Journal of Biomedical Science

Biomedical Vignette

In the current issue:

Trilinolein Inhibits Cardiac Hypertrophic Signals

Sympathetic stimulation, similar to norepinephrine, induces cardiac hypertrophy [14]. Of the diverse stimuli that lead to cardiac hypertrophy, a prototypical final molecular response of cardiomyocytes to hypertrophic signals involves an increase in protein synthesis and expression of the β-myosin heavy chain (β-MyHC) gene [23]. Liu et al. [13] studied the intracellular mechanism that underlies the cardiac protective effect of trilinolein, using primary culture of rat ventricular myocytes. Their results indicate that trilinolein inhibits norepinephrine-induced protein synthesis, β-MyHC gene promoter activity and intracellular oxygen radicals, and suggest that inhibition of norepinephrine-induced protein synthesis by trilionlein may be mediated through the attenuation of oxygen radical generation.

Antiplatelet Action of Magnesium Sulfate Involves Suppression of Protein Kinase C and Na^+/H^+ Exchanger

Intravascular thrombosis is one of the generators of a wide variety of cardiovascular diseases. At the same time, magnesium sulfate has been shown to reduce platelet aggregation both in vitro and ex vivo [8, 20]. Hsiao et al. [6] showed that magnesium sulfate inhibits aggregation of human platelets in a concentration-dependent manner, along with reduced phosphoinositide breakdown, intracellular Ca^{2+} mobilization, protein kinase C activation or thrombin-evoked increase in pHi. They conclude that these changes may be associated with the antiplatelet activity of magnesium sulfate.

Estrogen Downregulates Angiotensin II-Induced Endothelin-1 Gene in Aortic Smooth Muscle Cells

The risk of cardiovascular diseases in postmenopausal women on hormone replacement therapy is halved [1], possibly because of the protection provided by estrogens to the cardiovascular system. One possible underlying mechanism is that estrogens inhibit the proliferation and migration of vascular smooth muscle cells, partly by suppressing endothelin-1 gene expression induced by angiotensin II [28]. Hong et al. [5] propose a signal transduction cascade between angiotensin II treatment and cell proliferation that includes sequentially reactive oxygen species, ERK kinase, AP-1 and endothelin-1. This signaling mechanism provides an explanation for estradiol inhibition of vascular smooth muscle cell proliferation via downregulation of angiotensin II-induced endothelin-1 gene expression.

Ciliary Neurotrophic Factor Rescues Retinal Degeneration

Retinitis pigmentosa is characterized by progressive degeneration of the photoreceptors, leading to a combination of constricted visual field, night blindness and loss of central vision [25]. Huang et al. [7] investigated the effects of ciliary neurotrophic factor (CNTF), a powerful inducer of nerve fiber formation in retinal development [10], using Royal College of Surgeons rats, which exhibit recessive hereditary retinal dystrophy. They observed that both recombinant CNTF and adenovirus CNTF gene transfer exert a potent delaying effect on the process of photoreceptor degeneration, although the latter is more efficacious. These results suggest that adenoviral CNTF may be beneficial in diseases such as retinitis pigmentosa.

Induction of IL-8 Synthesis by Neutrophil Elastase

The large number of neutrophils consequent on exposure to potent neutrophil mediators, including neutrophil elastase, places the airspace in great jeopardy [24]. In addition, neutrophil-derived elastase, protein 3 or defensins induce IL-8 in lung epithelial cells [26]. Chen et al. [2] used cultured A549 epithelial cells to study the signal transduction pathway of neutrophil elastase-induced IL-8 expression. They report that neutrophil elastase activates p38 MAPK to upregulate NF-κB and AP-1 activities, leading to the induction of IL-8 expression. Furthermore, tyrosine kinase and protein kinase C are implicated in neutrophil elastase activation of the MAPK pathway.

Myeloperoxidase Gene Variation and Coronary Flow Reserve

Myeloperoxidase (MPO) is an oxidative enzyme that is able to form proatherosclerotic particles by its oxidative intermediates. An elevated MPO level in the blood is associated with coronary artery disease (CAD), and persons with MPO deficiency have a reduced risk of cardiovascular damage [30]. A sequence polymorphism affects the Sp1 binding site of the MPO transcriptional promoter, and leads to high (G/G genotype) and low expressers (A/A and A/G). The low expression genotype was recently correlated with protection against CAD [16]. The study by Mäkelä et al. [15] presents evidence for the involvement of the MPO genotype in early steps of CAD development, as measured by endothelial changes that affect the coronary flow reserve.

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Chromosomal Imbalance Aberrations in Gastrointestinal Stromal Tumors

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract [17]. Current criteria for the diagnosis of malignant GISTs do not always reliably predict patient outcomes. Except for a small rectal tumor, Chen et al. [3] identified the presence of chromosomal imbalance aberrations (CIAs) in all 28 patients with GIST they examined. Among these CIAs, losses of 13q, 10q (with minimal overlapping on q11–q22) and 22q are most likely the chromosomal loci potentially harboring the tumor suppressor gene(s) which may be related to early recurrence and/or metastasis during malignant transformation of GISTs.

Hepatitis C Virus Core Protein Activates RNA Polymerase I Transcription

Chronic infection with hepatitis C virus (HCV) is often associated with the development of severe liver diseases, including cirrhosis and hepatocellular carcinoma [22]. Kao et al. [9] investigated the implication that HCV core protein may be involved in the transregulation of RNA polymerase (Pol) I-dependent genes [27]. They report that the core protein is the only viral product that has the potential to activate RNA Pol I transcription. In particular, the fragment containing the N-terminal 1–156 residues and the integrity of the Ser^{116} and Arg^{117} residues of HCV core protein are critical for this transregulatory function. The proposed mechanisms that underlie the actions of the HCV core protein include recruitment of the upstream binding factor (UBF) and RNA Pol I to the rRNA promoter, hyperphosphorylation of UBF on serine residues, association with the selectivity factor via direct contact with TATA binding protein, and additional activation of RNA Pol II- and Pol III-mediated transcription. These results provide new insights into the role of HCV core in promoting cell growth and proliferation, and the progression of liver carcinogenesis.

Cell Cycle Inhibition by Triton X

Triton WR-1339, a cross-linked form of Triton X-100, has been shown to suppress the dissemination and metastasis of certain tumors [21]. Contrary to these results, others have reported that WR-1339 actually increases the chance that certain tumor cells will metastasize [19]. Picache et al. [18] report that Triton X-100 blocks cell proliferation through inhibition of cyclin-dependent kinase. This finding is of interest since it provides a molecular insight into the effect of Triton X-100 on tumor cell growth.

Downregulation of Human Negative Differentiation Regulator Gene in Megakaryocytic Differentiation

How hematopoietic stem cells choose between fates of proliferation and differentiation is not well understood. Using a complexity reduction approach, Liu et al. [12] identified a gene called negative differentiation regulator (NDR), which is highly expressed in the human erythroleukemia K562 cell line and in CD34+ umbilical cord blood cells. They found that NDR is downregulated in response to 12-O-tetradecanoylphorbol-13-acetate (TPA) and that overexpression of NDR partially blocks TPA-induced megakaryocytic differentiation in a protein kinase C-dependent manner. NDR therefore appears to be a novel regulator of hematopoietic cell differentiation.

Early Detection of Severe Acute Respiratory Syndrome-Associated Coronavirus

Severe acute respiratory syndrome (SARS), a newly emerged viral infectious disease, has recently raised a worldwide alert [4]. Analysis of the profile of IgM and IgG antibody responses to SARS-coronavirus (CoV) [11] indicated that all patients tested negative 1 week after the onset of symptoms. In order to identify specific antibodies to different viral proteins in SARS patients, Wu et al. [29] purified different recombinant viral proteins in *Escherichia coli* and detected various immunoglobulin classes in serum samples from SARS patients. Of note is that N protein of SARS-CoV was recognized in most of the sera, and IgA antibodies against SARS-CoV could be detected within 1 week after the onset of illness in a few SARS patients. Combining Western blot with RT-PCR greatly enhances the confirmation of SARS-CoV infection. These results provide clues to the development of a rapid and accurate laboratory test for SARS viral infection.

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