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The Vignette for V14 N5 Issue

Modulation of liver X receptor signaling as novel therapy for prostate cancer

Liver X-receptors (LXRs) are important regulators of cholesterol, fatty acids and glucose. Recently, it was found that a LXR agonist T0901317 suppressed proliferation of prostate tumor xenograft, which appeared to cause G-1 cell cycle arrest by reducing expression of SKP2 and inducing the accumulation of P27 KIP. T090137 also induced expression of ATP binding cassette transporter A1 and delayed the progression of androgen-dependent human prostate tumor xenograft towards androgen-independency in mice. Phytosterols such as β-sitosterols and campesteral have recently been shown to be the agonist for LXRs. This review [1] summarizes the potential use of LXR signaling as a therapeutic target in prostate and other cancers.

Characterization of monoclonal antibodies to hepatitis E virus (HEV) capsid protein and identification of binding activity

Infection of Hepatitis E virus (HEV) can cause acute hepatitis in developing countries. The mortality rate of hepatitis E during epidemics is between 0.4 and 4%; however, the highest mortality rate of hepatitis E occurs in pregnant woman with case-fatality as high as 30% [2]. Currently there is no licensed vaccine to prevent hepatitis E and no IVIG to treat the infected patients. The development of monoclonal antibody is a possible solution. HEV is a positive-sense RNA virus. The genome contains three open reading frames. He et al. [3] describes the generation and characterization of 27 monoclonal antibodies against the open reading frame 2 structural protein of the Pakistan strain of hepatitis E virus by hybridoma technique. These monoclonal antibodies have been characterized by ELISA, affinity-captured reverse transcriptase-polymerase chain reaction, immune electron microscopy, and a RT-PCR-based neutralization assay. Among them, no. 7 monoclonal antibody has the strongest binding activity and can inhibit the ability of HEV to attach to Alexander hepatoma cells (PLC-PRF-5). This clone may have a potential in passive immunization to treat HEV infection.

Potent inhibition of HIV-1 replication by backbone cyclic peptides bearing the Rev Arginine-Rich-Motif

Peptide-based therapeutic agents against HIV-1 have been developed that target the entry process into the cell [4]. The paper by Chaloin et al describes a series of Backbone Cyclic Peptide (BCP) analogs bearing a conformationally constrained arginine-rich motif of the essential viral Rev protein [5]. Potent suppression of HIV-1 replication was observed in T cells treated with these Rev-BCP's, which may represent an interesting approach for the design of novel antiviral compounds.

Efficient and persistent transduction of exocrine and endocrine pancreas by Adeno-associated virus type 8

Effective gene delivery into pancreatic tissue may serve as a potentially important therapeutic approach for pancreatic disorders. However, one of the major challenges facing pancreatic gene therapy is the efficiency of gene delivery by viral vectors. Here, Cheng et al. compared the efficiency of recombinant lentivirus and adeno-associated virus (AAV) 1, 2 and 8 vectors in pancreatic transduction. Their results showed that AAV8 represents the most effective vector among all the vectors tested for gene delivery into pancreatic tissue in vivo [6]. These findings serve as a foundation for potential clinical applications of pancreatic gene therapy.

Enhanced gene transfer into brain capillary endothelial cells using antp-modified DNA-loaded nanoparticles

Brain capillary endothelial cells (BCECs) have been considered as one of the primary targets for cerebral gene therapy. However, the cells are

difficult to be transfected by general non-viral vectors because of their poor function of endocytosis. To enhance the efficiency of transfection and gene expression in BCECs, Huang et al. [7] constructed DNA/polymer nanoparticles (NP) with highly positively charged polyethylenimine (PEI)- or relatively low positively charged polyamidoamine (PAMAM)-modified membrane penetrating peptide, antennapedia (Antp). They found that after a 20-min transfection, the efficiency, in terms of transfection and expression, of DNA/PEI NP or DNA/PAMAM NP was enhanced significantly. After a 3-h transfection of DNA/Antp/PEI NP, there was an enhancement in gene expression. Moreover, both the transfection and expression efficiencies of DNA/PAMAM NP were enhanced using Antp. These observations suggest that Antp can increase the membrane-penetrating ability of DNA-loaded nanoparticles, which can be employed as novel non-viral cerebral gene vectors.

Molecular evidence for the endosymbiont Wolbachia in a non-filaroid nematode, *Angiostrongylus cantonensis*

Angiostrongylus cantonensis is a parasitic worm of rats. People usually get infected by eating raw or undercooked snails that are infected by eating infected rat feces. Most of the known cases of infection in people have occurred in Southeast Asia. Based on alignment of the sequences of wsp, ftsZ, and 16S RNA genes, Tsai et al were able to identify a putative novel endosymbiont Wolbachia in this parasite [8]. Since Wolbachia had never been reported from nematodes other than filariae [9, 10], Tsai's observation may provide an insight to develop new therapeutic strategy against *A. canthonesis.*

Fibroblast-like cells derived from the gonadal ridges and dorsal mesenteries of human embryos as feeder cells for the culture of human embryonic germ cells

The development of human embryonic germ cells (hEG) is important for stem cell research and potential clinical applications such as transplantation of cells. Feeder cells are essential for the culture of hEG. Most studies have used mouse-derived feeder cells to support the growth of hEG. However, the employment of mouse-derived feeder cells may not be suitable for clinical application. Here, He et al. have successfully employed human fibroblast-like cells derived from the gonadal ridges and dorsal mesenteries as feeder cells for the culture of hEG [11]. These findings may facilitate the use of human embryonic germ cells in translational research.

Mediation of propofol-induced vascular permeability by NO

Propofol is frequently used for sedation and the induction and maintenance of anesthesia [12]. However, local inflammation is the prominent clinical symptom in the immediate response to intra-arterial propofol injection [13]. By studying vascular permeability in rats, Chen et al. [14] found that the propofol-induced vascular permeability and occluding phosphorylation were significantly attenuated by pretreatment of *N*-nitro-L-arginine methyl ester, indicating that the propofol-induced vascular permeability is at least in part mediated through NO. Therefore, NO synthetase inhibitors might be useful in the treatment of accidental intra-arterial injection of propofol in reduction of adverse effects.

Catechins bind ECM proteins and affect SMC's integrin β1 expression

Occlusive lesions of atherosclerosis that result in myocardial infarction, stroke, and peripheral vascular disease are the consequence of focal accumulation, within the innermost layer (intima) of the artery, of leukocytes from circulation and smooth muscle cells (SMCs) from the underlying media [15]. The pathogenesis of atherosclerosis and restenosis includes the abnormal production of ECM proteins by "synthetic" SMCs combined with modification of newly synthesized and preexisting ECM [16]. Previous studies showed that EGCG inhibits focal adhesion kinase activity and interferes with melanoma cell adhesion and movement processes [17]. However, the effects of other catechins such as (+)-catechin, and (−)-epicatechin-3-gallate (ECG) on SMC's functions have not been fully understood. Results of this study indicated that tea catechins, EGCG and ECG are relatively effective inhibitors of

SMC-ECM interaction, and their action mechanisms are through interference with SMC's integrin $\beta 1$ receptor and binding to ECM proteins [18].

Reduction of survivin expression by COX-2 inhibitor in hypoxic cancer cells

Hypoxia, a unique feature of solid tumors, diminishes therapeutic efficacy and plays a pivotal role in malignant progression. Hypoxic exposure can promote genetic instability and select for tumor cell populations with reduced apoptotic potential [19]. Because elevated levels of survivin are associated with increased resistance of tumor cells to conventional therapy [20], it becomes an important question whether hypoxia-driven down-regulation of survivin will make tumor cells more sensitive to cytotoxic effect. Kardosh et al. [21] studied the effect of the selective cyclooxygenase-2 (COX-2) inhibitor celecoxib on hypoxic glioblastoma cells, and found that the cells are more sensitive to killing by COX-2 inhibitor, and this effect is reflected by further decreased expression of survivin. These results introduce celecoxib as a drug with increased cytotoxicity against hypoxic tumor cells.

δEF1 represses BMP-2-induced differentiation of C2C12 myoblasts into the osteoblast lineage

δEF1 was originally identified as a chicken delta 1-crystallin enhancer binding protein. Member of δEF1 gene family are transcriptional regulators that can either activate or repress transcription, depending on the promoter and associations with coactivators and corepressors [22, 23]. Zhu et al [24] reported an interesting observation that δEF1 is significantly down-regulated as human mesenchymal stem cells (MSCs) are subjected to osteoblastic differentiation in the presence of BMP-2. They unambiguously showed that δEF1 suppresses osteoblastic cell differentiation through interference with the MAPK/AP-1 and NF-κB pathways.

Apoptotic cleavage of NuMA at the C-terminal end is related to nuclear disruption and death amplification

NuMA is a nuclear matrix protein in interphase and distributes to spindle poles during mitosis. Present studies [25] demonstrate that four apoptotic cleavage sites are clustered at a junction between the globular tail and central coiled-coil domain of NuMA, which could be responsible for apoptotic degradation of NuMA related to chromatin condensation and micro-nucleation. Cleavage of caspase-6-sensitive site at D1705 produced the R-form, a major coil-less product of NuMA during apoptosis, which showed the induction of chromatin condensation and activated the death machinery. It suggests that intact NuMA is a structural element in maintaining nuclear integrity.

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