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Hyaluronic Acid Suppresses the Reduction of \( \alpha2(VI) \) Collagen Gene Expression Caused by Interleukin-1\( \beta \) in Cultured Rabbit Articular Chondrocytes

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In order to investigate how \( \alpha2(VI) \) collagen gene is regulated by inflammatory cytokines in cultured rabbit articular chondrocytes, we examined the effect of interleukin-1\( \beta \) (IL-1\( \beta \)) on this collagen mRNA expression. Polylayer cultures of chondrocytes were exposed to IL-1\( \beta \) (0.1, 1, 10 ng/ml). Quantitative detection of specific mRNA for this collagen was carried out by reverse transcription-polymerase chain reaction (RT-PCR). Furthermore, to investigate the effect of hyaluronic acid (HA) on \( \alpha2(VI) \) collagen mRNA expression by IL-1\( \beta \), chondrocytes were exposed to IL-1\( \beta \) (10 ng/ml) in the presence of HA (0.01, 0.1, 1 mg/ml) with molecular weight of 900 kDa. Chondrocytes were also exposed to IL-1\( \beta \) (10 ng/ml) in the presence of HA (1 mg/ml) with molecular weights of 200, 900 and 2000 kDa. \( \alpha2(VI) \) collagen mRNA expression was decreased significantly in chondrocytes cultured with 1 and 10 ng/ml of IL-1\( \beta \). However, the addition of both IL-1\( \beta \) and HA (0.1, 1 mg/ml) or both IL-1\( \beta \) and HA (1 mg/ml) with all the molecular weight significantly suppressed these reduced mRNA levels. No tendency for this suppression to depend on the molecular weight was observed. These results suggest that suppression of transcriptional activity for type VI collagen will be associated with the reduction of cartilage matrix tissue and that HA will be associated with the suppression of the effect of IL-1\( \beta \).

Key words--- type VI collagen; interleukin-1\( \beta \); hyaluronic acid; articular chondrocytes

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Expression of MEF2 Genes during Human Cardiac Development

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To better understand the regulatory mechanisms in gene expression of human cardiomyocytes, we studied the expression of MEF2 genes encoding transcription factors during the course of cardiac development. Expression of all four MEF2 transcripts (MEF2A, MEF2B, MEF2C, and MEF2D) were detected in all developmental stage of the human heart, while Mef2b transcripts were down-regulated in mouse heart development. Although none of the MEF2 genes, besides mouse Mef2b, exhibited any remarkable quantitative change in their transcripts, qualitative changes in MEF2 transcripts were found during the course of cardiac development. In particular, MEF2D transcripts showed prominent changes by alternative splicing in the perinatal period. MEF2D transcripts containing the 21-base exon (exon b) were predominantly expressed after birth. At the same time, transcripts of the alpha myosin heavy chain (αMHC) gene increased after birth, as the splicing pattern in transcripts of the cardiac troponin T (cTnT) gene changed to decrease the transcripts of cTnT1 after birth. These changes seemed to be correlated with the alternative splicing changes of MEF2 genes, especially MEF2D. The alternative splicing as well as transcriptional regulation in MEF2 genes might be important for regulating the αMHC gene and the maturation of cardiomyocytes.

Key words--- transcription factor; alternative splicing; cardiac development; polymerase chain reaction

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Immunohistochemical Characteristics of Estrogen Receptorα Positive Cells in Glandular Epithelium of the Rat Seminal Vesicle

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Epithelial cells of the rat seminal vesicle stained positively for nuclear estrogen receptorα (ERα). We studied these cells using immunohistochemical means. We demonstrated in a previous study that some glandular epithelial cells of the seminal vesicles of immature castrated rats treated with estrogen for 1-2 weeks had multilayer features. The present study shows that these glandular epithelial cells are nuclear ER and basal cell-specific cytokeratin (34βE12) positive. These findings suggested characteristics of basal cells. Moreover, we demonstrated that these cells express transforming growth factorβ1 (TGFβ1) as a result of castration and estrogen treatment. Our findings indicate that glandular epithelial cells with multilayer features, which stained positively for nuclear ERα have basal cell features and may play an important role in the expression of TGFβ1 through an epithelial-stromal interaction.

Key words--- basal cell; seminal vesicle; estrogen receptorα; cytokeratin; TGFβ

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Endotoxin Contamination in Isolation of Lamina Propria Mononuclear Cells

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Because the beginning of extraction of lamina propria mononuclear cells is to obtain mucosal tissues that are exposed to luminal bacteria, the contaminated endotoxin in this step and/or the enzymes for mucosal digestion may activate mucosal macrophages and other cells. To address this issue endotoxin levels in isolation solutions were evaluated during the extraction of lamina propria mononuclear cells from 8 control, 7 Crohn's disease and 8 ulcerative colitis specimens. Endotoxin levels were measured using Toxicolor system based on the Limulus tests. Endotoxin levels were consistently below 500 pg/ml, and more importantly, these in enzyme digestion solutions were comparable among control, Crohn's disease, and ulcerative colitis. Therefore, comparative experiments using lamina propria mononuclear cells from these mucosae can be appropriately carried out, at least as far as in a comparable amount of contaminated endotoxin. However, careful consideration is required for the comparative and functional study using peripheral blood and lamina propria mononuclear cells.

Key words--- lamina propria mononuclear cells; endotoxin; lipopolysaccharide; inflammatory bowel disease; macrophage

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Point Nucleotidic Changes in Both the RET Proto-Oncogene and the Endothelin-B Receptor Gene in a Hirschsprung Disease Patient Associated with Down Syndrome

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A short-segment Hirschsprung disease (HSCR) patient associated with 21 trisomy showing point nucleotidic changes in both the receptor tyrosine kinase (RET) proto-oncogene and the endothelin-B receptor (EDNRB) gene is reported. A T to A heterozygous transition at the splicing donor site of the intron 10 in the RET proto-oncogene, and a G to A heterozygous substitution in non-coding region in the exon 1 of the EDNRB gene were observed. The familial analysis with these genes revealed that the origin of the former mutation was de novo and the latter one was maternal. No patient has been reported with two points mutations in different pathogenetically susceptible loci for HSCR. There is genetic evidence that the RET and EDNRB genes may interact in their susceptibility leading to HSCR.

Key words--- Down syndrome; Hirschsprung disease; receptor tyrosine kinase RET proto-oncogene; endothelin-B receptor gene; mutation

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Relation with Preoperative Fructosamine and Autonomic Nerve Function and Blood Pressure during Anesthesia in Diabetics: A Retrospective Study

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Many diabetics may have a high risk involving the cardiovascular system. In an attempt to predict the intraoperative risks of diabetics during anesthesia, we evaluated retrospectively the relationship among the biochemical assay or autonomic nerve function obtained as parts of the preoperative examination, and the blood pressure changes relating to the stimulation of intubation and extubation for anesthesia. In 40 diabetic surgical patients examined the biochemical assay (HbA1c, fructosamine level and blood glucose level) beforehand, the autonomic nerve function was quantified preoperatively by analysis of ECG R-R variability recorded in supine and subsequent standing position using an HRV analyzer, and some parameters of autonomic nerve function especially responsive sympathetic nerve activities were obtained. We assessed the correlation with systolic blood pressure changes in these cases at intubation for general anesthesia comparing to similar conditioned 40 non-diabetics. A diabetics with low vagal activity became larger systolic blood pressure afterdrop at tracheal intubation for anesthesia \( (r=0.513, p<0.001) \). Otherwise the blood pressure afterdrop at extubation became larger in a non-diabetics with high sympathetic activity \( (r=0.502, p<0.001) \). The preoperative fructosamine concentration in diabetics correlated positively with the responsive sympathetic nerve irritability index; "mRR(sup)-RRmin(std)" \( (r=0.432, p<0.05) \) and the responsive sympathetic nerve excitability index; "mRR(sup-std)" \( (r=0.448, p<0.05) \). However HbA1c had no correlation with these parameters of autonomic nerve function and blood pressure rise at tracheal intubation. Because of above correlation with blood pressure rise at intubation for anesthesia induction, the preoperative fructosamine examination and the responsive sympathetic nerve function test must be useful preoperative examination for detection of the unexpected heart events of diabetic patients during operation.

Key words--- fructosamine; sympathetic activity; heart rate variability; diabetes mellitus; anesthesia
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Rise in Plasma Oxidized Glutathione by Experimental Hypoglycemia

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Changes in plasma glutathione were investigated under hypoglycemic status. Twelve rabbits were randomly divided into hypoglycemic group (n=6) and saline-injected control group (n=6). Hypoglycemia was induced by intravenous injection of insulin as 10 U/kg and recovered by intravenous glucose injection after 60 minutes. In the control group, saline was intravenously injected in stead of insulin. Plasma levels of oxidized glutathione (GSSG) rose significantly (p<0.01) and remarkably decrease in plasma GSH/GSSG ratio (p<0.05) accompanying increase in serum enzymes in the hypoglycemic group. These results suggest that hypoglycemia might cause change in plasma GSSG which is related to increase of serum enzymes by hypoglycemia.

Key words--- hypoglycemia; reduced glutathione (GSH); oxidized glutathione (GSSG)

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Detection of Serum Antibody against Arrestin from Patients with Acute Disseminated Encephalomyelitis

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In our previous study, we found the presence of serum autoantibody against arrestin in patients with multiple sclerosis (MS), while such serum autoantibody was not detected from patients with other neurological diseases and control subjects. We suggested that serum arrestin antibody titers may be useful for the diagnosis and evaluation of the disease's course. In the present study we examined sera from 7 patients, who were initially diagnosed as having acute disseminated encephalomyelitis (ADEM), for the presence of serum antibody against arrestin, in order to study the specificity of the serum antibody among demyelinated diseases. High titers were detected from 2 patients out of 7. One of the patients, a 4 year-old girl, presented with an additional neurological attack during the 6 months after the initial attack, resulting in change of diagnosis to MS. During her disease course the serum titers against arrestin fluctuated in correspondence with the disease's activity. These observations suggest that the presence of serum autoantibody against arrestin may be specific to MS and be helpful for differential diagnosis of ADEM and MS.

Key words--- multiple sclerosis; acute disseminated encephalomyelitis; demyelination; arrestin; autoantibody

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Disseminated *Fusarium* Infection Identified by the Immunohistochemical Staining in a Patient with a Refractory Leukemia

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The difficulty and uncertainty encountered in diagnosing a systemic mycosis often lead to a delay in starting antifungal therapy. We reported a disseminated infection of multiple fungal isolates including *Fusarium* species during donor leukocyte transfusion (DLT) after allogeneic bone marrow transplantation in a 20-year-old woman with a refractory leukemia. Skin lesions are the feature of *Fusarium* and occur in the early period of the infection. In this case, during immunosuppression state after DLT, she presented with the whole body ache and erythematous lesions which appeared rapidly on her trunk and extremities. While administration of amphotericin B was started, her condition was further deteriorated and she died. Autopsy materials revealed that she had multiple fungal infection with different isolates, including *Aspergillus* and *Candida* in the brain, lung and liver, but not in the skin. With the immunohistochemical staining with specific antibody, *Fusarium* or *Aspergillus* infection was identified from the biopsy skin or autopsy brain, respectively. This rapid and specific immunohistochemical method may be useful for the diagnosis and treatment of invasive fungal infection without delay.

Key words--- disseminated *Fusarium* infection; refractory leukemia; donor lymphocyte transfusion

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A Case of Interferon Alpha-Induced Manic Psychosis in Chronic Hepatitis C

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It is well known that mood disorder such as depression occasionally develops during interferon (IFN) therapy for chronic viral hepatitis. So far, however, IFN-induced manic disorder has been rarely reported. We present a case of manic psychosis which developed during IFN treatment for chronic hepatitis C. A 35-year-old man with chronic hepatitis positive for hepatitis C virus RNA in serum was treated with natural IFN alpha with a daily dosage of 5 million units. Six weeks later he complained of insomnia, and then became exhilarated, talkative, restless and aggressive. Since the mental state was compatible with manic disorder, IFN therapy was immediately ceased. Simultaneously, psychotropic drugs were administered. One week later, the psychiatric disturbances disappeared. He has been keeping his usual social interactions without the psychotropic drugs after that. It is suggested that manic psychosis happened secondary to IFN alpha treatment.

Key words --- interferon; mania; hepatitis C

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Sensorineural Hearing Loss Associated with Byler Disease

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Progressive familial intrahepatic cholestasis, sometimes described as Byler disease, is a lethal liver disease and its inheritance is autosomal recessive. There is a previous report on the occasional association between this disease and sensorineural hearing loss without any audiological findings. We report here two siblings, an 18-year-old female and a 16-year-old male, suffering from Byler disease and hearing loss. Pure tone, Bekesy and speech audiometries and auditory brain stem response examination were performed. Audiometric data showed hearing characteristics of cochlear origin, high-frequency loss and progressiveness. This sensorineural hearing loss possibly results from a genetic mutation. The mechanism of cochlear disorder in patients with Byler disease is unknown, however, a novel gene responsible for deafness might be found to be related to Byler disease.

Key words --- Byler disease; sensorineural hearing loss; hereditary; audiology

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