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EDITORIAL

Medicine in the era of network science

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"Organisms are information networks."—Sir Paul Nurse, Nobel Laureate

Network medicine involves the application of the principles of network science to the analysis of large, heterogeneous-omics data sets with the aims of gaining novel, mechanistically significant insights into the causes of human diseases and developing new and more effective treatments. This rapidly expanding area of research is now mature enough to significantly transform medicine in the near future. Its potential for catalyzing fundamental changes in our approach to complex diseases of all types is truly exciting [1].

The current availability of massive sets of biomolecular-omics data, quantitative in silico methodologies, and powerful tools for the analysis of *big data* are blazing new trails on the frontiers of medicine that are nothing less than revolutionary. The new genomic technologies developed in recent years have enabled us to generate huge complex sets of biomedical data on a scale previously difficult to imagine. The challenge now is to integrate these data into biologically informative contexts that will truly deepen our knowledge of the molecular bases of disease. Innovative tools are essential if we want to meet this challenge, and of the numerous solutions proposed thus far, the *network medicine* approach is by far the most promising [2].

A network is graphically represented as a set of points (or nodes) that are coupled by lines (edges), which allows one to visualize and explore the potentially complex relationships between multiple variables of interest. The new field known as network medicine combines principles and approaches from systems biology and network science for more fruitful interrogation of human diseases, their causes, and their possible treatments. It reflects our growing awareness of the fact that human phenotypes and pathophenotypes are almost invariably driven by complex interactions among a plethora of molecular mediators.

The basic underlying hypothesis is that diseases arise as a consequence of the genetically and/or environmentally mediated perturbation of one or more biological networks operating within a target organ (or organs). Network medicine is inherently a holistic approach that considers the affected system as a whole instead of searching for a single "magic bullet" that will eliminate the disease—the principle that underlies so many reductionist approaches to disease. Understanding the relationships between the multiple components of a network can yield important new insights into many common diseases, such as cancer, heart disease, or diabetes [2, 3].

This issue of *Endocrine* includes a fundamental contribution to our understanding of the striking potential of network medicine by one of the field's early pioneers: cardiologist Joseph Loscalzo. His mini-review provides a comprehensive overview of the role network medicine is playing in the study of type 2 diabetes mellitus and the development of therapeutic strategies for this disease that can truly be described as precision medicine [4]. Loscalzo explains how he and his team are integrating mutation and protein–protein interaction data (the interactome) to explore type 2 diabetes data sets generated by genetic association studies.

Experimental evidence shows that loci linked to disease phenotypes frequently cluster together to form a subnetwork in the interactome, which can be analyzed in depth to discover novel pathways that play unexpected roles in disease pathogenesis and are therefore potential drug targets. Importantly, this approach is not restricted to the exploration of diabetes: it can in fact be used in any disease [1].

Previous issues of *Endocrine* have included several other articles in which network medicine has played key roles. Falcone et al. [5], for example, studied the correlation network of gene expression profiles in thyroid cancer to

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provide an unbiased network-based interpretation of clinical responses to vemurafenib in patients with different types of tumor (thyroid, lung, colon, and melanoma), all harboring the same driver mutation (BRAF V600E). Using the network medicine tool known as "Switch Miner," they identified different sets of genetic switches that are responsible for each tumor type's response to the drug. A similar approach was adopted by Zhai et al. [6] to identify prognostic biomarkers in metastatic papillary thyroid cancer. And weighted gene co-expression network analysis was used by Li et al. [7] to discover five novel genes that may be associated with the myocardial benefits of melatonin.

Network medicine is therefore a highly promising tool for increasing our understanding of complex pathophenotypes—understanding that should improve our ability to define an individual's risk for complex disease based on network-based signatures that contribute to that risk, understanding that could reveal pathways within the network that could be therapeutically targeted to prevent the disease from becoming manifest or arrest its progress. Potential benefits can be expected at all levels, from prevention to diagnosis and treatment. Medical research is on the verge of a paradigmatic change that will shift its focus towards the development of multilevel models. The challenge is enormous, and transdisciplinary, collaborative minds are essential if we are to reach the goal. In the words of Loscalzo himself: "*Network medicine is not simply a new strategy for analyzing mechanisms of biology and disease, but a unifying approach that interrogates the complexity of biology and disease in a uniquely informative way for diagnostic and therapeutic purposes*."

We at *Endocrine* are enthusiastic about the increasing use of this innovative approach for the analysis of omics data sets, and we look forward to publishing the new and exciting insights it will generate, as we stated in the January editorial [8].

Sebastiano Filetti Editor-in-Chief, Endocrine

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