



# Phenotypic Variation: Exploration and Functional Genomics

*Moyra M.D., Ph.D., MFA Smith*

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During the past two decades international collaborative studies have yielded extensive information on genome sequences, genome architecture and their variations. The challenge we now face is to understand how these variations impact structure and function of organelles, physiological systems and phenotype. The goal of this book is to present steps in the pathways of exploration to connect genotype to phenotype and to consider how alterations in genomes impact disease.

In this book the author reviews published research in functional genomics carried out primarily since 2006 that sheds light on aspects of phenotypic variation. The goal of functional genomics is to gain insight into mechanisms through which specific changes in genome transcripts and regulation induce changes in proteins, pathways, organelles, cellular and tissue functions, morphology and ultimately in phenotype.

Topics reviewed include investigations in genome architecture, gene structure, gene regulation epigenetic modifications and function of organelles including mitochondria, and the endosome lysosome system. New insights into neurodevelopment and neurobehavioral disorders gained through functional genomic research are presented. Aspects of genomic studies in complex common diseases are reviewed. Molecular genetic variations and aberrations in cellular mechanisms involved in protein quality surveillance play a role in late onset diseases and one chapter deals with this topic. Molecular analyses of genes and proteins continue to shed light on the pathogenesis of malformation syndromes and specific examples of such studies are presented.

There is growing evidence that late onset disorders such as Parkinson disease, are frequently the end result of defects in functioning of components in different pathways and examples of these are discussed. There is evidence that genetic variation determines differences in response to environmental insults. Genetic variations in complement factor genes are an example of this and are discussed in the context of macular degeneration and pathogenesis of hemolytic uremic syndrome in response exposure to E coli Shiga toxin. In the final chapter the author briefly summarizes key features of the cascade of events that constitute functional genomics.

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