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# Consistency between traditional Chinese medicine constitution-based classification and genetic classification

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## KEYWORDS

Yin-deficient constitution;  
Yang-deficient constitution;  
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**Abstract** *Background:* We studied the consistency between two classification systems for categorizing patients: traditional Chinese medicine (TCM) constitution-based methods, versus genetic clustering. Genetic classification in constitutional identification was also evaluated.

*Methods:* A TCM physician evaluated the constitution of each patient, according to four examinations (inspection, auscultation-olfaction, interrogation, and palpation). Those who met the criteria for Yang-deficient, Yin-deficient, and balanced constitutions were enrolled in the study. Peripheral blood samples were obtained from the participants, and peripheral blood mononuclear cells were separated from the samples within 2 hours. Total RNA extraction from the white blood cells was performed; and an Affymetrix HG-U133 Plus2.0 array was used to determine the peripheral blood gene expression profiles. The samples were classified using a support vector machine genetic classifier, and the “leave-one-out” method was used for validation.

*Results:* The global gene expression profiles of 32 samples were grouped into three categories, and the samples in each of the gene categories corresponded with the three constitution categories. The three constitution types were distinguished using the genetic classifier with 165 genes. The accuracy of the prediction classification was greater than 95% using mathematical method.

*Conclusions:* Participants with Yin-deficient, Yang-deficient, and balanced constitutions have varying physical characteristics and gene expression patterns. Additionally, the results from

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TCM constitution classification matched those obtained by genetic classification. Finally, our preliminary gene classifier distinguishes among Yin-deficient, Yang-deficient, and balanced constitutions, and provides a methodological basis for identifying the different constitutions. © 2015 Beijing University of Chinese Medicine. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Medicine's guiding model is anticipated to change in the twenty-first century from "disease-oriented" to "health-oriented" or "holistic" medicine, with an emphasis on the prevention, versus the treatment of diseases. Further, group treatment approaches are expected to be replaced by individualized medicine and more specific treatment approaches. Concurrent with modern medical science developments, the global medical community commonly believes that the best medicine is not curative, but rather is preventive.

TCM constitution in individuals can be changed when the inherited and acquired characters are affected after birth. Thus, an entity with relatively stable physiology, psychology and mentality is formed.<sup>1</sup> Chinese medicine constitution approaches for studying the status of an individual's health are well-developed. Individuals can be classified into nine constitution types according to an epidemiological study of the Chinese Han population<sup>2</sup>: balanced constitution, Qi-deficient constitution, Yang-deficient constitution, Yin-deficient constitution, phlegm-dampness constitution, damp-heat constitution, stagnant blood constitution, stagnant qi constitution, and inherited special constitution. Constitution classification facilitates the path toward personalized medical care. Constitution identification takes an individual's physical fitness as an observational object, assesses physical state and classifies different physical characteristics to elucidate the overall health factors and individual differences in human participants, which can then be used to develop preventative medicine principles. Thus, intervention can be based on the qualities presented by different people.

The biological basis and clinical relevance of the constitution system in TCM have been intensively investigated over the years.<sup>3–5</sup> TCM constitution may reflect genetic features, and different constitutions might result from differential gene expressions, an area that needs to be confirmed by further research. In previous studies, genetic classifiers have been assigned to classify participants using a mathematical model. Classifiers were assigned to known categories of unknown participants. Through a novel research approach, we aim to determine whether the classification schemes of TCM constitution conform to genetic differences, using a gene classifier system.

In TCM theory, when Yin and Yang are in equilibrium, positive health is achieved and sustained. People with Yang-deficient constitution are marked by aversion to cold while those with Yin-deficient constitution by aversion to heat. The study of these two constitutions is the foundation of all other TCM constitution-based research. Various

studies have demonstrated that the Yin-Yang phenomenon can be explained at least partially through molecular biology.<sup>6,7</sup> In one study, the nuclear transcription factor Yin-Yang1 (YY1) gene was shown to have similar regulatory functions to traditional Chinese Yin and Yang. The YY1 transcription factor was identified as targeting a plethora of potential target genes important for cell proliferation and differentiation which is similar to Yin and Yang in TCM.<sup>6</sup> Another study showed that YY1 possessed a wide range of regulatory functions, including a role as a critical negative regulator of excitatory amino acid transporter (EAAT) 1 in one of two glial glutamate transporter pathways.<sup>7</sup> So Yin and Yang can be partly explained by molecular biology.

Support vector machine (SVM) is used as a new approach for data mining. It is based on information provided by the limited sample in a complex model (i.e. the specific learning accuracy of training samples, and accuracy) and learning ability (i.e. any samples without error identification) to seek the best compromise and to obtain optimal generalization ability.<sup>8</sup> SVM can better solve the problems of small samples, nonlinear, high dimension and local minimum points. It is an important method in the field of machine learning to solve problems and estimation of nonlinear functions, and it is widely used in pattern recognition, signal processing and time series prediction.<sup>9</sup> It is an excellent classifier owing to its robust theoretical background, strong adaptability, and extensive generalized functions. Because of its suitability with small sample sizes and its generalized performance, SVM has recently been internationally used in the pattern recognition field.<sup>10</sup> Furthermore, its scalability and generalization capabilities make it very suitable for classification study.<sup>11–13</sup>

Our research aims to evaluate whether a relationship exists between TCM constitution-based classification and genetic clustering classification, and to explore the application of a genetic classifier to constitution identification. Genomics is the essence of biophysical research. This study has selected the Yin and Yang constitutions to carry out the biophysical genomics research. The results will provide a strong basis for further study of the TCM theory and clinical application.

## Methods

### Participants

Volunteer participants were chosen from students without compensation at Beijing University of Chinese Medicine and from staff at Beijing New Era Company, between February 17 and May 26, 2012. Participants were 18–28 years old,

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