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Integration of geonomics, proteomics, and metabolomics in the systems biology of lipid metabolism and signaling

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Abstract

The omics evolution began at the end of the 20th century with the cloning of the human genome. The 21st century has already seen the development of comprehensive proteomics analyses, but the emerging evolution is to metabolomics, the definition of which is the identification and quantification of all of the molecular constituents of the cell including its nucleic acids, amino acids, sugars, and fats. But by far, the largest number of distinct molecular species in cellular metabolism lies in the fats (or lipids) where tens of thousands of distinct molecular species exist in cells and tissues [Dennis, Proc.Natl.Acad.Sci.*U.S.A.*, **106**, 2089-2090 (2009)]. We have now applied novel liquid chromatographic-mass spectrometric based lipidomics techniques termed "CLASS" [Harkewicz & Dennis, Annual Reviews of Biochemistry, **80**, 301-25 (2011)] generally in the context of an overall omics analysis of immunologically-activated macrophages integrating transcriptomics, proteomics, and metabolomics of lipid metabolites [Dennis et al, J Biol Chem, **285**, 39976-85 (2010)]. As part of the LIPID MAPS Consortium [www.lipidmaps.org], our laboratory has developed a robust and comprehensive approach to the lipidomics analysis of hundreds of fatty acids, acylethanolamines and inflammatory eicosanoids, including their numerous metabolites arising from an array of cyclooxygenases, lipoxygenases, cytochrome P450s and non-enzymatic oxidation producing isoprostanes, as well as combinations thereof [*J. Lipid Res.* **50**, 1015-1038 (2009)]. We will discuss the application of lipidomic analysis to characterize cellular lipid signaling of Toll-like (TLR) and purinergic receptors and their "synergy" in endotoxin stimulated macrophages as models for inflammation and infection [*J. Biol. Chem.*, **282**, 22834-22847 (2007)]. New results comparing various primary macrophages [*J Leukocyte Biology*, **90**, 563-74 (2011)] and analysis of the fluxes of metabolites as well as "directed proteomics" [*Mol Cell Proteomics*, **11**, M111.014746, 1-9 (2012)] of the system will be presented. Also lipidomic analysis of cells supplemented with small amounts of the omega-3 fatty acids eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA) provides information on the overall effects of EPA and DHA on the inflammatory eicosadome [*Proc Natl Acad Sci U S A*, **109**, 8517-22 (2012)]. Human plasma has also been profiled to quantify almost six hundred distinct lipid molecular species present across all mammalian lipid categories and the implications for the future of clinical medicine and the understanding of the mechanisms of disease will be discussed [Quhenberger & Dennis, New Eng J Med, **365**, 1812 (2011)]. [Supported by LIPID MAPS Glue Grant U54 GM069338, R01 GM020501, and R01 GM064611]

Biography

Edward A. Dennis is 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 University in 1963 and a Ph.D. from Harvard University in 1967, a Doctorate in Medicine (honorary) from Goethe University in Frankfurt in 2008, and he served as a Research Fellow at Harvard Medical School.