Beyond Doctrine and Dogma
One Gene—Multisystem Effects
Henry J. Duff, MD

High-quality research frequently disproves dogma or provides a new insight as to mechanism or a biological framework. At one time, the dogma was 1 gene produced only 1 polypeptide product (1 gene–1 protein hypothesis). This dogma has been proven wrong. The study by Hu et al1 extends the complexity of biology framework by showing that 1 gene defect in 1 gene can affect multisystems in complex, unexpected, and interactive ways. The work by Hu et al is emblematic of a new era of biology that allows dissection of complex interplay with in multisystem syndromes using systems biology linked to genomic approaches. The power of this approach is that it exposes unexpected and potentially important biological networks.

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The study of Hu et al1 rightfully points out that the biology of sudden death is complex. It is shocking that disruption of a single gene Kcne2 can affect, in a complex interactive way, fundamental susceptibility elements that predispose to sudden death. These elements include: diabetes mellitus, excesses in the angiotensin signal transduction system, and hypercholesterolemia. The effect of this curiosity/discovery-based research has the potential to provide new targets to minimize not only risk for sudden death but also for ischemic heart and vascular disease and heart failure. Hu et al1 should be congratulated for a discovery that may lead to new diagnostics and therapeutics.

Curiosity-driven research and translational science are complementary. The underpinnings of translational science are that we need to understand at least at a practical level how a biological system works and how to manipulate it. In the new era of human genomics and systems biology, our working premise of how biological systems work can change in a New York minute. In the current era of focus on translational science, it will be important to fund strategies that provide a tight linkage between contemporary basic and translational science.

Of course the next challenge will be to translate discoveries of Hu into practical approaches to minimize morbidity and mortality. What approaches will foster the complementary interface between discovery and translational science? Obviously 1 method is to share information. However, the sheer volume of information currently available means that we need to translate information into insights. The systems biological approach is a pivotal tool to translate information into insight. A tight interface between discovery and translational biologists who have synergistic skills but common purpose may be necessary for to convert innovation into diagnostics and therapeutics.

Multiple methods are available to assess differential gene expression. One method is whole transcript microarray analysis. This approach uses probe hybridization methodology. A newer method involves next generation sequencing techniques (RNA-Seq). Further experience with both techniques will be required to assess which method is most appropriate for which experiment condition.

Disclosures

None.

Reference


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