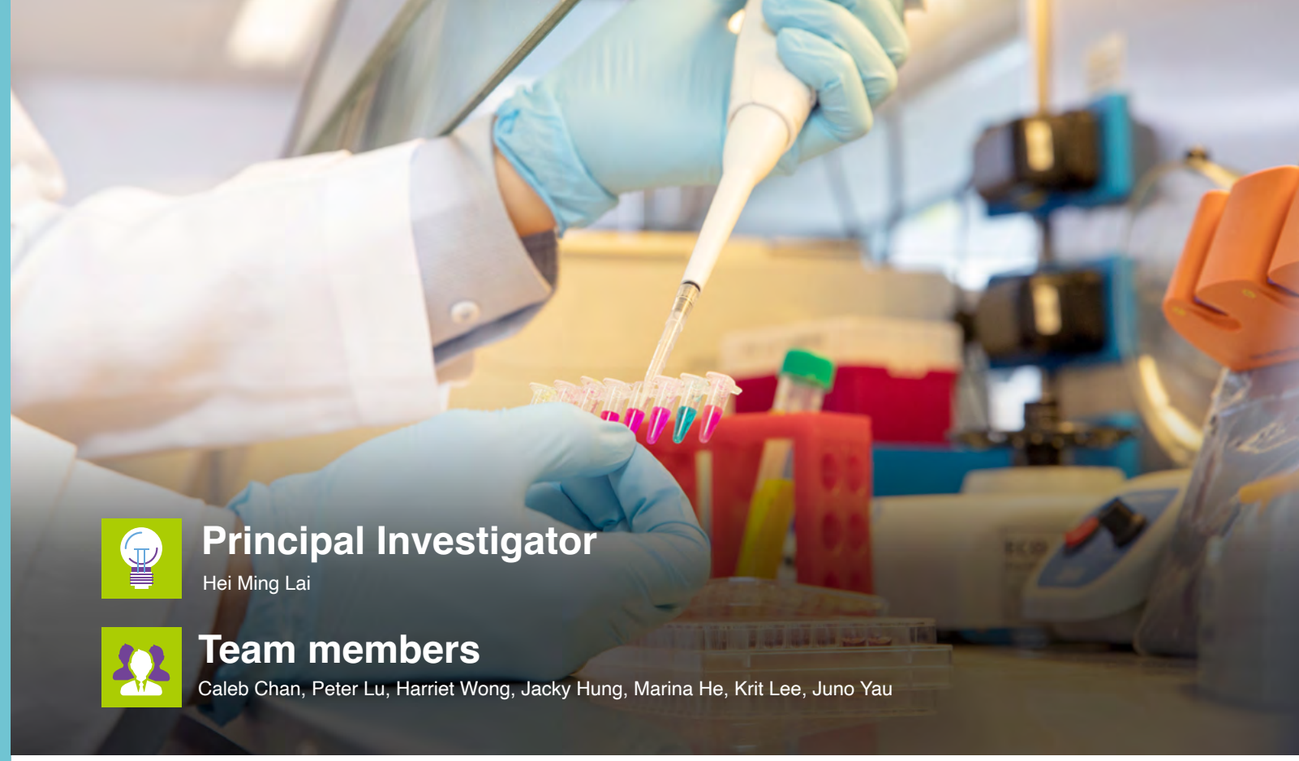
黎曦明

HEI MING LAI

08 NEUROSCIENCE AND NEUROTECHNOLOGY



Principal Investigator

Hei Ming Lai

Team members

Caleb Chan, Peter Lu, Harriet Wong, Jacky Hung, Marina He, Krit Lee, Juno Yau

Research Progress Summary

This is the first year of the establishment of the laboratory led by Hei Ming Lai at the Li Ka Shing Institute of Health Sciences. As the research team has been building the infrastructure for investigation of complex, abstract psychiatry disorders, they are pleased to report the significant progresses in pursuing that goal. In addition, various foundational technologies have been developed for mapping of the brain's neurocircuitry and molecular compositions.

Building Concrete Infrastructures for Understanding Abstract Mental Phenomena

One of the biggest problems in psychiatry is to link matter to mind. As the first psychiatry research laboratory in Hong Kong, they reflected deeply on what is the nature of mental phenomena, such as emotions, thoughts, social interactions, and their disorders. They went back to the basic scientific principle to plan their project: testable hypotheses based on the best-known evidence. They thus arrived at a creative yet practical experimental approach: rather than inferring mental states of animals based on human experiences, which can be biased and, on some occasions, non-testable, they seek to obtain unbiased observations and classification on the behavioural and mental processes that reflect a "mous-onality" – defined as a statistically biased way of action and reaction towards internal and external stimuli. They then took 3 approaches to monitor these processes, (1) the use of six high speed infrared cameras and thermal imaging cameras for 3D reconstruction of mouse behaviour round-the-clock in a sound-, smell- and light-proof enclosure, to minimise disturbances on their circadian rhythm and percepts, (2) the implantation of Neuropixels probe on the mouse subject being observed, which will stream thousands of neuronal spiking activities across multiple brain regions to

correlate with the behaviours, and finally (3) the use of an observer mouse co-behaving with the subject mouse and also with Neuropixels probe implanted – representing an evolutionarily tuned "sensor" that should ensure the extraction of most relevant cues on the subject mouse' mental and social state. This approach, inspired by the phenomena of transference and countertransference in psychiatry, has not been proposed by others and will provide a solid foundation on the investigation of abstract psychiatric symptoms that has been disruptive to patients' social lives but elusive to capturing by machines and algorithms.

The capturing system is currently around 80% completed and they very much look forward to kickstart the project next year.

Developing Necessary Technologies for Mapping Neurocircuits and Molecular Compositions

Another bottleneck in understanding neuropsychiatry is the complexity of brain structures and compositions. Since the technologies for mapping neurocircuitries in the desired resolution and throughput has yet to exist, the team aims to develop them in-house. One major challenge is the use of 3D fluorescent labelling strategies to label dozens of molecules in a whole intact brain, such that subsequent imaging using tissue clearing techniques would be useful. In contrast to the centuries-old wisdom that tissue immunostaining should be carried out at ambient temperatures, they developed thermo-immunohistochemistry where deliberate the use of high temperatures, along with a new chemical engineering method to stabilize commercial antibodies, which can help achieve fast, deeply penetrating immunostaining. They also generated proteins with unnatural amino acids for additional multiplexing capabilities and functionalities. Combined, these technologies can make high-throughput mapping of brain circuitries feasible, which is important to generate confident data for understanding molecular underpinnings of neuronal functions. In addition, the laboratory team is glad to announce that with the generous support from the Academic Equipment Grant, they are constructing a mesoscale selective plane illumination microscope (mesoSPIM) to image large, centimetre-scale cleared tissues – a platform of emerging significance to understand all kinds of tissues in their 3D context. Upon its completion, they will be honoured to make it open to serve other CUHK research groups.

Serendipitous Discoveries and Spin-off Technologies

Since they implemented a diversified approach to the development of novel technologies, with multiple trial and errors they inevitably stumbled across many interesting discoveries upon careful observations. These include an artificial chaperone that can potentially benefit industrial production of pharmaceuticals and biotechnology applications involving the use of enzymes, a room temperature synthesis method for producing cesium lead halide perovskite nanocrystals with record-high photoluminescent quantum yields – a very promising material for the next generation flexible LED displays and solar cells, as well as a low-cost synthesis method for producing molecular beacons for qPCR and other nucleic acid diagnostics. The development of 3D histology technologies is also benefitting renal hemodynamics and colorectal cancer research. Lai and his team very much look forward to more exciting science to come with their firm foundation laid in the Institute.

Research and Scholarship

Research Awards and Recognitions

Member's Name	Details	
	Award	Organisation
Hei Ming Lai	Faculty Innovation Award 2020	Faculty of Medicine, The Chinese University of Hong Kong

Reviewer of Journal / Conference

Member's Name	Details	
	Role	Journal / Conference
Hei Ming Lai	Reviewer	Laboratory Investigations

Grants and Consultancy

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hei Ming Lai	Developing Practical Next Generation Histology Chemical Technologies	Faculty Innovation Award, Faculty of Medicine, The Chinese University of Hong Kong	01/01/2021	31/12/2023	750,000
	Clearing the Way for Better Tissue Diagnostics – A Midstream Development Project on Accessible Three-dimensional Histology Methods and Platform	Innovation and Technology Commission – Innovation and Technology Fund for Midstream Research Programme for Universities	01/03/2021	31/08/2023	4,700,000
Hei Ming Lai, Caleb Chan	Clearing The Way for Better Tissue Diagnostics – A Midstream Development Project on Accessible Three-dimensional Histology Methods and Platform	Innovation and Technology Commission – Innovation and Technology Fund for Research Talent Hub	01/03/2021	31/08/2023	1,005,000

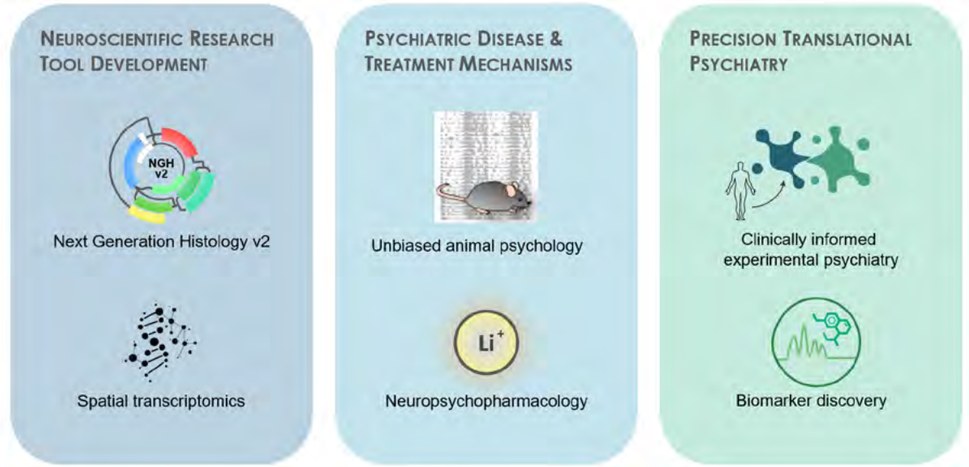
Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hei Ming Lai, Peter Lu	Clearing The Way for Better Tissue Diagnostics – A Midstream Development Project on Accessible Three-dimensional Histology Methods and Platform	Innovation and Technology Commission – Innovation and Technology Fund for Research Talent Hub	01/04/2021	31/08/2023	971,500
Hei Ming Lai, Yuan He	Clearing The Way for Better Tissue Diagnostics – A Midstream Development Project on Accessible Three-dimensional Histology Methods and Platform	Innovation and Technology Commission – Innovation and Technology Fund for Research Talent Hub	01/03/2021	31/08/2023	264,600
Hei Ming Lai	Development of A MesoSPIM Light Sheet Microscope v5.1-Based Next Generation Histology Tissue Diagnostic Platform	The Chinese University of Hong Kong – Academic Equipment grant (2020/21 2nd round)	01/02/2021	31/08/2021	1,063,000
	A Comprehensive Survey on Alpha-Synuclein Pathologies in Colonic Submucosal Biopsies of Prodromal Parkinsons's Disease Patients – An Exploratory Study	Food and Health Bureau – Health and Medical Research Fund	01/09/2021	31/08/2023	965,803

Publications

A. Journal Papers

1. Li Z, Chen X, Vong JSL, Zhao L, Huang J, Yan LYC, Ip B, Wing YK, Lai HM, Mok VCT, Ko H. Systemic GLP-1R agonist treatment reverses mouse glial and neurovascular cell transcriptomic aging signatures in a genome-wide manner. *Communications Biology*. 2021;4(1):1-6. doi:10.1038/s42003-021-02208-9.

2. Lo HS, Hui KPY, Lai HM, He X, Khan KS, Kaur S, Huang J, Li Z, Chan AKN, Cheung HHY, Ng KC, Ho JCW, Chen YW, Ma B, Cheung PMH, Shin D, Wang K, Lee MH, Selisko B, Eydoux C, Guillemot JC, Canard B, Wu KP, Liang PH, Dikic I, Zuo Z, Chan FKL, Hui DSC, Mok VCT, Wong KB, Mok CKP, Ko H, Aik WS, Chan MCW, Ng WL. Simeprevir potently suppresses SARS-CoV-2 replication and synergizes with remdesivir. *ACS Central Science*. 2021;7(5):792-802. doi:10.1021/acscentsci.0c01186.



Three main research directions of Hei Ming Lai and his team's laboratory.

Source: Hei Ming Lai