

P016 Tyrosine denitrase activity is enhanced by an inflammatory stimulus

Grace Osoata, Ian M. Adcock, Peter J. Barnes, Kazuhiro Ito

Airway Disease, NHLI, Imperial College

The formation of 3-nitrotyrosine residues has been shown to be a marker for oxidative damage in the pathogenesis of various diseases, such as atherosclerosis, Alzheimer disease and chronic inflammatory lung diseases. It has also been reported that nitration of proteins at tyrosine residue alter protein function and fate, and cause amplified inflammation. Here we demonstrate that a putative 'protein denitrase' activity, which catalyzes denitration of nitrotyrosine deposits on proteins, are detected in crude nuclear extracts of cultured epithelial cell lines (A549) and enhanced by low concentration of IL-1 β stimulation. A549 cells were starved overnight and then stimulated with various concentrations of IL1 β ... Denitration activity was detected by reduction of nitrotyrosine (nTyr) deposits on nitrated bovine serum albumin (nBSA) evaluated by SDS-PAGE/Western blot. IL-1 β enhanced denitrase activity in a concentration-dependent manner with the maximal activity observed at a very low concentration (0.01 ng/ml), which did not activate NF- κ B measured by NF- κ B-DNA binding ELISA. In contrast, higher concentrations (1, 10 ng/ml) diminished this activity. Induction of denitrase activity by IL-1 β at 0.0033 ng/ml was observed at 3h but not at 8h or 16h after stimulation. This activity was also enhanced by Fudosteine, a mucoactive agent. Taken together, low dose IL-1 β may enhance denitration activity without new protein synthesis, whereas higher doses of IL-1 β worsen the nitration status of proteins.