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Prof. Mei Hong

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Mei Hong obtained her BA degree in chemistry with *summa cum laude* from Mount Holyoke College in 1992 and her PhD from the University of California, Berkeley in 1996 (with Professor Alex Pines). After a one-year postdoctoral stint in Bob Griffin's lab at the Massachusetts Institute of Technology, she began her independent career at the University of Massachusetts, Amherst, before moving to Iowa State University in 1999. She became a full professor in 2005, held the first John D. Corbett Professorship in 2007-2010, and returned to MIT as a full professor in 2014. Mei Hong has received numerous awards for her creative development and application of solid-state NMR spectroscopy to elucidate the structure, dynamics and mechanism of membrane proteins, amyloid proteins and other biological macromolecules such as plant cell walls. Current research interests include membrane-bound ion channels and transporters involved in infectious diseases, structures and dynamics of the protein tau, and development of 19F NMR and other multinuclear NMR techniques for structural investigation.

Structures and Dynamics of the SARS-CoV-2 Envelope Protein from Solid-State NMR

Enveloped viruses encode membrane-bound ion channels, also called viroporins, that are important for the lifecycle and pathogenicity of these viruses. Elucidating the structure, dynamics and mechanism of action of these viroporins is important for advancing fundamental knowledge about ion channels as well as for developing antiviral drugs. Solid-state NMR spectroscopy is well suited to studies of small viral ion channels bound to phospholipid bilayers that mimic the native membrane in which these proteins function. In this talk Prof. Hong will present her lab's latest structure determination of the SARS-CoV-2 envelope (E) protein, a cation-conducting channel that is associated with the inflammation response of the cell to SARS-CoV-2 infection. Using multidimensional solid-state NMR and 19F-based distance measurements, they have determined the membrane-bound E structures at neutral pH and at acidic pH in the presence of calcium. These two structures show important differences in the N-terminal and C-terminal polar segments of the helical bundle, which give insight into the activation mechanism of this viroporin. Hexamethylene amiloride (HMA) is a known inhibitor of the E channel. Measurement of protein-drug distances using 19F-enhanced solid-state NMR techniques shows that HMA surprisingly binds the protein-lipid interface instead of the channel pore. This binding mode differs from the well-known amantadine binding to the pore of the influenza M2 proton channel. We discuss this HMA binding result in terms of an aromatic belt in the middle of the E channel, the distinct hydrophobic character of E from influenza M2, and the implication of the HMA binding mode for future design of E-targeting antiviral drugs to treat COVID infections.