香港城市大學
City University of Hong Kong
專業 創新 胸懷全球
Professional · Creative
For The World

# City University Distinguished Lecture Series

Speaker

## Professor Wen-Hwa Lee

*Chancellor of China Medical University, Taiwan*
*Fellow of Academia Sinica*

# Aberrant sugar metabolism triggers pancreatic oncogenesis through *KRAS* mutation

**on**

**Monday, 5 November 2018 at 4:30 pm**

**at**

**Senate Room**
**19/F Lau Ming Wai Academic Building**
**City University of Hong Kong**
**Tat Chee Avenue, Kowloon**

## *Abstract*


Pancreatic ductal adenocarcinoma (PDAC) is the highest mortality among all cancers, with a median survival of ~6 month and a 5-year survival rate of < 8%. PDAC exhibits few early symptoms, and over 80% of PDAC patients are diagnosed at a late stage beyond the curative resection treatment window when cancer cells have already metastasized, highlighting the need of fully understanding of this disease.

It is known that lesions in the *KRAS* gene are the earliest and the most frequently found in 92-3% of PDAC samples, and are required for both initiation and maintenance of PDAC. However, how KRAS mutation is triggered, why the mutation frequency of KRAS is preferentially high in PDAC, and what kind of factors are involved in KRAS mutation remain largely unknown. Since pancreas does not directly contact with potential carcinogens from air, food, and viral or bacterial pathogens, the most likely factors may be derived from metabolites. There are circumstantial evidences that abnormal carbohydrate metabolism seen with diabetes and impaired glucose tolerance associates with an elevated risk of pancreatic cancer. Under high-glucose conditions, cellular O-GlcNAcylation is significantly elevated in pancreatic cells that exhibit lower phosphofructokinase (PFK) activity than other cell types. This post-translational modification specifically compromises ribonucleotide reductase (RNR) activities leading to imbalance of dNTP pools, genomic DNA alterations with KRAS mutations, and transformation of cells. These results provide a mechanistic view of how aberrant sugar metabolism triggers *de novo* KRAS mutation in pancreatic cell and how dietary high sugar links to cancer in pancreatic cells.


## *Biography*

Professor Wen-Hwa Lee, born in Taiwan in 1950, is a molecular biologist and pioneer in the field of tumor suppressor in cancer research. In 1987, he discovered the first human tumor suppressor gene (TSG), Retinoblastoma gene (Rb). Up to now, he has continued his cancer research and made a great contribution to this field. Professor Lee completed most of his fundamental education in Taiwan. In 1981, he received his PhD in molecular biology from University of California, Berkeley. With his expertise in cancer biology, he had been on the faculty of UC San Diego, UT Health Science Center, and UC Irvine for 30 years. Professor Lee is the elected fellow of Academia Sinica, Taiwan, Texas Hall of Fame in Science, American Association for the Advancement of Science (AAAS), The World Academy of Sciences (TWAS), and National Academy of Inventors (NAI) in the United States of America. Currently, he serves as the Chancellor of China Medical University (CMU) in Taiwan.

**Online registration:**
**http://www.cityu.edu.hk/vprt/distinguished_lecture_series/upcoming.htm**


**Enquiries:**
Office of the Vice-President
(Research and Technology)
Tel: 3442 9049
Fax: 3442 0322
Email: vprtdl@cityu.edu.hk