Granulocyte Macrophage Colony-Stimulating Factor Plays a Priming Role in Murine Macrophage Growth Induced by Oxidized Low Density Lipoprotein

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INTRODUCTION

One of the characteristic events in the atherosclerotic lesion is the proliferation of cellular components. It is generally accepted that smooth muscle cells migrated from media into intima proliferate in the atherosclerotic lesions. It was recently demonstrated, however, that macrophages also proliferate in the early stage of atherosclerotic lesions.¹

Using an *in vitro* culture system, we have shown that macrophages obtained from mouse,²⁻⁵ rat,⁶ and human⁷ are able to proliferate upon incubation with oxidized LDL (Ox-LDL). It then becomes clear that the specific uptake of lysophosphatidylcholine (lyso-PC) of Ox-LDL through the macrophage scavenger receptor type A-I/A-II (MSR-AI/AII) is essential for Ox-LDL-induced macrophage proliferation.^{3,5,7} The activation of protein kinase C (PKC) was also shown to be involved in this phenomenon.⁸ These *in vitro* observations strongly suggest that Ox-LDL acts as a growth factor for macrophage *in vivo*. The present study was undertaken to elucidate the molecular cascade(s) leading to Ox-LDL-induced macrophage proliferation. The results indicate that Ox-LDL-mediated release of granulocyte macrophage colony-stimulating factor (GM-CSF) from macrophages may play an important role in macrophage proliferation.

MATERIALS AND METHODS

Cell Culture

Murine peritoneal macrophages were collected from male DDY mice with 8 ml ice-cold PBS and suspended in RPMI 1640 supplemented with 10% heat-inactivated

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