
GW26-e4756
Decreased Copper Concentrations But Increased Lysyl Oxidase in Rhesus Monkey Model of Myocardial Ischemic Infarction
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OBJECTIVES Ischemic injury leads to collagen deposition in the heart. Lysyl oxidase (LOX), a copper (Cu) dependent enzyme, catalyzes cross-linking of collagens. The present study was to investigate the relationship between Cu concentrations and LOX activities in the heart of ischemic infarction.

METHODS Rhesus monkeys were subjected to coronary artery ligation, developing ischemic infarction. At 8 weeks after the surgery, monkeys were sacrificed and the molecular changes in the hearts were determined by Western blot, polymerase chain reaction (PCR), LOX enzyme activity, and atom absorption spectrometry (AAS). Collagen deposition was detected by hematoxylin and eosin (HE) staining, Masson’s staining, and immunohistochemistry.

RESULTS Both type I and III collagen mRNA levels were increased along with increased collagen and cross-linking degree. LOX protein levels and enzyme activities were significantly increased. However, Cu concentrations were significantly decreased.

CONCLUSIONS The increase in the Cu-dependent LOX activity with the decrease in the total Cu concentrations would predict a redistribution of Cu under ischemic condition, leading to enhanced collagen deposition.

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GW26-e5321
Inhibition of PKR Impairs Angiogenesis Through a VEGF Pathway
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OBJECTIVES Peripheral artery disease (PAD) is a common clinical problem, and its pathophysiological mechanisms are incompletely understood. Double-stranded RNA-activated protein kinase (PKR) is a ubiquitously expressed serine/threonine protein kinase. Although PKR has been reported in antivirus and the immune system, the role of PKR in vascular function, especially in angiogenesis, is still unclear.

METHODS PKR activation was measured by Western Blot in hypoxic HUVECs. PKR siRNA was used to inhibit PKR expression in HUVECs. After transfected with PKR siRNA, Matrigel tube formation, wound healing and proliferation were tested in HUVECs.

RESULTS PKR+/− and WT mice were used in our experiments. Hind limb ischemia model was developed and Laser Doppler Imaging system was used to measure hind limb blood perfusion before and immediately after surgery and then at 7-day intervals, until the end of the study, for a total follow-up of 28 days after surgery. Proliferative endothelial cells in ischemic muscle were tested with immunohistochemistry stain of CD31. VEGF expression in HUVECs and muscle were measured by Western Blot in HUVECs.

RESULTS Blood flow recovery was significantly delayed in PKR/- vs. WT mice (n = 9, P < 0.01), accompanied by 34% reduced CD31-positive stain in ischemic muscle 28 days after procedure (n = 9, P < 0.05). PKR expression decreased in the first 12 h and increased to peak at 24 h in human umbilical vein endothelial cells (HUVECs) in response to hypoxia (n = 3, P < 0.05). Accordingly, phospho-PKR expression increased in HUVECs 24 h after treatment with hypoxia (Western blot analyses, n = 3, P < 0.05). Inhibition of PKR by siRNA reduced microtube formation (n = 3, vs. control siRNA, P < 0.05) and migration (wound healing, n = 3, vs. control siRNA, P < 0.05) by 33 and 59%, respectively. Vascular endothelial growth factor (VEGF) expression in ischemic muscle from PKR−/− mice was significantly decreased by 54% 1 day after procedure (n = 3, P < 0.05, vs. WT) and by 63% 7 days after procedure (n = 3, P < 0.01, vs. WT), respectively. At the same time, VEGF expression in HUVECs decreased by 21% (n = 3, P < 0.05, PKR siRNA vs. control siRNA).

CONCLUSIONS These findings demonstrate that PKR mediates angiogenesis through a VEGF pathway, which may form the basis for future intervention of PAD.

GW26-e5358
Apelin/APJ Signaling Promotes Hypoxia-Induced Proliferation of Endothelial Progenitor Cells Via PI3K/Akt Signaling
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OBJECTIVES To determine hypoxia culture promoting proliferation of EPCs via HIF-1α/Apelin/APJ signaling.

METHODS (1)EPCs of C57BL/c mice were isolated with density gradient centrifugation and adherence screening method.

RESULTS (1)Compared with Normoxia culture group, the molecules of Apelin/APJ expression on EPCs of Hypoxia culture group increased (P < 0.01). (2)Compared with Hypoxia culture group, the EPCs proliferation ability decreased (P < 0.01), while the EPCs proliferation ability increased (P < 0.01). Compared with Hypoxia culture group, the molecules of Apelin/APJ siRNA culture group on EPCs of Hypoxia-HIF-1α siRNA culture group decreased (P < 0.01). The Yiqihuoxuejiedu-treated rats had significantly reduced compared with the model group (0.263±0.037 mm2). At 28 days after injury, the areas of neointima and the whole vessel wall increased in the model group (versus the sham group, P < 0.01). The Yiqihuoxuejiedu-treated rats had significantly

GW26-e5382
Effects of Yiqihuoxuejiedu Formula on Proliferation and Secretion of Adventitial Fibroblast after Balloon Injury
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OBJECTIVES To investigate the effectivity and mechanism of Yiqihuoxuejiedu formula on inhibiting vascular remodeling, especially adventitial remodeling.

METHODS SD rats weighing 380-450 g were chosen for a common carotid artery model after balloon injury. Rats were administered the intervention for 7 or 28 days. The slices were stained with haematoxylin and eosin, Sirius Red, Masson and immunohistochemistry of smooth muscle α-actin.

RESULTS At 7 days after injury, the areas of neointima in the model group and two treatment groups were larger than those of the sham group (P < 0.01). The adventitial areas of the Yiqihuoxuejiedu formula group (2.021±0.91 mm2) reduced compared with the model group (2.63±0.037 mm2). At 28 days after injury, the areas of neointima and the whole vessel wall increased in the model group (versus the sham group, P < 0.01). The Yiqihuoxuejiedu-treated rats had significantly