Consequences of oxidation of plasma membrane lipids in cultured cells

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The lipid bilayer is a key site for oxidative damage; unsaturated lipids are particularly labile to oxidation. In vitro models have demonstrated that oxidation alters key properties of the lipid bilayer including permeability, morphology, and phase state. However, it remains unclear to what extent oxidation persists in the membranes of living cells, which incorporate mechanisms for preventing oxidative damage and regenerating plasma membrane lipids. Here, we expose cells in culture to a variety of oxidative environments, extract lipids from their plasma membranes, and use lipidomic techniques to quantify the extent of oxidation.

In our previous work, we have shown that at low degrees of oxidation (fewer that 3% of unsaturated lipids oxidized), bilayers demonstrate radically increased permeability to small molecules. This represents a potentially catestrophic compromising of the barrier properties of the plasma membrane. Oxidation is also capable of radically altering the morphology of lipid bilayers, altering the dimensions of lipids in a manner that leads to changes in membrane tension and subsequent pore formation. Similary, oxidation can lead to processes that inhibit the capacity of lipid bilayers to form high-curvature structures.

To better model modes of oxidative damage to the cellular plasma membrane, we have exposed cells in culture to both chemical oxidation and growth in a high oxygen partial pressure environment. Cell viability was analyzed and lipids were extracted from the cell to assess the mechanical properties and permeability of lipid bilayers constructed from them. Extracted lipids were also subject to lipidomic analysis to clarify the compositional changes that occur in plasma membranes in an oxidative environment.