Monograph

Precision Medicine: To Start the Era of Status Medicine to be the Mainstream Medicine

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Abstract

Through the analysis of the limitations and difficulties of disease medicine, the article stated the meaning of precision medicine is not based on precision of disease medicine. The core is to create a status medicine system that can describe and control personalized human body status, and open a mainstream medical era of status medicine. Traditional Chinese Medicine (TCM) has not been understood by the Western scientific and medical community. TCM is essentially a status medicine system. The human body status description system of TCM is established at a holistic level. It is different from the human body status description system of precision medicine that established at micro-level based on genome research, proteomics, metabolomics, etc. In recent years, progress in complexity science and uncertainty principle of in vivo is revealed, the “analysis–reconstruction” model of reductionist medicine are proved to be unworkable from the theoretical and practical point of view. Therefore, status medicine can only adopt TCM model to establish the holistic human body status description system, and to start from studying holistic human behaviour and function. Status medicine that based on holistic level has advantages that human status description established at micro-level cannot match, in terms of simplicity, comprehensiveness and precision of grasping human status, development of macro level drug, as well as integrity and simplicity of controlling human status. To establish a precision medicine system at holistic level based on TCM, by means of modern medi-
Keywords

Precision medicine; Traditional Chinese Medicine; Holistic Medicine; Status Medicine; Personalized Medicine; Disease Medicine

Introduction

Precision, by definition, means precise and accurate. In medical term, it means precise diagnosis, accurate knowledge of drug and treatment, as well as precise selection of methods and medical means during treatment process.

In fact, since the early beginning, medicine has been walking in the precision way. The introduction of new diagnostic tools, the discovery of a new pathogen and a new research drug, to a certain extent, leads human towards precision on disease diagnosis and treatment.

Today, modern medicine can make a diagnosis among 29,000 different diseases. Disease diagnosis should be regarded as quite accurate by the introduction of various detection technologies. However, modern medicine got no significant improvement of disease regulation and control capability. It is still remain in controlling rather than treatment for most diseases. For selected drug of a disease treatment, due to side effects, it turns into the cause of many other diseases.

Disease-centric medicine seems to have come to its end. People look forward to a new medical system. As early as a few decades ago, insight medical professionals recognized the limitations of disease medicine. They explore beyond what we call ‘science’ of modern medicine, such as, natural medicine, alternative medicine, translational medicine, Evidence-based medicine, etc. It reflected the fact that modern medicine trying to get rid of the shackles of traditional analysis medical based on anatomy, histology, cytology, physiology, and biochemistry, and to explore outwardly a new medical model.

Today, precision medicine greatly enhances the accuracy of diagnosis and treatment of disease by means of progress in technologies such as, modern detection analysis, artificial intelligence, and big data. It is not the core meaning at all. But it changes the frame of reference and the idea of precision. It heralded the end of 300 year ruling era of disease medicine. Thus, it will open the era of what we call a “body status medical system”, or the medical era of which “disease medicine” and “body status medicine” complementary co-existence.
The Background of Precision Medicine

For what a disease is, currently it still does not have a unified and clear definition. According to the International Classification of Diseases System (ICD), for 120 years of history, the classification of the disease is based on four major characteristics. That is the cause of disease, part, pathology and clinical manifestations (including, signs and symptoms, staging, type, gender, age, onset time of acute and chronic disease). Each of them constitutes a taxonomical standard, and a classification axis is formed, thereby forming a multi-axis classification system [1]. Since ICD is widely accepted in the international medical community, so far the modern medicine basically can be said has established the diagnostic, treatment and prevention system in response to ICD’s definition of diseases.

Today, clinical practitioner found that based on ICD system, modern medicine established a huge disease medical system contained more than 29,000 kinds of diseases. It is still far from enough to grasp the actual complicated clinical diseases. Due to individual differences, some specialized drugs of a disease are effective to some people but ineffective to others. Their side effects of one kind or another are always cannot be avoided as well.

The success of the Human Genome Project has greatly broadened people’s horizons. In research study, scientists found millions of gene mutation that may relate to human disease. Further studies showed that the vast majority of gene mutation associated with human disease has no absolute specificity [2]. In other words, the lifetime risk of suffering from a disease could not be fully determined by human gene. It is similar to plastic kitchenware manufacturing process. The mold design is the first priority, but mold manufacturing and product processing cannot be ignored. When product has problem, it may due to mold design flaw, or the mold does not meet the requirements, or it may be a problem with the production process. The problem may also be due to the worker technical standards, as well as the management control on production process. Similarly, a person suffering from a disease may be associated with the gene problem. It may be in the processing problem of protein synthesis and metabolism. It also may be due to all sorts of external pathogenic factors, or mental, diet, lifestyle that affecting the body’s normal physiological functions, as well as the organs and systems-level metabolic processes.

Obviously, find out genes is far from enough for understanding human life and disease processes. Thus, with the progress of genomic research, there are blustery omics researches on proteinomics, metabolomics, transcriptomics, lipidomics, Immunomics, glycomics and RNomics. Currently the study of millions of genes mutations and their correlation of human disease has just started. How-
ever, biologists knew that abnormal proteomics and metabolomics occur in human life process are much more than gene mutations. It is different from the relatively stable gene mutations, and it shows a significant dynamic characteristics.

If we put the abnormal indications found in omics research into further refinement for human diseases, we will get a disease classification system of astronomical scale with billions, or tens of billions disease classifications and it is not including the situation resulting from a group of single indicator. This will be the situation that cannot be faced by any science and human intellectual.

Preliminary study on the correlation of gene mutation and human disease showed a disease often associated with more than one gene mutation. That is to say, in most cases, human disease is not determined by a particular gene. Thus, different combinations of disease related gene mutations may affect the disease differently. If we put the differences between gene mutations for disease classification refinement, we not only have to consider the disease caused by the single gene mutation, but also have to consider the diseases caused by the different combinations of gene mutations. A two-to-two combination of millions gene mutations will reach mega digits. It will be an unthinkable astronomical number for a three-to-three, or four-to-four combination. We can imagine that, even though the vast majority of these combinations are not clinically significant, and it is only one thousandth of them are meaningful, then we still have to face a billions of disease classifications by taking the two-to-two combination only. Moreover, the recent gene related study found it is not uncommon for a disease to be affected by more than 3, or even more than 5 gene mutations. “Molecular Cancer Therapeutics” recently published results of a study to explain the problem. In the study, Schwaederle et al carried genetic test for 439 patients with different tumours, and the results showed there was 96% of patients had tumours with at least one gene mutation, and an average of three gene mutations and the gene mutations types of most patients are different [3]. Still, we have to face proteomics, metabolomics and so on, much larger than the genome. Obviously, with such a scale of complex human pathological states in disease process, the current disease classification system is not adaptable.

Disease-centric medicine has come to its end. The development of modern medicine requires not only new technologies and methods, but also looking forward to the birth of a new medical model. Thus, the concept of personalized medicine came into being.

**Precision Medicine: Transition from Disease Medicine to Status Medicine**

Precision medicine program is first proposed by the American scientific community—leading the world’s science and technology and treat Western medicine as the mainstream medical. Following the vigorous advocacy
of the world’s two most powerful economies—the United States President and the China Head of State, as well as the blitz of medical professionals, it has now become the hot topic of common concern worldwide.

For US precision medicine plan, the definition of precision medicine is to develop personalized treatment program that tailor-made and based on individual characteristics of each patient. Obviously, the purpose of precision medicine is not limited to precise diagnosis, or precise understanding and grasping of drug and treatment, or even accurate selection of treatment program. More importantly, it is the change in the precise frame of reference. That is, the precise frame of reference is no longer the disease classification system that we already knew. It is the establishment of a classification system independent of disease, and can be customized to describe the human characteristics. It is the human body status description system.

NIH Director, Francis Collins, when interpreting precision medicine plan, said that he envisioned a grand scale to collect one million or more volunteers involved in the large databases study. He said that participants would be required to render biological data as specimens including the number of cells, proteins, metabolites, RNA and DNA, full genome sequencing, behavioural data and electronic health records [4]. Obviously, the US scientists use big data analysis - with extensive statistical correlation between the various measurable indicators of human body in a variety of diseases - in order to reflect the overall status of the human body. It is the foundation of a more in-depth, accurate and comprehensive description of essential characteristics of the human body.

In general, from the perspective of modern science, to study any object or a system, we must first establish its status description. Let’s take the status description of a closed vessel as an example. We introduce 3 variables, temperature (T), humidity (W) and pressure (P). We refer them as status variables. These 3 variables formed the status description system of the closed vessel. Suppose the temperature may be taken as an integer value in the range of -99° to 100°; the humidity may be taken as the percentage ratio of the actual water pressure to the saturation vapour pressure under the temperature, i.e., the relative humidity in the range of 1% to 100%; the pressure may be taken as an integer value in the range of 1mPa to 100mPa. Thus, the status (Si) of the system at a time can be described as follows.

\[ Si = (Ta, Wb, Pc) \]

wherein, \( a = -99 \sim 100; \) \( b = 1 \sim 100; \) \( c = 1 \sim 100 \)

This is a status description system that can describe 1,000,000 system statues with 3 status variables.

Study of the human genome revealed that the human body has about 20,000 to 25,000 protein-coding genes. The original estimation was more than 100,000. With better-quality genome sequence and gene identification
technology found, it is now gradually revise downward to the current number. If we bring more than 20,000 coding genes as status variables, while the standard status and the mutation status of genes to represent different status values, then millions of genes mutation and the astronomical combinations can be represented by a status description system consisted of the 20,000 or more status variables. In this manner, for information on human behaviour and disease related data, such as, proteomics and metabolomics, we will face a much simpler status description system, and the human body status can be dynamically described better.

The problem is different mutations of the same encoding gene do not often exist a linear relationship in expression. The drugs targeting them vary in many cases. That means these relatively independent gene mutations can only be expressed by different status variables. That is, each relatively independent gene mutation of each encoding gene should be represented by one status variable. Thus, twenty thousand protein-coding genes constitute a subsystem of twenty thousand variables containing several statuses. The total of all status variables that belong to different subsystems constitute a status space represent human personalized gene mutations. In hundreds millions of status variables, we assume that only 1% of them got independence. Thus, in millions of independent status variables, even the number of two-to-two combinations will reach a trillion.

The introduction of status variables to describe a system, in particular, to describe the behaviour of a dynamic system, it is typically employed by science research on real system study. US precision medicine plan scheduled to start the Million Volunteer Project in fiscal year 2016. In order to express the huge personalized information, the algorithm design and processing technology is essential. Raising this technical aspect into the methodology level of a science subject development, the impact on the science subject will be disruptive.

Since there is a gap between disciplines, the medical profession has been stressed the special nature of medicine. It seems the methods and concepts that universal to other natural science, does not apply to medicine. Since the rise of modern medicine for 300 years, its medical framework and methodological level followed the tradition of Renaissance. Today, with the advent of precision medicine, personalized description of the human status is needed. The core method of traditional single factor analysis and disease description has been difficult to sustain. Modern medicine will have to make disruptive change for mainstream medicine: introducing status variables; through the establishment of status description system that can precisely control personalized status in disease process, to establish the body status medicine; to start a complementary coexistence medical era of disease medicine and status medicine.
Status Medicine: The Medical System Based on Status Description and Status Regulation

According to the Oxford English Dictionary, the definition of medicine is an applied science for disease diagnosis and treatment, and to prevent physical and mental illness, as well as to improve human body quality [5]. The establishment and development of disease medicine is based on disease classification of modern medicine. Treatment of disease required clear diagnosis, effective drugs and treatment. It also required studying the rules and conditions of drug and treatment methods selection according to disease. For disease prevention and prediction, we need to understand the disease, and its development and transformation pattern.

Treatment of disease has been the core of modern medicine. During the 300 years development process, while developing new disease types, it explores the more effective detection method based on a reference frame of disease and to find a more effective treatment. By establish more accurate disease classification, diagnosis and treatment rule, with more in-depth study of the law of disease development, thereby establishing a large clinical medical system.

Status medicine is based on human body status as a frame of reference. So, the detecting method for body status, diagnostic rule, treatment and drug application rule, the interrelated and mutual-influence of status variables during disease process, as well as the evolution of human body status, they all form essential parts of the status medicine.

Generally speaking, different set of status variables can be used in the same description system. There is a certain degree of freedom for status variables choice. The selected system status variables must have a specific meaning that can represent the basic features and behaviour of the system. Status variables vary with different systems. For status description system to describe human body status, the status variables should be selected to meet the 2 general requirements: 1) complete – the number of status variables is sufficient to fully and uniquely describe the status of the system; 2) independence – any status variable cannot be expressed as a function of other state variables. Here the former ‘sufficient’ is to ensure the integrity of the status description system, and not related to the number of status variables. That is the number of status variables introduced is large, does not mean the status variable system is complete. On the contrary, the number of the status variables introduced is small, does not mean the status variable system is incomplete. Integrity is any part of the body, and any function and behaviour, has a corresponding status variable to represent. Independence of status variable refers to any one of which cannot be formed by a combination of other status variables. When the status
description system without independent status variables, it will inevitably be redundant, overlapping, structural confusion and no rigorous logic. In order to ensure the integrity of status description system and the independence of status variables, people usually based on the model that can completely describe system behaviour, through rigorous logical analysis, and introduce status variables to establish status description system. Precision medicine of today introduces status variables and establishes status description system based on the human model established by modern molecular biology, cytology, physiology, biochemistry and other basic disciplines. As we will see later in our discussion, TCM has 2000 years of history in China. TCM called it syndrome differentiation and treatment system, is the status description and control system. It is also created with status variables and based on the ancient China functional model that describing human physiological and pathological activities.

It is a lengthy process for human to understand the nature including human beings themselves. Advancement of biology and medicine is deepening down along different levels: from functional level of external behaviour with overall performance, to system level, to organ and tissue level, to cellular level, to molecular level. There is also expand along the breadth direction include the feature of a body level found that was unknown in the past. For instance, under the effect of new pathogens, to figure out the human behaviour characteristics and disease development and transmission pattern inside human body. It also includes expand research on proteomics, metabolomics, etc. at the molecular level that people previously still do not understand. In the process of scientific development, we will never reach completeness in absolute sense. Especially, deep into our naked eyes cannot completely see and our senses cannot completely perceive the system, organ tissue, cellular and molecular levels. To this end, we can only based on the knowledge of human body at a particular level, to propose a set of the most completed status variables. With the new features of behaviour found, to introduce and supplement new status variables and make them perfect.

With status description system, we can identify the unique human body status in the course of disease with vary widely personalized statuses. For disease caused by single factor, we can approximately define the corresponding status variable is abnormal, and the other status variables are normal (or negligible), such as, disease caused by single gene mutation. For complex disease caused by multi-factor and at a plurality of abnormal parts, the personalized status can be easily made out of a unique combination of abnormal status variables.

The core of status medicine is status description system. To implement status-based control, the study of drugs and treatment for a variety of pathological conditions is also essential. Schwaederle et al carried gene research for cancer pointed out that, at least 90% of patients...
carrying a gene mutation that an approved drug or an on-going clinical trials drug is targeting at. This finding is not unique, for this phenomenon existed in many different malignancies cases. So, for most cancer patients, cancer genetic test can provide at least one treatment program for doctors and patients [3]. Obviously, due to the limitations of disease medicine, clear diagnosis cannot determine treatment uniquely. Since disease medicine cannot distinguish the drug for the same disease and its selectiveness for gene mutation, the clinical application of these drugs are indiscriminate and significantly reduced the effectiveness of the drugs. With the development of genetic medical research, people realized that the effects of these drugs are not satisfactory. It cannot be completely attributed to the drug itself. It is largely due to pharmaceutically applicable status (gene) inadequate identification and distinction. Similar problem existed in efficacy evaluation of Chinese medicine by the drug evaluation system that based on modern medicine. The effectiveness of TCM proprietary Chinese medicine is related to status description system of TCM. It is capable of treating a disease. But it is usually only applicable to the appropriate status type corresponding to the disease. Different drugs are required for the other status types. Most of the proprietary Chinese medicine that spread for thousands years in China and has good reputation, their effect is uncertain when reviewed by disease medicine drug evaluation system. The recent blocking Chinese medicine events in United States, Europe and Japan are due to adverse side effects. It is mostly holding the concept of disease medicine and neglect and abuse the status medicine usage provision of TCM. The Xiaochaihutang of Kampo carried huge side effects in the 90s, and strongly affected the Japanese society is a typical example.

In 1994, in view of the obvious effect on liver dysfunction improvement by Xiaochaihutang in long-term practice, the Japanese Ministry of Health stated it as liver disease drug in the national pharmacopoeia. Thereby forming a ‘grand occasion’ with thousands of liver disease patients throughout Japan took the drug. But two years later, there have been 88 cases of chronic hepatitis patients got interstitial hepatitis and 10 of them death caused by Xiaochaihutang in Japan. After that, Xiaochaihutang sales fell by a third, and it also suffered the risk of expulsion from the health insurance [6]. It is resulting from status drug being included in medical system and ignoring the selectiveness of status drug.

Clearly, the research on drug and medical treatment effectiveness in status medicine must take the corresponding status description system as reference. For selection of clinical medication (treatment), it must be based on the therapeutic effect for the status as well. That is, with the advent of status medicine, clinical pharmacology system is not only with the presence of drug for disease system, but also establishes the presence of drug for various body statuses.
Two Different Scopes of Human Body Status Description System

For human to understand their own is from the observation of the human overall external behaviour characteristics. In ancient, under the dominant view of holistic nature, people use similar things for analogy and predict, it was the main way for people to recognize the unknown. On one hand, it is from people's belief of the holistic natural world and the similarity of natural organization. On the other hand, it is subject to the limitation of scientific and technical development at that moment. Today, with the development of complexity science, it is recognized that, to establish a status model system through metaphor and analogy and to continuously improve and correct the model at empirical test, it is the only viable way for people to understand complex system and to grasp the holistic law. This is the profound understanding of modern science from its 300 years development, through analysis and decomposition of research object and integration based on the analysis and decomposition, thus gradually realized the limitation of the ‘analysis-integration’ cognitive style. TCM has 2000 years of history, it still able to create stunning medical miracles in today's highly developed modern technology. The reason is that TCM built the human body model and body status description system and adopted the approach thoroughly, and use the approach to reach the level that complexity science cannot match.

Modern medicine was originated in Europe. After the second half of the 15th century along with the beginning of the Renaissance in Europe, the establishment of the 17th century Newtonian physics system, and the first industrial revolution began in the mid-18th century, there was a complete change in the perception of the understanding of the world. With the rise of the mechanistic view of nature, the holistic form of exercise was replaced by low-level form of exercise, enabling reductionist scientific method to become the mainstream method. Anatomical decomposition and one-factor analysis medical methods were deemed to meet the contemporary concept of science. The analytical methodological medicine gradually developed, as holistic medicine was relatively weak in Europe, it became a scientific medical system, and occupied the position of mainstream medicine. The holistic approach of traditional medicine was considered to be unscientific, was marginalized and gradually faded out from the stage of history.

The first collision of Western analytical medicine and holistic medicine was about a hundred year ago. Since the Opium War in 1840, following the invasion of foreign powers, Western medicine entered China as a by-product of Western civilization and science. Defeated in the Sino-Japanese war in 1895, Chinese people was introduced the concept of Western science and technology as well as Western civilization. TCM is irrelevant to modern Western science concept, got an unprecedented impact.
In TCM, in order to explain the behavioural function of human body associated with disease, the basic life substances of five internal organs and six hollow organs as well as Qi, blood, body fluids, etc. was introduced. With analytical medicine's advancement in anatomy and physiology, it was found that the understanding of TCM in organs and basic life substances are totally different from the actual same named organs and body fluids under the scalpel. The description of TCM is far from the truth and details. Clearly, from the analytic empirical science perspective, the theory of TCM is not scientific. In modern times that analytical science dominated the mainstream civilization. Western medicine with the same strain of Western science, replaced TCM though TCM had two thousand years of history in China. Western medicine became the mainstream medicine in China and the status quo continued until today. TCM was developed from five thousand years of Chinese civilization and it had become one the world’s most powerful traditional medicine systems. It had played a significant role in the process of multiplication and prosperity throughout all the various Chinese dynasties. It had created numerous medical miracles that still could amaze the medical science of today. However, it still could not escape the fate of being suppressed, marginalized and some of the know-how were even abolished.

In modern medicine that characterized by anatomical analysis, the study of human body is started from organs and tissues level. However, this level of knowledge alone cannot fully reveal the human basic physiological and pathological activities as well as the mysteries of life process. With the advent of microscope, discovery of cell, and the rise of biochemistry, human understanding of life gradually deepened. Molecular biology mark the human understanding of life has gone deep into the most basic unit of life – the molecular level. From organ tissue and cell, to molecular level, human cognition about themselves is gradually moving away from where their senses can directly percept. To establish a human body status description system at the molecular level, we not only need to know the static information about which elements at this level the human body consists of, but also need to know the dynamic links of these elements on structural relationship, interaction, and mutual-effect, etc. within a human body. Genomics, proteomics, genomics lipids, carbohydrates genomics, transcriptomics and other genomics research is carried at this level. The US Million Volunteers Plan launched in 2016 to establish the human body status description is also based on this level.

Thus, we see there are status description systems of two different levels. One of them is relatively macroscopic and is established based on external behavioural characteristics of human holistic performance. Such as, TCM established a status description system based on the relatively macroscopic human body model – the syndrome system of TCM. The other one is established based on molecular level elements of human genes, proteins, and
metabolites. That is, the long-term goal to be achieved by the US precision medicine plan.

Generally speaking, the lower the level of status variables require the greater total number of variables to fully express the body’s physiological and pathological activities. On the contrary, the higher level of status variables gives a better level of abstraction and requires smaller number of variables. From the perspective of precise drug research point of view, drugs that are produced according to controlled macroscopic status variables research may function at relatively broader coverage. It will cover the micro level and has the sum of direct or indirect effects of multiple variables. From the control point of view, the more macroscopic status variables, the better the abstract, the simpler to describe the state of the system, and easier to understand and to control. Thus, the precision requirements to identify the body status will be lesser. The accurate requirements of understanding the role of drugs will be reduced based on the macroscopic status variables research. If we were to observe a soldier's beard on the ground from an orbiting satellite, we need a high-powered telescope. But if we were to observe a mountain or a river, we do not need to be so accurate. Similarly, if the missile aims at a vehicle, using the energy of ordinary shells, of course, it needs precise positioning and precise control trajectory. But if we use a bomb to bombard a city, then the accuracy of positioning and control will be greatly reduced [7].

Obviously, the micro level variable precision does not mean the precise description of human body status. Under the same accuracy, the higher the variable level, the higher precision of the overall human body status. The precision of human body control is closely related to the level of variables we have to control. The higher the level, the lower required precision, and the smaller side effects of drugs created. The reverse is true. This is why when we study TCM and Western medicine, we find TCM herbs are very vague, but they are good enough for TCM clinical usage. Western drugs functions are in great detail, from a higher level perspective, there is more uncertainty and side effects.

The US precision medicine plan currently required to collect biological specimens that are very microscopic, such as, the number of cells, proteins, metabolites, RNA and DNA as well as whole-genome sequencing. That is to say, the establishment of a status description system at this level means higher accuracy and the large amount of data magnitude. So, to achieve precision of detection and diagnosis, or precision of drug research, or precision of human body control, we have a long way to go. Comparing with previous medicine, it is down the road from microscopic analysis to holistic comprehensive change.

TCM theory system is originated from the basic functional division of human physiological and pathological activities at the holistic level. In recent years, the progress of body constitutional medicine research shows that, to
represent the relatively stable status of body constitution at the holistic level, a classification scale of about 10 types from TCM can cover all human basic body constitutional types. The human body status description system of TCM, i.e., the syndrome differentiation and treatment system has 100 basic syndromes (status variables) combinations to cover all the body’s basic pathological process. Clearly, the status description system of TCM has the top level of abstraction, i.e., the highest level. The requirement for precise diagnosis and precise drug research will be lower and the developed drug will have better macro and long-term effects.

Just think, if there is a status description system with 100 variables (such as the syndromes in TCM) as reference, and we precisely identify 80 of which for understanding of the patient status, then we can say we achieve 80% precision on the understanding. Whereas if the status description system has 10,000 variables (such as the detection indicators of modern medicine) as reference, to understand the patient’s status, even though we precisely identify 500 of which, we can only say that we achieve 5% precision on the understanding. That is why TCM can grasp the patient’s overall status a lot better than modern medicine, although the former precision of symptoms and signs identification are far less than modern medicine. Obviously, precise understanding of human status involves technical issues of measuring methods and instruments precision. Besides, the level of reference status description system and the total number of status variables are more vital related. The lower the status description system level, the more the total number of parameters and the more the difficulties to achieve precise identification.

TCM has mature status description system that can cover the human basic physiological and pathological activities (i.e., TCM theory model and syndrome differentiation and treatment system). It has a higher level and fewer status variables. More importantly, for thousands years of clinical practice from ancient to now, TCM established and improved a complete human body status control system through theory, treatment, prescription and drug usage. Obviously, TCM is closer to the goal of personalized treatment in precision medicine. To achieve the long-term goal of precision medicine, TCM has a higher starting point than modern medicine, and take the lead [8].

Complexity: The Problems have to be Faced in Precision Medicine Development

The methods and knowledge we applied in medical research and clinical practice is gradually formed by modern medicine during its development in the last 300 years. In recent decades, mainstream concept of natural science has gradually changed from dealing with simple to face the complexity directly. Before methodology of dealing with complexity is established and made perfect,
medicine as applied science, still have to use conventional scientific method to develop medical knowledge.

Conventional science is developed based on the belief of simple word and simple natural law. The analysis and decomposition methods of reductionism are suitable for relatively simple system research, or the complex system that can be decomposed into a plurality of relatively simple system problems. For objects or problems that cannot be decomposed, the less important factors and links will be ignored, boiled it down to a simple system problem to be addressed.

With the deepening of human understanding on the nature, scientists have come to realize that human is surrounded by natural systems: botany, human body system, ecological system and social system. All these are composite and numerous, with complex internal structure and interrelated complexity and systems that are difficult to be decomposed. Trying to reduce these complex systems to fit into the framework of simplicity science is just like cutting one’s toes to fit into one’s shoe. The traditional reductionist analysis cannot totally fully grasp and master completely the intricacy of the behaviours and internal laws of the systems. In the face of the deep oceans of complex systems, science must not forsake its own ideal and natural right to reveal the truth. Science must paves a path when a mountain is on its way, build a bridge when there is a river to cross, introduce new and suitable research methods and tools to expand its territories. Thus, complexity science comes into the scene.

As a “21st Century Science”, complexity science leads to the paradigm shift in science concepts and a reform in its way of thinking. Science expands from its linear and orderly domain to a non-linear and uncertain domain. Formerly considered to be non science and domains that are considered to be out of the reach of science are gradually incorporated into the science domain. Thus, the goal of science shifts from its original pursuit of simplicity to the current understanding of complexity [9].

Human, as the most advanced product of biological evolution on this planet, scientists estimate the human body consists of about 60 trillion cells. The elements of molecular level in human life involved are far more than that. There is a wide range of dynamic links between cells and molecules in human body. As an open system, human body keeps a closely link with external environment all the time. In such an open complex giant system, complexity become the problem have to be faced in medical development.

In recent centuries, the progress of Western medicine and Western science are almost synchronous. Every step of improvement in modern science method and technology will push forward the related fields of Western medicine. With the progress of mathematical model and big data analysis method, and advancement of artificial intelligence and computer simulation technology, human capacity for complex system integration has made great improvement. However, when face with the complex giant
system of a human, those improvement is still negligible. Genes, proteins, metabolites, lipids, carbohydrates, and RNA are the basic molecular level elements of a human body. The recent studies of these elements are basically in categories. That is, the genomics research of systems biology in today is still under the guidance of reductionism as a whole.

In reality, human body system is not an accumulation of categorized elements, such as genes, proteins, metabolites, lipids, carbohydrates, RNA, etc. Human body system is an ordered structure formed by a variety of different class molecules that was organized together in an organic intertwined way. Complexity science research shows the most important feature of complex system is that, the overall function and behaviour is not equal to the sum of each composited parts as well as their different class of function and behaviour. Inside the whole, since the mutual-effect of each part and each class will make some properties and functions of the part lose, and some new nature that do not belong to any part appear. In categorized genomics research, even though the features and functions of different genomics were found, uncertainty will be still existed when integrating them into the whole behaviour and function.

It is not feasible to understand the holistic human body by attempting to take the ‘analysis-integration’ route. The research of complexity science already gave a clear conclusion about it. To grasp the holistic human body, we only to face the complexity directly, take the complex human body as a whole. From examine its behaviour and function under natural conditions, to establish its model and its status description system.

The US precision medicine plan takes cancer treatment as the short-term goal. Cancer is a disease resulted from and restrict to abnormal part or factor. Precisely targeting disease and develop precise target drug usually can achieve more precise treatment. Even when cancer developed into affecting human body normal life activities, it will spread to and turn multiple parts and factor (i.e., status variables) into abnormal. The patients in clinic usually suffered more than one part or factor (i.e., status variables) lesions. Assuming that the precise diagnosis of the patient’s statuses A, B, C and D were done, and we select precision drug (or, other precision treatment) that was developed based on precision concept. Then how to prescribe precision medication?

Because the drugs or treatment effects are multifaceted, there are positive and negative effects. Drugs that are ‘precise’ for A, may not be ‘precise’ for B. Drugs that ‘precise’ for B may not be “precise” for C or D. When it is said to be not precise, it may refer to side effects. When we have to consider a number of parts and the various elements of the overall disease, the concept of precision may not have much sense. The more useful concept should be ‘optimal’. That is, for disease or for the patient as a whole, to select a relatively better but less side-effects comprehensive treatment solution [2].
Obviously, the precision we talked about in precision medicine is deeply stamped with reductionism method. For disease and patient resulting from single part or factor, precision medicine no doubt have great potential and is relatively easy to realize. Every concrete and valuable result will bring some major advancement in disease treatment and generate great social and economic benefits.

But the reality is that attribution to a single part or specific disease (or patient) with specific factors are very rare. Most diseases (or patients) may involve more than one part (factor) dysfunction. In this general case, even if there are ‘precise’ diagnosis, ‘precise’ drugs, ‘precise’ prescription, and a ‘precise’ treatment solution, precision medicine still have to face many technical hurdles. Serious consideration must be given to the possible hazard due to ‘precise’ diagnosis and the importance of maintaining life activities of the human body that determines treatment priorities and to consider the relevance of correlation, as well as the interrelationship between the structure and the function of each part of the disease and the treatment solution will have a better synergy. We also have to consider the various ‘precise’ drugs, in a holistic manner or in a total solution, enhance to set off their respective side effects. Obviously, by then, precision medicine may have been far beyond human comprehension now for it will not be the treatment of diseases caused by a single specific part or a specific factor, but in the overall level of the overall state of the ‘precise’ human body. It will be the day of the highest attainment of precision medicine [10].

In this sense, finally, precision medicine will become a ‘short-lived’ medicine in medical development process like the old natural medicine, translational medicine and evidence-based medicine do. More profound to reflect the characteristics of medicine methodology idea and name, such as status medicine and holistic medicine (we’ll talk about later) will be precipitated in the medical knowledge system. Precision medicine is indelible of its role in driving medical science forward.

Precision medicine is created in response to the medical science trend of simplicity to complexity. The change brought by the trend is subversive on scientific concepts and methods. We have to adapt the mainstream shift from disease medicine to status medicine. The more fundamental change in medical model is mainstream shift from analytic method to holistic method. Science is like human driving an aircraft towards the unknown world. To reach the destination, it is not only driving the aircraft straight ahead on the line, but also have to consider the destination position at a multidimensional space and to select the best route from the multidimensional directions.

**TCM: The Traditional Medicine that Today Science can Understand**

In fact, regardless of metaphors and analogies methods adopted by complexity science, or the cognitive model of complexity system model establishment, or the status medical model of the core of precision medicine to reflect-
ing the human personalized statuses, are having longer history of human cognitive model and medical tradition than modern science and medicine.

Today, with its magical clinical results, acupuncture has become popular around the world. Acupuncture is a branch of TCM treatment technology. The syndrome differentiation and treatment system of TCM is more profound and has a broader clinical value, but is still not understood by mainstream medicine, and accepted. The reason is that acupuncture is easily grafted onto the technical content of modern disease medical system, whereas the syndrome differentiation and treatment system of TCM involves the medical cognitive method and concept, which is irrelevant to disease medicine.

Now it seems that during the establishment of modern experimental medicine, the ‘unscientific’ ingredients of traditional medicine was abandoned. Naïve of science indeed has throw away something valuable in traditional medicine just like throwing away the baby together with the bath drained.

Metaphors and analogies are common approach in all fiction and poetry. No matter in the East or West, ancient or modern, it is a well-known cognitive style. The basic human theoretical model of TCM was built up through the analogy based on image similarity approach.

In the last two or three decades, metaphor become a scientific method for establishing a scientific theory. American Santa Fe Institute was first introduced to it as a holistic study method for complex systems, to describe the real system and as the basic scientific method for dynamics analogy. Recently, there are more than ten definitions using metaphors and analogies in dozens of complexity science basic definitions. Such as the butterfly effect, fractals, artificial life, the edge of chaos, and self-organized criticality, etc. becoming emerged. Scientists express complex things by analogy when it is difficult to express in precise language, describe complex phenomenon by metaphor concept when it is difficult to describe in language. Certain Important contemporary models of complexity science, such as Genetic Algorithms and Echo Model of John Holland are established by means of these methods.

Today, when we use metaphor and analogy as scientific method to re-examine the thousand years old TCM, we notice that metaphor and analogy were used in the “Huangdi Neijin” (Yellow Emperor’s Internal Canon). TCM called it ‘analogy based on image similarity’. It had all along been widely used to establish the theoretical system of TCM. The theoretical model system of TCM is based on ‘analogy based on image similarity’ of Yin and Yang, the Five Elements and the Eight Trigrams and is constructed through the holistic observation of human basic physiological and pathological phenomena [11].

In TCM, the basic substances of human life activity are Qi, blood, body fluids, and the essence of substance.
(1) Essence of substance – it is parents heredity; constantly replenish from acquired absorb nutrients; it is the most basic substance of human life activities; and it is also the most material basis of various body organs functional activities. (2) Qi – it is diffuse in the body; large and small both without boundary; it has promote, nutrition, warmth, and astringent effects. (3) Blood – it runs in blood vessel; and spread in the body; it provides nutrition for internal organs and limbs. (4) Body fluids – it runs in blood vessel and fluid passage; and spread in the body; it has moisture and nutrition functions.

For functional division based on the health-related behaviour, the human body is divided into several functional subsystems - heart, liver, spleen, lung, and kidney – the five internal organs. (1) Heart – pumping of blood; through blood vessel to spread nutrition substance throughout the body; and presides the mind and spiritual awareness of human body. (2) Liver – the main reservoir of blood; regulation the Qi of human body; regulating the wind, i.e., the ‘wind’ behaviours that related to human disease, such as spasms, convulsions and dizziness. (3) Spleen – for diet and liquid absorption, transport, and spread throughout the body; generating Qi, blood, and body fluids; and as the acquired replenishment for essence of substance. (4) Lung - for Qi and regulating breath; to delivery Qi and body fluid to the skin surface; Qi should be purges dropped in Lung as normal. (5) Kidney – to store essence of substance; create bone marrow through the brain; gasification of urine; separating clear and turbid stream. The six hollow organs are gallbladder, stomach, large intestine, small intestine, bladder, and triple burner. Among them, stomach is for food receiving and digesting; bladder is for storage and discharge of urine; large intestine is for transporting dietary compounds after digestion and absorption; and so on.

For characterization of each subsystem (or basic materials) performance and status, a set of status variables was introduced. Heart is the first of the five internal organs. In order to characterize its functional status, a set of status variables was introduced, heart Qi, heart blood, heart yin, heart yang, heart blood circulation status (if any blood stasis), heart fire (if any). Thus, it constitutes the status space of heart subsystem. Each status variable may be set as normal or several abnormal statuses. For example, heart Qi may be normal, heart Qi deficiency, or heart Qi serious deficiency. Each status is called syndrome in TCM. It is defined by a set of symptoms and signs that is sensible or observable. For instance, the corresponding cluster of heart Qi deficiency symptoms are, palpitations, shortness of breath even worse after the movement, looking Koushi and white. Heart Qi serious deficiency is corresponding to, palpitations, sweating, shortness of breath particularly when moving, lassitude, weak pulse or knotted pulse and so on [11].

The set of all human subsystems status variables constitute a human body status description system. There are
about 100 status variables. In clinical consultation, we can fully understand the health status of a patient by identifying the abnormal status variables through the patient’s symptoms and signs. If each variable represents no more than five abnormal statuses, the 100 status variables can be combined into and represent more than 10 billion different statuses. Although the scale is much smaller comparing with hundreds of millions of genetic mutations status description system, it would be a huge system that can describe more than 10 billion different statuses [12].

In the status description system, since the status variables introduced is based on a predetermined function of the human body model, the integrity of the human body model on human function description, determined the integrity of the system status variables. Structure and rigorous logic of the human body model can ensure the independence between status variables. In fact, there are some problems in the integrity and independence of the status variables of TCM. For instance, the core of the status description system are five internal organs and six hollow organs as well as Qi, blood, body fluids and the essence of substance. It is unable to express the behavioural law of the occurrence and evolution of exogenous disease. So, people have to improve and supplement the model structure and status variables system. For status description of exogenous pathogenic cold development and treatment process, Taiyang, Shaoyang, Yangming, Taiyan, Shaoyin and Jueyin were introduced. To express the status changes in the development and treatment process of exogenous febrile disease from outside to inside of human body, Wei Qi Ying Xue was introduced. To express the status changes in the development and treatment process of exogenous heat illness from upper to lower of human body, Sanjiao was introduced. These status description systems are different from each other and their structure are different from the status description system of five internal organs and six hollow organs as well as Qi, blood, body fluids, and the essence of substance. So, in TCM, it is still adopt different status description system to identify and regulate different disease categories.

Currently, the status description system of TCM is basically enough for clinical diagnosis and treatment. For vastly different individualized clinical diseases, good practitioners can always identify abnormal status variables and develop appropriate treatment program. Of course, due to the incompatibility of several status description systems, for patient that suffering various diseases, especially when the patient is suffering from exogenous and internal injuries diseases, it showed the limitations of overall control. In this case, practitioners often tell patients to treat exogenous disease first and then miscellaneous diseases. This is of course related to TCM treatment principle of ‘acute symptoms, slow the cure’. If there is a united status description system, in many cases, ‘both specimens’ is often the best therapeutic approach [7].

On the other hand, in the comparative clinical study of TCM and Western medicine noted that, TCM based on
the personalized clinical manifestations of a patient, and regarded different patients belonging to the same status (syndrome). But through modern medicine detection, it will find that the lesions and links of the disease are different. And even practitioners using the same treatment method, the effect will be different. Obviously, there are further refinement needs in the status variables system of TCM.

Precision medicine develops status description system based on modern medicine disease classification system, does not mean to abandon the classification system completely. Similarly, Syndrome differentiation and treatment system is the core of TCM that mainly based on the status description system. Since ancient times, there has been symptomatic treatment and disease treatment existed in TCM. The TCM principles of ‘acute symptoms, slow the cure’ and ‘diagnosis and treatment, subtraction with the symptoms’, show a medical model that based on status medicine and taking disease medicine into account.

Modern medicine is on the way returning to holistic medicine and moving towards the era that status medicine becoming the mainstream medicine. TCM itself is a status medicine system. In our previous analysis, the status description system of TCM is established at holistic level. Precision medicine is based on modern medicine and establishes the status description for molecular-level information of genomic, proteomic and metabolomic, etc. With further research, the holistic status description system can be gradually precise and refine. The microscopic molecular-level status description system is able to be abstracted and integrated upward. So, what kind of architecture will medicine be ultimately going to? How to avoid going astray during the process?

China has an old saying, “since ancient times, do not seek future who seek temporary insufficient; those who do not seek global, less than seek a field.” 300 years ago, scientific revolution brought medical progress in terms of analytic concept. To abandoned holistic medicine, the expense of human is enormous, substance, money, and time. Most importantly, countless lives could have been saved. Today, with another big medical change coming, we must not be ‘only bow to pull carts, rather than look up the road’. We should seriously study the problems, technical and economical feasibility of scientific development, and to find the best way for medical science development.

Ways to Holistic Medicine: Top-Down or Bottom-Up

Just a few decades ago, to most people, scientific theory describes a true picture of the real world, and science ultimately shows people the true colours of the nature. Today, with the theory of relativity and quantum mechanics, as incomplete scientific theories, are generally accepted by science community. The uncertainty principle of quantum mechanics has been widely recognized by people. With scientific and technological development, humanity is no
longer the omnipotent observer and controller. Whether to the vast universe or microscopic field of elementary particles, or human beings, what we can do in observation and control are limited.

The analysis reduction method adopted by biology and medical research, required strict control of experimental conditions and keeps only one variable to change at a time. If there were several factors change, we cannot determine the exact causes for the results. However, in vivo, we cannot strictly control experimental conditions. The human intervention for controlling condition will inevitably affect the functional activity that supposed to be decided by its own. Like uncertainty principle of quantum mechanics, to analysis the complex system of a human body, the same uncertainty issue existed.

The more in-depth understanding of the nature, the more recognize the limits of human capabilities. Today, scientific theory, no matter in the eyes of scientists or in the textbooks of primary and secondary schools, are defined as the model to reveal the real system inherent law from certain areas. It does not have to have any other relationship with the actual real world scenarios. After Einstein, the world greatest theoretical physicist, Stephen Hawking, discusses science theory in his classic work - A Brief History of Time. “A scientific theory is. I shall take the simpliminded view that a theory is just a model of the universe, or a restricted part of it and a set of rules that relate quantities in the model to observations that we make. It exists only in our minds and does not have any other reality (whatever that might mean). A theory is a good theory if it satisfies two requirements. It must accurately describe a large class of observations on the basis of a model that contains only a few arbitrary elements, and it must make definite predictions about the results of future observations” [12].

Medicine is an applied science based on prevention and treatment of diseases. The first thing to consider when establishing human model and status description system is practical and clinical values. Precision medicine based on modern medicine to establish a human body description at the molecular level. Its drug and treatment reference must be the abnormal status variables of molecular level. We mentioned earlier that there are hundreds of millions, billions and billions of billions abnormal variables. In the event of illness, even if there is only one thousandth of variables become abnormal, their number will be hundreds or thousands. The effective part or nature of future precision drug will not reach the control accuracy of missile. Because drug will normally affect more one part or element in the human body, side effects are inevitable for non-target part or element. Precision medicine drug research will undoubtedly continue to seek more precise drugs. The precision here must be relative to a particular status variable abnormal. To the point receiving side effects, it is not precision at all. Furthermore, when there is a plurality of variables abnormal in the body, precision for a specific status variable does not mean it also precision for other abnormal status variable or no adverse effects.
Just think, when we put several precision drugs that having a respective plurality of side effects to a patient, can we ensure their overall effect? Will it pulling the target abnormal status variables back to normal without producing a variety of side effects?

Today modern medicine is still in the era of not precisely grasping the drug effect. For a single abnormal variable in the vast molecular level, precision drugs are not yet available for clinical application. Advance in medical research, with continuing precision drugs discovery, the number will be exploded rapidly growth. According to current precision medicine research way, in order to achieve the long-term goal of precision medicine, medicine have to face the situation of using dozens or even hundreds of precision drugs. This is the fact that modern medicine often needs “combination therapy”. With the development of precision medicine, the scale of “combination therapy” will increase. Dealing with complex disease, the integrated drugs that targeting specific abnormal status variable with more or less side effects, the short-term and long-term effects in many cases is uncertain. The uncertainty also presents a personalized tendency. To clarify the issues, we will face hundreds millions of abnormal status variables combinations and an explosion of research works that may need tireless efforts of many generations to do. Even if we figure out the problems, it does not mean we have a viable solution of personalized medicine.

We talked about earlier, the human model and status description system of TCM is established based on human holistic behaviour and function. Compare with micro variables as reference, the drug found in macro status variable as reference is usually has control for body macro features and functions and has a broader scope. The research of viscera and syndrome of TCM as well as clinical study of integrative medicine were carried in China for decades. It showed that each TCM viscera will involve multiple anatomical tissues and organs functional activities. A TCM syndrome (status variable) will involve multiple abnormal elements and variables at the micro-level. Thus, take syndrome as a controllable and develop a drug that can deal with the syndrome, it is no doubt will provide treatment for micro-level abnormal elements and variables directly or indirectly. If we start from the microscopic variables of the lower level, in order to achieve the macro-level control effect, it means the research of drugs that dealing with multiple micro-variables. Even if we find all micro level variables related to this macro variable and developed the precision medicine against them, and taking them to the human body, it does not necessary mean the macro variables (syndrome) will restore to normal. The reason is that, complexity science already given a clear conclusion from theory, the control of upper-level elements does not equal to the sum of the lower-level elements control.

In this regard, it also has been proven in the modern Chinese medicine research. For example, the most important function of ginseng and astragalus is Qi. The modern pharmacological analysis and study of Qi drugs showed their functions at the micro level as follows: regu-
lation of glucose metabolism and lipid metabolism; pro-
more protein, DNA, RNA synthesis; increased albumin
and γ- globulin content; increased peripheral leukocytes,
increase phagocytosis of reticuloendothelial system; en-
hance cellular and humeral immune function and so on.
So, if we find a variety of Western drugs with functions
such as, regulate glucose metabolism and lipid metabo-
lism; promote protein; promote protein, DNA, RNA bio-
synthesis; increasing phagocytosis of reticuloendothelial
system; enhance cellular and humeral immune function;
and let the patient take in them altogether, can it be com-
bined to form the TCM Qi drug function? On this issue,
whether it is based on pharmacologist research or physi-
cian clinical practice, the answer is a very clear, no. Obvi-
ously, to lower the level of drug research control variables,
will greatly increase the complexity of the research and
increase the drug observation uncertainty from a macro
perspective. In searching for precision drugs, the TCM
top-down path is easier and more effective compared with
the bottom-up path of modern medicine. The researched
drugs have higher precision correspond to holistic status.

In fact, the precision drug research for a status variable
(syndrome) in TCM is not limited to the study of single
herb. Chinese medicine modern pharmacological stud-
ies suggested that same category Chinese medicines with
similar function may be different in functional mechanism
at the micro level. Therefore, in many cases, using together
several drugs that cope with the same pathological condi-
tion, due to synergy between different parts and aspects of
drugs, it will show a better therapeutic effect compared to
increasing the dose of a single drug. On the other hand,
each drug (or drugs of same category), may have their
own side effects or TCM refers as ‘bias’. Precision medici-
ne drug research not only requires therapeutic effect for
the target, but also to minimize the side effects in order to
avoid ‘hurting the innocent’. Actually finding such drugs
is not easy. Selection of better therapeutic effect drug or
drug combination for the target and effectively control the
side effects, it is usually the easier way to find precision
drug. It is in the unique way of TCM medicine prescrip-
tion. Prescription for a particular pathological condition,
due to a combination of different aspects and mechanisms
against the target, the drug effect is usually better than
single herb. Because prescription has constraints adjuvant
added to control the side effects (or bias) of the primary
and secondary drug, a good prescription often have better
accuracy both for the target or general condition.

In complexity science concept, each drug dose not
only playing a single role within a prescription. There is
chemical reaction in prescription composition and usage
process. There is also direct effect and secondary reaction
of each drug inside human body. The Interleaving conver-
gence of the causation chain resulting from direct effect
and secondary reaction, making the observed reaction of
prescription does not equal to the simple sum of compos-
itated drugs effects. Interaction between composited drugs
will make the overall prescription lose some of the com-posite drug’s effects, but emerge some new effects that individual components do not have. We observed the ef-fects of a prescription inside the human body, is its con-verging force of direct and indirect reaction, synergistic and antagonistic effects. It is not possible to understand such process by analysis and decomposition methods. So, similar to studying a single herb, we should study the prescription as a whole, and to analyse the status change with respect to status description system caused by the prescription [13].

The core of precision medicine is personalized medi-cine that is the status treatment based on status description system. The core of two thousand years history TCM is syndrome differentiation and treatment system. The latter is also the status treatment based on status description system, and is basically align with the long-term goal of precision medicine. However, its current precision is in-adequate. It is not yet capable to introduce the necessary molecular level abnormal variables into the status description system. The bottom-up approach of holistic human body status description system, due to absence of a rea-sonable top-level design, with the breadth of human body expansion at the micro level and model structure upward integration, we will find some control of micro-level study is unnecessary. We will also find the model structure is unreason-able. It is necessary to reconstruct the model partially according to more rational structure, and re-organize existing knowledge. Similar to building a city, if there is no pre-unified planning and design, endless demoli-tions will be certain during the construction process, and ongoing adjustment is needed for the city structure and the functional configuration of various parts. That means the workload and social costs are much larger. The most important thing is, during the long process before the study reach holistic level, the precision drug de-veloped based on micro-level status description system will be inaccurate and has side effects to human at the holistic level. The uncertainty of combination therapy with a vari-ety of precision drugs is always the problem that medicine has to face and cannot be properly resolved.

Well, is it possible to adopt the human model and status description system of TCM into the top-level de-sign for achieving the precision medicine long-term goal? By means of modern scientific testing and analysis tech-niques, from the top down, is it possible to establish more accurate human model and status description system that integrate Eastern and Western medicine?

Holistic Medicine: The way to Preci-sion Medicine through Chinese Learn-ing as the Essence and Western Learning as the Practical Application

The theory model and status description system of TCM are established based on the human holistic level and disease-related behavioural function. As mentioned
earlier, as a scientific status description system, the integrity and independence of status variables system is essential. In TCM, there are three status description systems, viscera; Qi, blood, body fluids, and the essence of substance; and exogenous disease. Obviously, each status description system has no integrity. Thus, for precision of status description system, the first thing to do is to implement a unified of the four status description systems. We have dealt with the specific program of the unification in detail at a relevant writing [14]. Just to point out here, based on a unified status description system, it will not lead to fundamental change TCM in related status identification standard, regulatory principle and clinical treatment program. It just changes the model structure and the explanation of pathological mechanism.

There is another problem in enhancing the independence of status variables and precision of TCM status description system. In TCM theoretical model, there is a conflict model function description and repeating doctrines. The status variables derived thereby are certainly having structural and independence problems. For spiritual awareness on human thinking activity, there is academic dispute on 'heart possession of mind' and 'brain dominating mind'. As a discipline, contending is allowed in academic. As a model and status description system, the function specified must be unique and the relationship must be structured. For the establishment of status description system based on TCM basic theory, we can only choose one of the different views of doctrine. We should choose the most reasonable rule and deal with the structure based on it, then introduce a status description system that has independency.

The top-down precision of TCM status description system is usually implemented by status variables refinement and restructuring. Status variables refinement is to further divide TCM syndromes into subtypes. Status variables restructuring is usually accompanied by model structure refinement and adjustment to attribute and function of model components. According to today’s scientific philosophy, it should be established based on statistical analysis of the empirical basis. To do this, we must first establish precise definition for abnormal status variables (syndromes), and then carry out correlation analysis based on this frame of reference.

The current syndrome differentiation and treatment system of TCM is defined by the status variables of symptoms and signs. It is difficult to eliminate the subjective interference of doctors and patients in collection of symptoms and signs information and it is difficult to express quantitatively. Therefore, the issue of objective and quantitative disease information is a problem. The solutions are, first, introduce an objective detection index; second, based on the differences in significant diagnosis, to classify the information by minimal applicable classification; third, the symptoms and signs related to a status variable usually not specific to the diagnosis of the status variable
abnormal, but rather related to the probability form. So, it is necessary to attribute the qualitative diagnosis into quantitative, or quantitative and qualitative issue, through fuzzy algorithm or a combined algorithm of fuzzy logic.

Just think, if we follow the design of American Million Volunteers plan, and add symptoms and signs that have diagnostic significance in TCM into the volunteer health information collection process. In the mean time, we increase the syndrome identification of TCM status description system as well as the treatment program development and efficacy evaluation. If we collect the same overall health and treatment information from the one million volunteers, base on this big data, what can we do?

Based on the correlation analysis of TCM syndromes, we can find the better related indicators for various syndromes, including genomic, proteomic, metabolomic and human health status routine testing indicators. A set of syndrome, signs and detection index of the disease was introduced. We found in the radiographic detection of cardiac hypertrophy that the detected electrocardiogram low voltage highly correlated to the deficiency of heart Qi and heart yang; and blood viscosity and cardiac angiography has better statistical relevance with embolization of blood stasis. Thus, the former can be used as one of the indicators for diagnosis of the deficiency of heart Qi and heart yang and the latter can be used as a diagnostic indicator of blood stasis. Hence, to introduce the objective detect indicators into the holistic status description system of TCM, will make the syndrome definition and identification out of the subjective decision by symptoms and signs.

Assumed as refers to syndrome treatment program and treatment evaluation, the response of a particular syndrome treatment is good to some people and poor to the others. If the clinical manifestation and detect indicator of poor response patients showed some kind of regularity, and the regularity cannot be expressed as other syndrome or disease class, then the syndrome needs refinement. To define new syndrome characteristic index by clinical manifestation and detect indicator that showing regularity, the syndrome will be further refined.

In addition, based on an analysis of various clinical manifestations and detection indicators of TCM syndromes, we can find the better relevant syndrome indicators for objective syndrome identification of TCM. The correlation value can also serve the quantitative basis of the indicator for the syndrome diagnosis. A group of necessary or sufficient logical rules for syndrome identification can be screened as well, making the establishment of TCM status identification move from experience-based to rigorous analysis and statistical basis.

To establish TCM syndrome based on empirical clinical statistics, the most important technical difficulty to overcome here is the problem of qualitative and quantitative standards for syndrome definition and diagnosis reference. The disease definition reference of modern medicine is usually through direct observation and objec-
tive testing to find the abnormal of human body structure functions. Therefore, the diagnostic criteria, clinical manifestations and detection index have relatively specific internal relationship. For coronary heart disease and diabetes, both has a clear internal body morphology or detected abnormalities of physiological and biochemical indicators. The introduced TCM syndrome is usually based on the functional description of the theoretical model. It generally has no specific relationship with observed clinical manifestations, but a many-to-many relationship. That is, a syndrome is usually defined by a plurality of non-specific symptoms and signs. These symptoms and signs are often present in the corresponding symptoms set of other syndrome. Thus, the syndrome boundaries are blurred. It is impossible to have a defined statistical regularity before statistical analysis.

The solution is to establish an empirical model. To determine the set of symptoms and signs associated with syndromes according to accepted TCM knowledge and expertise. Then identify the value of each symptom and sign for syndrome diagnosis. Through correlation process of symptoms and signs to ensure the relative independence of symptoms and signs in symptoms set. In addition, select logic rules that affecting syndrome confirmation. Based on this empirical model, through clinical validation and clinical cases repeated operation verification, to adjust and amend the parameters and logic rules continuously, making it in line with expert experience. Then it can be used as the reference for statistical analysis.

Furthermore, to optimize the parameters and rules from accumulating clinical cases big data analysis by artificial intelligence and machine learning technologies. When necessary, we should adjust the model structure by the way of man-machine combination. Thus, we can ensure that by means of modern scientific methods and techniques, the status description system of TCM is on the road to precision and integrate with the detection methods of modern medicine and biology.

To note here is that the purpose of establishing a status description system is to identify and control human personalized pathological status. It is not for revealing the actual life process of human body from macro to micro level. Therefore, the refinement for the status description system is limited and the same principle of the simplest applicable should be followed. To ensure that the human body status description system can meet the premise of identification and control of human status in disease, the simpler the system, the better it is.

Scientific TCM as the core, with modern medicine precise and objective testing indicators introduced, TCM will be into its precision medicine era. The core of this medical system is a holistic model. It will maximize the coherence of TCM and modern medicine knowledge, experience and technology. It has gone beyond the narrow geographical and cultural Eastern and Western medicine
concept and will lead to an unprecedented revolution in concept and thinking way of medicine. The concept and basic approach of this strict scientific medical system is rooted in TCM, but the theory is built on scientific evidence basis. So, it has a qualitative difference from TCM. In complexity science concept becoming the mainstream scientific idea of today, we will call this new medical system, the holistic medicine.

Science knows no boundaries. We still call it TCM today for it had not yet been incorporated into modern scientific system. With the rise of complexity science, mainstream medicine change from disease medicine to status medicine. TCM mystery has been lifted and revealing it is more profound than reductionist science and disease medicine. As a representative of the 21st century science and mainstream medicine, the name of TCM may become history. But the holistic level status medicine that based on TCM concepts, methods and system, i.e., the holistic medicine will be the mainstream modern medicine of the 21st century.

**Future Medical Structure**

Under the three major trends of times: the rise of complexity science, medical transition to personalized medicine, and rejuvenation of TCM, medicine is in the eve of an unprecedented change. So, what will be the structure of modern medicine in the 21st century?

As mentioned earlier, we know that the theoretical model of TCM has about 20 actors: heart, liver, spleen, lung, kidney, Qi, blood, body fluid, and the essence of substance, etc. The status description system has about 100 status variables. The study of human biology shows that the total number of cellular lever human body has about 60 trillion variables. At the molecular level, the kind of gene mutation has more than 100 million and there is far larger group of proteins, transcription group, metabolomics, etc. Obviously, the two levels are far apart. The road from analysis to synthesis is out of reach. Modern biology and medicine research on human body further revealed that the relationship of each part or element within the human body system is complicate and there is no strict hierarchy. In many cases, the interaction in molecular level directly affects the behavioural change in the organ and tissue level. For instance, the adrenal cortex hormones on the heart will directly cause heart beat rhythm accelerate; the serotonin in peripheral tissues will directly lead to vasoconstriction.

Also as previously mentioned, in order to achieve the long-term objective of precision medicine, it is impossible to achieve the human full dynamics holistic description by the bottom-up analysis-integration approach. For refinement of human body status description by top-down approach, it will not drill-down successively along the hierarchy of human body revealed by modern medicine, but will carry out refinement from human behavioural functions perspective. The description and definition of the
behavioural functions can be achieved through external symptoms, signs and detection index. These indicators may at the organ and tissue level, it may also at the cellular and molecular level. Like the US precision medicine plan, it is not only included the genomic, proteomics and metabolomics indicators, but also included the behavioural data of holistic human clinical manifestations.

From holistic status description of TCM, to molecular level, genomics, proteomics and metabolomics that reveal life activities, there is a vast unknown space. Science is not a panacea. Today’s science could not be expected to completely open the black box of human body and to expose under broad daylight the internal process of all functional activities from molecular level to holistic level. Scientists are just trying to examine the input and output of the black box and to presume the inherent laws. Then gradually validate and improve our understanding this laws and to achieve the purposes of health care and effective disease treatment.

The understanding of disease and the law of disease, as well as to reveal various possible status of life process, they are the two difference but both effective paths for exploration of the vast human body unknown spaces. So far, Medicine has made tremendous achievements along the two paths. In TCM, the syndrome differentiation and treatment system based on status description and control, as well as the disease identification and treatment system based on disease diagnosis, were combined for clinical practice application. The Western medicine with disease medicine developed till today is aware of disease medicine limitations and start introducing personalized medicine mechanism based on status identification and control. Disease medicine and status medicine are ‘moving forward in an orchestrated effort’ from different directions and angles to attack the unknown space inside human body. For personalized pathological process and control law that cannot be described by disease medicine, status medicine provides effective solution for it. For understanding of disease common law, as well as the development of common disease treatment, the role of disease medicine cannot be replaced by status medicine. Therefore, it will continue to be the era that disease medicine and status medicine co-exist in the 21st century modern medicine. But the future disease medicine will have a higher level of integration and unity of modern disease classification system and TCM disease classification system. The future status medicine will be based on holistic level but combine microscopic detect indicators and has strict and logical structure. It is a more scientific status medical system with empirical basis.

More specifically, status medicine is based on TCM theoretical model and status description system. Through scientific reconstruction of the structure, make it a scientific status description system that available for empirical test. Then introduce modern detection means including genomic, proteomic, and metabolomic, etc., the micro-level detection index, as well as the behavioural informa-
tion of human body symptoms and signs. Put the precision of human body status description into sustainable development. The control of the status description system is based on TCM syndrome differentiation and treatment system. With the introduction of modern medicine control methods and means in dealing with specific status, it gradually develops into a more precise status control system that integrating Eastern and Western medicine.

Disease medicine is mainly based on modern medicine disease classification system and combined with rational elements and ingredients of TCM disease classification system. Based on the co-existed medical structure of status medicine and disease medicine, scientific reconstruction of disease classification system is required as follows.

1. Before striping from status medicine, disease classification included ingredients classified based on status. That is, to avoid redundancy in disease classification system and status description system.

2. Re-regulate disease classification system by simplest applicable principle. It is no longer targeting on infinite disease refinement, but to meet the classification basis of human body status control requirement. Disease classification should be simple and disease classes should be less. Thus, the concept of classification solely based on the difference of pathological structure should be abandoned. The more subtle difference in morphology and function that aligned with treatment will not be the basis for further classification.

3. Introduce the clinically meaningful classification principles and disease types of TCM that does not included in modern medicine disease classification system.

Thus, it will form a more scientific and rational disease classification system that integrated Eastern and Western medicine combining all mankind experience and wisdom in fighting disease for thousands years.

Progressive development and theoretical system reconstruction are the two complementary and mutually irreplaceable models of scientific development. Science cannot develop without progressive quantity change. Quantity change is within certain limits. When quantity changes accumulated to a certain extent, new progressive development is impossible if there is no quality change and no reconstruction. The two medical systems originated in the East and West has utterly varies methodology and theoretical framework. Science belongs to all mankind and should not be divided by geographic. With the advent of status medicine in modern medicine and the concepts and methods return to TCM, the integration and reorganization of future medicine is inevitable.
Conclusion

Precision Medical opened the era of mainstream medicine from disease medicine to status medicine transition. In today’s world, when most people paying attention to the possible enormous progress in cancer treatment, the “million volunteers” plan of the US science community has start establishing the holistic human body status description system. It is exploring to achieve the long-term goal of precision medicine: the personalized medicine approach.

From the perspective of today scientific development, the concept of the American scientists is visionary. Following this exploration path and extend, people is surprised to find that on the way towards precision medicine, TCM was not understood and aware of by science in the past, is now far away in front of today science. TCM is itself a personalized status medical system. It is not only a identification system based on status description, but also a complete status control system with theory, treatment methods, drugs prescription, etc.

Perhaps it takes time for mankind consensus on this point. Perhaps science will still progress along the road of establishing human body status description system at the micro-level. On the one hand, to expand our understanding of human body from the breadth at molecular level include genome, proteomics, transcriptomics and metabolomics, etc. On the other hand, to seek for holistic integration based on microscopic analysis. We claim that after exploration and research for decades or even longer, our science will recognize the hardship of this road and the insurmountable technical obstacles. Then people will come back to deeply understand that TCM top-down approach is the most simple and most effective way for human body description establishment.

Today, artificial intelligence and big data analysis techniques have been widely used in massive data analysis of complex biological research. It is still inadequate for systems biologists to tackle the complexity in holistic biological research. They can do noting about the uncertainty of complex system adaptability. In TCM, practitioners have been in a very simple way to ease the control of complex human diseases since ancient times. Here, complex adaptability is not the obstacle that increases the difficulty of problem solving. It is the ‘exceptional right-hand man’ that helping us to deal with the control of complex system simpler and more effectively.

TCM is a precious heritage of ancient China that dedicate to today mankind. Today, scientists have begun to realize that it is more precious than acupuncture to human knowledge system. Along the precision medicine guidelines into the road of future, Chinese scientists and practitioners do not need to follow the footsteps of the US science community. They should instead draw the most valuable TCM ideas, methods and knowledge, combined with the most advanced modern scientific technological
means, to explore the best way towards precise personalized medicine for mankind.

The core of precision medicine is precise and personalized. It is not subjected to the restrictions of methodology and theoretical framework that similar to alternative medicine, translational medicine, and evidence-based medicine. We can develop precision medicine based on molecular biological research progress in genome, biology, proteomics, and metabolites, etc. We can also develop alternate precision medicine based on holistic human behavioural functions along the TCM path. Modern medicine of today is returning to Oriental medicine conceptually. With pursuit of truth in mind, set aside the fetters of traditional science concept, to show inclusive mind for unfamiliar method and system. Oriental medicine practitioners and scientists with holistic medicine background should lead modern medicine toward a new medicine that take status medicine as mainstream and integrate disease medicine. They should play an important historical role in the process.

Reference


