中研學術大會
AS Conference

Immunometabolism mini-symposium

Immune and Metabolic Control of Human Diseases

July 2, 2025, 13:30-17:00

中央研究院 人文社會科學館 第二會議室

Conference Room 2, Humanities and Social Sciences Building

會 議 議 程 / Symposium Schedule

徐 志 文 副研究員 Dr. Jr-Wen Shui	IBMS	**13:30-14:00** **Lysosome Dysfunction in Gut-to-Liver Metabolic Disorders**
翁 瑞 霞 助研究員 Dr. Jui-Hsia Weng	IBC	**14:00-14:30** **Harnessing Intercellular Communication to Balance Inflammation and Control Food Intake**
賴 時 磊 助研究員 Dr. Shih-Lei Lai	IBMS	**14:30-15:00** **Secrets of Heart Regeneration Revealed by Comparative Analyses in regenerative vs. non-regenerative models**
15:00-15:20 Coffee Break		
李 宜 靜 副研究員 Dr. Yi-Ching Lee	ICOB	**15:20-15:50** **Regulation of Connective Tissue Homeostasis**
王 維 樂 助研究員 Dr. Wei-Le Wang	IMB	**15:50-16:20** **Unveiling Novel Mechanisms of Immune Regulation in Gut Inflammation**
王 志 豪 助研究員 (新聘) Dr. Chih-Hao Wang	GRC	**16:20-16:50** **Thermogenic Adipocytes in Glucose Homeostasis and Inflammation Resolution**

Moderator: 陳 緯 助研究員 (GRC)

Host Institute: Genomics Research Center (GRC)

Organizers: 李志浩 中心主任/特聘研究員 (GRC)

陳 緯 助研究員 (GRC)

Participating Institutes:

Genomics Research Center (GRC)
Institute of Biomedical Sciences (IBMS)
Institute of Biological Chemistry (IBC)
Institute of Cellular and Organismic Biology (ICOB)
Institute of Molecular Biology (IMB)

Immunometabolism mini-symposium

Immune and Metabolic Control of Human Diseases

It has now been recognized that the interplay between immune and metabolic signaling plays key roles in many physiological and pathological processes. Targeting “immunometabolism” thus represents a new approach for therapeutic developments to treat human diseases. The Genomics Research Center is pleased to invite you to join the Immunometabolism mini-symposium, which is part of the 2025 Academia Sinica Conference series. In collaboration with the Institutes of Biomedical Sciences, Biological Chemistry, Cellular and Organismic Biology and Molecular Biology, the symposium brings together six rising scientists who will present their recent research findings focusing on immune and metabolic control of human diseases. Three main topics will be covered, which include: (1) metabolite transporters (e.g., NPC1 and SLC2A10) in metabolic homeostasis; (2) immune cells, such as macrophages and eosinophils, in heart regeneration and gut immunity; and (3) adipokines and hepatokines in tissue inflammation and metabolic diseases. Through these presentations, the audience will gain deeper insights into how the immuno-metabolic crosstalk is involved not only in homeostatic maintenance but also in mediating metabolic and inflammatory diseases.

Co-organizers: Chih-Hao Lee, PhD and Wei Chen, PhD
Genomics Research Center, Academia Sinica

Immunometabolism mini-symposium Moderator

Wei Chen, Ph.D.　陳　緯 博士

Assistant Research Fellow

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Position

- **2023-present *Assistant Research Fellow***, Genomics Research Center, Academia Sinica, Taiwan

Education

- **2020-2023 *Postdoctoral Researcher***, Center for Nanomedicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
- **2014-2019 *Ph.D.*** Department of Chemistry and Biochemistry, University of California Los Angeles (UCLA), Los Angeles, CA, USA
- **2009-2011 *M.S.*** Department of Chemistry, National Taiwan University, Taiwan
- **2005-2009 *B.S.*** Department of Chemistry, National Taiwan University, Taiwan

Expertise

- Nanomedicine, Biomedical engineering, Drug delivery syetem, Materials chemistry, RNA nanotechnology

Selected Publications

1. **Chen W**, Schilperoort M, Cao Y, Shi J*, Tabas I*, Tao W* "*Macrophage-Targeted Nanomedicine for the Diagnosis and Treatment of Atherosclerosis.*" ***Nature Reviews Cardiology*** 2022, *19*, 228–249.
2. He Z(#), **Chen W(*)(#)**, Hu K(#), Luo Y, Zeng W, He X, Li T, Ouyang J, Li Y, Xie L, Zhang Y, Xu Q, Yang S, Guo M, Zou W, Li Y, Huang L, Chen L, Zhang X, Saiding Q, Wang R, Zhang MR, Kong N, Xie T, Song X,* Tao W*. "*Resolvin D1 delivery to lesional macrophages using antioxidative black phosphorus nanosheets for atherosclerosis treatment.*" ***Nature Nanotechnology*** 2024, *19*, 1386-1398 (*: Corresponding author) (#: Co-first author, equal contribution)
3. Chen S(#), Li Y(#), Zhou Z, Saiding Q, Zhang Y, An S, Khan MM, Ji X, Qiao R, Tao W*, Kong N*, **Chen W(*)**, Xie T*. "*Macrophage hitchhiking nanomedicine for enhanced β-elemene delivery and tumor therapy.*" ***Science Advances*** 2025, *11*, adw7191. (*: Corresponding author)
4. Zhou Z, **Chen W(*)**, Cao Y, Abdi R, Tao W*. "*Nanomedicine-based Strategies for the Treatment of Vein Graft Disease.*" ***Nature Reviews Cardiology*** 2025, *22*, 255–272. (*: Corresponding author)
5. Li Y(#), **Chen W(#)**, Kang Y, Zhen X, Zhou Z, Liu C, Chen S, Huang X, Liu H, Koo S, Kong N, Ji X, Xie T, Tao W*. "*Nanosensitizer-mediated augmentation of sonodynamic therapy efficacy and antitumor immunity.*" ***Nature Communications*** 2023, *14*, 6973. (#: Co-first author, equal contribution)
6. He Z(#), Luo Y(#), Duan Z(#), Su B(#), Zeng W, Guo Y, Li Y, He X, Shi H, Zhou Z, Jiang C, Qin D, Zhang J, Kang Y(*), **Chen W(*)**, Song X* "*IRF5 siRNA Nano-Immunotherapy: Restoring Macrophage Efferocytosis in Atherosclerosis.*" ***Circulation*** (under minor revision) (*: Corresponding author)
7. **Chen W**, et al. "*In situ Engineering of Tumor-Associated Macrophages via a Nanodrug-Delivering-Drug (β-Elemene@Stanene) Strategy for Enhanced Cancer Chemo-Immunotherapy.*" ***Angew. Chem. Int. Ed.*** 2023, *62*, e202308413.
8. Shi Y(#), Zhen X(#), Zhang Y, Li Y, Koo S, Saiding Q, Kong N, Liu G, **Chen W(*)**, Tao W*. "*Chemically Modified Platforms for Better RNA Therapeutics.*" ***Chemical Reviews*** 2024, *124*, 929–1033.

Immunometabolism mini-symposium Speaker

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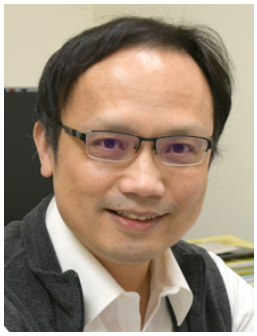

Position

- **2013-2014** ***Instructor*****,** La Jolla Institute, San Diego, USA
- **2014-2021** ***Assistant Research Fellow***, Institute of Biomedical Sciences, Academia Sinica
- **2021-present** ***Associate Research Fellow***, Institute of Biomedical Sciences, Academia Sinica

Education

- **2006-2013** **Postdoctoral Fellow,** La Jolla Institute, San Diego, USA
- **2004-2006** **Postdoctoral Fellow,** Baylor College of Medicine, Houston, USA
- **1998-2004** **Ph.D.** Department of Immunology, Baylor College of Medicine, Houston, USA
- **1993-1995** **M.S.** Institute of Immunology, National Taiwan University

Expertise

- Mucosal immunology, Intestinal inflammation, Gut epithelial barrier, Host defense, Paneth cell homeostasis, Microbiota dysbiosis, Metabolic disorder.

Selected Publications

1. HY Chiang, HH Lu, JN Sudhakar, YW Chen, NS Shih, YT Weng, and (**JW Shui**). "IL-22 initiates an IL-18-dependent epithelial response circuit to enforce intestinal host defense." ***Nature Communications*** 13:874 (2022) (https://doi.org/10.1038/s41467-022-28478-3)

2. JN Sudhakar, HH Lu, HY Chiang, CS Suen, MJ Hwang, SY Wu, CN Shen, YM Chang, FA Li, FT Liu, and (**JW Shui**). "Luminal Galectin-9-Lamp2 interaction promotes lysosome stabilization and facilitates autophagy to prevent pathogenesis in the pancreas and intestine." ***Nature Communications*** 11:4286 (2020) (https://doi.org/10.1038/s41467-020-18102-7)

3. (**JW Shui**), A Larange, G Kim, JL Vela, S Zahner, H Cheroutre, and M Kronenberg. "HVEM signalling at mucosal barriers provides host defence against pathogenic bacteria." ***Nature*** 488:222 (2012) (https://doi.org/10.1038/nature11242)

4. (**JW Shui**), JS Boomer, J Han, J Xu, GA Dement, G Zhou, and TH Tan. "Hematopoietic progenitor kinase 1 negatively regulates T cell receptor signaling and T cell-mediated immune responses." ***Nature Immunology*** 8:84 (2006) (https://doi.org/10.1038/ni1416)

Lysosome Dysfunction in Gut-to-Liver Metabolic Disorders

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Abstract

Lysosome dysfunction, accompanied with autophagy blockade, is a key and pathogenic factor leading to lysosomal storage disease (LSD), which includes many inborn errors of metabolism like Niemann-Pick type C1 (NPC), Fabry disease, and Pompe disease. NPC1 is a lipid-trafficking or storage disorder characterized by adult-onset progressive neurodegeneration, which is, however, typically preceded by early-onset systemic metabolic symptoms including neonatal jaundice or hepatosplenomegaly. NPC1, like Lamp2, is heavily N-glycosylated lysosomal membrane protein important for autophagy, intriguingly, how intestinal NPC1 regulates gut barrier or metabolic disorders is largely unexplored. Previously we reported that Lamp2-Galectin-9 axis regulates lysosome function in gut Paneth cells and pancreatic acinar cells to prevent organ pathogenesis (1). Here we reported a N-glycan-stabilized Lamp2-Galectin-9-NPC1 trimeric complex in Paneth cells as a novel regulator of lysosomal cholesterol trafficking and an intestinal origin of microbiota-associated hepatosteatosis. The NPC1 complex-mediated cholesterol egress acts upstream of lysosomal assembly of the Rab7-RILP motor to prevent autophagy blockade and thus maintain Paneth cells. Paneth-specific disruption of the NPC1 complex in mice causes a reduction of *Lactobacillus* leading to lipid accumulaton in ileum crypts, adipose and hepatic tissues. Gavage of *Lactobacillus*-mediated tryptophan metabolite, kynurenic acid (KA), in mutant or high-fat-diet mice restores damaged Paneth cells and barrier fucosylation, as well as reduces bacterial translocation and ameliorates steatosis. KA, as an AhR ligand, effectively promotes Paneth cells in organoid culture and mice, as well as rescues cholesterol-laden CMT93 cells harbouring a human $Npc1^{I1060T}$ hot-spot mutation or HepG2 cells treated with the NPC1 blocker U18666A. Therefore, we reveal that gut Paneth cells are a gatekeeper to maintain the gut-to-liver metabolism and that Paneth-directed *Lactobacillus* utilizes KA to feedback and maintain host $NPC1^{+}$ or AhR^{+} Paneth cells. NPC1, being a risk factor for Crohn's and liver disease (2), is crucial to protect cholesterol-sensitive Paneth cells to prevent gut-to-liver metabolic disorders.

References

(1) JN Sudhakar, HH Lu, HY Chiang, CS Suen, MJ Hwang, SY Wu, CN Shen, YM Chang, FA Li, FT Liu, and **JW Shui**. Luminal Galectin-9-Lamp2 interaction promotes lysosome stabilization and facilitates autophagy to prevent pathogenesis in the pancreas and intestine. ***Nature Communications*** 11:4286 (2020) (https://doi.org/10.1038/s41467-020-18102-7)

(2) A Cavounidis, HH Uhlig. Crohn's Disease in Niemann–Pick Disease Type C1: Caught in the Cross-Fire of Host-Microbial Interactions. ***Digestive Diseases and Sciences*** 63:811 (2018) (https://doi.org/10.1007/s10620-018-4953-3)

Immunometabolism mini-symposium Speaker

Jui-Hsia Weng, Ph.D.　翁瑞霞 博士

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Position

- **2021-present** ***Assistant Research Fellow***, Academia Sinica, Taiwan

Education

- **2014-2021** ***Postdoctoral Fellow***, Harvard Medical School, USA
- **2013-2014** ***Postdoctoral Fellow***, Academia Sinica, Taiwan
- **2006-2013** ***Ph.D.*** Biochemistry and Molecular Biology, Yang-Ming University, Taiwan
- **2006-2013** ***Ph.D.*** Institute of Biochemistry and Molecular Biology, Yang-Ming University, Taiwan

Expertise

- Chemical Biology, Inter-Organ Communication, Inflammation, Drug Discovery

Selected Publications

1. Weng JH*, Koch PD, Luan HH, Tu HC, Shimada K, Ngan I, Ventura R, Jiang R, Mitchison TJ*. (2021) **"**Colchicine acts selectively in the liver to induce hepatokines that inhibit myeloid cell activation." ***Nature Metabolism*** 3: 513-522.

2. Shi J, Weng JH, Mitchison TJ. (2021) "Immunomodulatory drug discovery from herbal medicines: Insights from organ-specific activity and xenobiotic defenses." *eLife* 10: e73673**.**

3. Tang HW, Weng JH, Lee WX, Hu Y, Gu L, Cho S, Lee G, Binari R, Li C, Cheng ME, Kim AR, Xu J, Shen Z, Xu C, Asara JM, Blenis J, Perrimon N. (2021) "mTORC1-chaperonin CCT signaling regulates m^6A RNA methylation to suppress autophagy." ***Proceedings of the National Academy of Sciences of the United States of America*** 118: e2021945118.

4. Mondal S, Tseng CJ, Tan JY, Lin DY, Lin HY, Weng JH, Lin CH*, and Mong KK*. (2023, Jan) "Tunable strategy for the asymmetric synthesis of sulfoglycolipids from mycobacterium tuberculosis to elucidate the structure and immunomodulatory property relationships." ***Angewandte Chemie International Edition*** 62: e202212514.

5. Xu C, Xu J, Tang HW, Ericsson M, Weng JH, DiRusso J, Hu Y, Ma W, Asara J, Perrimon N. (2023) "A phosphate-sensing organelle regulates phosphate and tissue homeostasis." ***Nature*** 617, 798-806.

Harnessing Intercellular Communication to Balance Inflammation and Control Food Intake

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Abstract

Hyperactivation of immune cells and imbalance of energy consumption pose serious threats to health, yet effective management strategies remain limited. Growth Differentiation Factor 15 (GDF15), a member of the transforming growth factor-β (TGF-β) superfamily, has been reported to regulate immunity, limit appetite, and alter behavior. Circulating levels of GDF15 are controlled by various physiological and pathological conditions, highlighting its potential role in helping the body adapt to diverse challenges. Despite these insights, the full spectrum of GDF15's functions is not yet completely understood. In this talk, I will discuss the systemic regulatory mechanisms governing GDF15 expression and examine its wide-ranging physiological effects[1]. By deepening our understanding of GDF15, we may uncover novel strategies for addressing metabolic and immune-related disorders.

References

1 Weng, J. H. *et al.* Colchicine acts selectively in the liver to induce hepatokines that inhibit myeloid cell activation. *Nat Metab* **3**, 513-522 (2021). https://doi.org:10.1038/s42255-021-00366-y

Immunometabolism mini-symposium Speaker

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Position

- **2018-present** ***Assistant Research Fellow***, Institute of Biomedical Sciences, Academia Sinica, Taiwan

Education

- **2014-2017** ***Postdoctoral Researcher***, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Hessen, Germany.
- **2009-2014** ***Postdoctoral Researcher***, Institute of Zoology, National Taiwan University, Taiwan
- **2007-2008** ***Visiting Scholar***, Pharmacology Department, University of Washington, Seattle, WA.
- **2001-2008** ***Ph.D.*** Institute of Zoology, National Taiwan University, Taiwan
- **1997-2001** ***B.S.*** Department of Biology, Fu-Jen Catholic University, Taiwan

Expertise

- Developmental genetics, cardiovascular development and regeneration, cardioimmunology, and zebrafish disease model.

Selected Publications

1. Wei KH, Lin IT, Chowdhury K, Lim KL, Liu KT, Ko TM, Chang YM, Yang KC, Lai SL*. "Comparative single-cell profiling reveals distinct cardiac resident macrophages essential for zebrafish heart regeneration." ***eLife***. 2023;12:e84679.
2. Chowdhury K, Lin S, Lai SL*. "Comparative Study in Zebrafish and Medaka Unravels the Mechanisms of Tissue Regeneration." ***Frontiers in Ecology and Evolution***. 2022. 10, 783818.
3. Lai SL*, Marín-Juez R, Stainier DYR*. "Immune Responses in Cardiac Repair and Regeneration-A comparative point of view." ***Cellular and Molecular Life Sciences***. 2019;76(7):1365-1380 (Co-corresponding)
4. Lai SL*, Marín-Juez R, Moura P, Kuenne C, Lai JKH, Taddese Tsedeke A, Guenther S, Looso M, Stainier DYR*. "Reciprocal analyses in zebrafish and medaka reveal that harnessing the immune response promotes cardiac regeneration." ***eLife***. 2017;6. pii: e25605. (Co-corresponding)

Biosketch

Dr. Ben Shih-Lei Lai is a developmental biologist by training who studied gastrulation cell migration and LR asymmetry during his graduate years in Dr. Jeff Shyh-Jye Lee's laboratory and obtained a Ph.D. from the National Taiwan University. Later, Ben did his postdoctoral research in Dr. Didier Stainier's laboratory at the Max Planck Institute for Heart and Lung Research, where he established a unique platform to investigate the mechanism of heart regeneration by reciprocal analyses in regenerative zebrafish and non-regenerative medaka. His research led to the discovery that differential immune responses critically shape regenerative outcomes, and the potential of promoting heart regeneration by manipulating immunity. In 2018, Ben joined the Institute of Biomedical Sciences in Academia Sinica as a junior research fellow. Ben's research group focuses on how immune response is involved in cardiac repair and regeneration and the feasibility of translating the knowledge into therapeutics. Ben has received several young scholar awards/scholarships and serves as the Secretary General of the Taiwanese Society of Developmental Biology, Board Director and committee member of several national and international societies and organizations, and reviewer for international funding agencies and prestigious journals.

Secrets of heart regeneration revealed by comparative analyses in regenerative vs. non-regenerative models

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Abstract

Heart failure is a major cause of morbidity and mortality, in part due to the inability of the human heart to replenish lost cardiomyocytes (CM) following myocardial infarction. Zebrafish display a distinct ability to regenerate their heart following injury. However, this ability is not shared by another teleost, the medaka. My laboratory compares animals capable or incapable of heart regeneration to understand the cellular and molecular bases of this process. Bulk RNAseq profiling revealed major differences between these animals during cardiac repair in angiogenesis and immune cell functions. Functionally, delay macrophage infiltration by clodrosome pre-depletion disrupted revascularization, cardiomyocyte (CM) proliferation, and scar resolution in zebrafish, while stimulating immune response by dsRNA analog poly I:C promoted de novo regeneration via macrophage function in medaka. Recent comparative scRNAseq analyses of inflammatory cells further identified unique resident macrophage subsets function in ROS-mediated CM survival and ECM remodeling during cardiomyocyte replenishment in zebrafish, while poly I:C enhanced macrophage function in debris clearance and inflammatory resolution to accelerate cardiac repair and overall survival after cardiac injury in medaka. Altogether, our research gains insights into the complex role of the immune response during cardiac repair and establishes a platform to identify and test novel regulators of heart regeneration.

References

1. Chowdhury K, Huang CL, Lin IT, Hung YJ, Lim KL, Liu HW, Wei KH, Yang KC, Chang YM and **Lai SL***. Immune Modulation Promotes Heart Regeneration via Macrophage-Derived Granulin in Medaka. (under review)
2. Wei KH, Lin IT, Chowdhury K, Lim KL, Liu KT, Ko TM, Chang YM, Yang KC, **Lai SL***. Comparative single-cell profiling reveals distinct cardiac resident macrophages essential for zebrafish heart regeneration. *eLife*. 2023;12:e84679.
3. **Lai SL***, Marín-Juez R, Stainier DYR*. Immune Responses in Cardiac Repair and Regeneration-A comparative point of view. *Cell Mol Life Sci*. 2019;76(7):1365-1380 (Co-corresponding)
4. **Lai SL***, Marín-Juez R, Moura P, Kuenne C, Lai JKH, Taddese Tsedeke A, Guenther S, Looso M, Stainier DYR*. Reciprocal analyses in zebrafish and medaka reveal that harnessing the immune response promotes cardiac regeneration. *eLife*. 2017;6. pii: e25605. (Co-corresponding)

Immunometabolism mini-symposium Speaker

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Position

- **2021-preesent *Associate Research Fellow*,** Institute of Cellular and Organismic Biology, Academia Sinica, Taipei, Taiwan
- **2013-2021 *Assistant Research Fellow***, Institute of Cellular and Organismic Biology, Academia Sinica, Taiwan
- **2011-2013 *Assistant Professor,*** Institute of Molecular Medicine, National Tsing Hua University, Hsinchu, Taiwan
- **2006-2011 *Group Leader*,** National Center for Genome Medicine, Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan
- **2003-2006 *Visiting Fellow***, National Institute of Child Health& Human Development (NICHD), National Institutes of Health (NIH), Bethesda, MD

Education

- **1995-2003 *Ph.D.*** Graduate Institute of Life Science, National Defense University, Taipei, Taiwan
- **1993-1995 *M.S.*** Graduate Institute of Agronomy, National Taiwan University, Taiwan
- **1989-1993 *B.S.*** Department of Botany, National Taiwan University, Taiwan

Expertise

- Human Genetic Diseases, Molecular Biology, Cell Biology

Selected Publications

1. Lin YW, Kao HJ, Chen WT, Kao CF, Wu JY, Chen YT, **Lee YC***, "Cell-based screen identifies porphyrins as FGFR3 activity inhibitors with therapeutic potential for achondroplasia and cancer.", ***JCI Insight***, 2023, 8(22), e171257.
2. Jiang CL, Tsao CY, and **Lee YC*.** "Vitamin C attenuates predisposition to high-fat diet-induced metabolic dysregulation in GLUT10-deficient mouse model." ***Genes & Nutrition***. 2022;17(1):10. (IF: 5.523; SCI ranking: 18.8%) NSTC 108-2320-B-001-022.
3. Jiang, C.L., Jen, W.P., Tsao, C.Y., Chang, L.C., Chen, C.H., **Lee, Y.C.*** "Glucose transporter 10 modulates adipogenesis via ascorbic acid-mediated pathway to protect mice against diet-induced metabolic dysregulation." ***PLOS Genetics***, 2020, 16, e1008823.
4. Syu, Y.W., Lai, H.W., Jiang, C.L., Tsai, H.Y., Lin, C.C. and **Lee, Y.C.*** "GLUT10 maintains the integrity of major arteries through regulation of redox homeostasis and mitochondrial function." ***Human Molecular Genetics***, 2018, 27, 307-321.
5. **Lee, Y.C.,** Kuo, H.C., Chang, J.S., et. al., Chen, Y.T.*, Tsai, F.J.*, Wu, J.Y.* "Two new susceptibility loci for Kawasaki disease identified through genome-wide association analysis". ***Nature Genetics***, 2012, 44, 522-525.

Regulation of Connective Tissue Homeostasis

Yi-Ching Lee 李宜靜

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Abstract

Connective tissue is a dynamic and responsive system that adapts to environmental changes to maintain structural and functional homeostasis. Disruption of this balance contributes to a wide range of age-related diseases, including cardiovascular disease, osteoporosis, and type 2 diabetes. However, the mechanisms by which connective tissue senses and adapts to environmental stress remain poorly understood. In this presentation, I will share insights from our investigation of a rare connective tissue disease, arterial tortuosity syndrome (ATS), caused by loss-of-function mutations in the GLUT10 gene (*SLC2A10*). Our research reveals a critical role for GLUT10 as a transporter of dehydroascorbic acid (DHA), the oxidized form of vitamin C, in regulating vitamin C/redox balance and mitochondrial function, particularly in responding to stress. This function is essential for modulating cellular behaviors and extracellular matrix (ECM) remodeling[1,2], key processes underlying connective tissues maintenance and adaptation. We further highlight GLUT10's protective effects against age-related cardiovascular complications and high-fat diet induced metabolic diseases[2-4]. Given the pivotal roles of ECM remodeling and cell behaviors in tumor progression, we further explore how GLUT10 expression influences cancer progression. Together, our findings position GLUT10 as a key regulator of connective tissue responses to environmental challenges, providing new mechanistic insight into tissue homeostasis and potential strategies for preventing and treating related metabolic, vascular and oncological diseases.

References

1 Lee, Y. C., Huang, H. Y., Chang, C. J., Cheng, C. H. & Chen, Y. T. Mitochondrial GLUT10 facilitates dehydroascorbic acid import and protects cells against oxidative stress: mechanistic insight into arterial tortuosity syndrome. *Hum Mol Genet* **19**, 3721-3733 (2010). https://doi.org:ddq286

2 Syu, Y. W. *et al.* GLUT10 maintains the integrity of major arteries through regulation of redox homeostasis and mitochondrial function. *Hum Mol Genet* **27**, 307-321 (2018). https://doi.org:10.1093/hmg/ddx401

3 Jiang, C. L. *et al.* Glucose transporter 10 modulates adipogenesis via an ascorbic acid-mediated pathway to protect mice against diet-induced metabolic dysregulation. *PLoS Genet* **16**, e1008823 (2020). https://doi.org:10.1371/journal.pgen.1008823

4 Jiang, C. L., Tsao, C. Y. & Lee, Y. C. Vitamin C attenuates predisposition to high-fat diet-induced metabolic dysregulation in GLUT10-deficient mouse model. *Genes Nutr* **17**, 10 (2022). https://doi.org:10.1186/s12263-022-00713-y

Immunometabolism mini-symposium Speaker

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Position

- **2022-present *Assistant Research Fellow*,** Institute of Molecular Biology, Academia Sinica, Taiwan

Education

- **2019-2022 *Postdoctoral Researcher*,** Department of Pathology & Immunology, Washington, University in St. Louis, MO, USA
- **2012-2019 *Ph.D.*** City of Hope, Los Angeles, CA, USA
- **2007-2009 *M.S.*** Graduate Institute of Immunology, National Taiwan University, Taiwan
- **2003-2007 *B.S.*** Department of Chemistry, National Taiwan University, Taiwan

Expertise

- Neuroimmunology, Mucosal Immunology, Immune regulation

Selected Publications

1. **Wei-Le Wang**†, Jun Kasamatsu†, Satoru Joshita†, Susan Gilfillan, Blanda Di Luccia, Santosh K Panda, Do-Hyun Kim, Pritesh Desai, Jennifer K Bando, Stanley Ching-Cheng Huang, Kentaro Yomogida, Hitomi Hoshino, Mana Fukushima, Elizabeth A Jacobsen, Steven J Van Dyken, Christiane Ruedl, Marina Cella, Marco Colonna. †Equal contributions. "The aryl hydrocarbon receptor instructs the immunomodulatory profile of a subset of Clec4a4^{+} eosinophils unique to the small intestine." ***Proceedings of the National Academy of Sciences of the United States of America***, 2022 Jun 7;119(23): e2204557119.

2. Simone Brioschi†, **Wei-Le Wang**†, Vincent Peng†, Meng Wang Irina Shchukina, Zev J. Greenberg, Jennifer K. Bando, Natalia Jaeger, Rafael S. Czepielewski, Amanda Swain, Denis A. Mogilenko, Wandy Beatty, Peter Bayguinov, James A.J. Fitzpatrick6, Laura G. Schuettpelz, Catrina Fronick, Igor Smirnov, Jonathan Kipnis, Virginia S. Shapiro, Gregory F. Wu, Susan Gilfillan, Marina Cella, Maxim N. Artyomov, Steven H. Kleinstein, Marco Colonna. †Equal contributions. "Heterogeneity of meningeal B cells reveals a lymphopoietic niche at the CNS borders." ***Science*,** 2021 Jul 23;373(6553): eabf9277**.**

Unveiling Novel Mechanisms of Immune Regulation in Gut Inflammation

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Abstract

Eosinophils have conventionally been perceived as effector cells mediating inflammatory responses, particularly those related to type II immunity, including asthma, allergic reactions, and antiparasitic defenses. Our recent study on intestinal eosinophils unveiled an unexpected role for these cells in modulating gut inflammation following parasitic infection. We identified two distinct eosinophil subsets in the small intestine: one expressing the inhibitory receptor Clec4a4 and the inhibitory ligand PD-L1, and the other exhibiting a pro-inflammatory profile. Analysis of parabiotic mice revealed that both subsets originate from the blood, rather than being tissue-resident. Remarkably, Clec4a4$^+$ eosinophils are unique to the small intestine and are instructed by the aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor that integrates environmental cues and imprints functional programs in many gut immune cells. Selective AhR depletion in eosinophils results in a marked reduction of Clec4a4$^+$PD-L1$^+$ eosinophils, enhanced worm clearance, and an elevated frequency of group 2 innate lymphoid cells (ILC2s). Moreover, mice with eosinophil-specific AhR deficiency exhibit increased susceptibility to anti-CD3-induced small intestinal inflammation, accompanied by an expanded Th17 cell population. These findings highlight a general immunoregulatory role for AhR$^+$ eosinophils in resolving intestinal inflammation, paving the way for targeted therapeutic strategies for food allergies, inflammatory bowel disease, and eosinophilic gastrointestinal disorders.

Immunometabolism mini-symposium Speaker

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Position

- **2025 Aug *Assistant Research Fellow***, Genomics Research Center, Academia Sinica, Taiwan
- **2020-2025 *Assistant Professor***, Graduate Institute of Cell Biology, China Medical University, Taiwan

Education

- **2016-2020 *Postdoctoral Researcher***, Joslin Diabetes Center, Harvard Medical School, MA, USA
- **2008-2014 *Ph.D.*** Institute of Biochemistry and Molecular Biology, National Yang-Ming Chiao Tung University, Taiwan
- **2006-2008 *M.S.*** Institute of Biochemistry and Molecular Biology, National Yang-Ming Chiao Tung University, Taiwan
- **2002-2006 *B.S.*** Department of Biotechnology and Laboratory Science in Medicine, National Yang-Ming Chiao Tung University, Taiwan

Expertise

- Adipocyte biology, Mitochondrial medicine, CRISPR gene editing, Metabolic disorders

Selected Publications

1. **Wang CH[#,*]**, Tsuji T[#], Wu LH, Yang CY, Huang TL, Sato M, Shamsi F, Tseng YH*. "Endothelin 3/EDNRB signaling induces thermogenic differentiation of white adipose tissue." ***Nature Communications***. 2024 Aug 22;15(1):7215.
2. Onikanni AS[#], Lawal B, Oyinloye BE, Mostafa-Hedeab G, Alorabi M, Cavalu S, Olusola AO*, **Wang CH***, Batiha GE*. "Therapeutic efficacy of Clompanus pubescens leaves fractions via downregulation of neuronal cholinesterases/Na^+-K^+ATPase/IL-1β, and improving the neurocognitive and antioxidants status of streptozotocin-induced diabetic rats." ***Biomedicine & Pharmacotherapy***. 2022 Feb 17;148:112730.
3. Shamsi F[#], **Wang CH[#]**, Tseng YH*. "The evolving view of thermogenic adipocytes - ontogeny, niche and function." ***Nature Reviews Endocrinology***. 2021 Dec;17(12):726-744.
4. **Wang CH[#]**, Lundh M, Fu A, Kriszt R, Huang TL, Lynes MD, Leiria LO, Shamsi F, Darcy J, Greenwood BP, Narain NR, Tolstikov V, Smith KL, Emanuelli B, Chang YT, Hagen S, Danial NN, Kiebish MA, Tseng YH*. "CRISPR-engineered human brown-like adipocytes prevent diet-induced obesity and ameliorate metabolic syndrome in mice." ***Science Translational Medicine***. 2020 Aug 26;12(558):eaaz8664.

Thermogenic Adipocytes in Glucose Homeostasis and Inflammation Resolution

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Abstract

Thermogenic adipose tissue, including brown and beige fat, regulates nutrient usage and energy metabolism. However, brown fat is scarce in humans and declines with obesity and aging. Promoting white fat browning is a promising strategy to enhance metabolism. Previously, we used CRISPR/Cas9 to activate UCP1 expression in human white adipocytes, generating human brown fat-like (HUMBLE) cells that mimicked human brown fat and improved glucose metabolism and energy expenditure in obese mice. The findings reveal the potential of CRISPR-engineered brown-like cell therapy as a treatment for obesity and diabetes. Recently, we identified endothelin3 (EDN3) and its receptor EDNRB as key regulators of WAT browning. EDNRB overexpression in human preadipocytes activates the cAMP-EPAC1-ERK pathway, enhancing thermogenesis. Cold exposure increased EDN3 and EDNRB levels in WAT, while adipose progenitor-specific EDNRB deletion impaired beige fat formation, leading to obesity and insulin resistance in mice. Direct EDN3 injections into WAT stimulated browning and improved glucose metabolism, highlighting a potential therapeutic target for obesity and metabolic diseases. Moreover, the induction of WAT browning alleviated hepatic steatosis and inflammation by enhancing lipid metabolism and reshaping immune cell populations in the liver. Taken together, these studies provide novel insights into the molecular mechanisms underlying white fat browning and offer new therapeutic avenues for treating obesity and metabolic disorders.

References

1. **Wang CH[#,*]**, Tsuji T[#], Wu LH, Yang CY, Huang TL, Sato M, Shamsi F, Tseng YH*. Endothelin 3/EDNRB signaling induces thermogenic differentiation of white adipose tissue. Nature Communications. 2024 Aug 22;15(1):7215.

2. Shamsi F[#], **Wang CH[#]**, Tseng YH*. The evolving view of thermogenic adipocytes - ontogeny, niche and function. Nature Reviews Endocrinology. 2021 Dec;17(12):726-744.

3. **Wang CH[#]**, Lundh M, Fu A, Kriszt R, Huang TL, Lynes MD, Leiria LO, Shamsi F, Darcy J, Greenwood BP, Narain NR, Tolstikov V, Smith KL, Emanuelli B, Chang YT, Hagen S, Danial NN, Kiebish MA, Tseng YH*. CRISPR-engineered human brown-like adipocytes prevent diet-induced obesity and ameliorate metabolic syndrome in mice. Science Translational Medicine. 2020 Aug 26;12(558):eaaz8664.