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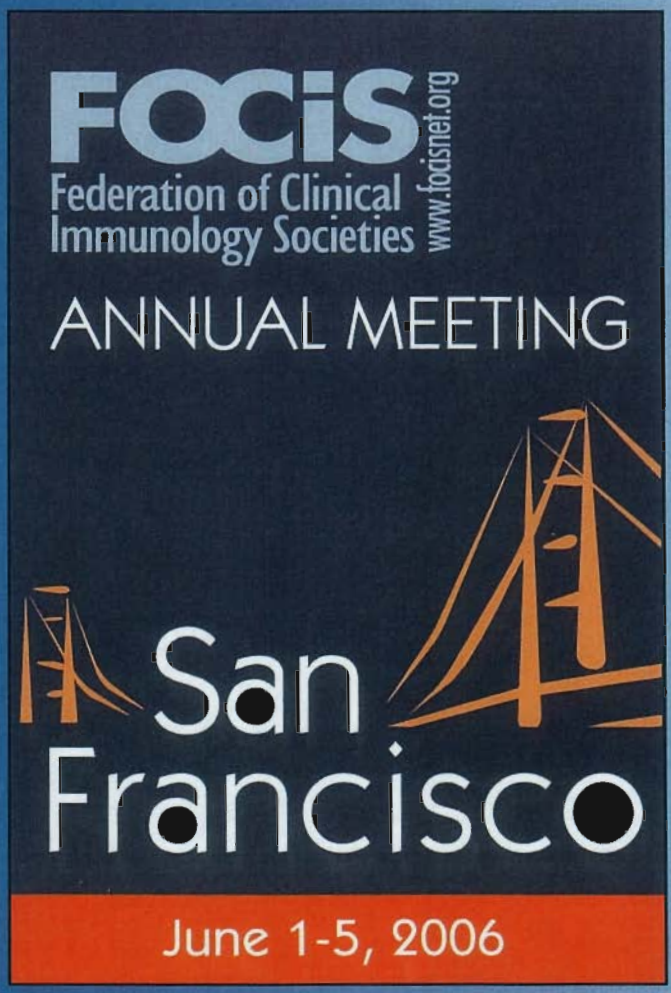

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臨床の免疫学会

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the IL-10 alteration seen in patients may be more consequence than cause of the disease.

doi:10.1016/j.clim.2006.04.535

Su.109. Prevention of Oxidative Stress-Induced Apoptosis in Lymphocytes By Hydroferrate Fluid from ACM Systems®.

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HydroFerrate fluid is an iron-based solution composed of bivalent and trivalent ferrates that is produced by ACM Systems®. The present study was carried out to examine the protective effects of HydroFerrate fluid against stress-induced apoptosis in murine splenic cells in vitro. Splenic lymphocytes from mice were cultured in the presence or absence of HydroFerrate fluid for 2 hrs and were subsequently exposed to hydrogen peroxide (H2O2) at a concentration of 2.5 μM for 24 hrs. Percent cell death was examined by flow cytometry and trypan blue exclusion. Results showed, as expected, that culture of splenic cells with H2O2 alone resulted in a significant increase in cell death (apoptosis) as compared to untreated control cells. In contrast, pre-treatment of cells with HydroFerrate fluid resulted in significantly reduced levels of apoptosis. The effect of HydoFerrate fluid was found to be dose-dependent and maximized at 100 μl/ml. We therefore conclude that HydroFerrate fluid may offer a protective effect against H2O2-induced apoptosis in murine splenic cells.

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Su.110. PKA and PKD Phosphorylation of CD43 in T-Cells.

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CD43 is one of the most abundant proteins expressed on the T-cell surface. Although CD43 is primarily expressed hematopoeitic cells, CD43 has recently been found on multiple tumors, and early upregulation of CD43 on colon adenomas suggests that aberrantly expressed CD43 could be one of the founding events in the rise of cancers. In T-cells, our laboratory has shown that CD43 acts as a negative regulator of T-cell activation through movement away from the immunological synapse through the action of its cytoplasmic tail. Despite clear evidence of the role of CD43 in T-cell function and tumorigenesis, the molecular mechanism of CD43 function in T-cells remains unknown. This lack of understanding of CD43 also limits our ability to explain the role of CD43 in immune function and tumorigenesis. In order to better understand the mechanism by which CD43 controls cellular function, we have analyzed the cytoplasmic tail of CD43. The cytoplasmic tail of CD43 contains 22 serines and theronines that may be modified to modulate CD43 effects on T-cell function. Using mass spectrometry and phosphate labeling, we now find that CD43 is phosphorylated at the serines at residue 72 (S72) and 76 (S76). We have identified two candidate kinases, PKA and PKD that can phosphorylate CD43 in vitro. PKA can phosphorylate at both S72 and S76 while PKD can specifically phosphorylate at S76. In vivo, we find that the PKA activator forskolin increases CD43 phosphorylation at S76. We have generated phosphorylation specific antibodies that can detect phosphorylation at S72 and S76. These phospho-specific antibodies will provide a powerful tool to investigate the physiological signals and kinases that regulate CD43 phosphorylation in vivo.

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Su.111. Novel Anti-Inflammatory Compounds from Endophyte Fungus in Inhibitions of Cytokine Responses in Macrophage RAW 264.7 Cells.

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Cytokines are pivotal proteins in regulating the homeostasis of immune system. Up- or down-regulation of cytokine production indicates modulation of the immune system in response to the environment. Many diseases are caused by excessive production of inflammatory cytokines in local or systemic tissues or organs. Here, two indole diterpenes, lolitrem B, produced by endophyte fungus, and its isomer. 31-epilolitrem B, were used to investigate their effects on pro-inflammatory cytokine interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF-a)responses in in vitro cultured murine macrophage RAW 264.7 cells. Our studies showed that both compounds have significant effects on inhibiting both IL-6 and TNF-a production at 24 hr in the presence of lipopolysaccharide (LPS) from the lowest concentration of 20 nm and up to 2 uM. In the absence of LPS, there were no significant increases in production of either cytokine. Statistical analysis showed that the effects we observed were not caused by the presence of the dimethyl sulfoxide used to dissolve both toxins. Paxilline, the precursor of lolitrems and known big conductance potassium channel activated (BK) blocker, also inhibited the cytokine responses but at a much higher concentration of 1 uM. Cell proliferation assays showed that the lolitrems alone did not inhibit the growth of the cells at concentrations as high as 1 uM. Cells treated with both toxins in the presence and absence of LPS did not undergo apoptosis with FACS analysis. This further demonstrated that inhibition was not through the apoptotic pathway, suggesting alternative cascades involved in the regulation of the anti-inflammatory response. The ability of these compounds to inhibit cytokine responses may have potential as immunotherapeutic drugs for inflammation diseases in the future.

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表題： ACM Systems®の HydroFerrate 液によるリンパ球における酸化ストレス誘導アポトーシス防止

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抄録本文： HydroFerrate 液は ACM Systems®が生産する 2 価ないし 3 価の鉄酸塩から構成される、鉄分を基礎とする溶液である。本研究は in vitro において、マウス脾臓細胞におけるストレス誘導アポトーシスに対する HydroFerrate 液の防護効果を調べる目的で実施した。マウス由来の脾臓リンパ球を HydroFerrate 液の存在／不在下で 2 時間培養した後、濃度 2.5μM の過酸化水素（H2O2）に 24 時間曝露させた。細胞死亡率はフローサイトメトリーおよびトリパンブルー色素排除法を使用して調べた。結果は予想したとおりで、処理を行わなかった対照細胞と比較して H2O2 のみを加えた培養脾臓細胞は細胞死（アポトーシス）が有意に増加した。対照的に HydroFerrate 液で前処理を行った細胞はアポトーシスの割合が有意に減少した。HydroFerrate 液の効果は用量依存的で、100μl/ml で最大となることが判明した。従って HydroFerrate はマウス脾臓細胞における H2O2 誘導アポトーシスに対する防護効果をもたらし得るとわれわれは結論した。