**THE PROTECTIVE ROLE OF PRX1 IN THE ATHEROSCLEROSIS BY REGULATING MACROPHAGE LIPOPHAGIC FLUX**

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**Objective:** Oxidative stress activates macroautophagy/autophagy and contributes to atherogenesis via lipophagic flux, a form of lipid removal by autophagy. However, it is not known exactly how endogenous antioxidant enzymes are involved in lipophagic flux.

**Method:** Consistent with this observation, apoe −/− mice transplanted with bone marrow from prdx1−/−apoe−/− mice had increased plaque formation compared with apoe−/− BM-transplanted recipients.

**Results:** Prdx1-deficient macrophages had higher intracellular cholesterol mass and lower cholesterol efflux compared with wild type. This perturbation in cholesterol homeostasis was due to impaired lipophagic cholesterol hydrolysis caused by excessive oxidative stress, resulting in the inhibition of free cholesterol formation and the reduction of NR1H3 (nuclear receptor subfamily 1, group H, member 3) activity. Notably, impairment of both lipophagic flux and cholesterol efflux was restored by the 2-Cys PRDX-mimics ebselen and gliotoxin.

**Conclusion:**We demonstrate that the antioxidant PRDX1 (peroxiredoxin 1) has a crucial role in the maintenance of lipophagic flux in macrophages. PRDX1 is more highly expressed than other antioxidant enzymes in monocytes and macrophages. We determined that Prdx1 deficiency induced excessive oxidative stress and impaired maintenance of autophagic flux in macrophages. This study reveals that PRDX1 is crucial to regulating lipophagic flux and maintaining macrophage cholesterol homeostasis against oxidative stress. We suggest that PRDX1-dependent control of oxidative stress may provide a strategy for treating atherosclerosis and autophagy-related human diseases.