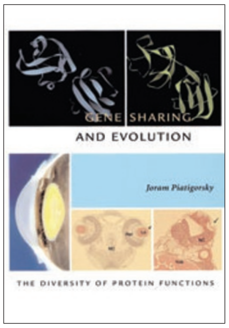
A general theory of gene sharing



Gene Sharing and Evolution: The Diversity of Protein Functions

By Joram Piatigorsky

Harvard University Press, 2007
336 pp., hardcover, $60.00
ISBN 0674023412

Reviewed by Laszlo Patthy

About twenty years ago Joram Piatigorsky coined the term 'gene sharing' to describe the situation when the same protein fulfils at least two markedly different functions; that is, different functions share the same gene. The first and most striking examples of gene sharing came from his studies on crystallins of the eye lens: these major water-soluble structural proteins of the transparent lens are responsible for refraction, but they are also expressed in lower amounts in other tissues of the same organism, where they have important nonrefractive, enzymatic roles.

Although all major textbooks of molecular evolution dedicate a section to gene sharing, a PubMed search with this term retrieves just a few dozen publications, the majority of which describe lens crystallins. It would be premature, however, to conclude that gene sharing is a rare phenomenon restricted to crystallins. In his new book Piatigorsky systematically explores the multifunctionality of proteins and argues that it is the rule rather than the exception.

Obviously, the generality of gene sharing, if valid, would have a huge impact on many aspects of molecular evolution. For example, in classical evolutionary biology it is frequently assumed that gene duplication usually precedes the evolution of new protein function, whereas studies on the evolution of gene sharing support the notion that functional diversity of a protein may exist before gene duplication. To be able to assess how this general theory of gene sharing might change current views of molecular evolution, the first three chapters of the book summarize basic principles of molecular evolution. The first chapter discusses, among other things, the role of gene duplication in the evolution of new functions and mechanisms for diversifying gene functions. The second chapter focuses on functional shifts and preadaptation, whereas the third chapter reviews the evolution of the gene concept.

Although the definition of gene sharing ("a process that expands the number of molecular functions that are performed by a polypeptide") is repeated and rephrased often, some ambiguity remains, as the definition of *function* is not always clear. Piatigorsky points out that "Jensen was a pioneer in considering multifunctionality of individual proteins by emphasizing substrate ambiguity of enzymes." If we equate substrate ambiguity of enzymes (very general among proteases) with multifunctionality, which in turn we equate with gene sharing, then we would come to the conclusion that proteases could be better examples of gene sharing than crystallins. Similarly, reference to the role of the multitude of protein-protein interactions in the many functions displayed by individual proteins highlights the problems associated with the definition of function. The chapters that discuss examples of gene sharing illustrate that this term is used both in a narrower sense (when the different functions of a protein exploit different molecular mechanisms) and in a broader sense (when different functions of a protein are associated with similar molecular mechanisms but different partners).

The most clear-cut, prototypical examples of gene sharing—the crystallins—are discussed in the fourth chapter. It provides an enjoyable description of the biology and evolution of diverse eyes and lenses and the role of crystallins in determining the optical properties of the lens. Crystallins are long-lived soluble proteins that have strictly structural roles inasmuch as they ensure transparency and high refractive index of the lens. The molecular mechanism of their optical function is based on their exceptional solubility and stability at high concentration. On the other hand, the function of the enzymatic crystallins in other tissues (where they fulfill metabolic roles) is based on their catalytic activity. The chapter surveys the diverse lens crystallins, provides compelling evidence for gene sharing and shows that a surprising number of proteins have biophysical properties that enable them to fulfill an optical role in the lens in different taxonomic groups.

The examples in the sixth chapter are intended to illustrate that multifunctionality (and gene sharing) is a common feature of proteins. The chapter discusses the multitude of interactions of hexokinase, citrate synthase, and other enzymes and cellular constituents to demonstrate that through these interactions they fulfill multiple functions. If we accept such a broad definition of multifunctionality and gene sharing, then it is quite clear that gene sharing is widespread. Xanthine oxidoreductase, however, qualifies as a case of gene sharing even in the narrower sense of the term. This is a housekeeping enzyme that catalyzes the oxidation of hypoxanthine to xanthine in many tissues, but in milk fat droplets of mammals it has primarily a structural role as a membrane-associated protein involved in milk fat droplet secretion.

In summary, Piatigorsky's book convincingly argues that most proteins perform a variety of different functions, and that the generality of protein multifunctionality sheds new light on the principles of molecular evolution. Accordingly, this stimulating book is highly recommended to those interested in molecular evolution. Ironically, if readers are convinced that gene sharing is a widespread phenomenon, valid for all proteins that are involved in more than one cellular process, the inflation of the term would actually deprive it of much of its power. It seems more likely that gene sharing will continue to be used in its original, narrower sense.

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COMPETING INTERESTS STATEMENT

The author declares no competing financial interests.