1. 김 수빈

Journal name: Biomaterials (2019)

RBC membrane camouflaged prussian blue nanoparticles for gamabutolin loading and combined chemo/photothermal therapy of breast cancer

Abstract: Due to the non-targeted release of anti-cancer agent gamabufotalin (CS-6), conventional chemotherapy using this drug can cause serious side effects, which accordingly result in poor therapeutic efficiency. Recently, the development of smart nanodrug systems has attracted more and more attention due to their significant advantages of high loading efficiency, controllable release behavior and targeted accumulation at tumor sites. In this study, a nanodrug system named as HA@RBC@PB@CS-6 NPs (HRPC) was constructed. In this system, Prussian blue nanoparticles (PB NPs) with hollow porous structure were used as the carrier for CS-6 and photothermal sensitizer simultaneously. The result indicated that the encapsulation of erythrocyte membrane on the PB NPs prolonged the blood circulation life to 10 h and improved the immune evasion ability for more than 60%, as well, which is beneficial for the targeting molecule (HA) to achieve high concentration accumulation of HRPCs at tumor sites. Moreover, we also disclosed that loading drug of CS-6 performed its ultra-strong antitumor function partly through markedly suppressing the expression of HSP70, which conversely amplified the efficiency of photothermal therapy. The in vivo study demonstrated the outstanding performance of HRPC in synergistic photothermal/chemotherapy of cancer without side effect to normal tissues.

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2. 김현수

JVIR (Journal of Vascular and Interventional Radiology, 2018

Chitosan-Based Hydrogel Microparticles for Treatment of Carcinoma in a Rabbit VX2 Liver Tumor Model

Abstract
Purpose: To investigate potential of chitosan hydrogel microparticles (CHI) for treatment of VX2 carcinoma.

Materials and Methods: Two weeks after liver VX2 implantation, contrast-enhanced computerized tomographic scanning was conducted. Rabbits (n = 2) with successful tumor growth were treated with different sizes of ^{99m}Tc-labeled CHI (60–80 μm and 100–120 μm) via intra-arterial hepatic catheterization. Liver distribution of ^{99m}Tc-labeled CHI was determined by means of autoradiography, a radiation-based photographic technique. In the next part of this study, therapeutic effectiveness was examined with the use of CHI with the size range of 60–80 μm (n = 11). Tumor growth response and levels of blood liver enzymes were studied at baseline and 1 and 2 weeks after CHI treatment.

Results: Successful tumor growth was confirmed in all rabbits (24/24). Intrahepatic CHI with the size range of 60–80 μm resulted in liver localization in more close proximity to tumor nodule versus 100–120 μm. Baseline tumor volume was 1,909 ± 575 mm^3 in animals receiving CHI versus 1,831 ± 249 mm^3 in control animals (P ¼.342). In control animals, tumor volume markedly increased by 1,544 ± 512% at 2 weeks after sham operation versus baseline. In animals receiving CHI, tumor volume remained relatively unchanged (54 ± 6% increase; P = .007 vs control). Levels of blood aspartate transaminase (AST) and alanine transaminase (ALT) in animals receiving CHI increased 1 week after treatment (P = .032 vs control for AST; P = .000 vs control for ALT), but returned to control levels at 2 weeks.

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3. 임용운

Circ Res. 2014

Regulation of acetylation of histone deacetylase 2 by p300/CBP-associated factor/histone deacetylase 5 in the development of cardiac hypertrophy.

Abstract

Rationale: Histone deacetylases (HDACs) are closely involved in cardiac reprogramming. Although the functional roles of class I and class IIa HDACs are well established, the significance of interclass crosstalk in the development of cardiac hypertrophy remains unclear.

Objective: Recently, we suggested that casein kinase 2α1-dependent phosphorylation of HDAC2 leads to enzymatic activation, which in turn induces cardiac hypertrophy. Here we report an alternative post-translational activation mechanism of HDAC2 that involves acetylation of HDAC2 mediated by p300/CBP-associated factor/HDAC5.

Methods and Results: Hdac2 was acetylated in response to hypertrophic stresses in both cardiomyocytes and a mouse model. Acetylation was reduced by a histone acetyltransferase inhibitor but was increased by a nonspecific HDAC inhibitor. The enzymatic activity of Hdac2 was positively correlated with its acetylation status. p300/CBP-associated factor bound to Hdac2 and induced acetylation. The HDAC2 K75 residue was responsible for hypertrophic stress-induced acetylation. The acetylation-resistant Hdac2 K75R showed a significant decrease in phosphorylation on S394, which led to the loss of intrinsic activity. Hdac5, one of class IIa HDACs, directly deacetylated Hdac2. Acetylation of Hdac2 was increased in Hdac5-null mice. When an acetylation-mimicking mutant of Hdac2 was infected into cardiomyocytes, the antihypertrophic effect of either nuclear tethering of Hdac5 with leptomycin B or Hdac5 overexpression was reduced.

Conclusions: Taken together, our results suggest a novel mechanism by which the balance of HDAC2 acetylation is regulated by p300/CBP-associated factor and HDAC5 in the development of cardiac hypertrophy

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4. 조단비

Sci Rep. 2017

Palmitic Acid-BSA enhances Amyloid-β production through GPR40-mediated dual pathways in neuronal cells: Involvement of the Akt/mTOR/HIF-1α and Akt/NF-κB pathways.

Jeong Yeon Kim1,2, Hyun Jik Lee1,2, Sei-Jung Lee3, Young Hyun Jung1,2, Dae Young Yoo2,4, In Koo Hwang 2,4,5, Je Kyung Seong2,4,5, Jung Min Ryu6 & Ho Jae Han1,2

Abstract

The pathophysiological actions of fatty acids (FAs) on Alzheimer's disease (AD), which are possibly mediated by genomic effects, are widely known; however, their non-genomic actions remain elusive. The aim of this study was to investigate the non-genomic mechanism of extra-cellular palmitic acid (PA) regulating beta-amyloid peptide (Aβ) production, which may provide a link between obesity and the occurrence of AD. In an obese mouse model, a high-fat diet (HFD) significantly increased the expression levels of APP and BACE1 as well as the AD pathology in the mouse brain. We further found that PA conjugated with bovine serum albumin (PA-

BSA) increased the expression of APP and BACE1 and the production of Aβ through the G protein-coupled receptor 40 (GPR40) in SK-N-MC cells. PA-
BSA coupling with GPR40 significantly induced Akt activation which is required for mTOR/p70S6K1-mediated HIF-1α expression and NF-κB phosphorylation facilitating the transcriptional activity of the APP and BACE1 genes.
In addition, silencing of APP and BACE1 expression significantly decreased the production of Aβ in SK-N-MC cells treated with PA-BSA. In conclusion, these results show that extra-cellular PA coupled with GPR40 induces the expression of APP and BACE1 to facilitate Aβ production via the Akt-mTOR-HIF-1α and Akt-NF-κB pathways in SK-N-MC cells.

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5. Tan-Huy Chu

International Journal of Biological Sciences 2019

IL-15 Generates IFN-γ-producing Cells Reciprocally Expressing Lymphoid-Myeloid Markers during Dendritic Cell Differentiation.

Abstract
Recently, interest in IL-15-differentiated cells has increased; however, the phenotypic definition of IL-15-differentiated bone marrow-derived cells (IL-15-DBMCs) is still under debate, particularly the generation of IFN-γ-producing innate cells such as premature NK (pre-mNK) cells, natural killer dendritic cells (NKDCs), interferon-producing killer dendritic cells (IKDCs), and type 1 innate lymphoid cells (ILC1s), all of which are IL-15-dependent. Here, we revisited the immunophenotypic characteristics of IFN-γ-producing IL-15-DBMCs and their functional role in the control of intracellular *Mycobacterium tuberculosis* (Mtb) infection. When comparing the cytokine levels between bone marrow-derived dendritic cells (BMDCs) and IL-15-DBMCs upon stimulation with various TLR agonists, only the CD11cint population of IL-15-DBMCs produced significant levels of IFN-γ, decreased levels of MHC-II, and increased levels of B220. Neither BMDCs nor IL-15-DBMCs were found to express DX5 or NK1.1, which are representative markers for the NK cell lineage and IKDCs. When the CD11cintB220+ population of IL-15-DBMCs was enriched, the Thy1.2+Sca-1+ population showed a marked increase in IFN-γ production. In addition, while depletion of the B220+ and Thy1.2+ populations of IL-15-DBMCs, but not the CD19+ population, inhibited IFN-γ production, enrichment of these cell populations increased IFN-γ. Ultimately, co-culture of sorted IFN-γ-producing B220+Thy1.2+ IL-15-DBMCs with Mtb-infected macrophages resulted in control of the intracellular growth of Mtb via the IFN-γ-nitric oxide axis in a donor cell number-dependent manner. Taken together, the results indicate that IFN-γ-producing IL-15-DBMCs could be redefined as CD11cintB220+Thy1.2+Sca-1+ cells, which phenotypically resemble both IKDCs and ILC1s, and may have therapeutic potential for controlling infectious intracellular bacteria such as Mtb.
