

Cardiac morphogenesis and development

The Editors wish to thank Dr. J. M. Icardo for coordinating this review.

Introductory comments

Through the years descriptive embryology has provided an impressive amount of data concerning the development of the vertebrate heart. Analysis of the developmental problems arising from this wealth of information is the main task we face today when studying cardiac embryology. However, despite continuing interest in this area of research, our understanding of heart development does not appear to have advanced as much, or as quickly, as we had hoped. Progress seems to have come to a standstill, waiting for some definitive breakthroughs to occur. For example, it is unclear whether we need much more information or whether the answers may come from looking at the same things from different points of view. Perhaps the first question that must be posed is at which level (tissue structure, cell, gene) we should start to analyze these data. In other words, are we looking at the right things? And, are we asking the right questions?

Although descriptive embryology currently constitutes a part of our own work, we must admit that while descriptive studies do increase factual knowledge they are unlikely to answer any fundamental questions. On the other hand, the statement that development is under the control of the genome does not help us much to achieve a deeper understanding of embryonic mechanisms. Gene regulation occurs at several hierarchical levels, and its complexity is becoming increasingly apparent. Moreover, there is the risk of losing sight of the distinct organ anatomy as the end product of gene activity. The purely descriptive and the purely reductionistic approaches to development coexist in the embryological literature today. The first can be accused of sometimes being boring and repetitive. The second, of being too cryptic. Yet, the two developmental viewpoints need to complement each other. One wonders, however, how there can be enough sharing of ideas when researchers cloister themselves within the confines of their own immediate projects. Nevertheless, there is no doubt that embryology is abandoning pure description; it is searching, for the molecular

mechanisms behind developmental facts; and there is an increasing amount of research being devoted to understanding how genes control the development of different structures. That is to say, investigators are looking at the conditions under which genes become activated (or repressed), how gene products control cell differentiation and cell behavior, and how these products influence morphologic events which are often remote in both time and space.

Some of these questions may be relatively easy to answer in simple systems. Organ development, however, appears to be far more complicated. It depends upon the sequential expression of genes or gene families whose products interrelate and establish cooperative influences. These products and the activity of the cells under their control, in turn, influence the expression of genes. Furthermore, extrinsic factors are superimposed on the genetic substrate so as to modulate the activity of the genome. Similarly, the mechanisms which ultimately result in heart shape are exceedingly complex. It may be that the formulation of a unified theory to explain heart development is simply not possible. However, we may be able to obtain partial answers at the various levels of biological organization: the mechanisms of cell differentiation; the relationship between the cells and their immediate micro-environment; the formation of the different tissue structures and their temporo-spatial assembly; the role of extrinsic factors, like the flow of blood through the heart and the hemodynamic workload; the production of congenital defects as failures in the transfer of developmental information in time and/or space, etc. The following set of reviews evidences progress in this direction. Although we may still be uncertain about whether this is the right path to follow, I am hopeful that this kind of thinking will provide answers that will lead to a better understanding of heart development. My thanks to all the contributors of this multi-author-review.

Jose M. Icardo