The Promise and Challenges of Biobanking in Digestive Disease Research

Advances in biomedical research require the use of many different model systems in the laboratory, ranging from the simplest eukaryotes, yeast, to the most complex, humans. In general, basic biological mechanisms are most efficiently studied in simple model systems where the genetic background can be controlled and manipulated, and large numbers of organisms can be quickly characterized. Profound discoveries have been made in yeast (Saccharomyces cerevisiae), nematodes (Caenorhabditis elegans), fruit flies (Drosophila melanogaster), and zebrafish (Danio rerio). Mammalian models largely focus on the use of either in vitro tissue culture or rodent models such as mice. Under certain circumstances, studies in non-human primates are performed to study disease processes such as hepatitis C virus and Simian immunodeficiency virus, as well as evaluate pharmacologic interventions that parallel the biology in humans. Here, too, basic mechanisms of normal biology and disease can be probed in experiments under carefully controlled conditions. Nevertheless, it is the application of knowledge to human biology that counts the most. Despite compelling evidence for the functional mechanisms in these model systems, direct relevance to humans is sometimes difficult to predict. For example, the efficacy of pharmacologic agents clearly useful in rodent models may not translate into meaningful results in humans. Furthermore, deleterious side effects of pharmacologic agents in rodents may not be observed in humans. Finally, just because a model of disease in a mammalian system phenotypically seems to have similar characteristics of human disease does not mean that this model is relevant to human biology. Enormous expense, hard work, and effort may be expended studying these model systems later to find out that the relevance to humans is limited.

As basic discoveries are made in simplified model systems, it seems intuitively obvious that a concerted attempt should be made to determine their relevance to humans. Many types of these studies require the collection of human tissue from healthy subjects, as well as from patients with disease processes, to perform genomic studies and characterize patterns of gene expression at the mRNA or protein level for their use in biomarker discovery. One example of biobanking blood that has been extremely successful, leading to novel discoveries relevant to gastrointestinal disease pathogenesis, are the genome-wide association studies that have identified a growing number of genes associated with the development of inflammatory bowel disease (IBD).1 These discoveries have led to new paradigms in disease pathogenesis, some of which would not have been predicted by decades of research in cell culture and various animal models. In addition, this new information has provided a strong impetus for basic science investigators to focus research projects on areas that are new to the field of mucosal immunology such as autophagy.2–4 Immediate applications of this new knowledge include genotypic–phenotypic studies that may lead to genomic tests to predict patterns of disease in patients that may help to direct therapeutic interventions. The identification of interleukin-23R as a gene associated with the development of Crohn’s disease has also helped to identify a new immune regulatory pathway as a target for the generation of novel pharmaceutical agents.5

With advances in transcriptome profiling to examine patterns of gene expression at the mRNA level as well as proteomics, significant advances in biomarker discovery are now much more feasible. The identification of these markers may provide useful in clinical practice by prognosticating disease phenotype, predicting response to pharmacologic therapy (as has been demonstrated in the treatment of tumors),6 and in identifying patients that may have adverse reactions to specific medical therapies. These types of studies can be performed not only on blood, but also on tissue samples obtained from the gut, which are fortunately easily accessible. The accessibility of tissue from the luminal digestive tract has facilitated important discoveries such as the progression of adenomas to carcinomas in the pathogenesis of colorectal tumorigenesis, a paradigm for the development of many epithelial tumor types. More recently, it now seems that even biobanks of human stool samples may ultimately lead to important discoveries in the role that the gut microbiome plays in diseases such as IBD, diet-induced obesity, and diabetes. To support such initiatives, the human microbiome project, supported by a National Institutes of Health roadmap initiative, has recently been initiated.7

Despite the promise of research based on human tissues, however, there remain significant challenges in the field. First, it is critical that procedures are in place to protect patient confidentiality as mandated by the Health Insurance Portability and Accountability Act. Careful scrutiny by institutional review boards is critical in this regard. Second, the collection of tissues requires the cooperation of clinicians, pathologists, surgeons, and basic researchers. Increasing pressure in academic medical centers to maintain high levels of revenue generation has made it difficult for clinicians to justify the addi-
Comment From the Editor continued

The substantial impact of digestive disease research. Nevertheless, given the biobanks will facilitate research that will reveal invaluable new information on disease pathogenesis, hopefully facilitating the development of novel approaches to diagnostics and therapeutics for our patients.

References


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