

In memory of Professor Louis LIM (1940 - 2021)

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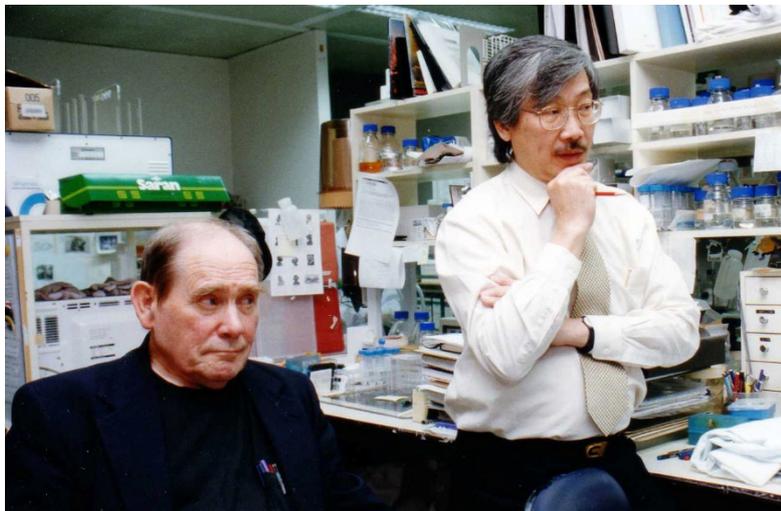
Emeritus Professor Louis LIM (1940-2021)

Louis Lim passed away on January 29th 2021. We mourn the loss of one of the founders of molecular neurobiology and a great colleague. Among his various scientific and administrative achievements, Louis' contribution to IMCB is particularly noted, since he was with us from the beginning. Here we briefly survey Louis' long career, and give perspective on what made him a unique scientist of his time, and consider his legacy.

After graduating in Biochemistry at the University of Malaya, Singapore (1964), Louis Lim fled to the Institute of Psychiatry, King's College London for his PhD (1967). Dr Lim's research career in molecular biology took off with a fellowship to Yale University with Evangelos Canellakis. In a paper published in Nature (1970) they reported that mammalian mRNAs curiously contained an extensive poly(A) tail. This insight allowed purification of mRNA from any tissue, free of contaminating rRNA and DNA, which could then be translated into radio-labelled proteins using reticulocyte lysate. Louis returned to London in 1971 as a lecturer at the Institute of Neurology, now part of University College London (UCL), and began to apply these methods to neuroscience.

During this time Louis' lab moved to Wakefield Street near Kings cross, where he remained. With the discovery of reverse transcriptase by David Baltimore (IMCB scientific advisory board 1998-2002), mRNA could be converted to DNA in the lab for subsequent cloning and sequencing.

Louis used the reticulocyte lysate system to investigate abundant brain mRNAs (primarily synaptic metabolic enzymes), then began sequencing many uncharacterized brain-specific mRNAs, which became the focus of his interest. As a scientist and a mentor, Louis Lim had a larger than life personality. In London he would arrive to work on his Harley-Davison



perhaps after a successful night of cards, and ruminate in his office proudly bearing the sign "smoking allowed".

Louis Lim and Sydney Brenner reflect on some new findings in 1992

Louis played a central role with another maverick Sydney Brenner, then Director of LMB Cambridge, in establishing and recruiting for IMCB from 1985 onwards. After IMCB was inaugurated Louis discussed with Richard Sykes, the Research Director of Glaxo PLC, possibilities for starting an R&D partnership in the biosciences. This led to the signing on 31

March 1989 of the 'Glaxo-IMCB research venture', together with the EBD headed by Philip Yeo. This was an early international collaboration with industry R&D to support basic discovery research aimed at identifying molecular targets involved with neurodegeneration.

Louis had a keen instinct for scientific discovery, but he combined this with disarming warmth, directness and generosity. He attracted and empowered an eclectic array of scientists over the years. Among many others, Thomas Leung and Edward Manser were brought from London to help run Louis' Neurobiology lab in Singapore. Aside from Principal Investigators past and present, several PhD students recruited to IMCB over this period remain in academia. For example Chen Weining is now Chair in Food Science and Technology at NTU, and Soong Tuck Wah served as Head of the Department of Physiology, NUS. Lim Kah Leong, moved into Parkinson's disease research, and is now Vice-Dean at the LKC School of Medicine. He reflects "*we have lost a great scientist, mentor and friend*".

The Glaxo-IMCB group made seminal discoveries in the area of signal transduction and neuronal architecture. This started with the serendipitous finding that an 'interesting' brain genes cloned by Christine Hall, coined chimaerin, was similar to a RhoGAP purified in a lab 'down the road' by Alan Hall (Institute of Cancer Research). The labs published a joint paper in Nature (1991) indicating these proteins share a common motif underlying their activity (we now know of 66 RhoGAPs in humans).

Although the prevailing view was that the small GTP-binding protein Ras and Rho signalled 'downstream' through these GAPs, experiments in Singapore proved otherwise. In two remarkable Nature papers in 1993 and 1994 the Glaxo-IMCB group proposed an alternate view, describing how protein kinases ACK and PAK1 bound tightly to a Rho protein - but only in its active form (i.e. when Rho bound GTP). For those in the Rho field the light had been switched on. The group then reported two larger kinases (ROK and MRCK, 1995-8), that followed similar principles, and thereby regulated the actin cytoskeleton. Because such proteins exhibit an amino-acid motif (CRIB) that could be identified by eye (now termed bioinformatics), it opened the floodgates for other researchers in the field. The PAK CRIB is seen on the \$10,000 note: as Louis would say 'putting some research back into money'.



Glaxo-IMCB team leaders in 2008, and the PAK peptide

Though leading a vibrant and productive research group, Louis Lim was the first to admit that luck played a large part in his scientific success - and in courting serendipity the journey was as important as the destination*. His photographic memory was a key advantage in the age before Pubmed. He never forgot an experiment or result, particularly the ones that made no sense to us. Today the reformed sGSK group led by Edward Manser is studying how these important protein kinases contribute to disease processes such as Fragile-x syndrome and cancer.

Louis was appointed by Philip Yeo as the first Executive Director of the Biomedical Research Council (BMRC) from 2001-2002. Under his guidance BMRC developed all its varied functions in promoting biosciences, including a generous extramural funding scheme. Outside of IMCB he served on the International Advisory Panel of the National Neuroscience Institute (1995-1998) and the National Biotechnology Committee (1995-1999) among others. He retired in 2009, but was delighted with last year's news of a revamped neuroscience program in IMCB, working with scientists across A*STAR research institutes.

Louis Lim is fondly remembered by many in science and pharma.

Suresh **Sachi**, current A*STAR DCE sums up his legacy - *"Louis was a great friend, coach, and mentor to me, and has done so much for ASTAR and Singapore"*

Jackie **Hunter**, previous GSK Head of Neurology, and A*STAR board member - *"It was a pleasure to know Louis Lim, whom I first met at the Astra Neuroscience Unit in Wakefield Street. Louis was a real supporter of science, especially for Singapore"*

Chris **Tan**, the founding Director of IMCB and fellow lover of durians echoes these sentiments succinctly - *"I dearly miss Louis' jokes and humour"*

Alice **Huang** from Caltech who served on the IMCB SAB - *"Louis Lim at times could be sweet, tough or acerbic, and all with a smile. I shall miss this good man"*

Sir David **Lane**, A*STAR **Chief Scientist** puts it poetically - *“Louis walked lightly through the world, I never saw him without a smile, he saw the best in everyone, loved life and found us all very amusing. His research ROKed and so did he”*



Louis Lim with colleagues Hong Wanjin, Qi Zeng, Walter Hunziker, Tay-Png Hong Lan and Henry Yu.

Finally from **Hong Wanjin**, current Executive Director of IMCB - *“Louis was a complex scientist; combining at once a general and a soldier, a boy and a man, insightful and inspiring to so many of us. We remember his contributions well and his charming personality better”*

Over the years Louis' avuncular attitude endeared him to all staff – for he was in fluent in Malay, Singlish, and some vernacular Hokkien. Combined with his unique sense of humour, his celebratory Friday evening sessions were renowned.

Thank you, Louis, for adding sparkle to our lives. Rest well – we will miss your impish smile and conspiratorial walk to the courtyard.*

- By Edward **Manser** and Alice **Tay**