Physiome and Sasang Constitutional Medicine

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Abstract: Sasang Constitutional Medicine (SCM) is a traditional Korean form of medicine widely used in the clinical diagnosis and treatment of disease. This paper reviews the main aspects of SCM and "physiome" with emphasis on integrative and holistic characteristics. Methodological and physiological aspects of SCM are summarized with reference to existing studies. The main characteristics of SCM, such as the four physical constitutions and diagnostic methods, are introduced. Moreover, physiome and systems medicine are introduced as plausible candidates for integrative medicine and are compared to reductionism-based molecular biology. We also discuss the conceptual similarity of SCM with predictive, preventive, personalized, and participative (P4) medicine. It is emphasized that the integrative and creative combination of SCM and physiome will unlock a new era of holistic medicine.

Key words: Sasang Constitutional Medicine, physiome, integrative holistic approach.

Western medicine was founded by the collective works of Hippocrates, who developed a humoral system of medicine in which the treatment goal was to restore the balance of humors in the body. Similar views were espoused in China and India; however, these ideas of medicine were challenged in Europe by the rise of experimental investigation originating from the works of Andreas Vesalius and William Harvey. Modern medicine was revolutionized in the nineteenth century by advances in chemistry and germ theory by Ignaz Semmelweis and Louis Pasteur, and although the germ theory was not appreciated until the antiseptic method was discovered, its validity was supported by the discovery of penicillin in the midtwentieth century.

The scientific method in Western medicine was established by Claude Bernard, and his ideas were conveyed in his famous book An Introduction to the Study of Experimental Medicine in 1865. He emphasized the importance of "milieu interieur" (internal environment), with the goal of medicine being the restoration of homeostasis. However, discoveries in classical genetics and molecular biology and technological revolutions such as the X-ray, the electrocardiogram (ECG), and other modern instruments, have changed medicinal practices from their original holistic form. Moreover, the mass production of penicillin-based antibiotics and other drugs has further changed the principles of medical practice. Nevertheless, the overall ineffectiveness of modern Western medicine in the treatment of chronic complex diseases such as metabolic syndrome, heart disease, and cancer suggests a need for alternative medicinal approaches [1–3].

Alternative medicine is now incorporated into the curriculums of educational institutions in several nations. In Asian countries, traditional oriental medicine is taught in parallel with Western medical programs of study, and in Korea, oriental medicine is recognized and approved for public use. Oriental medicine in Korea has a few theories, with "Sasang Constitutional Medicine (SCM)," initiated by Jema Lee in 1894 [4], being one of the most popular of traditional medicines there. In his book titled Donguisucesbowon (東醫壽世保元, Longevity and Life Preservation in Oriental Medicine) [4], Lee constructed the framework of SCM by evaluating the oriental medical literature of China and Korea and classified the physical constitution of a human into four types. Although SCM enjoys little scientific support, studies to test the applicability and effectiveness of SCM in modern science are being performed at the Korea Institute of Oriental Medicine (KIOM).

The methodology of modern medicine is based on reductionism introduced by René Descartes, a well-known French philosopher and scientist. Reductionistic approaches attempt to understand the nature of complex things by breaking problems into several pieces and
solving each piece separately. For instance, in life sciences it may be assumed that if we understand the inner workings of the lowest-level elements, genes, and proteins, the mechanisms of more complex life forms will then become clear. Thus unveiling these molecular events may be essential for understanding health and disease. In spite of this, the primary limitation of reductionism is its ignorance or rejection of the integrative nature of life. This approach is particularly ineffective in the diagnosis and treatment of complex diseases such as heart disease, cancer, and diabetes, which arise from the combined action of many genes, environmental factors, and risk-confering behaviors. Therefore integration-oriented approaches such as physiome (or systems biology) have emerged as alternatives to overcome the limitation of reductionistic medical approaches.

In this paper, we first introduce SCM and the present status of physiome research. The limitations of this research are then discussed in the context of a systems medical approach. Lastly, we provide arguments for the need to incorporate the physiome and SCM in a nonconflicting context with modern life science and medical approaches.

1. Introduction to SCM
1.1. Historical background of SCM

In all ages and countries, the classification of physical constitution into certain types has been attempted for the effective diagnosis and treatment of disease. Hippocrates and Galen of ancient Greece proposed classification through the Four Humors, whereas the modern scientists Ernst Kretschmer and William H. Sheldon classified humans into three categories according to their body shape. In traditional Indian medicine (Ayurverda medicine), a classification theory of physical constitution was suggested; it was based on therapeutic measures that relate to physical, mental, social, and spiritual harmony.

Unlike these theories, SCM classified the physical constitution according to the traits of an individual’s mind and body, indicating that personal sensitivity to a certain drug can be different according to physical constitution. The establishment of this physical constitution theory differentiates SCM from the other theories mentioned above [4]. Even before the appearance of SCM, personal sensitivity to certain drugs had been noticed. Traditional Chinese Medicine (TCM) established the “Differentiation of the syndrome (論證) theory” and analyzed each symptom, classifying them into symptomatic types (證型). If patients with similar dominant complaints showed different symptomatic types, they were treated with different therapies. Although traditional Korean medicine before SCM was influenced by TCM in many aspects, it progressively developed a unique constitutional view that the mind and body are inseparable and the physical state of the human body can be remarkably changed by mental factors. This belief of traditional Korean medicine led to SCM in the latter half of the nineteenth century.

1.2. Classification of human physical constitution

Although SCM was also influenced by Taoism and neo-Confucianism, some of its key concepts, such as four organ systems and human psychological nature, were adopted from the oriental philosophical theory of “Confucianism.” SCM intended to delineate human physiological and pathological phenomena by employing the characteristics of four organ systems: lung, pancreas, liver, and kidney. In the SCM view, each organ represents a functional group representing the respiratory, digestive, preservative, and excréptive systems, respectively. The mind is a very important factor in SCM. The harmonic interrelation among peoples is emphasized in SCM, whereas TCM takes a definite view in the relationship between people and environment based on the Five Elements Theory (五行說), one of the traditional Chinese branches of philosophy. Jema Lee explicated four physical constitutions in the chapter entitled “Organ Theory (臟腑論)” of the book Donguisusebowon, introducing balancing mechanisms among the four organs (lung, pancreas, liver, and kidney). In this concept, the lung and the liver pair to control some physiological processes, and the pancreas and the kidney compose another pair (Fig. 1). The pancreas and kidney are related to the digestion of food and the excretion of metabolites and perform in a counteractive manner (see-saw). Thus in this view, if one organ system is relatively hyper-active, the other becomes hypo-active. A similar metaphor to the seesaw in the pancreas and the kidney is applied to the lung and the liver. These organ systems relate to and regulate the usage and storage of energy in the human body. According to the SCM theory, every person is born with one unbalanced seesaw, and there can be four different types of physical constitution. Jema Lee termed

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**Fig. 1.** An example of the seesaw metaphor to explain physical constitution in SCM.
these types as Tae-yangin, So-yangin, Tae-eumin, and So-eumin, as shown in Table 1 [5]. This terminology was adopted from the well-known Chinese philosophical writing *Book of Changes* (周易).

Jema Lee also emphasized that the human mind and body are not separate, but that they closely reflect each other. He mentioned in the chapter “Origin of Oriental Medicine (醫原論)” of *Donguisusebowon* that a disease can be provoked by environmental factors, but of more importance is the influence of psychogenic factors such as sorrow (憂), anger (怒), gladness (喜), and enjoyment (樂). In scientific sense, the seesaw metaphor between organ systems may be explained by the balancing mechanism of hormonal and nervous systems, which has not been scientifically revealed. The system biological approach will be useful for delineating the balancing mechanism between organ systems.

A disease occurs when the inherent imbalance between body and mind are triggered by a certain external condition. Under this view, the physical constitution of a patient is therefore diagnosed in advance, and then an understanding of the inherent imbalance of the patient should be the next step to be undertaken for treatment. Food and medicine to complement these imbalances can be prescribed while the mental state of the patient is maintained or treated. In *Donguisusebowon*, Lee emphasizes the importance of regulation of the mind during treatment, especially in chronic diseases. Although SCM is a medical theory suggested more than 100 years ago, it is highlighted in the present situation. Assuming that immune system dysfunction and psychogenic disorders are the main causes of chronic disease, treatment based on SCM using natural herbal medicines and regulation of the mind could be effective.

### 1.3. Classification of physical constitution

Classification of physical constitution is performed by oriental medical doctors based on the traditional diagnostic methods involving seeing, listening, questioning, and touching (Four Diagnoses; 四診). Seeing (inspection) is inspecting appearance and color. It includes observing the shape of the face, the body, the hands, and the feet for the determination of physical constitution, and examining the color of the face for a diagnosis of plausible symptoms. Listening (auscultation) is inspecting vocal sounds such as voice, breathing, and coughing. Personal voice depends on physical constitution. Voices have different pitches, tempos, and volumes according to physical constitution. Breathing and coughing are checked for the diagnosis of likely symptoms. Questioning (interview) involves asking patients how they feel in order to determine whether pathological symptoms may exist. The personal traits and habits obtained from interviewing patients are highly important factors to determine their physical constitution. Touching (palpation) is inspecting the skin and the pulse. However, these traditional diagnostic methods are conducted by subjective observation and are catechetic methods, thus making the method difficult to objectify and quantify.

### 2. Scientific approach for SCM

#### 2.1. History

Quantification and objectification of diagnostic methods are the critical problems to be solved in traditional medicine. In SCM, this emerges as a more serious problem because there are no clear guidelines for treatment without physical constitutional classification. Research over the past 10 years dealing with this matter is described below.
2.1.1. Seeing diagnosis (inspection). Oriental medicine after the *The Yellow Emperor’s Internal Classics* (黃帝內經) asserted that the functional strengths and weaknesses of the human body are expressed by the face and the physical features. Efforts to diagnose physical constitution by analyzing facial features have been in progress since 1994. Analyses were performed based on the length and the angle of features in the front and side views of the face; however, the accuracy of diagnosis has not been adequate for clinical applications and requires further investigation. In the Far Eastern societies, facial features have never been used for racist purposes and are regarded as a means of diagnosing disease or physical constitution. Moreover, the classification of physical constitution according to the size and form of other body parts is another area of study. Although picture data for these investigations have been accumulated over decades, quantitative analyses are lacking [6–10].

2.1.2. Listening diagnosis (auscultation). Voice is a specific characteristic that depends on physical constitution and health condition. The voice itself, the speed of speech, the crying sounds during infancy, and the sharpness of the voice differ according to physical constitution. There has been research to investigate differences in voice frequency, volume, and pitch according to physical constitution since 1996. Analyzing algorithms for these factors have been developed to a certain extent, but emphasis is now placed on obtaining methodological diversity in the analysis of data [11–13].

2.1.3. Questioning diagnosis (interview). The objectification and quantification of traditional diagnostic methods have been regarded as the most important category of SCM research. The Questionnaire for Sasang Constitution Classification (QSCC) is a program widely used in this field, and it has been shown that physical constitution changes according to appearance, character, common symptoms, and reactions to certain foods. More than 30 papers have been published since 1991 in this field, and many scientific methodologies have been introduced from consultations with psychologists, Korean language experts, and statisticians [14–21].

SCM is a medical system with philosophical and psychological components. Therefore it is inferred that the Sasang physical constitution may be related to modern psychology. Over the years, Sasang medical doctors and psychologists have worked together and published many papers comparing and analyzing the relationships between the Sasang physical constitution and the MMPI (Minnesota Multiphasic Personality Inventory) test, the MBTI (Myers-Briggs Type Indicator) test, the 16PF (personality factors), and Beck’s depression criteria [22–24]. Nevertheless, little progress has been made in this research, probably because temperament and character were not properly evaluated. Recently, for the psychological study of SCM, many researchers have been interested in the Temperament and Character Inventory (TCI) criterion, which distinguishes inherited temperament and acquired character.

2.1.4. Touching diagnosis (palpation). Pulse objectification research is beginning to develop a scientific approach in oriental medicine. Three companies currently market a pulse analyzer, and the use of these instruments is covered by insurance programs in Korea. In traditional oriental medicine, the symptoms of a patient are evaluated through pulse variations, but SCM claims that even the baseline type of normal pulse differs according to physical constitution.

Recently, a pulse analyzer with a robot arm has been developed by KIOM that detects and analyzes pulse waves (Fig. 2).

Furthermore, based on the observation that skin, muscle, and bone development differ according to physical constitution, diagnoses using this principle are now being made. We believe that recent developments in sensor technology will expedite the progress of this research.

2.1.5. Biochemical research related to physical constitution. Over the past 10 years, remarkable progress has been made in the search to find biochemical indexes related to physical constitution. It was reported that the density of white blood cells (WBC), red blood cells (RBC), and platelets is relatively low in certain physical constitutions and that cytokines that stimulate the growth and differentiation of cells may also be indexes of physical constitution. Moreover, an analysis of body fat and indexes of patients have shown that certain physical constitutions are prone to obesity.

Recently, many researchers have been searching for certain genes related to the physical constitution. Clinicians can now investigate correlations between genes and physical constitution by DNA chip analysis. Although much experimental research has been conducted to delineate relationships between angiotensinogen (AGN) genes, polymorphisms of the apolipoprotein E (ApoE) gene, and physical constitution in stroke patients, no notable correlation has been found. It was shown that interleukin (IL)-4 and IL-6 in blood decreased and assisted the recovery of damaged neuronal cells [25, 26]. Furthermore, studies related to the regulation of cytokine secretion have been performed [27–30]. Although these studies have not been productive because of the technological limitations of standard molecular biology, SCM experiments using existing clinical data of Western medicine combined with gene information may reveal relationships worthy of further study. It may be necessary to also perform research using integrative and holistic approaches rather than relying solely on the methodologies of Western reductionism. Life scientists in developed countries have developed new integrative and holistic methods, such as physiome and systems medicine. Complementary and synergistic combinations of physiome and SCM hold promise in uncovering higher-level biological functions.
2.2. Universe Human Mapping theory

Scientific approaches for physical constitution classification are based on the premise that physical constitutional features, which are modulated by the strengths and weaknesses of internal organ systems, are expressed by face, body, voice, skin, pulse, and personality. This perspective is popular in oriental medicine and is based on an oriental philosophical theory called the Universe Human Mapping (UHM) theory (天人相應論). In the UHM theory, human beings are regarded as a small universe in themselves, with all the factors in the actual universe having corresponding pairs or parts in humans as well. For example, the human mind and body correspond to the sky and the earth, changes in emotion correspond to changes in climate, and a disease is compared with abnormal weather. One noticeable example of this correspondence can be found in ventricular reentry waves and in recirculating air waves of tornados. During ventricular tachycardia or fibrillation, scroll waves of electric potential in tissue are generated through the ventricular tissue layer between the epicardium and the endocardium, which can be compared to the airflow dynamics of a tornado (Fig. 3) [31].

This theory is applied not only between universal systems and human systems, but also between organs inside the body. A typical example is pulse diagnosis, which is a popular method in oriental medicine. By palpation of the arterial pulse, doctors are able to diagnose the pathological state of the patient. The five viscera and six bowels (五藏六腑) are mapped within the small area on the wrist, as shown in Fig. 4. The vital gate (命門) has traditionally been referred to the right kidney, which is supposed to originate the primordial Yang (元陽).

According to the UHM theory, universal systems and individual systems always have similar structures and show similar dynamics.
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posed an integrative circulation model connecting cellular
events to circulation hemodynamics and autonomic nerve
control. Thus the works of several researchers have led to
an understanding of the interrelatedness of biological and
pathological phenomena.

3.3. Limitations of physiome research
A variety of physiome models has been presented, but
they have mainly focused on reproducing existing clinical
and experimental results. Although physiological pertur-
bations such as arrhythmias have been predicted in clini-
cal settings on the basis of physiome-type theories [43,

3. Physiome and SCM
3.1. Background of physiome research
It is well recognized that biotechnology is a promising
cutting-edge industry that could dramatically improve hu-
man life and welfare. Genomics, proteomics, and metabo-
lomics are examples of fields that have evolved from mo-

dular biology. Physiome, however, is a new approach to
the understanding of human biology and life that differs
from methods in molecular biology. Physiome promotes
integrative and holistic methods and is progressively
spreading throughout the world. As termed by James B.
Bassingthwaighte from the University of Washington, physiome was devised as a combination of “physio,”
which means life, and “ome,” which means whole in Latin
and, in total, conveys the meaning “life as a whole.” As re-
viewed by Hunter and Borg [32], the goal of the Physiome
Project is to make computational programs and databases
that gather and analyze data from genes, proteins, cells,
and organs to get a macroscopic view of total body func-
tion. The human genome project (HGP) initiated this vi-
sion for the recognition and treatment of fatal diseases by
providing a complete human genetic map. Unfortunately,
data gathered from the HGP have limited utility, and the
complexity of life makes it difficult to explain biological
phenomena by genetic parameters alone. As remarked in
the book *The Music of Life* [33] written by Noble, genes
code for proteins, but protein synthesis itself is extraor-
dinarily complex and is not a linear phenomenon. Although
approximately 30,000 genes exist in humans, there are
more than 100,000 different proteins, suggesting that a
one-to-one relationship between a gene and a protein can-
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3.2. Examples of the physiome study
Research related to physiome is under way in various
biological fields. Cardiome is derived from the physiome
of the cardiovascular system, and the cancer physiome
applies physiome technology and knowledge to analyze
the production, growth, and metastasis of tumors. Further
fascinating fields have arisen from the physiome initia-
tive. Theoretical studies of cellular signal transduction
and cellular electrophysiological modeling of exciting–
contraction coupling mechanisms integrate mathematical
equations to understand physiology and disease.

In 1952, Sir Alan Hodgkin and Andrew Huxley made
the first mathematical model about electrophysiological
phenomena and were awarded the Nobel Prize for their
contribution. In 1960, Denis Noble at Oxford University
studied the mathematical model for the ion channels of
cardiac pacemaker cells [34]. Theoretical studies on the

cellular electrophysiology of cardiac cells have been pub-
lished by DiFrancesco & Noble [35], Kimura et al. [36],
Hilgemann & Noble [37] and Earm & Noble [38]. Models
at the cell level were integrated into tissues and eventu-
ally into the whole heart. Hunter et al. [39] formulated
electrical propagation and mechanical contraction of the
heart using the partial differential equation solved by the
finite element method. Various mathematical models for
electrical conduction and arrhythmias in the heart were
also presented and were used to reproduce and predict
pathological phenomena, such as ventricular tachycardia
or fibrillation [40]. At the systems level, Guyton et al. [41]
presented an overall circulation model including a variety
of physiological factors, and recently Shim et al. [42] pro-
posed an integrative circulation model connecting cellular
events to circulation hemodynamics and autonomic nerve
control. Thus the works of several researchers have led to
an understanding of the interrelatedness of biological and
pathological phenomena.

Fig. 4. Measurement locations in pulse diagnosis and their
corresponding internal organs.

The Music of Life

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bations such as arrhythmias have been predicted in clini-
cal settings on the basis of physiome-type theories [43,
44], many limitations remain in physiome research. Deficient information on the kinetics and dynamics of systems is one of the most serious problems, but this is primarily due to a lack of data-based observations. Though new information is continually being generated, the information required for the modeling either cannot be found or has never been obtained [45]. Specifically, holistic models that integrate physiological functions with scientific meanings have not been presented.

3.4. Systems biology and medicine

Systems biology involves understanding the manner in which the parts of an organism interact in complex networks, and the application of systems biology to medicine is termed systems medicine. Systems medicine was proposed to overcome the limitations of modern Western medicine, which depends mostly on biostatistics [46]. It tries to understand perturbed physiological systems and complex pathologies in their entirety by integrating all levels of quantitative functional, structural, and morphological information into a coherent model. In contrast to systems biology, systems medicine seeks an integrative and systemic approach for the diagnosis, therapy, and prevention of diseases [47]. It investigates the physiological network of diseases from gene to organ systems with four main goals — predictive, preventive, personalized, and participative medicine (P4 medicine). This approach to medicine arose by reflection of the averaged and statistical diagnosis/treatment systems in Western medicine and is regarded as an ideal paradigm to be pursued in future medicine.

4. Discussions

In this paper, we introduced SCM and addressed the possibility of SCM being a useful holistic medical theory and database for physiome research. First, we discussed the general aspects and characteristics of SCM with the four types of physical constitution and diagnostic methods. The background and current status of physiome research were also briefly described.

Hodgkin and Huxley’s first model concerning electrophysiological phenomena demonstrated that mathematical predictions could be used in clinical applications. Although some models were successful in the clinic, others proved useful only for teaching medical students. For example, Guyton et al. [41] presented a pioneering model for overall circulation that included a variety of physiological factors (circulatory dynamics, autonomic control, metabolism, pulmonary dynamics, kidney dynamics, blood flow control, electrolytes balances, capillary membrane dynamics, and others). Recently it was shown that this model provides useful simulations for the treatment of hypotension during anesthesia [48]. Despite this success, as reviewed by Bassingthwaighte [45], this model has not been widely accepted as a research tool for clinical applications.

Overall, little research has been performed on holistic and integrative models. To make a plausible mathematical model in a holistic manner, more advanced physiological theories for integrative life functions and databases of clinical data are needed; however, these requirements are unlikely at the present time to be met in Western medicine.

Regardless, empirical data of human physiological functions observed from holistic viewpoints such as SCM do exist, but these data have not been scientifically analyzed. The holistic theories, such as SCM, have been used for years in Korea and other Asian societies. In this sense, SCM may be an important candidate that could provide holistic data for human physiological functions. It may be difficult, however, to integrate physiome with SCM because of differences in theoretical systems. Nevertheless, it is probable that SCM may provide holistic theories that promote the advancement of physiome research. It is noteworthy that diagnosis and treatment in SCM already adopts the concept of P4 medicine. First, SCM is a personalized medicine that classifies individuals by four types of physical constitution (personalized medicine). Second, it emphasizes prevention before therapeutic treatment. Thus through analysis of the physical constitution of a patient, susceptibility to certain diseases may be predicted. This is similar to the predictive concepts and viewpoints of P4 medicine (predictive medicine). Based on predictions, its goal is to prevent disease by changing the lifestyle of a patient to promote health. These changes may be as simple as prohibiting some foods and promoting others based on the physical constitution of the patient. During the process of questioning (interview), patients can deliver their opinions and feelings about pathological symptoms and get responses from clinicians. This kind of interview enhances the interaction of clinicians with patients, which can encourage diagnostic and therapeutic processes (participative medicine).

Based on the view that life phenomena can be well understood by using integrative approaches, systems medicine pursues an integrative diagnosis and treatment approach for human disease, with the goal being similar in scope to SCM. Physiome research tries to construct the framework of integrative physiology and supports the fundamental scientific basis for systems medicine and SCM, and both approaches could contribute to accumulating clinical data supporting holistic models for physiome research. This kind of interaction between physiome and SCM as well as systems medicine could expedite the construction of a holistic framework for P4 medicine and promote scientific studies to verify the efficacy of SCM. Scientists and clinicians with an interest in these fields could therefore both contribute and benefit from this synergism. We therefore believe that new interest in holistic and integrative medicine could increase our understanding of the physiological and pathological bases of health.
and disease.

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