2019-12-04 Happy Hour Seminar

김수빈

ACS NANO (2018)

Erythrocyte Membrane Cloaked Metal–Organic Framework Nanoparticle as Biomimetic Nanoreactor for Starvation-Activated Colon Cancer Therapy.

Abstract

Shutting down glucose supply by glucose oxidase (GOx) to starve tumors has been considered to be an attractive strategy in cancerous starvation therapy. Nevertheless, the *in vivo* applications of GOx-based starvation therapy are severely restricted by the poor GOx delivery efficiency and the self-limiting therapeutic effect. Herein, a biomimetic nanoreactor has been fabricated for starvation-activated cancer therapy by encapsulating GOx and prodrug tirapazamine (TPZ) in an erythrocyte membrane cloaked metal–organic framework (MOF) nanoparticle (TGZ@eM). The fabricated TGZ@eM nanoreactor can assist the delivery of GOx to tumor cells and then exhaust endogenous glucose and O_2 to starve tumors efficiently. Importantly, the resulting tumor hypoxia by GOx-based starvation therapy further initiates the activation of TPZ, which is released from the nanoreactor in the acid lyso/endosome environment, for enhanced colon cancer therapy. More importantly, by integrating the biomimetic surface modification, the immunity-escaping and prolonged blood circulation characteristics endow our nanoreactor dramatically improved cancer targeting ability. The *in vitro* and *in vivo* outcomes indicate our biomimetic nanoreactor exhibits a strong synergistic cascade effect for colon cancer therapy in an accurate and facile manner.

Han XUEHAO

Cellular biochemistry (2019)

The role of P2Y6 receptors in the maintenance of neuropathic pain and its improvement of oxidative stress in rats

Aabstract:

AIM:
To explore the role of P2Y6 receptors in the maintenance of neuropathic pain and progression of oxidative stress, we investigated the efficacy of the selective P2Y6 receptors antagonist MRS2578 on the antiallodynic effects and improvement of pathological neuropathic pain-induced oxidative stress, thereby finding a potential therapeutic target in neurological disease.

MATERIALS AND METHODS:

The mechanical allodynia in the ipsilateral spinal dorsal horn (SDH) of rats was observed in rats after chronic constriction injury (CCI). Meanwhile, the messenger RNA (mRNA) levels of biological parameters, including superoxide dismutase (SOD), glutathione (GSH), and heme oxygenase-1 (HO-1) in the SDH of rats were measured by real-time polymerase chain reaction (RT-PCR). In addition, the mRNA expression and protein levels of P2Y6 were measured by RT-PCR and Western blot assay,

respectively. Next, the rats subjected to CCI were intrathecally infused with MRS2578 to block the expression of P2Y6 receptors. The positive expression of P2Y6 receptors was examined by immunohistochemistry.

RESULTS:

In the present study, the results revealed that the P2Y6 expression in the ipsilateral SDH of CCI rats was significantly upregulated. In addition, inhibition of the P2Y6 receptor in SDH increased CCI-induced tactile allodynia. Furthermore, the levels of SOD, GSH, and HO-1 which were correlated with oxidative stress produced by CCI were also decreased.

CONCLUSION:

The results demonstrated that inhibition of the P2Y6 receptor can generate antiallodynic effects and improved the pathological neuropathic pain-induced oxidative stress. Thus, this study provides a potential approach for the therapy of neurological disease.

Li LAN

Journal name: Journal of Ocular Pharmacology and Therapeutics (2018)

Comparison of 0.1%, 0.18%, and 0.3% Hyaluronic Acid Eye Drops in the Treatment of Experimental Dry Eye

Abstract

Purpose: To compare the efficacy of 0.1%, 0.18%, and 0.3% hyaluronic acid (HA) artificial tear in the treatment of experimental dry eye (EDE).

Methods: EDE was established in female C57BL/6 mice through an air draft and subcutaneous scopolamine injection. The mice were divided into 5 groups according to topical treatment regimens (n=5 each): EDE control, balanced salt solution (BSS), preservative-free 0.1% HA, 0.18% HA, and 0.3% HA. The tear film break-up time (TBUT) and corneal fluorescein staining scores were measured 5, 10, 14, 21, and 28 days after treatment. The corneal smoothness scores were measured. In addition, periodic acid–Schiff (PAS) and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining were performed.

Results: The values for TBUT and corneal fluorescein staining showed greater improvements in all the HA groups ($P < 0.05$) than in the EDE and BSS groups after 10 days of treatment. Mice treated with 0.3% HA showed a more significant improvement in all clinical parameters than did those in the EDE control, BSS, 0.1% HA, and 0.18% HA groups (all $P < 0.05$) after 28 days of treatment. The goblet cell counts were higher in the 0.3% and 0.18% HA groups than in the 0.1% HA group. The number of TUNEL-positive cells was the lowest in the 0.3% HA group.

Conclusions: In EDE, 0.3% HA artificial tears are more effective than the 0.1% and 0.18% HA in improving tear film instability and ocular surface staining and irregularity, in increasing the number of conjunctival goblet cells, and in decreasing corneal epithelial apoptosis.

Ayeskanta Mohanty

ACS Nano (2019)

Construction of Dually Responsive Nanotransformers with Nanosphere–Nanofiber–Nanosphere Transition for Overcoming the Size Paradox of Anticancer Nanodrugs

Abstract

Tumor microenvironment (TME)-responsive nanosystems represent a category of intelligent nanomaterials for precise anticancer drug delivery. Herein, we report a smart size-/morphology-switchable nanodrug that can respond to the acidic TME and near-infrared (NIR) laser irradiation for effective tumor ablation and tumor metastasis inhibition. The nanoagent is physically assembled by a cytolytic peptide, melittin (MEL); an NIR-absorbing molecule, cypate; and tumor-targeting ligand, hyaluronic acid (HA). At pH 7.4, the as-formed MEL/Cypate@HA complexes are negatively charged nanospheres (~50 nm), which are suitable for long-term systemic circulation. When these nanospheres actively target tumors, the weakly acidic TME triggers an *in situ* transformation of the nanospheres to net-like nanofibers. Compared with the nanospheres, the nanofibers not only exhibit an inhibitory effect on tumor cell mobility but also significantly prolong the retention time of MEL/Cypate@HA in tumor tissues for MEL-based chemotherapy. Moreover, the nanofibers can be photodegraded into small nanospheres (~25 nm) by NIR laser irradiation during cypate-mediated photothermal therapy, which enables deep tumor penetration of the loaded MEL and thus achieves effective tumor eradication. This work provides a facile strategy for converting naturally occurring therapeutic peptides into a TME-responsive drug delivery system and may inspire the development of nanomaterials with changeable structures for therapeutic purposes.

Nguyen Phuoc Quang Huy,

Gynecologic Oncology (2019)

Cytokine-induced memory-like natural killer cells have enhanced function, proliferation, and *in vivo* expansion against ovarian cancer cells

Abstract:

OBJECTIVE: Natural killer (NK) cells are lymphocytes well suited for adoptive immunotherapy. Attempts with adoptive NK cell immunotherapy against ovarian cancer have proven unsuccessful, with the main limitations including failure to expand and diminished effector function. We investigated if incubation of NK cells with interleukin (IL)-12, IL-15, and IL-18 for 16h could

produce cytokine-induced memory-like (CIML) NK cells capable of enhanced function against ovarian cancer.

METHODS: NK cells were preactivated briefly with IL-12, IL-15, and IL-18, rested, then placed against ovarian cancer targets to assess phenotype and function via flow cytometry. Real-time NK-cell-mediated tumor-killing was evaluated. Using ascites cells and cell-free ascites fluid, NK cell proliferation and function within the immunosuppressive microenvironment was evaluated in vitro. Finally, CIML NK cells were injected intraperitoneal (IP) into an in vivo xenogeneic mouse model of ovarian cancer.

RESULTS: CIML NK cells demonstrate enhanced cytokine (IFN-γ) production and NK-cell-mediated killing of ovarian cancer. NK cells treated overnight with cytokines led to robust activation characterized by temporal shedding of CD16, induction of CD25, and enhanced proliferation. CIML NK cells proliferate more with enhanced effector function compared to controls in an immunosuppressive microenvironment. Finally, human CIML NK cells exhibited potent antitumor effects within a xenogeneic mouse model of ovarian cancer.

CONCLUSIONS: CIML NK cells have enhanced functionality and persistence against ovarian cancer in vitro and in vivo, even when exposed to ascites fluid. These findings provide a strategy for NK cell-based immunotherapy to circumvent the immunosuppressive nature of ovarian cancer.

Presentation Requirement

No later than one week before each class, speakers are required to send me an e-mail regarding journal name, publication year, title and abstract. Then I will collect the information and upload it home page. If you cannot make it, you will have to prepare copies for other students. Students need to print-out and bring their own copy for the class.

**** Please tear off along the dotted line below and submit after class.**
