that CD137-CD137L/Cyclophilin A (CYPA) activation accelerated the formation and progression of atherosclerosis plaque. Here we explore to detect the effect of their interaction on the endothelial cells.

METHODS Reactive oxygen species (ROS) generation, apoptosis and necrosis, proinflammatory and prothrombic properties, the levels of the apoptotic signaling proteins and the transcription factors in human umbilical vein endothelial cells (HUVECs) were measured after exposure to anti-CD137 in the presence or absence of CYPA-silencers or ROS inhibition.

RESULTS The results showed that anti-CD137 markedly induced CYPA expression, ROS production, mitochondrial depolarization and apoptosis in HUVECs; significantly increased the LDH leakage, the expression of CD54 and CD62E, the release of TNF-α, IL-6, IL-10 and VCAM-1; and activated NF-kappaB, increased Bax expression and suppressed Bcl-2 protein. Moreover, CYPA knock out attenuated anti-CD137-induced ROS enrichment, apoptosis, inflammation and the activation of NF-kappaB similar to the ROS inhibition.

CONCLUSIONS In summary, our findings demonstrated that CD137-CD137L/Cyclophilin A activation could induce dysfunction of endothelial cells through oxidative stress via NF-kappaB pathways, and their interaction may serve as a potential target for atherosclerosis therapy.

GW26-e0711

Ticagrelor Prevents Endothelial Dysfunction of Aortas in Hypertension Rats

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OBJECTIVES The aim of the study was to investigate the effect of ticagrelor on function of the aortas in 2-kidney, 2-clip hypertension rats.

METHODS Male Sprague Dawley rats were made hypertension after partial renal artery constriction (2-kidney, 2-clip method). After 1 week, systolic blood pressure of rats was measured. Hypertension rats were simultaneously treated with ticagrelor (10 mg/kg ig.q24h) or vehicle at 1weeks. Systolic blood pressures (mmHg) of rats were measured at 1.4 and 8 weeks. Endothelium-dependent relaxation induced by 2-MeS-ADP (selective $P2Y_{1/12}$-receptor agonist) was examined in horacic aorta rings from hypertension and normal rats. Western blot was used to exam the expression of $P2Y_1$ and $P2Y_{12}$ protein.

RESULTS At 1, 4, 8 weeks systolic blood pressure (mmHg) were increased in hypertension rats. Ticagrelor or vehicle did not change the systolic blood pressure (mmHg) of hypertension rats. 2-MeS-ADP induced endothelium-dependent relaxations were decreased in aorta from hypertension rats, compared normal rats. In the same time, L-NAME and indomethacin augmented 2-MeS-ADP induced contraction in hypertension rats, compared to normal rats. Ticagrelor did not normalize contractile responses and relaxation induced by L-NAME, indomethacin and 2-MeS-ADP in aorta from hypertension rats. $P2Y_1$ and $P2Y_{12}$ protein expression was significantly increased, but P2Y13 receptor expression was reduced in aorta of .hypertension rats. Endothelium-dependent relaxation by acetylcholine-stimulation was reduced in hypertension rats, and ticagrelor could improve endothelial function of aorta of hypertension rats.

CONCLUSIONS Our data suggested that ticagrelor ameliorates aortic endothelium function of 2-kidney, 2-clip method hypertension rats, but it was not through inhibition of $P2Y_{12}$ receptors in this vessel.

GW26-e2102

Gut microbiota alter cholesterol metabolism and regulate NPC1L1 by inducing the expression of Cyp7a1

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OBJECTIVES To investigate the function of intestinal bacteria in NPC1L1 mediating cholesterol.

METHODS Germ Free mice and Specified Pathogen Free (SPF) mice were treated with western diet and ezetimibe, cholesterol metabolism related data were tested in different ways. Metagenome Sequencing was used to test the differences between the feces of SPF mice and L1-KO mice treated with chow diet and High fat diet.

RESULTS Findings from these animals definitively establish that intestinal bacteria play a significant role in cholesterol metabolism and have affected ezetimibe action by increasing the expression of Cyp7a1 in C57BJ/6J mice. Additionally, The abundances of Anaeroplasma, Odoribacter, Clostridium_XlVb, Oscillibacter and Ruminococcus were significantly increased in NPC1L1 knockout mice.

CONCLUSIONS Gut microbiota may alter cholesterol metabolism and regulate NPC1L1 by inducing the expression of Cyp7a1.

GW26-e4406

Influence of different intensity treadmill training on myocardial energy metabolism substrate transition in rats

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OBJECTIVES To observe the influence of different intensity of treadmill training on key myocardial fatty acid and hybocardrate metabolism factors in rats and discuss the relationship between training intensity and myocardial substrate transition.

METHODS We divided 19 male rats into 3 groups randomly, control group(C, n=7), moderate training intensity group (M, n=7), and high intensity training group (H, n=7). M and H groups undertook treadmill exercise. M group run at the speed of 9 mile per minute, equally 45% VO_{2max}, and H trial run at 18 miles per minute, equally 78% $VO_{2max.}$ Every trial exercised for 8 weeks. After the last time training, rats were anesthetized. Serum was collected and the hearts were removed preserving at -80°C for further analyses. The levels of carbonhydrate and fatty acid in the serum were detected by ELISA. The expression of GLUT4, Cpt-1, FAT/CD36 were determined.

RESULTS Compared with C group, the carbonhydrate level in the serum of M group is significantly decreased, and the carbonhydrate in H group is significantly increased. Compared with C group, the fatty acid level of M group is decreased significantly and the fatty acid level of H group is decreased significantly. Compared with the C group, the GLUT4 mRNA and protein content of M group decreased insignificantly, and the GLUT4 mRNA and protein content of H group increased significantly. Compared with C group, CPT1 and FAT/CD36 mRNA and protein content of M group were increased significantly and decreased significantly in H group.

CONCLUSIONS A greater reliance on fat source occurred moderate exercise and a greater reliance on carbohydrate source during high intensity exercise in rat heart myocardial energy metabolism.

GW26-e4408

The protective effects of salidroside from exhaustive exercise-induced heart injury by enhancing the PGC-1α–NRF1–NRF2 pathway and mitochondrial respiratory function in rats

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OBJECTIVES We aimed to investigate the effects of exhaustive exercise and salidroside interference on myocardial mitochondrial respiratory function and the key regulators of mitochondrial biogenesis in rats.

METHODS Adult male SD rats were randomly divided into four groups. Cardiomyocyte ultrastructure was observed by optical microscopy and transmission electron microscopy. The levels of the cardiac marker enzymes CK, CK-MB, LDH, cTn-I and MB were determined by ELISA. Muscle oxidative capacity was measured in permeabilized bers. The expression of the mitochondrial biogenesis master regulator PGC-1α and its downstream transcription factors, NRF1 and NRF2, were measured.

RESULTS Salidroside ameliorated myocardium ultrastructure injury induced by exhaustive exercise, reduced the levels of CK, CK-MB, LDH, cTn-I and MB, increased mitochondrial respiratory function, elevated the mRNA expression levels of PGC-1α, NRF1 and NRF2, and increased the protein content of PGC-1α, NRF-1 and NRF-2.

CONCLUSIONS Salidroside can dose-dependently protect the heart from exhaustive exercise-induced injury. It might act by improving myocardial mitochondrial respiratory function by stimulating the expression of components of the PGC-1α-NRF1-NRF2 signaling cascade.