 influences the cell membrane and resulted in retention in the endoplasmic reticulum. However, the retention and retention was much more serious in the cells expressing heterogeneous L539fs/47-hERG compared to the cells expressing WT-hERG.

Conclusions: The compound mutation L539fs/47-hERG obviously enhanced the susceptibility of hERG channels to d-sotalol hydrochloride. This may explain the drug-induced LQTS and TdP related symptoms during the administration of sotalol.

GW25-e2511

The activation of the G protein-coupled estrogen receptor subsequently triggers the PKA/CREB phosphorylation pathway causes decline in collagen deposition and a parallel stimulation of elastogenesis in cultures of human cardiac fibroblasts

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Objectives: It has been previously reported that the activation of G-protein coupled estrogen receptor (GPER) can alleviate the maladaptive ventricular hypertrophy and fibrosis that develops in mice after experimental cardiac infarction.

Methods: Our present studies, performed on cultures of human cardiac fibroblasts investigated whether such beneficial effects of this receptor would be exercised through the mechanisms interfering with deposition of major components of extracellular matrix, collagen and elastin.

Results: We found that treatment with 10-7 to 10-5 mol/L G1 (agonist of the GPER) not only resulted with a significant inhibition of collagen deposition, but also enhanced production of new elastic fibers. Knockdown of GPER using short hairpin RNAs (shRNAs) significantly reduced this effects of G1. Interestingly, we further demonstrated that the pro-elasticogenic effects occurs after the selective activation of GPER subsequent initiates the downstream PKA/CREB phosphorylation pathway. PAKA knockdown using shRNAs significantly blocked CREB subunit phosphorylation at Ser-133 and abolished the GPER-mediated expression of elastin. We also demonstrated that G1 induces phosphorylation of CREB contributed to suppression of collagen I synthesis by phosph-CREB-mediated competition for the transcriptional activator CBP1 to Smad transcriptional complexes contributing to collagen I gene transcription.

Conclusions: In summary, our data validate a novel mechanisms in which both anti-collagenogenenic and pro-elasticogenic effects occurs after the selective activation of GPER further initiated the PKA/CREB pathway, induces a crucial balance between collagenous and elastic fibers that would allow for the best possible resiliency of the post-infarct scars and the optimal cardiac function.

GW25-e2521

ApoE knockout mice of different weeks of atherosclerosis of blood lipid and pathological histology observation

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Objectives: The ApoE knockout mice progress of atherosclerosis in different time points, to explore different diet of ApoE knockout mice to progression of atherosclerosis.

Methods: 8 weeks of age 40 ApoE gene defects in mice, only 20 is given only to a high-fat diet, and 20 groups of normal diet. And 20-week-old mice were randomly divided into 2 groups: to explore different diet of ApoE knockout mice to progression of atherosclerosis.

Results: After two-kidney one-clip (2K1C), rats were treated with valsartan for 3 weeks. The results showed that valsartan significantly attenuated 2K1C-induced increase in the tumor necrosis factor (TNF)-α, interleukin-1β (IL-1β) and interleukin-6 (IL-6) expression. Furthermore, valsartan reduced the nuclear factor-kappa B (NF-κB) expression in the heart tissues of 2K1C rats.

Conclusions: Our results demonstrated that valsartan not only had a significant effect on the expression of pro-inflammatory cytokines, but also reduced the activation of NF-κB in the heart tissues of 2K1C rats. These findings suggest that valsartan may be a potential therapeutic agent for the prevention and treatment of cardiac remodeling after myocardial infarction.

GW25-c3165

Lack of non-symmonymous mutation in OrAil gene of patients with atrial fibrillation

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