Raft Busters: A Molecular Role for DHA in Biological Membranes?

Jacob J. Kinnun[1], Justin A. Williams[1], William Stillwell[2], Robert Bittman[3], Saame Raza Shaikh[4], and Stephen R. Wassall[1]

[1]Department of Physics, Indiana University–Purdue University, Indianapolis, IN 46202
[2]Department of Biology, Indiana University–Purdue University, Indianapolis, IN 46202
[3]Department of Chemistry and Biochemistry, Queens College of CUNY, Flushing, NY 11367
[4]Department of Biochemistry and Molecular Biology and East Carolina Diabetes and Obesity Institute, East Carolina University, Greenville, NC 27834

Dietary consumption of fish oils rich in omega-3 polyunsaturated fatty acids (n-3 PUFAs), such as docosahexaenoic acid (DHA, 22:6), has a wide variety of health benefits. However, a complete molecular mechanism is yet to be elucidated. One model that has emerged from biochemical and imaging studies of cells postulates that n-3 PUFAs are taken up into phospholipids in the plasma membrane of cells and, due to their high disorder and aversion for cholesterol, reorganize lipid rafts. Lipid rafts are ordered domains within biological membranes which contain high amounts of sphingomyelin (SM) and cholesterol. To investigate this model, we studied lipid bilayers composed of SM, PDPC (a DHA-containing phospholipid), and cholesterol (1:1:1 mol). The molecular organization of each lipid was investigated with solid-state ^{2}H NMR using deuterated analogs of the lipids. Spectral components assigned to ordered raft-like domains and disordered non-raft domains were resolved, from which the composition of the domains and the order within them could be determined. Most of the SM (84%) and cholesterol (88%) was found in the raft-like domain, together with a substantial amount of PDPC (70%). Despite the infiltration of PDPC there appears to be minimal effect on the order of SM or cholesterol. We speculate that PDPC molecules sequester into small groups minimizing the contact of DHA chains with cholesterol, thereby interrupting the continuity of the raft-like environment.