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TNF receptor-associated factor 6 (TRAF6) mediates the angiotensin-induced non-canonical TGFβ pathway activation and differentiation of c-kit+ cardiac stem cells

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Objectives: TNF receptor-associated factor 6 (TRAF6) acts as a multifunctional regulator of the transforming growth factor (TGF-β) signaling pathway, and mediates signals linked to G protein-coupled receptors (GPCRs) activation via Gα12/13. This study was performed to test the hypothesis that TGF-β/TRAF6 is essential for angiotensin-II (Ang II)–induced differentiation of rat c-kit+ cardiac stem cells (CSCs).

Methods: c-kit+ CSCs were isolated from neonatal Sprague Dawley (SD) rats, and then treated with c-kit+ CSCs and Ang II in control and c-kit+ CSCs and Ang II concentrations. A TGF-β– and c-kit+ receptor inhibitor (SB431542) or the small interfering RNA (siRNA)–mediated knockdown of TRAF6 were used to investigate the role of TRAF6 in TGF-β signaling. Rescue of TRAF6 siRNA transfected cells with a 3′UTR deleted siRNA improved the responsiveness of the siRNA TRAF6 dominant negative (TRAF6ΔD) vector was constructed and used to infect c-kit+ CSCs, and western blotting was used to assess the expression of TRAF6, JNK, p38, cardiac-specific proteins, and Wnt signaling proteins. Physical interactions between TRAF6 and TGFβ receptors were studied by coimmunoprecipitation.

Results: Cardiac differentiation was suppressed in the absence of TRAF6. Forced expression of TRAF6 enhanced the expression of TGF-β–activated kinase (TAK1), and inhibited Wnt signaling. Furthermore, TRAF6 increased the expression of cardiac-specific proteins (cTropin and Cx43) but inhibited the expression of Wnt signaling proteins.

Conclusions: Our data suggest that TRAF6 plays an important role in Ang II induced differentiation of c-kit+ CSCs via the noncanonical signaling pathway.

GW25-e1647

Effects of Herbal medicine Aconite Compound on Heart failure

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Objectives: Cardiology and Cardiology-Derived Cells Can Be Derived from The Cadaver Autopsy

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Objectives: Cardiology and Cardiology-Derived Cells (CDCs) are mainly obtained through myocardial biopsy and surgical, but there is limited access to tissue size, technical requirements and faced with infection, trauma and other problems assume that there is still a large number of dead cells survival in the cadaveric heart, we can get a sufficient amount of functional CDCs and CDCs through cadaver autopsy methods.

Methods: Mouse (C57BL/6) were sacrificed and placed in a refrigerator at 4°C for 0 to 3 days, cardiac tissue was removed at different time points (D0, D1, D2, D3), cut into small pieces (approximately 1.5 cm3) and placed into dishes to culture explant-derived cells (CDCs) with complete explant medium. Flow cytometry analysis the expression of stem cell surface markers of EDCs such as CD117, CD133, CD105, Sca-1, CD90. EDCs were cultured with Cardiosphere growth medium to form CSP. CDCs were prepared from cadaveric cardiac were successfully isolated and cultured. Each group of EDCs are rich in stem cell surface markers expressing such as CD117, CD133, CD105, and D3. No significant difference in proliferation when detect by cck-8 and c-TnI, vWF expression respectively, the amount of EDCs could harvest at D3 decreased significantly lower for acute (P=0.24, 0.25, 0.24) and TIMI myocardial perfusion grade (P=0.01, 0.01) immediately after PCI MACES rate in intravenous group was lower than control group (P=0.03). And MACES rate between intragroup and intragroup, intragroup and across group are all significantly different (P<0.05, respectively). The incidence of bleeding events among 3 groups was similar.

Conclusions: Intracoronary tibolfin compared to the intravenous group, can effectively reduce the number of PMPs in patients with acute ST-segment elevation myocardial infarction undergoing emergency interventional treatments. The purpose of the inhibition of activated platelets quickly, and reduce total MACES events rate, but did not increase the risk of bleeding.

GW25-e4404

Cardiosphere and Cardiosphere-Derived Cells Can Be Derived from The Cadaver Autopsy

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Objectives: Unstable angina (UA), an acute coronary syndrome caused by disruption of atherosclerotic plaque triggered thrombosis. The blood vessel narrow and reduction of blood flow lead to the symptoms. Statin therapy benefits UA patients by cholesterol independent effect. Yet the mechanism of statin pleiotropic effect remained to be study. MicroRNAs (miRNAs), small non-coding RNAs, are post-transcriptional regulators of gene expression. In this study we aim to investigate statins’ novel mechanism mediated by miRNAs. Moreover we carry out systematic analysis of the mRNAs functional networks in atherosclerotic lesions.