biology
- OLET1504 Health Challenges: Diabetes
- BIOL1996 Life and Evolution (Talented Student Program)
- NEUR3X06 Neural Information **Processing**
- NUTM3X01 Nutrition and Metabolism
- PHSI2008 Integrated Physiology
- PHSI3X09 Frontiers in Cellular Physiology
- PHSI3X11 Frontiers in Whole Body Physiology

Extensive teaching experience, with numerous responsibilities, including teaching tutorials, laboratory practicals, leading problem-based learning sessions, marking and student consultations. Invited "Diabetes Expert" for 3rd year physiology research workshops and served as one of four academics on the examining panel for 3rd year Frontiers in Cellular Physiology final assessments.

PUBLIC ENGAGEMENT

The Court of St James's

2025

Nominated by The High Commission of Australia to the United Kingdom to serve as a representative at a Garden Party hosted at Buckingham Palace by His Majesty The King, 'in recognition of excellent contributions made' in my field.

The High Commission of Australia to the United Kingdom

2025

Invited to meet the High Commissioner of Australia to the United Kingdom and Deputy High Commissioner at Australia House in London, to discuss my research and detail the work being performed in science by high-performing Australians in the United Kingdom as part of celebrations for Australia Day 2025.

IF Oxford: The Oxford Science and Ideas Festival

2024

Participated in the organisation and running of a stall at the IF Oxford Science and Ideas Festival on behalf of the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM), to engage with lay audience members about diabetes and islet research.

Diabetes UK 2024

Delivered a seminar to the Diabetes UK – Winchester & Eastleigh Patient Support Group about my research in diabetes, especially adapted for an audience of people living with diabetes.

Diabetes UK 2023

Participated in the organisation and running of a site visit by Diabetes UK to the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM), including donors and people living with diabetes.

ACADEMIC SERVICE

Wolfson College, Oxford

2021-2023

Garden Building Project Steering Committee Member

One of two students elected to participate on the Steering Committee formed to investigate the feasibility and plan the construction of a new accommodation block for the college, in consultation with college leadership and project architects. These efforts proved fruitful, and the 'Garden Building' has received planning approval and is currently <u>under construction</u> for opening in Autumn 2027.

The University of Sydney

2013

Student Liaison Officer, Faculty of Science

Elected to the faculty board as a student representative, communicating student feedback for first-year biology units of study.

LEADERSHIP EXPERIENCE	
Oxford University Australia & New Zealand Society	2021-
President	
Sydney University Disney Appreciation Society	
President	2014–2016
Vice–president	2014
General executive officer	2013
Sydney University Wind Orchestra	
Publicity officer	2015
Sydney University Chocolate Society	
General executive officer	2013–2015
	_
Professional memberships	
Australian Diabetes Society	2017–

LANGUAGES

- English (native)
- Cantonese (conversational)

RESIDENCY STATUS

- Australia (citizenship)
- Hong Kong SAR (Right of Abode)
- United Kingdom (Tier 4 visa)

ACADEMIC REFEREES

Professor David Hodson

Robert Turner
Professor of Diabetic
Medicine, Oxford
Centre for Diabetes,
Endocrinology and
Metabolism (OCDEM),
Radcliffe Department
of Medicine;
Senior Research
Fellow, Green
Templeton College
University of Oxford
+61 2 8627 4629
david.hodson@ocdem.
ox.ac.uk

Professor Peter Thorn

Chair of Cellular and Molecular Physiology, School of Medical Sciences; Head, Discipline of Physiology The University of Sydney +61 2 8627 4629 peter.thorn@sydney.ed u.au

A. Professor Melkam Kebede

Associate Professor, Head, Islet Biology and Metabolism Lab The University of Sydney +61 2 8627 0164 melkam.kebede@sydne y.edu.au

Dr. Daniela Nasteska

Principal Investigator,
Oxford Centre for
Diabetes,
Endocrinology and
Metabolism (OCDEM),
Radcliffe Department
of Medicine;
Research Fellow,
Wolfson College
University of Oxford
daniela.nasteska@ocde
m.ox.ac.uk