

## Bioinformatics Analysis on Molecular Mechanism of *Poria Cocos* in Treatment of Jaundice

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**Abstract.** Objective: To study the molecular mechanism of *P.cocos* in the treatment of Jaundice by building molecular networks and comparing canonical pathways. Methods: Target proteins of *P.cocos* related genes of Jaundice were searched from Pubchem and Gene databases online respectively. Molecular networks and canonical pathways comparison analyses were performed by IPA. Results: The molecular networks of *P.cocos* and Jaundice were complex and multifunctional. The 14 target proteins of *P.cocos* and 33 Homo sapiens genes of Jaundice were found in databases. There were 56 common pathways both related networks. *P.cocos* could regulate endothelial differentiation Tumor Necrosis Factor (TNF), Interleukin-1 $\beta$  (IL-1 $\beta$ ) and Interleukin-6 (IL-6) in these pathways. Conclusions: *P.cocos* treat Jaundice by regulating many effective nodes of Metabolism pathway and Immunity related pathways.

**Keywords:** *Poria Cocos*; Jaundice; IPA; PubChem.

### 1. Introduction

Jaundice is a kind of Common symptoms and signs caused by heat/ damp capsici in Traditional Chinese Medicine, it's typical expression are face yellow, eyes yellow, urine yellow and red [1-2]. Comparing with modern western medicine, Significance are almost the same.

At present, there are lots of prescriptions in treatment of jaundice, and mostly used eliminating dampness and diuresis treatment [3]. In Traditional Chinese medical treatment of Jaundice, *P.cocos* is high use of frequency drug. [4], and takes good effect on recent clinical research. [5-6]. In order to explore the mechanism of *P.cocos* in treatment of Jaundice, building molecular networks and comparing canonical pathways of *P.cocos* and Jaundice by Bioinformatics. The methods and results are shown below.

### 2. Materials and methods

#### 2.1 Retrieve the target protein and related gene

Logged into PubChem Database, entered "*P.cocos*". Acquired molecular information and corresponding biological testing and got GI number of target protein. Then logged into Gene Database, entered "Jaundice", acquired related gene and its Gene Symbol or ID.

#### 2.2 Molecular networks analysis

Import the target protein of *P.cocos* and Jaundice related gene into IPA (Ingenuity Pathway Analysis) software as excel format. Then, molecular networks of these were performed respectively by Network analysis module of IPA.

#### 2.3 Canonical pathways comparison analyses and action sites analysis.

Canonical pathways of the target protein of *P.cocos* and Jaundice related gene were analyzed conjointly by Comparison of IPA and the combination pathway were chosed to further research. In order to definite the molecular mechanism of *P.cocos* in the treatment of jaundice, analysis of both in the common role of the canonical pathway, Found action sites from the combination pathway.

### 3. Results

#### 3.1 The target protein and related gene

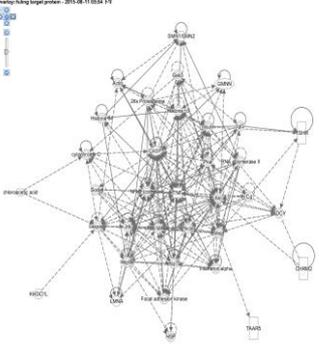
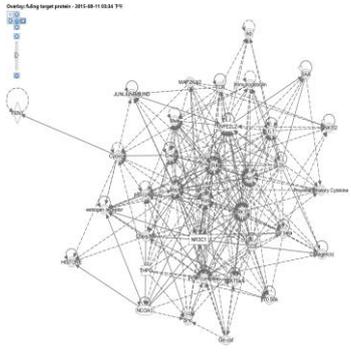
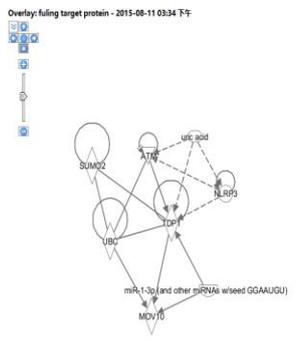
By 2015.4.9, there were 14 target protein of *P.cocos* in PubChem Database, and 33 Jaundice related gene in Gene Database

#### 3.2 Molecular networks analysis

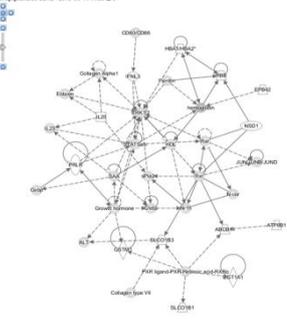
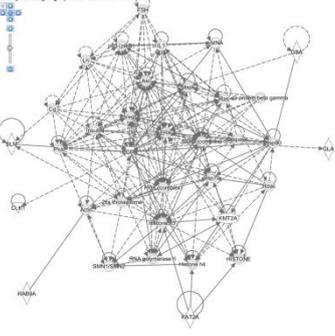
The results showed that, the *P.cocos* build 3 networks of different function; Jaundice constructed 6(Select the top three) (Table.1A, B). The graphs of Molecular networks showed that, the moleculars of *P.cocos* mostly involves to Cell Death and Survival, Developmental Disorder, Hematological Disease, etc. Moreover, the moleculars of Jaundice mainly involves to Drug Metabolism, molecular Transport, Developmental Disorder Tissue Development, etc.

Table.1 The graph of Molecular networks and function of target proteins of P.cocos and related genes of Jaundice

A Molecular networks and function of target proteins of P.cocos

Mole-cular network-ks			
	Neurological Disease, Organismal Injury and Abnormalites, Skeletal and Muscular Disorders	Connective Tissue Development and Function, Hematological System Development and Function, Hematipoiesis	Cell Death and Survival, Developmental Disorder, Hematological Disease

B Molecular networks and function of related genes of Jaundice

Mole-cular network-ks			
	Drug Metabolism, molecular Transport, Developmental Disorder	Tissue Development, lymphcid Tissue Structure and Development, Organ Morphology	Cell-To-Cell Signaling and Interaction, Cellular Development, Cellular Growth and Priliferation

#### 3.3 Canonical pathways comparison analyses

The Comparison Analysis module of IPA performed that, there were 56 canonical pathways of the target protein of *P.cocos* and Jaundice related gene that involes Metabolism, Cellular immunity,etc. (Fig.1)

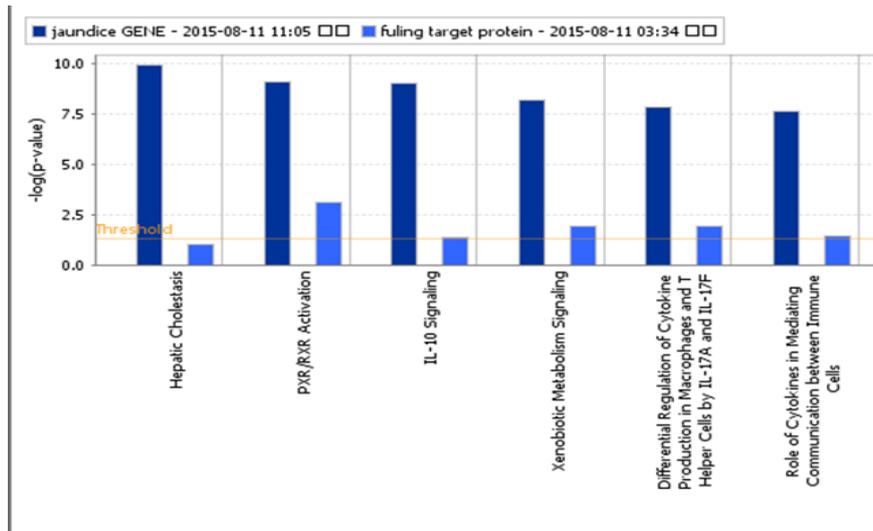
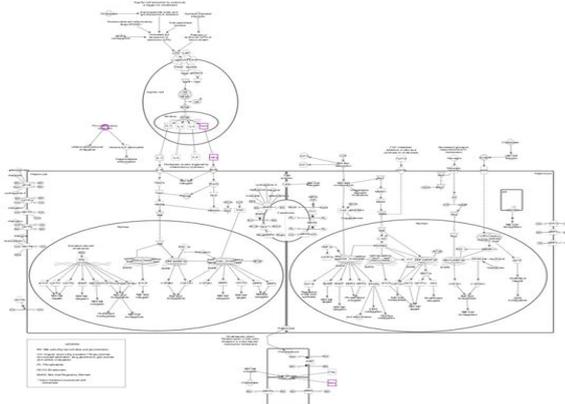


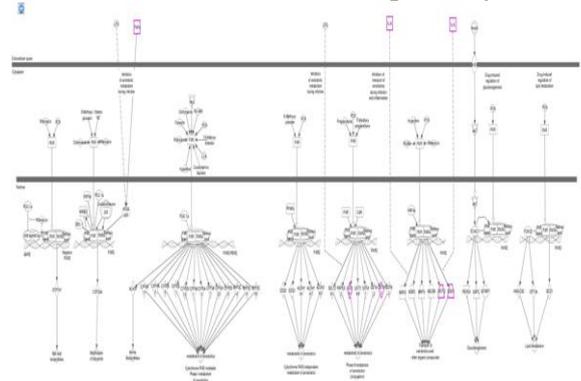
Fig.1 Canonical pathways of the combined action between target proteins of *P.cocos* and related genes of Jaundice

### 3.4 Action sites of canonical pathways

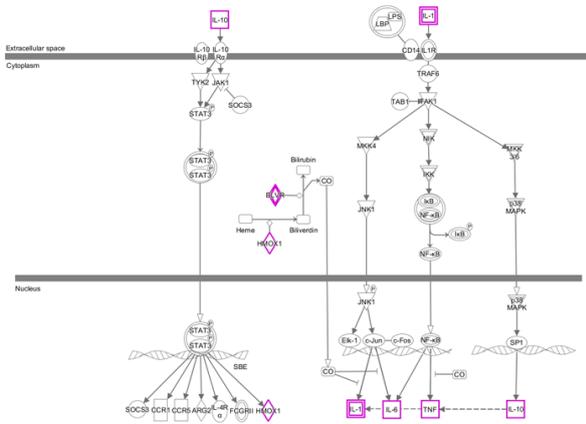
In order to define the action site of the common canonical pathway of *P.cocos* in the treatment of jaundice, take further research on canonical pathways as Hepatic cholestasis, PXR/RXR Activation, IL-10 signaling, Xenobiotic metabolism signaling based on previous results (Fig. 2A, B, C, D). The analysis results indicate that TNF, IL-1B, IL-6 may be the action sites of canonical pathways.



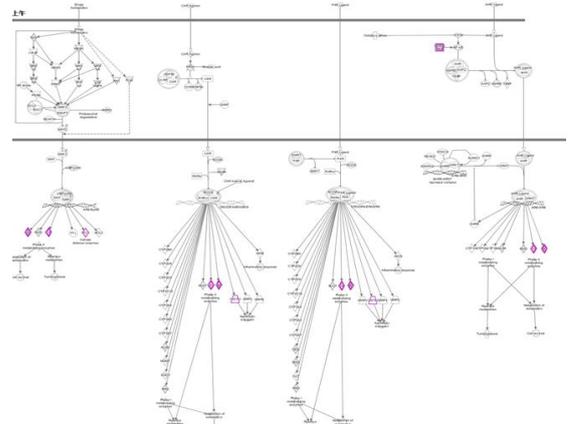
A. Hepatic cholestasis



B. PXR/RXR Activation



C. IL-10 signaling



D. Xenobiotic metabolism signaling

Fig.2 Action sites of canonical pathways of the combined action between target proteins of *P.cocos* and related genes of Jaundice

#### 4. Summary

Jaundice often involves various illnesses in modern western medicine, such as: hepatocellular jaundice, obstructive jaundice, hemolytic jaundice, viral hepatitis, liver cirrhosis, cholecystitis, cholelithiasis [7]. The *P.cocos* is widely used as a traditional medicine in treatment of Jaundice. Its extract has beneficial effects on inflammation, cancer and immune function [8-11]. The combination of *P.cocos* and western drug for patients with Jaundice also receive a good therapeutic effect. [12] In the research at home and abroad, by means of bioinformatics methods such as database and IPA software, the network fit and interact with the related genes of disease and the active target of compounds, which can be used to explore the potential target for the treatment of the disease. [13-15]

The results of networks illustrate that there are common and different molecules between molecular networks of both, and their biological functions are complicated.

There were 56 combination canonical pathways between the target protein of *P.cocos* and Jaundice related gene that involves Metabolism, Cellular immunity, etc. by means of Comparison module. According to the most relevant 4 canonical pathways analysis, TNF, IL-1 $\beta$ , IL-6 may be the action sites of canonical pathways. The research of LIU-C show that, high dose of *P.cocos* play a good role in anti-jaundice in the rat model of jaundice induced by alpha-naphthylisothi (ANIT) duct, and inhibit mRNA expression of IL-1 $\beta$  and TNF- $\alpha$ , improved mRNA expression of IL-4. The effect maybe take from immune regulation [16]. WANG-LS used drug of removing heat from blood (include red peony, Herba Artemisiae Scopariae, Salvia miltiorrhiza, *P.cocos*, Rheum officinale, Pueraria) to eliminate effectively toxicity to cure severe jaundice in patients with chronic hepatitis B, TNF- $\alpha$  and IL-6 depressed. [17] The effect of *P.cocos* in treatment of Jaundice may associate with material metabolism. [17] Pregnane X receptor (PXR) binds as a heterodimer with the 9-cisretinoic acid receptor (NR2B) to DNA response elements in the regulatory regions of CYP3A genes. Although PXR evolved to protect the body, its activation by a variety of prescription drugs represents the molecular basis for an important class of clinical drug interactions [18]

The bioinformatics results are quite consonant with the previous theoretical and experimental studies. Therefore, bioinformatics analysis will provide the beneficial reference for Pharmacology of Chinese medicine and prescription mechanism.

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