2019. Oct 2 Happy Hour agenda

1. PIAO HELONG

Current Eye Research (2016)

Mangiferin Protects Retinal Ganglion Cells in Ischemic Mouse Retina via SIRT1

Abstract

Objective: To investigate whether mangiferin can increase the viability of retinal ganglion cells (RGCs) in ischemic mouse retina, and to determine the possible mechanism of neuroprotection.

Methods: C57BL/6J mice underwent constant elevation of intraocular pressure for 60 min and received saline or mangiferin (30 mg/kg) intraperitoneally once daily until sacrifice. HIF-1a, GFAP and SIRT1 expression was assessed at 1, 4, and 7 days after retinal ischemia. Bax and Bcl-2 expression was also analyzed at 1 and 4 days. RGC survival was assessed by labeling flat-mounted retinas with Brn3a at 2 weeks after retinal ischemia. The effect of co-treatment with mangiferin and sirtinol (SIRT1 inhibitor) was also evaluated.

Results: The expression of HIF-1a and GFAP was upregulated in saline-treated retinas within 7 days after ischemia. Mangiferin treatment suppressed this upregulation. The expression of SIRT1 was downregulated in saline-treated ischemic retinas. This downregulation was reversed by mangiferin treatment, resulting in a significant difference from saline-treated ischemic retinas. In mangiferin-treated ischemic retinas, Bax expression was downregulated, whereas Bcl-2 expression was upregulated in comparison with saline-treated ischemic retinas. Mangiferin treatment protected ischemic retinas against RGC loss. Treatment of sirtinol decreased the neuroprotective effect of mangiferin.

Conclusions: Our findings suggest that mangiferin has a neuroprotective effect on RGC through downregulation of HIF-1a and GFAP, and upregulation of SIRT1 in ischemic mouse retinas. We suggest that mangiferin might be a potential neuroprotective agent against RGC loss under oxidative stress.

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2. Sah Dhiraj kumar

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Scientific Reports (2019)

Metformin inhibits lithocholic acid induced interleukin 8 upregulation in colorectal cancer cells by suppressing ROS production and NF-kB activity

ABSTRACT

Metformin, an inexpensive, well tolerated oral agent that is a commonly used first-line treatment for type 2 diabetes, has become the focus of intense research as a potential anticancer agent. In this study, we describe the inhibitory effect of metformin in interleukin 8 (IL-8) upregulation by lithocholic acid(LCA) in HCT116 colorectal cancer (CRC) cells. Pharmacological inhibition studies indicated that reactive oxygen species (ROS) were involved in LCA-induced IL-8 upregulation through activation of the transcription factor NF-kB. Metformin was demonstrated to block LCA-stimulated ROS production, in turn suppressing NF-kB signaling that was critical for IL-8 upregulation. An NADPH oxidase assay proved that the inhibitory effect of metformin on ROS production was derived from its strong suppression of NADPH oxidase, a key producer of ROS in cells. Compared conditioned media(CM) derived from HCT 116 cells treated with LCA lost all stimulatory effect on endothelial cell proliferation and tubelike formation. In conclusion, metformin inhibited NADPH oxidase, which in turn suppressed ROS production and NF-Kb activation to prevent IL-8 upregulation stimulated by LCA; this prevention thus obstructed endothelial cell proliferation and tube like formation.

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3. Shah Rajesh 188823

Cell (20**)

Growth Differentiation Factor 11 Is a Circulating Factor that Reverses Age-Related Cardiac Hypertrophy

Abstract

The most common form of heart failure occurs with normal systolic function and often involves cardiac hypertrophy in the elderly. To clarify the biological mechanisms that drive cardiac hypertrophy in aging, we tested the influence of circulating factors using heterochronic parabiosis, a surgical technique in which joining of animals of different ages leads to a shared circulation. After 4 weeks of exposure to the circulation of young mice, cardiac hypertrophy in old mice dramatically regressed, accompanied by reduced cardiomyocyte size and molecular remodeling. Reversal of age-related hypertrophy was not attributable to hemodynamic or behavioral effects of parabiosis, implicating a blood-borne factor. Using modified aptamer-based proteomics, we identified the TGF-β superfamily member GDF11 as a circulating factor in young mice that declines with age. Treatment of old mice to restore GDF11 to youthful levels recapitulated the effects of parabiosis and reversed age-related hypertrophy, revealing a therapeutic opportunity for cardiac aging.

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4. Tung Nguyen Thanh Uong

Nature Immunology (2018)

Blockade of the checkpoint receptor TIGIT prevents NK cell exhaustion and elicits potent anti-tumor immunity

Abstract

Checkpoint blockade enhances effector T cell function and has elicited long-term remission in a subset of patients with a broad spectrum of cancers. TIGIT is a checkpoint receptor thought to be involved in mediating T cell exhaustion in tumors; however, the relevance of TIGIT to the dysfunction of natural killer (NK) cells remains poorly understood. Here we found that TIGIT, but not the other checkpoint molecules CTLA-4 and PD-1, was associated with NK cell exhaustion in tumor-bearing mice and

patients with colon cancer. Blockade of TIGIT prevented NK cell exhaustion and promoted NK cell–dependent tumor immunity in several tumor-bearing mouse models. Furthermore, blockade of TIGIT resulted in potent tumor-specific T cell immunity in an NK cell–dependent manner, enhanced therapy with antibody to the PD-1 ligand PD-L1 and sustained memory immunity in tumor re-challenge models. This work demonstrates that TIGIT constitutes a previously unappreciated checkpoint in NK cells and that targeting TIGIT alone or in combination with other checkpoint receptors is a promising anti-cancer therapeutic strategy.

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5. Arathy Vasukutty

Nature Materials (20 **)

Hyaluronic acid–bilirubin nanomedicine for targeted modulation of dysregulated intestinal barrier, microbiome and immune responses in colitis

Abstract

While conventional approaches for inflammatory bowel diseases mainly focus on suppressing hyperactive immune responses, it remains unclear how to address disrupted intestinal barriers, dysbiosis of the gut commensal microbiota and dysregulated mucosal immune responses in inflammatory bowel diseases. Moreover, immunosuppressive agents can cause off-target systemic side effects and complications. Here, we report the development of hyaluronic acid–bilirubin nanomedicine (HABN) that accumulates in inflamed colonic epithelium and restores the epithelium barriers in a murine model of acute colitis. Surprisingly, HABN also modulates the gut microbiota, increasing the overall richness and diversity and markedly augmenting the abundance of **Akkermansia muciniphila** and **Clostridium** XIVα, which are microorganisms with crucial roles in gut homeostasis. Importantly, HABN associated with pro-inflammatory macrophages, regulated innate immune responses and exerted potent therapeutic efficacy against colitis. Our work sheds light on the impact of nanotherapeutics on gut homeostasis, microbiome and innate immune responses for the treatment of inflammatory diseases.

!! Please remember you are required to send the abstract by a week before the presentation, so I can collect them and upload for the class. If you cannot make it, you will have to bring your copies for all students.

Again, you don't need to follow this requirement for Professor Lee's class.

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