The phospholipase A₂ (PLA₂) superfamily exhibits a large array of functions, but of special interest is the inflammatory cascade which is initiated by the release of free arachidonic acid by some types of phospholipase A₂, all of which interact with membrane phospholipids. However, different PLA₂ types have unique three-dimensional structures and unique catalytic residues as well as specific tissue localization, distinct biological functions, and with which membrane phospholipids have unique allosteric interactions. Understanding how the different PLA₂s associate with phospholipid membranes, specific phospholipid substrate molecules, and inhibitors on a structural and molecular basis has advanced in recent years due to the introduction of hydrogen/deuterium exchange mass spectrometry approaches. We will emphasize recent results utilizing hydrogen/deuterium exchange approaches and molecular dynamics on the major types of PLA₂, including secretory s-PLA₂, cytosolic c-PLA₂, lipoprotein-associated LpPLA₂, and calcium-independent iPLA₂ with inhibitors and substrates. We will also discuss new results on the precise nature and molecular dynamics of the interaction of these enzymes with specific substrate phospholipids pulled into the catalytic site from membranes and how new potent specific inhibitors block substrate phospholipid binding. Phospholipase A₁ is the initiator of eicosanoid formation in inflammatory processes, so it is a critical enzyme and inhibitors could provide new approaches to disease treatment.

Biography
Edward A Dennis is a distinguished Professor of Chemistry and Biochemistry and of Pharmacology in the School of Medicine at the University of California at San Diego (UCSD). He received his BA from Yale and a PhD from Harvard and was a Post-doctoral fellow at Harvard Medical School. He has served as Chair of the Department of Chemistry and Biochemistry. His research focus has been on the mechanism of the enzyme phospholipase A₂, signal transduction, inflammation, lipid metabolism, eicosanoid action, and lipidomics. He authored over 380 publications, is Editor-in-Chief of the Journal of Lipid Research and Director of the LIPID MAPS Consortium.

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