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Immunotherapy for head and neck cancer

In the current review by Wu et al. [1], recent advances as they pertain to therapeutic intervention of human head and neck cancer are described. The authors started by describing tumor-specific antigens that are unique to head and neck cancers. Using these tumor-specific antigens as targets, a comprehensive coverage of beneficial immune responses is presented. With estimated 600,000 cases of head and neck cancer cases annually in the world and the relative lack of effective treatment, this review is not only timely but also brings into the picture on-going as well as potentially exciting treatment directions.

Antiviral activity of pyridyl imidazolidinones against enterovirus 71 variants

Enterovirus 71 (EV71) has emerged as the major causative agent of hand-foot-and-mouth disease (HFMD) fatalities worldwide, and it has also been associated with severe neurological diseases. For example, there was a large-scale HFMD outbreak in 1998 in Taiwan with 78 deaths [2]. Pyridyl imidazolidinones have previously been described as a novel class of EV71-selective inhibitors [3]. These compounds bind in a hydrophobic pocket of the viral VP1 capsid protein, which can acquire resistance mutations. The current study by Chen et al. [4] provides a comprehensive analysis of the effect of 11 drug variants on VP1-mutated EV71 variants. It confirms the importance of hydrophobic forces and the fit into the hydrophobic pockets of VP1 for drug efficacy. Whereas amino acid substitutions at VP1 position 192 can provide resistance, some drugs were identified that remain active on this VP1 variant.

Expression and membrane integration of SARS-CoV M protein

SARS-associated coronavirus (SARS-CoV) is a new member of coronavirus family. Infection of SARS-CoV causes severe acute respiratory syndrome (SARS), which is an emerging infectious disease and characterized by a cascade of immunological events leading to pulmonary inflammation and respiratory failure [5]. Expression of M and E proteins of SARS-CoV in insect cells is able to form virus-like particles, indicating that the M protein plays a crucial role in virion assembly [6]. Ma et al. [7] demonstrates that the translated products of M protein contain full-length un-glycosylated and glycosylated protein. The glycosylation of M protein occurs co-translationally in the presence of microsomes. The second and third transmembrane regions (a.a. 46–68 and 78–100) are able to insert a cytoplasmic protein into the endoplasmic reticulum membrane more efficiently than the first one (a.a. 14–36).

Morphogenesis of hepatitis B vrion and subviral particles in the liver of transgenic mice

Infection of human hepatitis B virus (HBV), a hepatotropic non-cytopathic DNA virus, causes acute hepatitis. Persistent human hepatitis B viral infection leads to a high risk of developing chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Three different kinds of viral and subviral particles are present in patients' sera. The 42-nm Dane particle, infectious virion, is composed of a 31-nm nucleocapsid with genome inside and a lipid bilayer envelope containing large, middle and major (small) surface antigens. The 22-nm subviral spherical and filamentous

particles, which are 1,000- to 10,000-fold excess of Dane particles, do not contain nucleocapsid. However, electron microscopy (EM) studies on the morphogenesis of these particles are few due to the low rate of virion production in livers and transfected cells [8]. Liou et al. [9] described the morphogenesis of HBV virion and subviral particles in the liver of transgenic mice using cryo-ultrathin section EM. Their results demonstrate that the morphogenesis of virions and subviral particles are through two separate pathways.

Discovering implicit protein–protein interactions in the cell cycle using bioinformatics approaches

The high throughput experimentation on genome-wide scale has generated enormous data. To develop bioinformatic tools are urgently needed to identify critical information to extract useful biological messages for life scientists to design appropriate experiments. Recently, several developments in text-mining tools have been made to automatically extract information from free-excess database such as PubMed [10, 11]. BioMap is an integrated software system that performs basic literature mining tasks on Medline database [12]. Palakal et al. [13] developed several new features as well as a new interface for BioMap. They used cdc2 interacting protein in Xenopus laevis as an example to show that this new version of BioMap indeed generated more homologue sequences for interacting proteins for cdc2 and suggested that these results are more reliable and are also consistent with the public domain software.

Inhibitory role of TGIF in the As_2O_3-regulated p21WAF1/CIP1 expression

Arsenic has been reported to be a chemotherapeutic agent for patients with acute promyelocytic leukemia by inhibiting cell growth and triggering apoptosis. In the present study it was found that AS_2O_3-induced c-Jun (Ser 63/73) phosphorylation can recruit TGIF/HDAC1 to the SP-1 binding sites and suppress p21 promotor activation [14]. It suggests that after AS_2O_3 treatment, the N-terminal domain of c-Jun phosphorylation by JNK recruits TGIF/HDAC1 to the SPI sites and then represses p21 expression. Therefore, TGIF is involved in AS_2O_3 -inhibited p21 expression, and then blocks the cell cycle arrest.

The transcriptional factor Snail simultaneously triggers cell cycle arrest and migration of human hepatoma HepG2 cells

Several transcriptional factors including Snail have been shown to induce epithelial-mesenchymal transition (EMT) and to repress expression of E-cadherin in many human carcinomas [15]. Activation of protein kinase C by phorbol ester can induce expression of Snail in human melanoma cells [16]. Hu et al. [17] provides experimental evidence suggesting that Snail is not only upregulated by phorbol ester in human hepatoma HepG2 cells but also is responsible for phorbol-ester-induced expression of cell cycle G1 inhibitor p15INK4b. This interesting result is contradictory to the recent observations that Snail is required for tumor growth and lymph node metastasis of human breast carcinoma cells [18]. Whether Snail plays a different role with respect to growth control in human hepatoma cells deserves more vigorous investigations.

Lysophosphatic acid induces IL-1β expression in macrophages

Lysophosphatic acid (LPA) is known to regulate inflammation and atherosclerosis by binding to its cognate receptors. Recent studies demonstrated that LPA is an important regulator of atherosclerosis by activating monocytic cells [19] and inducing neointimal formation in a rat carotid artery model [20]. Chang et al. [21] studied the effect of LPA on the upregulation of IL-1β expression in mouse J744a.1 macrophages. Gi/Rho activation and subsequent reactive oxygen species production were involved in LPA-induced expression of IL-1β. The LPA-induced expression of IL-1β was also observed in human primary macrophages. These results suggested that LPA regulates inflammation-related functions in both mouse and human macrophages.

In situ delivery of stem cells in hypertensive rats

Ischemic heart disease is the leading cause of death worldwide and also an important cause of heart failure [22]. The aim of the present study was to evaluate the effects of two different kinds of adult stem cell populations, administered in situ, on cardiac morphology, function and histology of SHR submitted to surgical coronary occlusion, in an attempt to investigate this therapeutic approach in a more physiological animal model of myocardial infarction. Results of this study demonstrated that the treatment with MSC and BMC groups had significantly reduced lesion tissue score, increased capillary density and normal (not-atrophied) myocytes, as compared to NM and C groups. The survival rate was higher in C, NM and MSC groups as compared to MI and BM groups. In situ injection of both MSCs and BMCs resulted in improved cardiac morphology, in a more physiological model of myocardial infarction represented by surgical coronary occlusion of spontaneously

hypertensive rats. Only treatment with MSCs, however, ameliorated left ventricle dysfunction, suggesting a positive role of these cells in heart remodeling in infarcted hypertensive subjects [23].

Isoeugenodilol inhibits neointimal formation

Abnormal vascular smooth muscle cell (VSMC) proliferation within the arterial intima plays a key role in the progression of atherosclerotic lesions, hypertension, and restenosis [24]. Thus, this study was to determine the efficacy and the possible mechanism of action of the synthesized drug isoeugenodilol (a new third-generation β-adrenoceptor blocker) on the growth factor-induced proliferation of cultured rat vascular smooth muscle cells (VSMCs) and neointimal formation in a rat carotid arterial balloon injury model. Results demonstrated that isoeugenodilol shows an inhibitory effect on neointimal formation due to inhibition of both migration and proliferation of VSMCs. This study suggests that isoeugenodilol has potential for the prevention of atherosclerosis and restenosis [25].

Methamphetamine-elicited alterations of dopamine- and serotonin-metabolite levels within μ-opioid receptor knockout mice: a microdialysis study

Methamphetamine (MA) is a powerful psychostimulant. A number of studies have indicated that μ-opioid receptor (μ-OR) can regulate the behavioral effects of MA on locomotor activity and behavioral sensitization [26, 27]. However, little is known regarding the role of μ-OR on the alteration of neurotransmitter dopamine (DA)/serotonin (5-HT) metabolism induced by MA. In this communication, Lan et al. [28] reported that μ-opioid receptors play a critical role in regulation of MA-induced alterations of the extracellular concentration of DA and 5-HT metabolites in the mouse striatum. These findings may have important neurochemical implications regarding the role of the μ-opioid receptors in MA-induced behavioral changes.

Gastroprotective effect of leptin in indomethacin-induced gastric injury

Gastric injuries associated with the use of nonsteroid anti-inflammatory drugs (NSAIDs) are common occurrences. So far, the main treatments for these complications are the suppression of acid secretion, the use of prostaglandin analogues and cyclooxygenase-2 (COX-2) inhibitors. However, this gastropathy has also been reported to be caused by neutrophil activation, leading to the production of reactive oxygen species (ROS) and nitric oxide (NO). Recently, leptin has been reported to have protective effects in several gastric injuries. This study [29] examined the gastroprotective effects of leptin in indomethacin-induced gastric ulcer and found that it did have protective effects through the production of mucin and induction of SOD (superoxide dismutase) and glutathione peroxidase. These results suggest that leptin can prevent indomethacin-induced injury through interfering with neutrophil infiltration, NO production and oxidative stress. This study offers a potential new preventive measure against NSAIDs-associated side effects.

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