

NITRATE/NITRITE AND PEROXYNITRITE IN SARCOIDOSIS, RELATED TO MYCOBACTERIA'S STATIONARY-PHASE

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Sarcoidosis SA is a granulomatous disease with unknown etiology. We recently evidenced that the same mycobacterial heat shock proteins (Mtb-HSPs), especially HSP16, the main marker of dormant stage of mycobacteria, occurring in sarcoid tissues and in precipitated immune complexes CIs were inducing immune response dependently on different genetic background of host (HLA and non-HLA-NRAMP, FCGRIIA, IIC, IIIA), developing acute sarcoidosis/Lofgren syndrome, chronic SA, latent or active TB. In contrast to TB, decreased clearance of antigens CIs by resistant to apoptosis monocytes with their decreased production of microbicidal degradable nitric oxide were detected in sarcoidosis. Because a low level of nitrate nitrite NO_x may result from a rapid reaction of NO_x and superoxide with following production of peroxynitrite ONOO⁻, we evaluated NO_x and ONOO⁻ levels in supernatants of PBMC cultures treated with Mtb-hsp from SA patients TB patients and healthy volunteers using Griess and rhodamine fluorescence methods. We found a significantly increased NO_x and ONOO⁻ concentrations with and without Mtb-hsp stimulation in SA and TB than in controls but significantly lower NO_x and higher ONOO⁻ levels after Mtb-hsp induction were shown SA than TB. In summary, in contrast to active TB lower level of NO_x may induce M tuberculosis genetic dormancy program via higher Mtb-hsp expression in SA. Following increased ONOO⁻ concentration induced by Mtb-hsp may explain the low level of NO_x and initiate an (auto)immune response in SA related to mycobacteria stationary-phase. Funding grant 5160/B/P01/2010/39 to A D and N-N401-047137 to L.K.