Transcription, Translation, and Transitions

It seems a bit odd to use the word 'era' in the context of just a few decades, but we are now said to be in a transition stage between the genomics era and the newly arriving proteomics era. The articles presented in this issue aptly illustrate that transition. Now that we have learned how to read, or transcribe, the genes, the call is for research that will translate the information gathered from the international genome project into knowledge about biological function and ultimately, into effective therapies that prevent and cure genetic disease, including hearing loss.

In the development of human medical genetics, mutation analysis has played a prominent role, and it is reasonable to expect that the utility of such investigations will increase. Mutation discovery has its first impact in the area of diagnosis. In this issue, Cryns and van Camp review the status of molecular diagnosis and hearing loss disorders. Hundreds of mutations in many genes have been identified, underscoring the extensive heterogeneity in the genetic etiology of hearing loss. This heterogeneity is a diagnostic nightmare, because testing for known and novel mutations is labor intensive and expensive. Unfortunately, mutation studies have taken a back seat to other investigations, to the detriment to both the families involved as well as science. However, more rapid, and less expensive, chip-based methods of diagnosis of syndromic and nonsyndromic forms of hearing loss will soon become available.

Mutation analysis (as exemplified by the papers by Bischoff et al. and Frei et al.) can be an extremely useful approach to study the regulation of gene expression as well as the structure-function properties of the protein coded for by that gene. By virtue of their detrimental impact on the phenotype, specific sequences in or near the gene, or within introns, may be revealed that are important in the regulation of gene expression or that could con-

trol gene splicing to produce isoforms. Missense mutations will provide insight into the function of different domains of the protein being produced as well as the importance of its steric properties. It was the analysis of mutations that provided much of the insight into the structure-function properties of hemoglobin as well as the regulation of its expression during development. It is reasonable to expect similar benefits in the study of mutations involved in hearing loss disorders.

Phenotype/genotype correlations are an important part of mutation analysis and help in trying to understand the in vivo function of the gene and its product. The research reported by Bischoff et al. and Pennings et al. are both good examples of the utility of this approach. The breadth of phenotypic variation gives an indication of the extent to which one can possibly modify the phenotype through therapy. The study of background genes promises to be an important avenue of future investigation in this regard. Pickles' review of the role of mitochondria in presbycusis is an especially appropriate example of transition to the genetics of the 21st century. Common disorders have become far more important as targets for research, simply because the success of the genome project has provided us with the tools of finally being able to dissect these complex disorders and to identify and quantify both their genetic and environmental etiologies. The genetics of aging and age-related disorders has also become an important issue for our society.

The papers in this issue show the transition of hearing science research, from gene discovery to gene function, the transition from transcription to translation. As genetic hearing research progresses, the interaction of genes, the mechanisms by which their products interact, and their impact on hearing will become increasingly apparent.

William J. Kimberling, Omaha