CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
R1103

Project Title:
Recruitment of First-Time, Tenure-Track Faculty Members

Award Mechanism:
Recruitment of First-Time, Tenure-Track Faculty Members

Principal Investigator:
Yu, Yonghao

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Dr. Yonghao Yu is an analytical biochemist who uses quantitative mass spectrometric techniques to uncover how signal transduction networks wire in cancer cells.

Born and raised in Shanghai, he inherited his passion for science and engineering from his father, who is a mechanic engineer. Dr. Yu later became fascinated by molecules, leading him to pursue his Bachelor's degree in Chemistry at Fudan University. He was named a "Chun-Tsung Scholar" by the Hui-Chun Chin and Tsung-Dao Lee Endowment, and performed undergraduate research in design and characterization of nanoporous materials.

Never having left the city of Shanghai, his first long trip in fact took him over the Pacific Ocean to the San Francisco Bay area in 2001, to attend graduate school at the University of California, Berkeley. There he joined the lab of Dr. Julie Leary in the Department of Chemistry and began his career as an analytical chemist. He developed FT-ICR mass spectrometric techniques to characterize protein-protein, protein-carbohydrate and protein-drug interactions. In addition, he design and developed the first general method for pinpointing protein tyrosine sulfation. He characterized the sulfation pattern of a series of human chemokine receptors. The results led to a critical understanding of the role of tyrosine sulfation in regulating proteinprotein interaction.

To pursue postdoctoral training, he joined Steve Gygi and John Blenis labs in the Department of Cell Biology at Harvard Medical School where he continued to be involved in mass spectrometry technology development and its application in the field of cancer signal transduction. In the first project, he developed a multiplexed, mass-spectrometry-based in vitro kinase assay which allows concurrent measurement of hundreds of site-specific peptide phosphorylation rates, reporting a diagnostic fingerprint for activated kinase pathways. He applied this unique kinome-activity profiling strategy in a variety of cellular settings, including mitogen stimulation, cell cycle, pharmacological inhibition of pathways, and to a panel of breast cancer cell lines. Using this technology, he also made a novel discovery that PI3K regulatory subunit is phosphorylated by Src in vivo. These results might provide a novel mechanism formodulating the activity of the PI3K pathway, which is one of the most frequently mutated pathways in human cancers.

His second project as a postdoctoral fellow is focused on the mTOR signaling. The evolutionarily conserved Ser/Thr kinase mTOR exists in two complexes, mTORC1 and

mTORC2, which play a critical role in regulating cell growth, proliferation, migration and survival. Numerous upstream genetic alterations converge on mTOR, leading to its hyperactivation in a broad spectrum of human cancers. Functional characterization of the mTOR signaling pathways, however, has been hampered by the paucity of known substrates. Using SILAC-based quantitative phosphoproteomics, he characterized for the first time the mammalian TOR phosphoproteome (both mTORC1 and mTORC2) and identified hundreds of previously unknown targets of mTOR. These results provided critical insights to how mTOR signals downstream and contributes to tumorigenesis.

At UT southwestern, Dr. Yu will continue to develop novel mass spectrometric technologies and characterize cancer signal transduction. By performing these experiments, he hopes to provide better strategies for therapeutic intervention of human cancers.