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KATHY LUI



Principal Investigator

Kathy Lui



Team members

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Research Progress Summary

During the past years, Kathy Lui and her team have been uncovering the potential of using human pluripotent stem cells for cell therapy, disease modeling, and drug screening. The below two research projects are examples of this effort:

Research on pancreatic beta cell therapy and functional regeneration

There has been a continuous debate over whether there is an adult progenitor or stem cell for the generation of pancreatic beta cells to treat diabetes particularly insulin-dependent diabetes. Compared to insulin therapy, pancreatic beta cell therapy is more appealing given that these cells can respond to the changing blood glucose levels to prevent complication such as hypoglycemia. However, pancreatic beta cells were not able to regenerate after injury. In 2021, the team has

reported that there is no endogenous adult stem cell for beta cell (re)generation as demonstrated by a new genetic lineage tracing mouse model (*Nature Metabolism*, 2021; *Cell Metabolism*, 2021). Adult beta cells are mainly derived from the rare process of pre-existing beta cell replication. Therefore, additional therapeutic approaches should be developed to replenish adult beta cells after injury. In 2020, they have reported a new differentiation protocol for generating human pancreatic beta-like cells from human pluripotent stem cells, and uncovered a cell surface marker for negative purification of the mature and functional human beta-like cells (*Stem Cell Reports*, 2020). Recently, pharmaceutical companies such as Semma Therapeutics, Viacyte, Inc, etc have reported FDA approval to launch clinical trials for testing the safety and therapeutic efficacy of human stem cell derived pancreatic progenitor cells. These mark the beginning of using human

10 STEM CELLS AND TISSUE REGENERATION

Stem Cell and Vascular Regeneration

stem cell derived beta cells as personalized cell based therapies to treat diabetes. Besides making new beta cells from human pluripotent stem cells, they have further studied the endogenous regulatory pathways to understand how insulin is produced, facilitating the search for the pathophysiological origin of diabetes.

cells by generating human pluripotent stem cell derived endothelial cells for *in vitro* disease modeling and drug screening. While ACE2 is indispensable for SARS-CoV-2 infection in these cells, they found that the virus can directly induce endothelial inflammation and dysfunction independent of ACE2 expression.

Research on COVID-19 related vascular disease and dysfunction

In view of the unknown impact of the SARS-CoV-2 virus on vascular function in COVID-19 patients, the team has also investigated whether the virus has a direct effect in impairing endothelial cell function or a secondary effect in inducing the dysfunction through immune over-reaction. They have written a concise review to summarise the arguments on both sides of this topic (*Journal of Molecular and Cellular Cardiology*, 2021). Moreover, they have also collaborated with Leo Poon's team at The University of Hong Kong to study the effect of SARS-CoV-2 on the infectivity, function and inflammation of vascular cells. Importantly, they model SARS-CoV-2 infection in these

Conference presentation

Despite that the pandemic has not ended, Kathy has been invited to give several virtual lectures in some international and regional conferences, including a lecture for the Federation of Immunological Societies of Asia-Oceania (FIMSA) in Korea; a lecture for the Immunity and Infection Seminar in University of Freiburg, Germany; a lecture for the exchange programme between The Chinese University of Hong Kong and Monash University, Australia; a lecture for the 24th Annual Scientific Meeting of Institute of Cardiovascular Science and Medicine, Hong Kong. The scientific meeting for the Hong Kong Society for Immunology (HKSI) has been organised by the team in 2021 as she has been serving as the chairman of HKSI.

Research and Scholarship

Research Awards and Recognitions

Member's Name	Details	
	Award	Organisation
Kathy Lui	Young Researcher Award 2020	The Chinese University of Hong Kong
	Young Investigator Award	The Chinese University of Hong Kong
	2021 Circulation Research Extraordinary Reviewer	American Heart Association, U.S.A.

Fellowships

Member's Name	Details	
	Fellowship	Organisation
Wenchu Ye	RC Postdoc Fellowship	The Chinese University of Hong Kong

Academic Editorship

Member's Name	Details	
	Role	Journal
Kathy Lui	Editorial Member	Circulation Research
		Cardiovascular Research
		Frontiers in Immunology
		Scientific Reports
	Associate Editor	Stem Journal
		Journal of Immunology and Regenerative Medicine

Reviewer of Journal / Conference

Member's Name	Details	
	Role	Journal / Conference
Kathy Lui	Grant Reviewer	Sir Henry Dale Fellowship, Wellcome Trust, United Kingdom
		Spark Funding Scheme, Swiss National Science Foundation, Switzerland
		New Talent Programme, Dutch Research Council, Netherland
	Journal Reviewer	Circulation Research
		Diabetes
		Theranostics
		Acta Pharmaceutica Sinica B
		Pharmacological Research
		China Science Life Science
Kevin Yang	Journal Reviewer	Immunology Letters

Grants and Consultancy

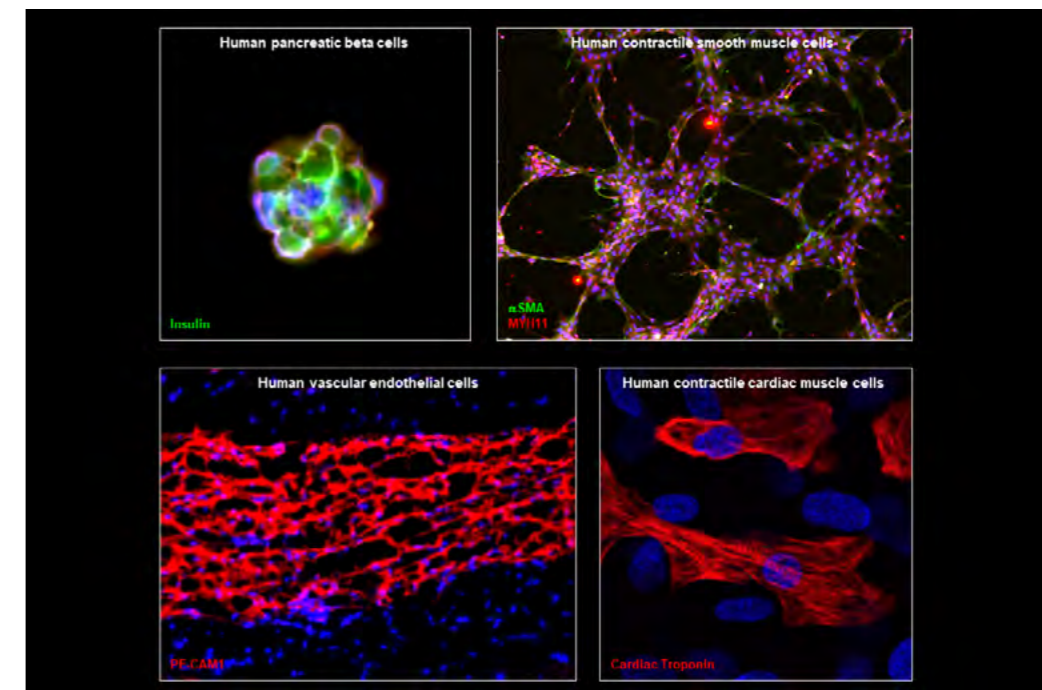
Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Kathy Lui	Vascular Diseases and Regeneration	National Natural Science Foundation of China – Excellent Young Scientist Fund	01/01/2020	31/12/2022	RMB 1,300,000
	Studying the Functional Mechanism of Endothelial YY1 in Postischemic Angiogenesis	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,195,542
	Studying the Role of m6A RNA Modification in Vascular Diseases and Regeneration	National Natural Science Foundation of China – Research Fund	01/01/2021	31/12/2023	RMB 550,000
	Aging, Skeletal Degeneration and Regeneration	Research Grants Council – Areas of Excellence Scheme	01/05/2021	30/04/2029	64,889,000
Wenchu Ye	平滑肌細胞焦亡在動脈粥樣硬化中的作用及機制研究	National Natural Science Foundation of China – Excellent Young Scientist Fund	01/01/2021	31/12/2023	RMB 240,000

Publications

A. Journal Papers

1. Yan Y, Tang R, Li B, Cheng L, Ye S, Yang T, Han YC, Liu C, Dong Y, Qu LH, Lui KO, Yang JH, Huang ZP. The cardiac translational landscape reveals that micropeptides are new players involved in cardiomyocyte hypertrophy. *Molecular Therapy*. 2021;29(7):2253-2267. doi:10.1016/j.ymthe.2021.03.004.
2. Zhao H, Huang X, Liu Z, Pu W, Lv Z, He L, Li Y, Zhou Q, Lui KO, Zhou B. Pre-existing beta cells but not progenitors contribute to new beta cells in the adult pancreas. *Nature Metabolism*. 2021;3(3):352-365. doi:10.1038/s42255-021-00364-0.
3. Han DSC, Ni M, Chan RWY, Wong DKL, Hiraki LT, Volpi S, Jiang P, Lui KO, Chan KCA, Chiu RWK, Lo YMD. Nuclease deficiencies alter plasma cell-free DNA methylation profiles. *Genome Research*. 2021;31(11):2008-2021. doi:10.1101/gr.275426.121.
4. Weng W, Liu X, Lui KO, Zhou B. Harnessing orthogonal recombinases to decipher cell fate with enhanced precision. *Trends in Cell Biology*. Published online 2021. doi:10.1016/j.tcb.2021.09.007. (Review, Epub ahead of print)

5. Lui KO, Huang Y. Chaperone mediated autophagy regulates eNOS uncoupling in cardiovascular events. *Circulation Research*. 2021;129(10):946-948. doi:10.1161/CIRCRESAHA.121.320212. (Editorial)
6. Zhao H, Lui KO, Zhou B. Pancreatic beta cell neogenesis: Debates and updates. *Cell Metabolism*. 2021;33(11):2105-2107. doi:10.1016/j.cmet.2021.10.007. (Editorial)
7. Zhang S, Li Y, Huang X, Liu K, Wang QD, Chen AF, Sun K, Lui KO, Zhou B. Seamless genetic recording of transiently activated mesenchymal gene expression in endothelial cells during cardiac fibrosis. *Circulation*. 2021;144(25):2004-2020. doi:10.1161/circulationaha.121.055417. (Epub ahead of print)
8. Li Y, Zhu H, Zhang Q, Han X, Zhang Z, Shen L, Wang L, Lui KO, He B, Zhou B. Smooth muscle-derived macrophage-like cells contribute to multiple cell lineages in the atherosclerotic plaque. *Cell Discovery*. 2021;7(1):1-4. doi:10.1038/s41421-021-00328-4. (Letter)
9. Ma Z, Yang KY, Huang Y, Lui KO. Endothelial contribution to COVID-19: An update on mechanisms and therapeutic implications. *Journal of Molecular and Cellular Cardiology*. 2022;164:69-82. doi:10.1016/j.yjmcc.2021.11.010. (Epub ahead of print)



Functional organoids generated from human pluripotent stem cells from Kathy Lui and her team's laboratory

Source: Kathy Lui and her team