Institute of Chemistry
Academia Sinica

Sunney Chan Lecture

Sunney Chan Lecturer

2004 – Douglas C. Rees
2005 – Gary W. Brudvig
2006 – Harry B. Gray
2007 – Carolyn R. Bertozzi
2008 – Dennis A. Dougherty
2009 – Edward I. Solomon
2010 – Michael P. Sheetz
2011 – Michael A. Marletta
2013 – James C. Liao
2014 – Kenneth D. Karlin
2015 – Chad A. Mirkin
2017 – David Milstein
2018 – Jennifer A. Doudna
2019 – Mark E. Davis
2020 – Peter H. Seeberger
2023 – Michael K. Rosen
2024 – Joseph J. Falke

Lipid Signals in Immunity and Cancer: Insights from Single Molecule Biophysics

Lipid signaling pathways on cell membrane surfaces control a wide array of cell processes in health and disease. These pathways begin with cell surface receptors or intracellular sensors that activate lipid kinase enzymes on the target membrane. The kinases, in turn, generate signaling lipids that diffuse in the membrane plane, recruit downstream signaling proteins, and trigger a cascade of pathway activation and information transfer. My talk will describe our recent studies of three lipid signaling pathways central to immune cell migration, engulfment of pathogens, cell growth and renewal, and oncogenesis. Our approach begins by reconstituting each signaling pathway from purified components on the target membrane. Subsequently, we use tools of single molecule biophysics developed by our lab and others to monitor the membrane-bound signaling proteins and directly measure their 2-dimensional diffusion, interactions, activation, and output lipid signals in real time. This approach provides fundamental new insights that expand our basic understanding of lipid signaling on molecular, dynamic, and mechanistic levels. Such understanding may also facilitate new therapeutics that target defective lipid signaling in autoimmune and inflammatory disorders, and in many human cancers.

The 17th Annual
Sunney Chan Lecture

2024
09/24 14:30
Venue: Ta-shue Chou Memorial Hall

Joseph J. Falke

Department of Biochemistry
University of Colorado, Boulder

Lipid Signals in Immunity and Cancer: Insights from Single Molecule Biophysics

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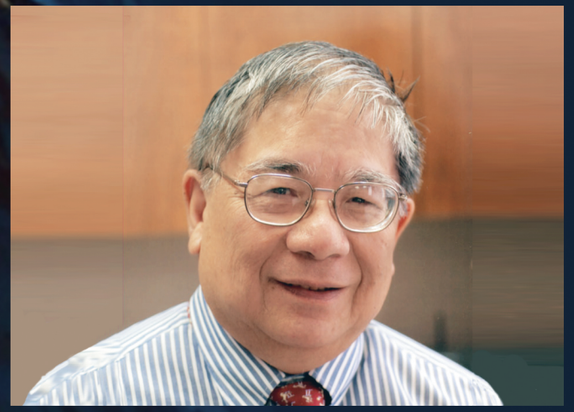

The Sunney Chan lecture was established at Academia Sinica in 2003 to honor Sunney for his six years of dedicated service to Academia Sinica and Taiwan during his term as Vice President of Research at Academia Sinica. Sunney took an early retirement from Caltech in 1997, where he spent essentially the bulk of his professional career, to work in Taiwan. Aside from rebuilding the Institute of Chemistry in a modern image, he established the Taiwan International Graduate Program and led the development of biotechnology in Taiwan. He helped the National Science Council of Taiwan put together the National Research Program in Genomic Medicine to promote basic and applied research in genomics, proteomics, and bioinformatics within the life science community in Taiwan. He also led the effort to create a Research Center on Genomics at Academia Sinica. Largely through Sunney's vision and hard work, Taiwan has now in place a research infrastructure to promote and support research in biomedical sciences and modern life sciences on this Island.

As expected, Sunney has also been active in the chemical community, promoting modernization of the undergraduate curriculum in chemistry, raising the standards of graduate research in the national universities, nurturing young scholars and junior faculty, and pointing the way to improving the infrastructure for basic and applied research in the molecular sciences. He has been particularly inspirational to young scientists, and the generosity, with which he has shared his chemistry, insights about science, wisdom on life, and his knowledge about wine, food, gourmet dining, and restaurants, is well known throughout the community here.

In recognition of these efforts, President Yuan T. Lee has established the Sunney Chan Lecture in Chemical Biology in order to bring to the Taiwan Scientific Community an eminent scientist who best exemplifies Sunney's enthusiasm as a scientist, teacher and mentor, and his devotion to public service.

The 2024 Lecturer

Joseph J. Falke

Joseph J. Falke was a National Merit Scholar at Earlham College where he received his B.A. in Chemistry in 1978 with admission to Phi Beta Kappa Honor Society. He was a National Science Foundation Graduate Fellow in the laboratory of Sunney I. Chan at Caltech where in 1984 he completed his Ph.D. and received the McKoy Award for Outstanding Ph.D. Thesis in Chemistry. His Ph.D. research with Chan developed and applied a ^{35}Cl NMR approach to elucidate structural and mechanistic features of the human red blood cell membrane anion exchange transporter (Band 3 / AE1). Subsequently, from 1985-87 he was a National Institutes of Health Postdoctoral Fellow in the laboratory of Daniel E. Koshland, Jr. at UC Berkeley where he began the development of site-directed cysteine and disulfide methods and applied them to the study of bacterial chemoreceptors. In 1987, Falke started his independent laboratory at the University of Colorado, Boulder in the Department of Chemistry and Biochemistry. In 1999 he became Full Professor and founded the University of Colorado Interdepartmental Molecular Biophysics Program with 43 member laboratories in 5 departments, serving as Director from 1999-2024 and now as Co-Director. In 2001, he was Chair of the Annual Biophysical Society Meeting (Boston), was elected Society President in 2007, and was named Society Fellow in 2015. Since its inception, the Falke Laboratory has developed new physical / chemical methods and has used them to probe structure, dynamics and mechanism in membrane-based cell signaling pathways. Early studies applied site-directed cysteine and disulfide engineering and other biophysical-biochemical approaches to investigate bacterial chemoreceptors and their receptor-kinase lattice. This work revealed the piston transmembrane signaling and electrostatic adaptation mechanisms of bacterial chemoreceptors, as well as the ultrastability of their receptor-kinase lattice.

The next phase of research developed FRET, EPR and EPR-guided molecular dynamics methods to investigate two membrane targeting domains each found in hundreds of human signaling proteins: the Ca^{2+}-activated C2 domain and the PIP-lipid sensing pleckstrin homology (PH) domain. These efforts yielded C2 and PH domain membrane-binding thermodynamics, kinetics, lipid specificities, docking geometries, and 2-D surface search mechanisms. The latest phase of research has developed single molecule fluorescence methods to investigate three essential human lipid signaling pathways reconstituted on their target membranes: the Ca^{2+}-PKC-MARCKS-PI3K(I)-PIP_3-PDK1-AKT1 pathway of innate immunity, cell growth, and oncogenesis; the GTP-Rab5-PI3K(III)CII-PI3P-p40Phox pathway of phagocytosis; and the GTP-Rab1-PIP-PI3K(III)CI-PI3P- (PX/FYVE/WD40) pathway of autophagy. This ongoing research provides a new window into the dynamics and regulatory mechanisms of each pathway, thereby advancing the molecular understanding of lipid signaling and revealing potential targets for therapeutics.

Selected Honors and Awards

- Career—130+ Publications
- Career—150+ Seminars
- Career—20+ NIH Study Sections
- CU College Scholar Award, 2018
- Biophysical Society Fellow, 2015
- President, Biophysical Society, 2007
- Chair, SGP Woods Hole Meeting, 2006
- Chair, Keystone Membrane Protein Meeting, 2003
- Feigen Lecturer, Stanford University, 2003
- Chair, Biophysical Society Meeting, 2001
- NIH Postdoctoral Fellow, 1985-87
- NSF Predoctoral Fellow, 1979-82
- National Merit Scholar, 1974-78