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[Novel type of antimicrobial mechanism in host macrophages against mycobacterial infections].

[Article in Japanese]

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Source

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Abstract

Macrophages (M(phi)s) play a central role as anti-microbial effector cells in the expression of host resistance to mycobacterial infections. With respect to antimicrobial effector molecules of host M(phi) against mycobacterial pathogens, recent studies suggest the possibility that the reactive nitrogen intermediates (RNI)--and reactive oxygen intermediates-independent antimycobacterial mechanism(s) may be crucial for the antimycobacterial function of host M(phi). In this context, we previously found that free fatty acids (FFAs) such as arachidonic acid (AA) and linolenic acid exhibited potent antimicrobial activity against mycobacterial organisms, including Mycobacterium tuberculosis (MTB) and Mycobacterium avium complex (MAC). In addition, FFAs in combination with RNI played critical roles in manifestation of the activity of M(phi) against mycobacterial organisms. Moreover, our recent studies have shown the following findings. First, anti-MTB activity of IFN-gamma-activated M(phi)s was specifically blocked by arachidonyl trifluoromethylketone (aTFMK), an inhibitor of cytosolic phospholipase A2 (cPLA2). Second, ATP potentiated the anti-MAC bactericidal activity of M(phi)s cultivated in the presence of clarithromycin and rifamycin. This effect of ATP was closely related to intracellular Ca2+ mobilization and was specifically blocked by aTFMK. Third, intramacrophage translocation of membranous AA molecules to MAC-containing phagosomes was also specifically blocked by aTFMK. In the confocal microscopic observation of MAC-infected M(phi)s, ATP enhanced the intracellular translocation of cPLA2 into MAC-containing phagosomes. These findings suggest that FFAs (especially AA) produced by the enzymatic action of cPLA2 play important roles as antimycobacterial effectors in the expression of M(phi) antimicrobial activity against mycobacterial pathogens.

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