Myeloperoxidase-induced Modification of Phosphatidylserine

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Polymorphonuclear leukocytes release the heme enzyme myeloperoxidase at inflammatory sites. This enzyme binds to the surface of apoptotic and necrotic cells, but not to vital cells. Phosphatidylserine epitopes were determined as binding domain for myeloperoxidase on non-vital cells as revealed by flow cytometry and confocal fluorescence microscopy. Upon phagocytosis of non-vital polymorphonuclear leukocytes by macrophages, conditions will be created in the phagosomes favoring a high activity of myeloperoxidase such as production of hydrogen peroxide and acidic pH value. The myeloperoxidase product hypochlorous acid (HOCl) as well as the myeloperoxidase-hydrogen peroxide-chloride system convert the serine residue in phosphatidylserine into an aldehyde and nitrile species at neutral and acidic pH values as shown by MALDI-TOF mass spectrometry. The reaction includes the formation of transient *N*-monochlor- and *N*-dichloramines as well as the formation of a chlorimine derivative. Decay rates of these transient products were determined by UV-VIS spectroscopy using O-phospho-L-serine as model substance. Other amines and ammonia ions may interfere with this pathway due to a transhalogenation reaction. In case of ammonia ions, the lipophilic, membrane permeable monochloramine (NH_2Cl) is produced. Thus, myeloperoxidase is able to modify phosphatidylserine. Some of the products are assumed to be involved in regulation of cell functions during inflammation.