ACS Local Section
New York
Long Island Subsection

A PCSK9 Vignette: from mRNA Display to Passively Permeable Macrocycles

Dr. Yuhua Huang
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Tuesday, March 17th, 2026
6:30-7:30 PM on Zoom
Register to receive Zoom link:
https://suny-ow-edu.zoom.us/meeting/register/CfGdysD_QEuXnIy8bkUdtg

Abstract: PCSK9 inhibition is a validated strategy for lowering LDL-cholesterol, yet current antibody therapies require injections, underscoring the need for oral alternatives. Using mRNA display, we identified macrocyclic peptide binders to the PCSK9:LDL-R interface and applied structure-guided optimization to enhance potency, stability, and physicochemical properties, ultimately enabling advancement of the formulation-enabled candidate MK-0616. In parallel, iterative design—incorporating strategies such as cross-linking and targeted reduction of hydrogen-bond donors to promote passive permeability—yielded the first PCSK9 macrocycles with measurable MDCKII/PAMPA permeability and low but quantifiable oral bioavailability.

Biography: Dr. Yuhua Huang received a Master's degree from the University of Minnesota and a Ph.D. from Rutgers University. As a co-inventor of Victrelis (boceprevir), the first-in-class HCV NS3 protease inhibitor, and narlaprevir, a second-generation protease inhibitor developed by R-Pharm, her contributions were recognized with the Schering-Plough President's Award (2002) and the Thomas Alva Edison Patent Award (2006). Her recent work on delivering high-quality molecules to advance drug discovery across stages and modalities was presented at the 27th American Peptide Symposium in 2022.

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