**SAM-1**

## CHOLESTEROL: A MULTIFACETED PHOTOOXIDIZABLE LIPID

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Unesterified cholesterol (Ch) is found in all membrane compartments of mammalian cells, most of it in the plasma membrane (PM). Like all unsaturated lipids, Ch is susceptible to oxidation, either physiological (e.g. enzymatic hydroxylation associated with steroid hormone and vitamin D synthesis) or potentially pathological (non-enzymatic conversion to hydroperoxides (ChOOHs) and other oxides). The latter aspect has attracted considerable interest over the past half-century, including interest in photosensitized Ch oxidation. Some key findings from work beginning in the 1950s are that (a) photogenerated ChOOHs, like phospholipid hydroperoxides (PLOOHs), disrupt PM structure/function, as observed in numerous erythrocyte model studies; and (b) individual ChOOH positional isomers can serve as *in situ* mechanistic reporters, 5α-OOH and 6α/β-OOH indicating singlet oxygen ($^1O_2$) intermediacy (Type II reactions) and 7α/β-OOH free radical intermediacy (Type I reactions). Development of cutting-edge analytical techniques such as HPLC with chemiluminescence detection or reductive electrochemical detection has greatly facilitated analysis of these species in cells and other complex systems. PLOOHs may also be used as reporters, but product analysis is more difficult than with ChOOHs. Of added interest, [$^{14}$C]Ch exchanged into a cell PM can serve as a highly sensitive *in situ* probe for free radical lipid peroxidation triggered by iron-catalyzed reduction of $^1O_2$-generated lipid hydroperoxides. It was recently recognized that ChOOHs can undergo spontaneous and protein-facilitated transfer between membranes, which greatly expands their cytotoxic and redox signaling ranges. Each of these aspects will be discussed from a photochemical biology perspective. (Grant support: NIH CA70823, CA72630)