5088

EFFECT OF AGE, DIET RESTRICTION AND AMINOGUANIDINE ON PENTOSIDINE IN THE SKIN OF BROILER BREEDER HENS.

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Non-enzymatic glycosylation contributes to the formation of cross-links which leads to the deterioration in the structure and function of tissue protein. Whether the elevated concentrations of plasma glucose in chickens accelerates the accumulation of cross-links has not been determined. The objectives of this study were to determine the effect of diet restriction (DR) and the cross-linking inhibitor aminoguanidine (AG) on the rate of accumulation of the glycoxidation product, pentosidine, in the skin of naturally hyperglycemic broiler breeder (BB) hens. BB female chicks (n=450) were randomly assigned to four groups from 8 to 125 wks after hatch. *ad libitum* (AL), diet restricted (DR); *ad libitum* and diet restricted groups supplemented with 400 ppm AG each (AL+ AG and DR+AG respectively). Skin pentosidine was isolated by HPLC and oxidative stress was measured by luminometery. Results showed that the accumulation of pentosidine increased linearly ($P<0.001$) with age. DR significantly ($P<0.001$) retarded the rate of accumulation of pentosidine. The concentration of pentosidine in AL+AG group was comparable with that of DR group and skin pentosidine was lowest ($P<0.001$) in DR+AG group. Oxidative stress was significantly lower ($P<0.001$) in both DR and DR+AG groups as compared to AL and AL+AG groups. It was concluded that the rate of accumulation of pentosidine can be retarded by DR and AG. In addition, the data supports the view that pentosidine can be used as a biomarker for the study of aging in chickens. Supported by Hatch 368

CHEMOKINES (5089-5091)

5089

IL-8-BINDING PROTEINS IN ALVEOLAR FLUID FROM PATIENTS WITH THE ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS).

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IL-8, a potent neutrophil attractant and activator, has been implicated in the pathogenesis of ARDS. Our previous studies show that a significant portion of IL-8 in lung fluids from patients with ARDS is associated with α-2-macroglobulin (α-2-M) and anti-IL-8 autoantibodies (α-2-M:IL-8 complexes and anti-IL-8:IL-8 complexes). To further define the function of these proteins in ARDS, we measured concentrations of free and complexed IL-8 in bronchoalveolar lung (BAL) fluids from patients at risk for ARDS and with well-defined ARDS (1, 3, 7, 14 and 21 days after onset of ARDS). Patients at risk for ARDS had less anti-IL-8:IL-8 complexes than patients with ARDS (day 1), and the concentration of these complexes in ARDS patients (day 1) was lower in survivors than nonsurvivors. In addition, the increased amount of anti-IL-8:IL-8 complexes was associated with the development of ARDS and death. Furthermore, both free IL-8 and anti-IL-8:IL-8 complexes correlated with concentrations of neutrophils (PMN) ($p<0.05$; $r^2=0.60$ and 0.30, respectively) in patients at risk for ARDS. In patients who subsequently developed ARDS α-2-M:IL-8 complexes and PMN concentrations were correlated ($p<0.05$; $r^2=1.00$). In addition, concentrations of complexed IL-8 were positively correlated with PMN concentrations in patients diagnosed with ARDS (day 1, 3 and 7). These data suggest that α-2-M and anti-IL-8 autoantibodies might contribute to the inflammatory process and lung injury in ARDS.
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5090

INHIBITION OF GROα INDUCED HUMAN ENDOTHELIAL CELL PROLIFERATION BY THE α-CHEMOKINE INHIBITOR ANTILEUKINATE.

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We report here that GROα acts as a growth stimulating factor for human umbilical vein endothelial cells (HUVEC) *in vitro*. The proliferation of HUVEC was significantly stimulated by adding 100 nM of recombinant human (r) GROα and was significantly inhibited by adding 100 μg/ml of anti-human GROα monoclonal antibody (mAb). However, the addition of rIL-8, rIP-10, anti-human IL-8 mAb, and anti-human ENA-78 mAb did not affect to the proliferation of HUVEC. When Antileukinate, a potent α-chemokine inhibitor, was added to HUVEC, binding of radiolabeled GROα to its receptors was displaced, and the proliferation of HUVEC was suppressed in a dose-dependent manner. Antileukinate was not cytotoxic and there was no decrease in viability of any of the cells in the presence of 100 μM Antileukinate. These findings suggest that GROα is an essential growth factor for HUVEC. Furthermore, Antileukinate inhibits growth of HUVEC by preventing GROα from binding to their receptors. This raises the interesting possibility of α-chemokine receptor inhibitors, such as Antileukinate in the treatment of cancer where angiogenesis is important for tumor growth.
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5091

ISOLATION OF A BETA-CHEMOKINE LIKE cDNA FROM RAINBOW TROUT (Oncorhynchus mykiss).

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Attempts to identify teleost cytokines based on sequence identity with their mammalian equivalents have met with limited success, we have therefore adopted an alternate approach to the question. 185 clones picked randomly from a stimulated lymphocyte cDNA library were sequenced with the T7 primer. The sequences were compared with the Genbank database to determine similarity to known genes: 51% of the sequences matched no known sequences, 30% of the sequences obtained matched ribosomal RNAs or proteins, 16% were from housekeeping genes and 3% showed similarity to immunological molecules. The clone O14 had 46% sequence identity with beta-chemokines, a family of small proteins which are chemoattractants for lymphocytes. The full sequence of this clone possessed 10 of 11 absolutely conserved family specific amino acid residues, and 65% amino acid sequence similarity if conserved substitutions are considered. The 3' untranslated region contained three repeats of the 'AUUUA' RNA destabilisation motif, which is specific to cytokines and oncogenes. Screening a cDNA library using O14 as a probe produced no closely related clones, therefore it may not be a member of a conserved multi-gene family in fish. Screening of a genomic library produced 6 genomic clones. Four clones have a 109 bp intron and two have a 111bp intron equivalent to the first intron of mammalian beta chemokine genes. We are producing a recombinant protein in a bacterial expression system in order to test whether this molecule attracts lymphocytes from trout and other species. This research is supported by NIH grant R01 A124258 and fellowships from the MRC (BD) and the NSERC (KM).

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ABSTRACTS

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Abstracts 3618-6467
Tutorials T1-T18

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