GW29-e0001
Cinnamaldehyde Attenuated Endothelial Dysfunction through Nrf2 Activation as a TRPA1 Agonist
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OBJECTIVES Advancing age is characterized with the development of vascular endothelial dysfunction which is the major risk factor for the development of cardiovascular diseases. TRPA1 is involved in lifespan and its agonist cinnamaldehyde (CA) mediates endothelial vasorelaxation. Therefore, we hypothesized that TRPA1 is involved in aging-related endothelial dysfunction and CA administration would improve endothelial function.

METHODS Human umbilical vein endothelial cells (HUVECs) were cultured until 14th passage and the 6th passage were used as control. Twenty-four months-old male Sprague Dawley (SD) rats were given dietary CA (0.2%) and six months-old rodents were used as young control. Ratent carotid arteries vasorelaxation was detected by wire myograph. TRPA1, Nrf2, UCP2 and its target genes as well as ENOS, p-eNOS were analysed by immunoblotting.

RESULTS Immunoblotting and immunofluorescence confirmed the TRPA1 expression in HUVECs and vascular endothelium. CA (10 μM) promoted Nrf2 nuclear translocation and eNOS phosphorylation, led to the up-regulation of HO-1, GPx-1, NQO-1 and a reduction in ROS production in HUVECs. However, these effects of CA could be reversed by TRPA1 antagonist, HC030031 (10 μM), Nrf2 inhibitor brusatol (40 nM) or UCP2 inhibitor. NO level was found decreased, and endothelium dependent relaxation was impaired in carotid arteries of aged rats, but both improved after 12 weeks of CA administration. Immunoblotting showed the expression of TRAP1, Nrf2, UCP2 and p-eNOS significantly decreased in vascular tissue of aged rats but partly restored after CA treatment.

CONCLUSIONS TRPA1 may be involved in aging related endothelial dysfunction and CA improved endothelial dependent vasorelaxation through Nrf2 activation as a TRPA1 agonist.

GW29-e0011
The effect of nicorandil on myocardial ischemia-reperfusion injury in isolated rat hearts
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OBJECTIVES To investigate the effect of nicorandil of potassium channel opener on myocardial ischemia-reperfusion injury in rats and to explore the mechanism of nicorandil on cardioprotective effect relative with mitochondrial ALDH2.

METHODS Wistar rats were randomly divided into four groups: normal group (N Group), ischemia-reperfusion group, nicorandil + ischemia-reperfusion group, adenosine + ischemia-reperfusion group by establishing Langendorff system. Normal group: continued perfusion of Krebs-Henseleit liquid for 70 minutes; IR group: stable perfusion for 30 minutes followed by ligating LAD for 30 minutes, then reperfusion for 90 minutes. Recorded the expression level of ALDH2, Bcl-2 and Bax of each group.

RESULTS 1. LVEDP in IR group was lower than the other groups after 30 minutes and 45 minutes of perfusion (P < 0.05). In the drug-post-conditioning groups: N/IR and N/IR + N group in 30 minutes and 45 minutes of perfusion were higher than the other groups after 30 minutes and 45 minutes of perfusion (P < 0.05). dp/dtmax in N/IR group were significantly higher than those in IR group and A/IR group at 30 minutes and 45 minutes after reperfusion. 3. Comparison of RA score: IR group score [5 (3.6), 57.36] was significantly higher than the drug post-conditioning groups. N/IR group [1 (1.3), 22.05] and A/IR group [2 (1.3), 23.14] (P < 0.0001, P < 0.0001). The N/IR group had the lowest score. There was no significant difference between N/IR group and A/IR group (P = 0.771). 5. The expression of the gene and protein about mitochondrial ALDH2 and apoptosis: IR group and mitochondrial ALDH2 gene expression increased significantly. The expression of Bcl-2 and Bax increased. The expression of mitochondrial ALDH2 in N/IR group increased, but A/IR group decreased; the expression of Bcl-2 and Bax both increased; Compared with IR group, the ratio of Bcl-2 / Bax in N/IR group and A/IR group increased (all P < 0.05); In the terms of anti-apoptosis, N/IR group and A/IR group had no significant difference (P > 0.05).

CONCLUSIONS On myocardial ischemia-reperfusion injury, we found that N/IR group can improve ischemia-reperfusion heart pump function, reduce the occurrence of reperfusion arrhythmia and reduce myocardial infarct size so that reduce myocardial ischemia-reperfusion injury. The effect of nicorandil is better than adenosine overall; Ischemia-reperfusion injury in myocardial mitochondrial ALDH2 gene protein is significantly reduced. Nicorandil can increase the expression of mitochondrial ALDH2, while raising the expression of B-catenin and down-regulating the expression of Bax in order to resist ischemia-reperfusion injury suggesting that the protective effect of nicorandil on myocardial ischemia-reperfusion injury may be related to this mechanism.

GW29-e0036
Xanthine Oxidase Induces Foam Cell Formation through LOX-1 and NLRP3 Activation
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OBJECTIVES Xanthine oxidase catalyzes the oxidation of xanthine to uric acid. In this process there is generation of reactive oxygen species (ROS) that play an important role in atherogenesis. Recent studies show that LRR and PYD domains-containing protein 3 (NLRP3), a component of the inflammasome, may be involved in the formation of foam cells, a hallmark of atherosclerosis. This study was designed to study the role of various scavenger receptors and NLRP3 inflammasome in xanthine oxidase and uric acid-induced foam cell formation.

METHODS Human vascular smooth muscle cells (VSMCs) and THP-1 macrophages were treated with xanthine oxidase or uric acid. Xanthine oxidase treatment (of both VSMCs and THP-1 cells) resulted in foam cell formation in concert with generation of ROS and expression of CD6 and LOX-1, but not of SRA. Uric acid treatment resulted in foam cell formation, ROS generation and expression of CD6, but not of LOX-1 or SRA.

RESULTS Further, treatment of cells with xanthine oxidase, but not uric acid, activated NLRP3 and its downstream pro-inflammatory signals-caspase-1, IL-1β and IL-18. Blockade of LOX-1 or NLRP3 inflammasome with specific siRNAs reduced xanthine oxidase-induced foam cell formation, ROS generation and activation of NLRP3 and downstream signals.

CONCLUSIONS Xanthine oxidase induces foam cell formation in large part through activation of LOX-1 - NLRP3 pathway in both VSMCs and THP-1 cells, but uric acid-induced foam cell formation is exclusively through CD6 pathway. Further, LOX-1 activation is upstream of NLRP3 activation.

GW29-e0059
Attenuation of diabetes-induced cardiac microvascular injury by TRPV1 and the role of OPA1 in this process
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OBJECTIVES Cardiac microvascular injury often occurs in patients with type 2 diabetes mellitus (T2DM) who are suffering hyperglycemia and hyperlipidemia. Transient receptor potential vanilloid 1 (TRPV1) plays a contradictory role in cardiac diseases. This study was performed to determine the role of TRPV1 in cardiac microvascular endothelial cells (CMECs) in patients with T2DM and elucidate the underlying mechanism.

METHODS Experimental mouse model was established by multiple injections of low-dose streptozotocin (STZ) and fed with high-fat Chow. Cohorts of diabetic mice received a 24-week treatment of capsaicin. CMECs was isolated from mice of wild-type and TRPV1-/-, and cultured separately in normal-glucose medium, high-glucose medium (HG), and HG plus HF medium.