GW26-e1830
Effects of Unilateral Noninvasive Vagus Nerve Stimulation on the Left Ventricular Post-Ischemic Remodeling
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OBJECTIVES Our previous study demonstrated that bilateral low-level transcutaneous electrical stimulation of the auricular branch of the vagus nerve (LL-TS) could substitute for vagus nerve stimulation and inhibit matrix metalloproteinase 9 expression, resulting in improved cardiac remodeling.

METHODS Thirty adult beagle dogs were randomly divided into an MI group (myocardial infarction was induced by permanent ligation of the left coronary artery, n=8), an R-LL-TS group (MI plus intermittent right-sided LL-TS treatment, n=8), an L-LL-TS group (MI plus intermittent left-sided LL-TS treatment, n=8) and a control group (sham ligation with left-sided LL-TS group, n=6). Auricular vagus nerve stimulation was unilaterally delivered to the right- or left-sided tragus via ear-clips connected to a custom-made stimulator. The LL-TS treatment was initiated three hours after the induction of MI and lasted two hours. Starting the following day, four hours of stimulation was administered from 7-9AM and 4-6PM daily for 4 weeks.

RESULTS At the end of 4 weeks post-MI, both the right- and left-sided LL-TS treatment significantly attenuated sympathetic nerve activity, reduced the left ventricular dilation and improved left ventricular systolic function. The unilateral LL-TS treatment significantly attenuated interstitial fibrosis, inhibited the expression of the matrix metalloproteinase 9 and increased the expression of the tissue inhibitors of matrix metalloproteinase 1.

CONCLUSIONS Both right- and left-sided LL-TS could attenuate LV remodeling in a post-ischemic beagle dog model.

GW26-e12188
miR-21 Contributes to Cardiac Aging by Targeting PTEN
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OBJECTIVES Given the potential of microRNAs (miRNAs) to influence large gene networks and modify complex developmental and disease phenotypes, we searched for miRNAs that were regulated during the process of heart aging.

METHODS Microarray analysis revealed subsets of miRNAs that were up- or down-regulated in cardiac ventricles from mice at 8 weeks and 15 months of age (young and aged). Dramatically, miR-21 was highly up-regulated during this period, with expression levels almost 3-fold higher in 15 months ventricles relative to 8 weeks. Over-expression of miR-21 in the neonatal rat cardiomyocytes (NRCM) shortened the telomere length, attenuated and strengthened the activity of telomerase and senescence-related beta-galactosidase respectively. Interestingly, this phenomenon is similar to the aging caused by doxorubicin (DOX). Using the quantitative PCR and Western-blot approaches, we found that miR-21 regulates the expression of enzyme phosphatase and tensin homologue (PTEN) gene, which was identified as a highly conserved direct target of miR-21.

RESULTS Finally, we demonstrated that knockdown of PTEN using siRNA functioned as a similar effect of miR-21 overexpression in the NRCM. Delightedly, we also found that knockdown of miR-21, as well as up-regulation of PTEN, repressed NRCM aging induced by DOX.

CONCLUSIONS These findings suggest that ectopic up- or down-modulation miR-21 may be an important regulatory mechanism governing heart aging by directly targeting PTEN gene.