Preface

This book explores gene sharing—a term originally coined to describe the observation that structural proteins (called crystallins) responsible for the transparent and refractive properties of the cellular lens in the eye also perform nonrefractive stress-related or metabolic functions in other tissues. In short, a lens crystallin has distinct molecular functions that share the identical gene-coding sequence. The term "gene sharing" emphasizes that a protein's function may be directly affected by the differential expression of its gene.

Although crystallins are clearly not alone among proteins that serve more than one biological role, I was uncertain as to what extent multiple molecular functions are common among proteins. Determining whether a protein engages in gene sharing is complicated by the need to distinguish between two alternatives: Does the protein perform distinct molecular (cf. biochemical/biophysical) functions, or does it exploit precisely the same properties (a specific enzymatic reaction, for example) with different phenotypic consequences? This can be a tricky question to answer, especially because mechanisms of protein action are often not known in detail. As I read the extensive scientific literature on proteins, I became increasingly convinced of the widespread use of the same protein for different molecular functions. Protein specialization and molecular diversity seem to go hand-in-hand as a general rule and be a fundamental characteristic of evolution. My original idea was to provide an extensive list of multifunctional proteins. I soon realized the futility of that approach: I would have had to include most, if not all, proteins!

A theme of this book, then, is that distinct specialized functions required for life are carried out by the same proteins cast as different characters, much as in a Peter Sellers movie. Specialization of an individual protein neither fixes its functional boundaries in a molecular sense nor prevents it from changing functions under different circumstances. In addition, the fact that the molec-

ular function of a protein may be dictated by the differential expression of its gene affects the very definition of its gene. How should we identify a gene—by its structure or by its function? Do the boundaries of a gene include its regulatory elements? What is the influence of gene expression on natural selection of protein functions, and how is variation in gene expression selected in evolution? These are neither new nor resolved questions in biology. I wrote this book to examine these questions from the vantage point of the principle of gene sharing. I believe that the extensiveness of gene sharing and protein multifunctionality argues against rigid compartmentalization in biology and introduces a fluid concept of genes and proteins.

The multiple functions of an organism's proteins, neatly encoded within the genome, ultimately lead to the visible phenotypes of its cells, tissues, organs, body, and behavior. This book concerns the vast biological space between genotype and phenotype. I have considered implications of gene sharing, but there is a lot of ground to cover between molecular and systems biology. Therefore, forgive me if I have missed an important issue or dwelled on a lesser one. Some topics may be a bit detailed, but I felt that it was important to document carefully because the thrust of the book is to explore. I recognize that I have left gaps in detail and scope, but I hope that I have shed some light on the complex interrelationships between gene regulation, protein functions, and evolution. There are many topics covered here that I had to learn as I wrote, and I take responsibility for the errors that are no doubt present. I hope that my efforts will be useful to students and seasoned scientists alike who are interested in the interplay between pragmatism and serendipity within living systems and evolutionary processes.

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