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Biography : Dr. Wenshe Ray Liu completed his BS degree in Peking University in 2000 and his PhD in the University of California, Davis in 2005. After two-year postdoctoral work in the Scripps Research Institute, he started his independent career at Texas A&M University in 2007. How is now a full professor, the current holder of the Gradipore Chair in chemistry, and the director of Texas A&M Drug Discovery Laboratory.

Abstract title: Phage-displayed noncanonical amino acids for drug discovery

Abstract: Phage display is a widely used tool for the selection of peptides from large, combinatorial peptide libraries. Its unique biology that physically links displayed peptides to their coding DNAs allows rapid enrichment and identification of peptides that bind potently to selected therapeutic targets. Although powerful, the phage display technique has its intrinsic limitations. Phages rely on bacterial hosts for production and therefore confine their displayed peptides to 20 canonical amino acid building blocks that have limited chemical diversity. Phage-displayed peptides are usually linear and unstructured leading to concerns such as low binding affinities to targets due to entropy penalty and proneness to proteolytic digestion when used in vivo. Although methods based on chemical modifications of canonical amino acids have been developed to expand chemical diversity and implement conformational constraints to phage-displayed peptides, they are limited by chemistry available to canonical amino acids. In this presentation, we will describe our recent progress in the integration of the phage display technique with the amber suppression-based noncanonical amino acid mutagenesis technique for drug discovery. By incorporating a Michael acceptor noncanonical amino acid into phage display peptides that also contained a preinstalled cysteine, we showed that peptides were simultaneously cyclized for selection of potent cyclic peptide inhibitors of HDAC8. Using a genetically incorporated butyryl-lysine in phage-displayed peptides to serve as an anchor to bind SIRT2, several potent ligands with nanomolar K_d values were selected. Inhibitors derived from these ligands have IC_{50} values as low as 10 nM.