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IN THE LAB

A Push to Back Traditional Chinese Medicine With More Data

Researchers Marry Modern Analytical Techniques to Centuries-Old Theories on What Makes People Sick

Chinese licorice root is used in traditional Chinese medicine with other herbs in a combination known as PHY906, which has been studied by Yale University researchers.
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By **SHIRLEY S. WANG**

Updated Nov. 3, 2014 7:36 p.m. ET

Hong Kong

Traditional Chinese medicine teaches that some people have hot constitutions, making them prone to fever and inflammation in parts of the body, while others tend to have cold body parts and get chills.

Such Eastern-rooted ideas have been developed over thousands of years of experience with patients. But they aren't backed up by much scientific data.

Now researchers in some the most highly respected universities in China, and increasingly in Europe and the U.S., are wedding Western techniques for analyzing complex biological systems to the Chinese notion of seeing the body as a networked whole. The idea is to study how genes or proteins interact throughout the body as a disease develops, rather than to examine single genes or molecules.

“Traditional Chinese medicine views disease as complete a pattern as possible,” says Jennifer Wan, a professor in the school of biological sciences at the University of Hong Kong who studies traditional Chinese medicine, or TCM. “Western medicine tends to view events or individuals as discrete particles.” But one gene or biological marker alone typically doesn’t yield comprehensive understanding of disease, she says.

To reach these goals, the overall quality of research on traditional Chinese medicine must improve. With studies of Chinese herbal remedies, for instance, rarely are scientists expected to provide authentication of herbs they’re studying, which makes it difficult to know what’s really in the concoctions. This hurdle also makes it harder for other scientists to replicate the findings, says Qihe Xu, a professor in renal medicine at King’s College London. Dr. Xu served as the coordinator of a recent 200-scientist consortium to study good practices for studying traditional Chinese medicine, dubbed GP-TCM.

TCM treatments of herbal concoctions could be authenticated and standardized with more scientific study, and could serve as leads for drug development, experts say.

One example of this possible development is Yale University pharmacology professor Yung-Chi Cheng's work looking at four-herb combination known as PHY906 for reducing the side effects of chemotherapy. The treatment appears to contain more than 60 chemicals. Researchers are studying it for its ability to reduce nausea and diarrhea and to enhance colon-cancer treatment.

EVA TATCHEVA

The field also must develop standard definitions and ways of measuring TCM syndromes, important for research and clinical care, Dr. Xu says. His European Union-funded consortium published a set of guidelines for good practices last year in the journal *BMC Complementary and Alternative Medicine*, one of about 50 papers published by the consortium since 2010.

“If it's not reproducible, it's not science,” he says.

According to traditional Chinese medicine, disease arises from imbalances in the body due to unhealthy factors in the natural environment and one's lifestyle. General symptoms like dry mouth or film coating the tongue are signals that certain bodily systems are out of whack. While these signs may be ignored by Western doctors more focused on more specific ailments, TCM doctors often use the symptoms as guides for treating patients.

A doctor practicing TCM who knows whether someone has hot or cold syndrome could use that as a first clue in testing for problems involving the immune or metabolic system. Those problems could

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include gastritis, colitis, rheumatoid arthritis or cancer. One day there also may be effective treatments if a person's constitution is taken into account when treating them, says Shao Li, deputy director of the bioinformatics division at Tsinghua University in Beijing.

In cities throughout China, doctors practicing Western and Chinese medicine can both be found. Many patients go to Western doctors for certain situations, such as acute illness, but seek out TCM guidance in others, often to prevent disease.

TCM was largely ignored by Western medicine until recent years, but is slowly gaining traction among some scientists and clinicians. The Cleveland Clinic in Ohio recently opened a herbal therapy center. The U.S. government established the National Center for Complementary and Alternative Medicine in 1998. The organization now has a budget of over \$120 million to fund research on the efficacy and safety of alternative medicines, including those rooted in traditional Chinese medicine.

Dr. Shao Li of Beijing's Tsinghua University delivered a keynote speech at the International Conference on Bioinformatics and Biomedicine in 2013. *CHENGJUN WANG*

One promising area of TCM research several independent groups of scientists are investigating is the notion of hot and cold syndromes. The work is still in its early stages. But it could result in a new direction

for TCM research by using the systems biology approach and integrating it with experience gleaned from TCM patient care, says Yale's Dr. Cheng, who also serves as chairman of the Consortium for the Globalization of Chinese Medicine.

In a series of studies, Tsinghua's Dr. Li and his colleagues examined people with hot and cold syndromes and whether they exhibited different signs of illness, including gastritis, a common digestive disorder in which the lining of the stomach becomes inflamed or irritated.

To gauge whether gastritis patients had cold or hot syndromes, researchers asked questions like whether individuals had chilly body parts or exhibited a preference for hot beverages or a susceptibility to catching colds. Doctors dug into their subjects' emotional states, asking whether they experienced so-called cold feelings like apathy. The scientists also measured proteins linked to gastritis and took measurements of the bacteria in the gut and imaged the bacteria in the tongue's coating.

They found some variations depending on whether patients were identified as hot or cold. They also found differences in the bacteria of patients' tongues that corresponded with tongue coating color and whether patients had been diagnosed with hot or cold syndrome.

These results suggest that some easily detectable and nonspecific symptoms could be clinically useful, Dr. Li says. However, it remains to be seen whether gastritis patients classified as having hot syndrome would actually respond to different treatment than those

classified as cold.

In the Netherlands, Jan van der Greef, a professor of analytical biosciences at Leiden University, and his colleagues have looked at how getting classified as having hot or cold symptoms relates to rheumatoid arthritis.

They had a Chinese medicine expert identify participants by type and studied a network of chemicals produced by the body related to the immune system. They found higher levels of one steroid and 11 other molecules in the urine of arthritis patients depending on their TCM diagnosis.

That could mean that they would benefit from different disease-management strategies. Cold patients might benefit more from hormone treatments like prednisone, while hot patients might benefit from immune therapies, says Herman van Wietmarschen, a postdoctoral researcher at the Netherlands Organization of Applied Scientific Research and the first author on the paper. They published their work in PLOS One in 2012.

In another study, published in Molecular BioSystems in 2012, Dr. van der Greef's group looked at another important TCM construct known as Qi, known as life energy, or the forces within the human body and the environment. Again, they found differences between biological markers in the urine of people with different body classifications. TCM-based symptom patterns could be suitable for early detection of health problems, the authors say.

Dr. Li's group continues to test the biomarkers associated with cold

and hot syndrome to subtype other kinds of diseases, including cancer. The next step would be to develop more individualized treatment for such complex diseases based on syndrome type.

The researchers believe that “in such a big-data era, a new way can be eventually found to connect Eastern and Western medicine at the molecular and systematic levels,” Dr. Li wrote in an email.

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