(6-months-old) mice were used as control (n =8 in each subgroup). The effect of brain aging and Rb1 on the learning and memory of C57BL/6J mice was tested by different behavioral tests including Y maze and Morris. The aged neuron was examined by the enzyme staining and electron microscope scanning, oxidative stress in brain tissue was tested by ELISA or spectrophotometer, and the plasticity-related proteins and the mTOR signaling pathway in hippocampus were tested by immunohistochemistry staining and Western blot.

RESULTS

1. Long-term low dose oral supplementation of Rb1 increased the average and maximum lifespan and improve aged-related cognitive decline.
2. Rb1 reduce the levels of MDA, protein carbonylation and improve SOD activity on brain tissue.
3. In the brain tissues of old controls, Rb1 reverse the over expression of mTOR/p70S6K pathway activation, then improve the cognitive function.

CONCLUSIONS Rb1 could prolong the lifespan and protect mice brain via restraining mTOR pathway activation. Consequently, Rb1 may be a effective and safe effective health medicine for anti-aging.

GW26-e2313

CD137 promotes angiogenesis by modulating endothelial CD137/NFATc1 signaling

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OBJECTIVES To observe whether CD137 promotes angiogenesis by modulating endothelial CD137/NFATc1 signaling.

METHODS Agonist-CD137 antibody and anti-CD137 antibody were used to activate or block CD137 axis respectively in $ApoE^{-/-}$ mice or HUVEC. The expression of CD137 mRNA and NFATc1 mRNA were measured by real-time quantitative PCR (RT-qPCR). The levels of phospo-Smad1/5 (Ser463/465), phospo-Smad2(Ser465/467) and NFATc1 of the HUVECs were determined by Western blot. Eukaryotic expression vector were constructed and co-transfected to the 293T with mimics or inhibitors to measure the protein level. Stable HUVEC cell line which knock-down NFATc1 or overexpress NFATc1 and control were built by lenti-virus. CCK-8 assay and transwell assay were performed to detect the proliferation and migration of cell. the Matrigel human umbilical vein endothelial cell (HUVEC) tube-formation assay and aortic rings assay were did to investigate whether LRG1 promotes blood vessel growth. Agonist CD137 antibody were used in $ApoE^{-/-}$ mice and Immunohistochemistry or Masson's trichrome assay were performed to observe the plaque stability.

RESULTS phospo-Smad2(Ser465/467) expression was downregulate (0.40±0.08 VS 1.00±0.00, p <0.05), whereas expression of nuclear factor of activated T-cells c1 (NFATc1) and phospo-Smad1/5 (Ser463/465) were significantly up-regulated(2.12±0.21 VS 1.00±0.00, 2.56±0.23 VS 1.00±0.00). Overexpression of NFATc1 by plasmid transfection demonstrated that NFATc1 independently contributed to HUVEC tube and branch formation. Inhibition of Smad1 downregulated NFATc1 in vitro. Knockdown NFATc1 suppressed the proliferation and migration of HUVEC induced by CD137. Up-regulating NFATc1 through agomir in Apoe-/- mice significantly increased angiogenesis in atherosclerotic lesion areas induced by CD137 in multi ways.

CONCLUSIONS Results indicate that CD137/NFATc1 pathway plays an important role in angiogenesis and Smad1/5 is involved in this progression cooperates with NFATc1.

GW26-e2339

miR-199a-3p, a Biomarker of Simulated Microgravity Induced Cardiac Remodeling

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OBJECTIVES Physiological adaptations to microgravity involve alterations in cardiovascular, neuromuscular, and neuroendocrine systems. These adaptations result in cardiac remodeling and orthostatic hypotension. Recent studies have found that microRNAs emerged as powerful and important modifiers of cardiovascular diseases. However, the role of microRNAs in weightlessness-induced cardiac remodeling is unknown. The purpose of this paper was to identify weightlessness-responsive microRNAs and to explore their role in weightlessness-induced cardiac remodeling.

METHODS In mice, hindlimb unloading (HU) mimics the effects of microgravity. Three groups mice were subjected to HU by tail suspension for 28 days and two of these three groups recovered 7 and 14 days respectively after HU (HU, n=10; R7, n=9; R14, n=9), the control group (n = 11) were treated equally, with the exception of tail suspension. Cardiac structure and function were detected in all groups by echocardiography on 4th, 5th and 6th week after HU respectively, and the microRNAs levels of serum and heart were detected by Q-PCR.

RESULTS Echocardiography revealed cardiac enlargement and decreased contractility in HU group. Compared with control, the HU group mice showed higher HW/BW (ratio of heart weight to body weight), LVIDs (systolic left ventricular internal diameter) and LV Vols (systolic left ventricular volume), lower LV EF (left ventricular ejection fraction) and LVFS (left ventricular fractional shortening). However, mice recovered 7 days after HU (R7) showed much higher HW/BW, LVIDs and LV Vols than both control and HU group. Mice recovered 14 days after HU (R14) returned to the normal state. Meantime, the results of Q-PCR demonstrated that miR-199a-3p of serum was upregulated in HU group, continued to be increased in R7 group, and returned to normal state in R14 group. More interestingly, variation trends of miR-199a-3p in left ventricle were consistent with the serum.

CONCLUSIONS These results indicate that simulated microgravity lead to cardiac remodeling, and the remodeling could be recovered, but in the early stage of recovering, cardiac remodeling may be more intensified because of increased pressure load. Meanwhile, miR-199a-3p is likely to play an important role in cardiac remodeling induced by simulated microgravity, miR-199a-3p may act as a biomarker of simulated microgravity induced cardiac remodeling.

GW26-e2399

The Use of Noninvasive Vagal Nerve Stimulation to Inhibit Sympathetically Induced Sinus Node Acceleration

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OBJECTIVES Hyperactivity of the cardiac sympathetic nerve system may underlie the pathogenesis of inappropriate sinus tachycardia (IST) and stellate ganglion (SG) block has been reported therapeutic for medically refractory IST. Investigations have proved that cervical vagal stimulation could inhibit SG activity.

METHODS Sixteen anesthetized dogs were randomly divided into the noninvasive vagal nerve stimulation (NVNS) group (n=8) and the control group (n=8) to receive 3 hours of right side noninvasive vagal nerve stimulation (at the voltage 80% below the threshold that defined as the minimal voltage to slow the sinus rate or atrioventricular conduction) or sham stimulation. The maximal sinus rate acceleration induced by high frequency stimulation (HFS) of right stellate ganglion (RSG) and RSG neural activity were measured at baseline and the end of each hour of stimulation. SK2, c-fos and NGF protein expression in RSG were examined in both groups.

RESULTS After 3 hours of stimulation, the maximal sinus node acceleration induced by HFS of RSG and RSG neural activity were significantly attenuated in NVNS group compared with those at baseline(P <0.05), no significant changes of these indices were observed in the control group (P >0.05). SK2 expression in RSG was significantly higher and c-fos and NGF expressions were significantly lower in the NVNS group than in the control group (P <0.05).

CONCLUSIONS Noninvasive vagal nerve stimulation may suppress RSG activity possibly by modulating SK2, c-fos and NGF expressions in RSG, thus inhibiting sympathetically induced sinus node acceleration.

GW26-e2443

Changes in gene expression of calreticulin in the myocardium of streptozotocin-induced diabetic cardiomyopathy

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OBJECTIVES Calreticulin (CRT) is major Ca2+ -binding protein mainly resident in the endoplasmic reticulum (ER) lumen. Evidences