INTERVIEW

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Interview with a Thought Leader on Systems Medicine—Weiniu Gan, PhD

*Program Director, Division of Lung Diseases, National Heart, Lung, and Blood Institute,
National Institutes of Health, Bethesda, Maryland.*

Dr. Weiniu Gan is the Program Director of the Genetics, Genomics, and Advanced Technologies Program for the Lung Division within the National Heart, Lung, and Blood Institute of the U.S. National Institutes of Health. Dr. Gan provides scientific oversight to multiple NIH-funded projects that are utilizing Systems Medicine approaches to analyze multiple Omics data, including the NHLBI Trans-Omics for Precision Medicine (TOPMed) Program and the COPDGene Study. He is widely respected for his scientific vision and molecular genetics expertise.

Why Does Systems Medicine Matter?

The main mission of the National Institutes of Health (NIH) is to generate and use biological knowledge to improve public health. That mission presumes that we can relate abnormalities and interventions at the molecular level to changes in function at the tissue and organismal levels. In the past, scientists relied mainly on animal models to identify the functional implications of molecular changes, but development and testing of animal models cannot keep up with the avalanche of molecular information that is now being produced. That is where systems medicine comes in—we need to develop highly detailed *in silico* systems that mimic biological systems to efficiently integrate the vast amount of data now available and translate that information into approaches for improving the health of people worldwide.

What Is the Main Gap?

Modern technologies are capable of producing huge amounts of data with incredible spatial and molecular resolution. What we are lacking is an understanding of how tens of thousands of genes, RNAs, proteins, and metabolites are assembled and function at the whole animal/human level. We will need systems medicine approaches to connect those biological molecules

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into cohesively integrated systems that can explain the underlying biology of disease. Systems medicine will hopefully yield a modern parallel for Kepler's law of planetary motion or Newton's theory of universal gravitation—a way of summarizing fundamental principles in a predictive model.

How Can It Be Filled?

NIH will continue to support studies that generate high-quality data in well-designed research projects using unbiased high-throughput methods, including latest technologies for omics and single-cell analysis. We will encourage the development of novel

mathematical algorithms to explore connections and interactions among genes and/or proteins. We will work to bring experimental and computational biologists together to work cooperatively. But all of this may not be enough. We may also need a change in attitude, perhaps a change in culture, through which investigators recognize the value of systems medicine approaches for interpreting data and generating new hypotheses.

What Will Be the Impact?

Systems medicine has the potential to open many doors, but I will mention only two. The first is the elusive goal of redefining diseases at the molecular level. Traditional

disease classifications emphasize symptoms and organs, rather than the molecular abnormalities that are assumed to underlie most disease. Systems medicine may provide a framework for establishing a new taxonomy of human disease that is based on molecular biology. Replacing organ-based disease definitions with alternative that focus on molecular systems would aid our understanding of multiorgan involvement in human diseases and of comorbidities. It could revolutionize the practice of medicine. Second, systems medicine has great potential for supporting precision medicine. Traditional scientific approaches are best suited for discovering what is common among individuals and species. Systems medicine may yield a scientific understanding that is much more powerful—one that can explain the differences among humans and show us how to treat individual patients in a personalized way.

Is There Anything Else Relevant to Systems Medicine That You Find Important to State?

To fulfill its potential, systems medicine will need examples of success—providing proof of principle that this approach can answer questions and provide understandings that cannot be gained in any other way. That

is where a journal like *Systems Medicine* can play a critical role. It can provide a platform for communication among researchers and a means of disseminating discoveries from this rapidly developing field. National Heart, Lung, and Blood Institute (NHLBI) will continue to do its part by supporting the training and research of investigators and by providing scientists with invaluable data resources, such as NHLBI's Trans-Omics for Precision Medicine (TOPMed) program. TOPMed includes data from tens of thousands of well-phenotyped humans with broad racial and ethnic representation and will soon make available multiomic data from these subjects, including more than 120,000 whole genome sequences.

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Abbreviations Used

NHLBI = National Heart, Lung, and Blood Institute
NIH = National Institutes of Health
TOPMed = Trans-Omics for Precision Medicine

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