The following letters refer to an “In focus” article by H. Ehmke (Developmental physiology of the cardiovascular system. Am J Physiol Regulatory Integrative Comp Physiol 282: R331–R333, 2002).

The Chicken Embryo in Developmental Physiology of the Cardiovascular System: A Traditional Model with New Possibilities

To the Editor: In the February 2002 issue of American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, Ehmke (7) focuses on unsolved issues and interesting findings in the field of developmental physiology of the cardiovascular system. Ehmke addresses the need for new useful models to study embryonic/fetal cardiovascular structure and function and rightly points out the potential of the zebrafish (Danio rerio) as an experimental model. The merits of this model organism for integrative physiology were reviewed by Briggs (4).

The chicken (Gallus gallus) is a species that deserves attention when the developmental physiology of the cardiovascular system is considered. The attractiveness of the chicken embryo as an experimental model to study angiogenesis (1), heart formation (11, 20), and the development of neurohumoral cardiac control (12, 19) has long been recognized. Recent studies have shown that the chicken embryo, like the zebrafish (9), can also be used to study developmental changes in local vascular tone and hemodynamic control. Reactivity of isolated femoral and carotid arteries of chicken embryos can be studied by means of wire myograph techniques from embryonic day 15 of the 21 days of incubation (15), and precise surgical preparation and intravital microscopy enable the measurement of mesenteric vascular diameter in the intact fetus at even earlier stages of development (22). Very recently the changes in pulmonary arterial reactivity during the transition from in ovo to ex ovo life (which takes more time than in mammals and therefore can be studied in more detail) have been investigated in the chicken embryo (25).

Other studies have used fluorescent microspheres and cannulation procedures (branches of chorioallantoic vein) to investigate time-dependent changes in cardiac output distribution, blood pressure, and heart rate in early and late stages of incubation (2, 3, 18, 26). These studies have provided methods that give important insights in the development of cardiovascular physiological mechanisms in the chicken embryo. In addition, they demonstrate substantial comparability in basic mechanisms of fetal cardiovascular control between the chicken and mammalian species (6). The response to acute hypoxia has been extensively studied in this respect (6, 10, 17).

As Ehmke (7) mentions and argues is the case for the zebrafish (4), a good experimental model should also give the opportunity to study the developmental function of single genes or complex genetic pathways. The role of specific genes and transcription factors, like endothelial PAS protein 1, in cardiovascular development has been investigated in the chicken embryo (8). A “chicken alternative” for the endothelin (ET)-1 and ET type A receptor null mice has even been made by pharmacological in ovo inactivation of the gene product (14). Over the past few years, worldwide collaborations have made large progress in the production of a molecular map of the chicken genome and provide new molecular tools (e.g., microarray) (24). This and the large diversity in genotypes (due to natural and experimental selection) that are also phenotypically characterized (for instance, see Refs. 16, 21) will only increase the potential of the chicken embryo to be used as a model to unravel the role of specific genes in developmental physiology.

As the chicken embryo, like the zebrafish, develops outside the mother, effects of external stresses on cardiovascular development can be studied without interferences of maternal hormonal, metabolic, or hemodynamic alterations. The most common causes of prenatal stress, namely malnutrition and chronic hypoxia (as seen in placental insufficiency), can be studied independently (13, 23, 27), and pharmacological or toxic substances are easily applicable via injections of compounds into the air cell (5). These practical advantages make the chicken embryo and the adult chicken, in which cardiovascular pathology has been observed (16, 21), important animal models to study mechanisms in the intriguing new field of developmental physiology that deals with the prenatal programming of cardiovascular pathology. This tractability for experimental manipulation, its rich history in developmental biology, the short incubation time, and the new possibilities of genomic tools emphasize the importance of the chicken embryo as a model organism in developmental physiology of the cardiovascular system alongside traditional models, such as the fetal sheep, and promising new models, like the zebrafish.

REFERENCES

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REPLY

To the Editor: I thank Ruijtenbeek et al. for their comments. They rightly make the point for the chicken embryo as a model system to study cardiovascular integrative physiology and homeostasis during development. The chicken embryo shares several features with the zebrafish, like an external development, a relatively short incubation time, and a wide availability, which substantially facilitate its investigation. Furthermore, later stages of embryological development are very similar in the chicken and mouse embryo, and many fundamental mechanisms of development (e.g., those of limb formation) have been discovered in this species. Indeed, the major textbook Principles of Development by Wolpert and colleagues (16) lists the chicken embryo, together with Xenopus laevis, Drosophila melanogaster, Caenorhabditis elegans, Aradobopsis thaliana, the mouse, and the zebrafish, as one of the canonical model systems of developmental biology.

Nevertheless, the virtues of the chicken embryo and the zebrafish as model systems of developmental physiology should not be confused. For many reasons, the zebrafish will remain the dream system for genome-wide screens (2, 6, 12). Its short generation time and large progeny size, high permeability to molecules added to the water, external development, and trans-
parenthood mean that zebrafish are ideally suited for large-scale random mutagenesis screens. Over the past 20 years, a huge amount of genomic information has been accumulated, and it is expected that the entire zebrafish genome will become available in the near future. Because the gene order appears to be conserved in most parts of zebrafish and human chromosomes, genetic screens in zebrafish will most likely help us to understand the function of human genes.

However, the cardiovascular system of the chicken resembles the human cardiovascular system much more closely than does that of the zebrafish. As emphasized by Ruijtenbeek et al., the basic mechanisms of cardiovascular control seem to be very similar in chicken and mammalian species (1), and cardiovascular physiology and pathology can be well studied in adult chicken. In addition, much physiological information is available for the chicken. This is also reflected by a surge of recent studies on chicken embryos published in American Journal of Physiology-Regulatory, Integrative and Comparative Physiology (1, 3–5, 7–11, 13–15). Thus the chicken appears to be particularly suited for studies investigating the long-term consequences of factors acting during embryogenesis.

REFERENCES


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