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Macrophage antioxidant protection within atherosclerotic plaques.

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Abstract

Macrophage cells within inflammatory lesions are exposed to a wide range of degrading and cytotoxic molecules including reactive oxygen species. Unlike neutrophils, macrophages do not normally die in this environment but continue to generate oxidants, phagocytose cellular remains, and release a range of cyto-active agents which modulate the immune response. It is this potential of the macrophage cell to survive in an oxidative environment that allows the growth and complexity of advanced atherosclerotic plaques. This review will examine the oxidants encountered by macrophages within an atherosclerotic plaque and describe some of the potential antioxidant mechanisms which enable macrophages to function within inflammatory lesions. Ascorbate, a-tocopherol, and glutathione appear to be central to the protection of macrophages yet additional antioxidant mechanisms appear to be involved. Gamma-Interferon causes macrophages to generate 7,8-dihydroneopterin, neopterin and 3-hydroxyanthranilic acid both of which have antioxidant properties. Manganese superoxide dismutase is also upregulated in macrophages. The evidence that these antioxidants provide further protection, so allowing the macrophage cells to survive within sites of chronic inflammation such as atherosclerotic plaques, will be described.