PERSPECTIVE

# All systems go

Systems science can provide guidance in capturing the complementary approaches to healthcare, says **Jan van der Greef**.

Various cultures have developed their own philosophies of science and, consequently, practices in medicine. The twentieth century has seemed to vindicate the Western approach, bringing huge advances in our understanding of physiology and biochemistry. This knowledge has fuelled the development of medicines and vaccines against countless diseases that had once wreaked havoc on humanity.

But in recent decades, the Western model has hit some turbulence. In particular, the concept of 'one disease — one target — one-size-fits-all' is shifting towards more personalized medicine tailored to individual patients, including the use of multiple therapeutic agents and the consideration of nutritional, psychological and lifestyle factors when deciding the best course of treatment. This shift in strategy has been most obvious in the prevention and management of chronic diseases such as diabetes and cardiovascular disease. The intellectual underpinnings for such a transition in medical practice are being laid in the discipline of systems science — and systems biology in the biomedical domain.

Systems science aims to understand both the connectivity and interdependency of individual components within a dynamic and non-linear system, as well as the properties that emerge at certain organizational levels. The relation to medicine is clear. Systems biology is particularly useful when it comes to describing homeostasis — the regulation of a system's internal environment to maintain a stable condition. In turn, the ability to cope with changing environments and stress is encompassed in the principle of allostasis — the physiological or behavioural changes required to stabilize the biological system.

The concepts and practices of systems biology align very closely with those of traditional Asian medicine. Consider the very idea of 'health'. The current World Health Organization definition of the term is based on a 1948 consensus: "A state of complete physical, mental and social well-being and not merely the absence of disease or infirmity." However, an emerging concept of health in the scientific literature describes an ability to adapt and self-manage in the face of social, physical and emotional challenges[1]. This perspective has, of course, long been central to the concept of health in traditional Chinese medicine (TCM), which further includes spiritual fulfilment and a sense of individual well-being.

TCM is descriptive and phenomenological — it typically diagnoses patients using concepts based on the relationship between signs and symptoms, obtained through questioning, listening, palpation, visual inspection and smelling. In contrast, Western-style, modern medicine has mainly used single biomarkers to describe disease states, for example diagnosing type 2 diabetes by measuring glucose levels. But there is a growing realization in the West that single biomarkers are not enough. A better approach is to look at patterns of biomarker responses to a challenge. These data will provide insight into the resilience of allostatic mechanisms, and hence into a person's health, an approach not unlike the tenets of TCM.

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**A flock of starlings relies on connectivity, dynamics and communication; these elements are embedded in TCM.**

In addition to giving Western medicine a basis for adopting some concepts of TCM, systems biology is also pushing the convergence from the other direction. Increasingly, TCM uses modern biochemical measurements and tools to refine or augment diagnostic descriptions. This is starting to facilitate the translation of TCM concepts into Western concepts based on biochemical, pathway or regulatory processes.

For instance, take diagnosis: the Sino-Dutch Centre for Preventive and Personalized Medicine in Zeist, the Netherlands, has conducted several studies that attempt to unify Eastern and Western diagnostic principles. In one such study of rheumatoid arthritis patients, selected according to Western (American College of Rheumatology) guidelines, TCM practitioners categorized patients into 'heat' or 'cold' pattern — based on the results of a questionnaire concerning joint issues, level and quality of pain, response to weather, and other symptoms such as fever and thirst, as well as the results of a tongue and pulse inspection. A systems biology investigation of the two groups found statistically significant differences between them in the expression of genes related to apoptosis and metabolite profiles[2].

Systems biology can also provide insight into the multi-target pharmacology of herbal formulae. A metabolomic study investigated changes in lipid levels in transgenic mice with mild hypercholesterolaemia given either a herbal concoction or a known drug (for example, rimonabant, atorvastatin or niacin). The study found that the herbal formula caused decreases in plasma cholesterol and triglycerides, and increases in high-density lipoprotein. How the herbal formula does this should help researchers pinpoint novel ways to treat metabolic disorders, especially those related to lifestyle[3].

These early systems biology investigations suggest that the TCM method of qualitative subtyping could be of use in deciding the course of treatment for patients in modern medicine[4], and provide momentum for the move towards personalized medicine. Furthermore the concept of health promotion alongside disease management will help to improve the current system of healthcare. ■

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