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RESEARCH ARTICLE

# Differential gene expression profile of Buyanghuanwu decoction in rats with ventricular remodeling post-myocardial infarction

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## Abstract

**OBJECTIVE:** To investigate the effect of Buyanghuanwu decoction (BYHWD) on gene expression in ventricular remodeling post-myocardial infarction in rats.

**METHODS:** Animal models of myocardial infarction were established by permanent ligation of the left anterior descending coronary artery. Echocardiography measurements were performed after the treatment of BYHWD (18 $g \cdot kg^{-1} \cdot d^{-1}$) for 90 days. Myocardial collagen was observed by mallory trichrome staining. Capillary density was quantified by using Factor Ⅷ immunohistochemical staining. Differentially expressed genes were explored by a short-read sequencing technology combined with a tag-based digital gene expression profiling (DGE) system. Real-time quantitative polymerase chain reaction detecting system (qPCR) was used to validate the sequencing results. After assembling the gene information from Sham, model and BYHWD groups, we constructed three DGE libraries based on each group. The sequencing of three libraries generated 66 000-73 000 unique tags, which were mapped to reference sequences for annotation of expressed genes.

**RESULTS:** Among them, 511 and 352 differentially expressed genes were found in comparison with sham/model and model/BYHWD, respectively. Fifty-five genes exhibited reversed direction of gene expression differences between Sham/Model and Model/BYHWD groups. We found that transforming growth factor beta receptor-1, junctophilin-2, monocyte chemotactic protein 1, neuropeptide Y, arachidonate 5-Lipoxygenase, arachidonate 15-Lipoxygenase were significantly modulated, which suggested the involvement of these genes in BYHWD treatment.

**CONCLUSION:** The DGE profiling data provide comprehensive gene expression information at the transcriptional level that could facilitate our understanding of the pharmacological mechanisms of BYHWD in ventricular remodeling post-myocardial infarction.



**Keywords:** Ventricular remodeling; Myocardial infarction; Gene expression; Buyanghuanwu decoction

## INTRODUCTION

Myocardial infarction (MI) is one of the major risk factors for heart failure. Chronic ventricular remodeling has been shown to play a key role in the pathological process of heart failure.[1] Due to the rapid development of the diagnosis and treatment of cardiovascular diseases, numerous patients could survive through acute MI and experience remodeling of left ventricle (LV). Acute MI usually leads to histopathological changes in left ventricular remodeling,[2] which can be effectively relieved by drug therapies. It is reported that Traditional Chinese Medicines (TCM) exerted protective effects on ventricular remodeling.[3,4] Therefore, elucidation of the underlying mechanisms of effective TCM formulae on ventricular remodeling would not only provide a better understanding on TCM, but also provide scientific support for the ancient TCM formulae.

Buyanghuanwu decoction (BYHWD) is a TCM formula that has been used for centuries. From TCM viewpoint, it can benefit *Qi*, activate blood circulation and dredge collaterals. A number of clinical evidences have indicated that BYHWD can be used for the treatment of ischemic disease including ischemic stroke and coronary heart disease (CHD).[5,6] BYHWD can be used for the treatment of CHD by the elimination of free radicals and regulating apolipoprotein metabolism.[7] Our previous study found that BYHWD could alleviate ventricular remodeling induced by left anterior descending artery ligation.[8] The anti remodeling effect of BYHWD was conferred by decreasing the area of MI through affecting multiple targets including B-cell lymphoma-2/ Bcl-2-associated X protein (Bcl-2/Bax) ratio and caspase 3 activity *via* upregulation of PRDX6, phosphorylation of HSPB6 and subsequently reduction of Atrial Natriuretic Factor (ANF).[8] Furthermore, BYHWD significantly decreased the level of C-reactive protein in serum and the expression of CD40 in coronary heart diseases with *Qi* deficiency and blood stasis syndrome rat model.[9] It also inhibited inflammatory pathway such as CD40 and CD40L expressions in model of myocardial ischemia rats.[10] However, the underlying mechanisms of BYHWD treatment still remain elusive.

In this study, digital gene expression (DGE) profiling was used to identify the responses of differentially expressed proteins to BYHWD treatment in ischemia-induced ventricular remodeling in rats model.

## MATERIALS AND METHODS

### *Preparation of drugs*

BYHWD is composed of [Huangqi (*Radix Astragali Mongolici*), Inner Mongolia, China], [Danggui (*Radix Angelicae Sinensis*), Gansu, China], [Chishao (*Radix Paeoniae Rubra*), Sichuan, China], [Chuanxiong (*Rhizoma Chuanxiong*), Sichuan, China], [Taoren (*Semen Persicae*), Hunan, China], [Honghua (*Flos Carthami*), Henan, China], and [Dilong (*Pheretima Aspergillum*), Guangdong, China]. The raw herbs for BYHWD were purchased from the affiliated Nan Fang Hospital of Southern Medical University produced by Zhixin Medicine Health Co., Ltd., (Guangzhou, China). BYHWD was prepared as previously described.[8]

### *Animals and experimental myocardial infarction*

Male Wistar rats, each weighing 200-250 g (specific pathogen-free, Certificate No. 2011A036), were obtained from Laboratory Animal Centre, Southern Medical University. They were provided with free access of water and rodent chow at 20-22 ℃ through a 12 h light-dark cycle. All procedures involving laboratory animal use were performed in accordance with the guidelines of the Instituted Animal Care and Use Committee of Southern Medical University. Before conducting the experiment, rats were allowed to adapt the new environment for 1 week. MI was induced by permanent ligation of the left anterior descending coronary artery as described previously.[8] The rats were anesthetized with an injection of 4% chloral hydrate [2 mL/kg, supported by Tianjin Zhiyuan biological technology Co., Ltd., (Tianjin, China)] into the abdominal cavity before operation and sacrifice to relieve the animal's suffering. Totally 36 rats were randomly divided into 3 groups by random number method: sham group ($n$ = 12), model group ($n$ = 12), and BYHWD group ($n$ = 12). BYHWD group was administered with BYHWD