2020年李卓皓院士紀念演講會
The 2020 Choh Hao Li Memorial Lectures

Prof. Hsing-Jien Kung

Arginine, mitochondria
and cancer metabolism

Aug, 21th (Fri), 2020 15:45-16:45

103 Auditorium Institute of Biological Chemistry
Academia Sinica
中央研究院生物化學研究所103講堂

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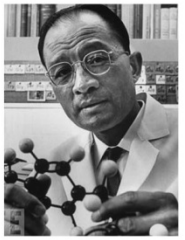

Prof. Choh-Hao Li
(1913-1987)

The Choh-Hao Li Memorial Lectureship was established and organized by the Institute of Biological Chemistry, Academia Sinica, and co-sponsored by the Graduate Institute of Biochemical Sciences, National Taiwan University, and the Taiwan Society for Biochemistry and Molecular Biology. The purpose of this Lectureship is to honor Dr. Li and to promote the study of proteins at the molecular level. The lectureship provides an opportunity to invite to Taipei an eminent scientist who has made original and important contribution to our understanding of the science of proteins and the mode of actions.

Dr. Choh-Hao Li graduated from the University of Nanking in 1933 and received his Ph.D. in Chemistry from the University of California, Berkeley in 1938. He joined the staff in Berkeley immediately thereafter and rose through the academic ranks to become Professor of Biochemistry in 1949. The world-famous Institute, Hormone Research Laboratory was organized at the Berkeley campus for him in 1950, and later on moved to UCSF in 1967. Dr. Li served as the Director of the Laboratory for thirty-three years until his retirement in 1983. However, he continued to conduct his research at his new Institute, Molecular Endocrinology Laboratory in UCSF until his death on November 28, 1987.

Dr. Li was among the first to isolate and identify eight of the nine hormones of the anterior pituitary. He isolated and synthesized the human pituitary growth hormone in 1971, the largest protein molecule synthesized at that time. The synthesis of the human growth hormone was hailed at the time as a scientific breakthrough, with tremendous possibilities in many areas of medical research. The pituitary gland, a small gland at the base of the brain, controls nearly every function in the body. The gland has been implicated in cancer, rheumatoid arthritis, allergies and metabolic diseases. In addition, Dr. Li and his associates did research on many other hormones used in disease treatment. In 1976, Dr. Li discovered β-endorphin, a substance produced in the brain that acts as a painkiller. He not only published over 1,000 scientific papers, but was also editor of many journals, and series of books.

In Taiwan, Dr. Li also made great contributions in initiating protein research in early 1958 and founding of biochemistry programs as he served on the Scientific Advisory Board of the Institute of Biological Chemistry, Academia Sinica, Taiwan, as well as the National Science Council of Taiwan. Dr. Li continued to give his endless efforts promoting the progress of protein research here in Taiwan until his death. This memorial lectureship is thus established as an annual event and leveraged to keep this unique strength.

李卓皓 博士
(1913–1987)

李卓皓院士紀念演講會是由中央研究院生物化學研究所、臺灣大學生化科學研究所，以及台灣生物化學及分子生物學學會共同創辦。此演講會目的為紀念李卓皓博士在生物化學研究的貢獻，並推動台灣在分子層次研究蛋白質的發展。一年一度的演講會邀訪對蛋白質研究有重大貢獻之世界知名學者來台演講。

李卓皓博士1933年畢業於南京大學，並於1938年獲頒美國加州大學柏克萊分校化學博士學位。他隨即加入該校開始其研究生涯，並於1949年升任生物化學教授。柏克萊分校於1950年為他成立了世界知名的荷爾蒙研究實驗室，此實驗室後來在1967年遷移至加州大學舊金山分校。至1983年退休為止，李博士領導該實驗室長達33年的時間。此後直到1987年11月28日逝世之前，他仍於舊金山分校內所設分子內分泌學研究室繼續進行研究。

腦下垂體的九種荷爾蒙中，就有八種是由李博士首先發現並分離。他於1971年成功合成人體生長荷爾蒙，為當時人工合成的最大蛋白質，並為醫藥科學研究帶來重大突破與貢獻。腦下垂體位於人腦底部中央位置，此微小腺體分泌的荷爾蒙能控制人體幾乎所有的功能，並與癌症、風溼性關節炎、過敏及多種代謝疾病相關。李博士與許多專家合作，將荷爾蒙運用在多種疾病的治療。他於1976年發現β-腦內啡，這是一種由大腦分泌具止痛功能的物質。李博士不但發表了1000多篇研究論文，還擔任許多科學期刊與書籍系列的編輯。

早在1958年李卓皓教授應胡適博士之邀回國以蛋白質化學與腦下腺荷爾蒙為題在臺大講學八週共24次演講，介紹蛋白質研究為主的最新生物科學發展概況，帶給國內生物科學新方向之啟示。李教授向相關單位建議國內應加速發展生物化學研究及人才培育，這成為中研院生化所及臺大生化科學所成立的最大動力。李教授擔任中研院生化所設所諮詢委員會主任委員，直接參與籌畫，正式成所後擔任學術諮詢委員會召集人直到過世為止，晚年仍持續推動台灣蛋白質研究。為了保持這項重點研究，相關單位於是創辦李卓皓院士紀念演講，成為每年四月的活動。

Prof. Hsing-Jien Kung

Arginine, mitochondria and cancer metabolism

Hsing-Jien Kung, Chialin Chen and many others
Taipei Medical Univeristy

As well described by DeBeradinis and Chanedel in a recent commentary (We need to talk about Warburg effects, Nature Metabolism, Feb, 2020), mitochondrial OXPHOS activities are required for tumor cells, even in the face of strong Warburg effects.

Arginine is vital in cellular physiology. However, as a non-essential amino acid, arginine has been used as a health supplement, and arginine-deprivation, as a therapy for cancer. We have been studying how tumor cells maintain mitochondrial activities through arginine metabolism, and have a series of papers demonstrating that a primary and immediate target of arginine-starvation therapy is mitochondria OXPHOS functions. We have now identified the detailed mechanisms whereby arginine stimulates OXPHOS activities and unexpectedly found that transcriptional factor TEAD4 as a central mediator. We show that arginine globally stimulates histone acetylation and coordinately upregulates nuclear encoded OXPHOS genes. This process is guided by TEAD4, but not TEAD1-3, and interestingly, in a YAP1-independent but mTOR-dependent and acetylation dependent manner. Arginine retains TEAD4 in the nucleus and facilitates TEAD4′s recruitment to the promoter/enhancer regions of OXPHOS genes. Our data also indicated TEAD4′s oncogenic role in prostate cancer and its knockdown compromises the growth of castration-resistant prostate cancers. These results shed light on the fundamentals of OXPHOS gene regulation by metabolite and uncover TEAD4 as a potential therapeutic target for prostate cancer.