重金属による食細胞フリーラジカル産生刺激と細胞内情報伝達機構

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1998 Fiscal Year Final Research Report Summary

Free radical producing activity and intracellular signal transduction mechanisms of phagocytes by heavy metals

Research Project

Project/Area Number

08457114

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Hygiene

Research Institution

Kanazawa University

Principal Investigator

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Project Period (FY)

1996 – 1998

Keywords

Free radicals / Zinc oxide / Phagocytes / Intracelluar signal transduction pathway / Monoamine oxidase / Glutathione / Nitric oxide synthase / peroxynitrite

Research Abstract

The activation mechanisms of intraperitoneal-eluted rat neutrophils and mouse macrophage -like cell line Raw 264.7 by zinc oxide (ZnO) was investigated to explore the etiological mechanisms of metal fume fever induced by ZnO.The activation of phagocytes by ZnO was enhanced by the addition of glutathione (GSH) and thiol compounds. Superoxide (O2^-) and hydrogen peroxide (H2O2) may be produced by NADPH oxidase via the intracellular signal transduction pathway such as GTP-binding protein, protein kinase C, tyrosine kinase, and intracellar calcium and membraneous CR3 if ZnO was added as a stimulant to neutrophils. If GSH was added to ZnO, the production of acitive oxygen species was dependent on FcgammaR in addition to CR3. The differnce in the activation of neutrophils by ZnO and ZnO plus GSH was investigated. The activation of neutrophils by ZnO may be dependent on the production of O2^- and peoxynitrite (ONOO^-) via NADPH oxidase and nitric oxide synthase (NOS). The activation of neutrophils by ZnO plus GSH may participated in the elevated H2O2 via the activation of monoamine oxidase (MAO) mainly localized in mitochodrium. These results suggest pot only the new evidence of the origin of H2O2 associated with the activation of nuclear transcription factor and the etiology of apoptosis but also the discovery of the relationship between MAO and intracellar signal transduction mechanisms. Moreover, from the results of Raw 246.7, GSH promoted the cleaning of ZnO particles by phagocytosis.
From this research project, it is speculated that zinc fume fever may be caused by the intrinsic factor GSH in addition to ZnO particles.

Research Products (17 results)

All | Other

All | Publications (17 results)

[Publications] Nakamura H et al.: "Central administration of interleukin-1 Breduces natural killer cell activity in non-pregnant rats,but not in pregnant rats." Psychoneuroendocrinology. 23. 651-659 (1998)

[Publications] Nakamura H et al.: "Opioid peptides mediate heat stress-induced immunosuppression during pregnancy." Am J Physiol. 274. R672-R676 (1998)

[Publications] Ikeda Y et al.: "Immunological features and inhibitory effects on enzymic activity of monoclonal antibodies against helicobacter pylori urease." J Ferment Bioeng. 86. 271-276 (1998)

[Publications] Nakamura H et al.: "Natural killer (NK) cell activity and NK cell subsets in workers with a tendency of burnout." J Psychosom Res. in press.

[Publications] Nakamura H et al.: "Natural killer cell activity reduced by microwave exposure during pregnancy is mediated by opioid systems." Environ Res. in press.

[Publications] Ogino K et al.: "Sodium azide inhibits nitric oxide production by rat neutrophils." J Phy Fit Nutr Immunol. in press.

[Publications] Keiki Ogino: "Role of free radicals in the pathogenesis of adult disease." Hokuriku J Public Health. 23. 1-5 (1996)

[Publications] Sugino N et al.: "Progesteron inhibits superoxide radical production by mononuclear phagocytes in psudopregnant rats." Endocrinology. 137. 749-754 (1996)

[Publications] Sugino N et al.: "Changes in activity of superoxide dismutase in hyman endometrium through the menstrual cycle and in early pregnancy." Hum Reprod. 11. 1073-1078 (1996)

[Publications] Ishiyama H et al.: "Histopathological changes induced by zinc hydroxide in rat lungs." Exp Toxic Pathol. 49. 261-266 (1997)

[Publications] Nakamura H et al: "Inhibitory effect of pregnancy on stress-induced immunosuppression through corticotropin releasing hormone (CRH) and dopaminergic systems." J Nureoimmunol. 75. 1-8 (1997)

[Publications] Nakamura H et al.: "Central administration of interleukin-1 B reduces natural killer cell activity in non-pregnant rats, but not in pregnant rats." Psychoneuroendocrinology. 23. 651-659 (1998)

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