Happy hour seminar 2019-12-11

PIAO HELONG

Journal: Investigative Ophthalmology & Visual Science (2018)

YAP/TAZ Are Essential for TGF-β2–Mediated Conjunctival Fibrosis

Abstract

Purpose: To investigate the roles of Yes-associated protein (YAP)/transcriptional co-activator with PDZ-binding motif (TAZ), the major effector molecules of the Hippo pathway, in TGF β2–mediated conjunctival fibrosis.

Methods: Primary human conjunctival fibroblasts were treated with TGF-β2. The expression of YAP/TAZ was examined by Western blot analyses and immunocytochemistry. The expression of fibrotic proteins and genes were evaluated by Western blot analyses and quantitative real-time PCR, respectively. The effects of YAP/TAZ on fibrotic changes were examined by knockdown experiments and the YAP/TAZ inhibitor, verteporfin.

Results: TGF-β2 stabilized YAP/TAZ and subsequently activated Smad2/3, which led to the transcription of fibrotic genes in human primary conjunctival fibroblasts. These fibrotic genes were differently regulated by YAP/TAZ. Notably, a-smooth muscle actin, fibronectin, collagen I, and collagen IV were primarily regulated by YAP. In contrast, CCN family proteins (CTGF and CYR61) depended on both YAP and TAZ. Mechanistically, YAP/TAZ were located in close proximity to Smad2/3, and in particular, YAP was required for TGF-β2-mediated phosphorylation and the nuclear translocation of Smad2/3. Furthermore, a YAP/TAZ inhibitor markedly suppressed TGF-b2-mediated fibrotic changes in conjunctival fibroblasts.

Conclusions: YAP/TAZ acted as a molecular hub of TGF-b2 signaling in a cellular model of conjunctival fibrosis. Moreover, verteporfin, a YAP/TAZ inhibitor exerted potent antifibrosis effects by suppressing TGF-β2-YAP/TAZ-Smad signaling. Our study highlights YAP/TAZ as essential regulators of conjunctival fibrosis and shows that inhibition of YAP/TAZ might potentially improve the outcomes of glaucoma filtration surgery.

Sah Dhiraj kumar

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Apigenin Suppresses the IL-1β-Induced Expression of the UrokinaseType Plasminogen Activator Receptor by Inhibiting MAPK-Mediated AP-1 and NF-κB Signaling in Human Bladder Cancer T24 Cells

ABSTRACT

The urokinase-type plasminogen activator receptor (uPAR), a glycoprotein localized on the cell surface with a glycosylphosphatidylinositol anchor, plays a crucial role in cell invasion, and the metastasis of several cancers, including bladder cancer, and its expression are significantly negatively correlated with patient survival rates. Apigenin, a naturally produced phytochemical compound found in fruits, vegetables, and plant leaves, has been shown to mediate a variety of cancer-metastasisrelated molecules in various cancers. The effect of apigenin on uPAR expression is still unknown. In this study, we examined the effects of apigenin on IL-1β-induced uPAR expression and investigated its potential mechanisms. We discovered in this study that IL-1β could remarkably induce uPAR

expression in bladder cancer T24 cells and that apigenin-inhibited IL-1β could induce uPAR expression concentration-dependently. Interestingly, NF-κB and AP-1 transcription factors were critically required for IL-1β-induced high uPAR expression. Apigenin suppressed the transcriptional activity of both AP-1 and NF-κB by inhibiting ERK1/2 and JNK signaling pathways. These results suggest that apigenin can exert anti-invasion effects by inhibiting uPAR expression via mediating (ERK1/2, JNK)/AP-1 and (ERK1/2, JNK)/NF-κB signaling pathways in human T24 cells. Our present study generated novel and valuable biological insight into anti-invasion through treatment with a small native compound.

Arathy Vasukutty

Journal- ACS Nano Letters

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MnCaCs biomineralized oncolytic virus for bimodal imaging guided and synergistically enhanced anticancer therapy

Oncolytic adenovirus (OA) is an ideal candidate for clinical anticancer treatment because it can specifically replicate in tumor cells with high titer. However, its systemic administration is still hindered due to severely compromised antitumor efficacy. Herein, an engineered OA was innovatively developed by enwrapping OA with calcium and manganese carbonates (MnCaCs) biomineral shell, which could protect virus from removal of the host immune system and prolong its in vivo circulation. Upon accumulating in tumor sites, MnCaCs readily dissolved under the acidic microenvironment, releasing Mn^{2+} that could convert endogenous H_2O_2 into oxygen (O_2) and then enhance the duplication ability of OA, thus significantly increased the antitumor efficacy. Meanwhile, Mn^{2+} and the increased O_2 individually endowed the T1 modal magnetic resonance imaging (MRI) and photoacoustic imaging (PAI) feasibility, providing real-time monitoring information for the therapy. This versatile engineered OA demonstrated its promise for visible and efficient oncolytic virotherapy by systemic administration.

Amal Babu

Janus Nanobullets Combine Photodynamic Therapy and Magnetic Hyperthermia to Potentiate Synergetic Anti-Metastatic Immunotherapy

Advanced science ( )

Photodynamic therapy (PDT) is clinically promising in destructing primary tumors but ineffective against distant metastases. This study reports the use of immunogenic nanoparticles mediated combination of PDT and magnetic hyperthermia to synergistically augment the anti-metastatic efficacy of immunotherapy. Janus nanobullets integrating chlorine e6 (Ce6) loaded, disulfide-bridged mesoporous organosilica bodies with magnetic heads (M-MONs@Ce6) are tailored for redox/pH-triggered photosensitizer release accompanying their matrix degradation. Cancer cell membrane cloaking enables favorable tumor-targeted accumulation and prolonged blood circulation time of M-MONs@Ce6. The combination of PDT and magnetic hyperthermia has a strong synergy anticancer activity and simultaneously elicits a sequence of immunogenic cell death, resulting in synergistically tumor-specific immune responses. When combined with anti-CTLA-4 antibody, the biomimetic and biodegradable nanoparticle enables the notable eradication of primary and deeply metastatic tumors with low systematic toxicity, thus potentially advancing the development of combined hyperthermia, PDT, and checkpoint blockade immunotherapy to combat cancer metastasis.