

Functional Development and Embryology

Abbreviation: Func. Dev. Embryol.

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Scope and target readership: *Functional Development and Embryology* deals with all aspects of developmental phenomena in all other organisms, including microorganisms, excepting for plants.

Manuscripts in any of the following fields will be considered:

- 1) Axial patterning, embryonic induction and fate maps;
- 2) Cell interactions and cell-matrix interactions;
- 3) Developmental diversity and evolution;
- 4) Developmental endocrinology;
- 5) Evolution of developmentally relevant genes;
- 6) Genes and pattern formation in invertebrates and vertebrates;
- 7) Growth factors and oncogenes;
- 8) Neural development and cell lineages;
- 9) Morphogenetic movements, the cell surface and fine structure of tissues and organs;
- 10) Regulation of stem cell populations;
- 11) Transcriptional control mechanisms;
- 12) Other topics: division, dormancy, germination, metamorphosis, regeneration and pathogenesis, developmental genetics, growth, differentiation, morphogenesis, cellular kinetics and cell-cell interactions, growth factors and signal transduction, fertilization or neuroanatomy, all at the molecular, biochemical, biophysical and analytically morphological levels.

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Cover photo: Defective vascular remodeling in *Man1*-deficient embryo. Whole-mount immunostaining of the yolk sac (A, B) and embryo proper (C, D) at E10.0. with an antibody to platelet endothelial cell adhesion molecule 1. *Man1* Δ/Δ indicates homozygous *Man1*-deficient (B, D). More details in Osada, pp 14-25.

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Caroline R. Kemp, Marijke Hendrickx, Erik Willems, Danuta Wawrzak, Mourad Métioui, Luc Leyns (Belgium) The Roles of Wnt Signaling in Early Mouse Development and Embryonic Stem Cells (pp 1-13)

ABSTRACT

Special Feature: The Wnt family of secreted signaling molecules is conserved throughout the animal kingdom. Wnt signaling plays critical roles during embryonic development and mutations leading to the overactivation of the Wnt pathway have been linked to cancer. Wnt signals are transduced intracellularly by the Frizzled family of receptors. Moreover, proteoglycans and the co-receptors LRP5 and -6 participate in the transmission of Wnt signals, whereas a series of secreted antagonists can block Wnt signaling directly (i.e. Frzb and Sfrps) or indirectly (i.e. Dkks). Some of the biochemical interactions of the Wnts with their receptors and antagonists have recently been characterized, permitting further elucidation of how these proteins function *in vivo*. Expression pattern analyses in mouse embryos have shown that Wnt genes are active during most, if not all, developmental processes and gene inactivation has uncovered some of their key roles throughout mouse embryogenesis. Importantly, knock-out and overexpression studies have proven the importance of Wnt signaling during mesoderm, neurectoderm and body axis formation. With their ability to differentiate into all adult cell types *in vitro*, mouse embryonic stem (ES) cells have been used to mimic the developing embryo. In this ES cell system, it has recently been shown that Wnt signals contribute to mesoderm induction and neural inhibition. Here we will provide an overview of the Wnt signaling pathway and its roles during mouse embryonic development, focusing on gastrulation. Functional studies in the mouse, including gene ablation and overexpression experiments, will be reviewed. Finally, we will discuss the latest reports on the application of ES cells to study the Wnt pathway during development.

Shin-Ichi Osada (Japan) Integral Nuclear Membrane Proteins in Vertebrate Development (pp 14-25)

ABSTRACT

Invited Review: The nuclear envelope is composed of the outer and inner nuclear membranes, nuclear lamina, and nuclear pore complexes. Recent studies show that the nuclear envelope is more than a capsule for protecting genetic information or a gatekeeper for molecular traffic between the cytoplasm and nucleus. The outer and inner nuclear membranes contain unique integral transmembrane proteins. The number of such transmembrane proteins is estimated as many as 80. However, a dozen of them have been characterized in detail. Nesprins, the first outer nuclear membrane proteins identified, are involved in nuclear positioning by connecting the nuclear envelope to the cytoskeletal system. A growing number of integral inner nuclear membrane proteins have been implicated in diverse cellular functions, such as gene regulation, chromatin organization, and signal transduction through interactions with their binding partners. In addition, mutations in the nuclear envelope proteins cause a wide variety of human diseases. Analysis of experimentally altered animal models of the integral nuclear membrane proteins is essential to understanding their functional roles at the whole-organism level and pathogenesis of the diseases caused by mutations in these proteins. However, only several such animal models are available in vertebrates. This review highlights recent progress in the field of integral nuclear membrane proteins from the view of vertebrate development.

Kristine A. Henningfeld (Germany), Morgane Locker, Muriel Perron (France) *Xenopus* Primary Neurogenesis and Retinogenesis (pp 26-36)

ABSTRACT

Invited Review: In the past, significant advances in our understanding of vertebrate neurogenesis have been obtained using the amphibian model system *Xenopus laevis*. Today, *Xenopus* continues to serve as an excellent system to study the molecular mechanisms of neural cell fate determination and differentiation owing to the accessibility of the earliest events of neurogenesis, amenability of the organism to manipulations such as microinjection, electroporation, explant isolation and cultivation. In *Xenopus*, the first neurons are born within the induced neuroectoderm shortly after gastrulation in three longitudinal domains on each side of the midline and are termed primary neurons. In addition to primary neurogenesis, the retina, in which six classes of neuronal cells and the Müller glial cell sequentially differentiate, also serves as an outstanding system to study the molecular events of neurogenesis. In this review we will detail the current knowledge of events that control neuronal and glial cell fates in *Xenopus*, with an emphasis on intrinsic factors, cell cycle regulators and the Notch pathway in the context of primary

neurogenesis and retinogenesis.

Eugenia C. Olesnick, Claude Desplan (USA) Gaining New Insights into Primitive Strategies for Embryonic Axis Specification Using the Wasp *Nasonia* (pp 37-48)

ABSTRACT

Invited Review: The evolution of genetic networks is a fascinating and complex topic that has long intrigued researchers. The genetic network controlling early embryonic patterning in *Drosophila* represents one of the best understood networks in developmental biology. Thus, the realization that major components of the network are not conserved features of insect embryogenesis provided the scientific field with an incredible opportunity to begin comparative studies between the well-studied *Drosophila* network and the genetic networks of other insect species. Moreover, the tremendous diversity among insects provides a wide variety of species to sample the conserved and novel developmental features that have evolved over time. The application of genetic screens, transgenic analysis and in particular, the development of pRNAi in various insect model systems has also contributed significantly to the advancement of the field of evolution and development. The results presented in recent reports regarding *Nasonia*, *Tribolium*, *Oncopeltus* and *Gryllus* embryonic patterning have shown the power of comparative studies between different insects for studying evolution and development. This review will focus on the establishment of the wasp *Nasonia vitripennis* as a powerful model system for elucidating the various biological strategies employed during insect embryogenesis. Moreover, work presented throughout this review will highlight important results regarding comparative studies between the fruit fly and the wasp.

Rebecca Lyczak (USA) Anterior-Posterior Polarity in *Caenorhabditis elegans*: Establishment of Asymmetries at the One-Cell Stage and Beyond (pp 49-56)

ABSTRACT

Invited Review: The *Caenorhabditis elegans* one-cell embryo is a model system for understanding how cells are polarized during development. Polarity establishment is regulated with the cell cycle and involves sperm donated products and changes in the actomyosin cytoskeleton. Sperm entry results in completion of meiosis II in the embryo and the sperm donated centrosome polarizes the axis by triggering local destabilization of the cortical actomyosin cytoskeleton. This leads to cortical flows and localization of the cortical PAR proteins to distinct domains. Following the establishment of cortical polarity, the cytoplasm is polarized through protein movement and selective degradation of developmental regulators. The establishment of polarity in *C. elegans* is complete prior to the first cell division and is crucial for cell fate decisions in daughter cells. Further AP polarities in the embryo require cell-cell communication and the Wnt signaling pathway plays a pivotal role in many of the AP cell fate decisions throughout development.

Marlene Benchimol (Brazil) *Giardia lamblia* Under Microscopy - How This Primitive Protist Divides (pp 57-69)

ABSTRACT

Invited Review: *Giardia lamblia* is a parasitic protozoan that infects thousands of people all over the world, causing a disease known as Giardiasis. *Giardia* trophozoites are pear-shaped cells with two nuclei located at the anterior region of the cell body. *Giardia* is an amitochondrial flagellate and possesses a complex cytoskeleton based on several microtubular systems. In the interphase, these microtubules include the axonemes of the eight flagella, the median body and the funis, both formed by a set of microtubules and the ventral adhesive disc built on a helicoidally turned layer of parallel microtubules. There are several questions still open to debate concerning the basic biology of *Giardia* and a fundamental one among these is its process of division. *Giardia* presents a semi-open type of mitosis, in which the nucleus elongates and an extranuclear spindle is formed. Some of the spindle microtubules penetrate through small openings in the nuclear envelope. The mode of *Giardia* cytokinesis and karyokinesis has been discussed in several papers due to the controversy of how the cells maintain their left-right (dorsal-ventral) asymmetry. Recently, progress has been made and it has been shown that *Giardia* divides with mirror-image symmetry. Elegant experiments were performed using a single clone of trophozoites transfected with a plasmid and also the spindle was finally demonstrated by electron microscopy. Although molecular data and the genome project have provided advances in *Giardia* knowledge there are still several questions to be answered concerning *Giardia* division. Thus, this review presents an analysis of the advances made on the knowledge of how *Giardia* divides and the behavior of the two nuclei in interphase and mitosis.

Klaus B. Rohr (Germany) Morphogenesis of an Epithelial Organ: Budding and Relocation of the Thyroid Gland during Vertebrate Embryonic Development (pp 70-77)

ABSTRACT

Invited Mini-Review: During early embryonic development, a common body plan is established in all vertebrates. Subsequently, complex morphogenetic programmes together with tissue growth dominate further foetal development, and differences in these morphogenetic processes result in anatomical variations between species. Our current view is dominated by the discovery that many morphogenetic processes are based on conserved molecular mechanisms. However, plasticity of such conserved molecular mechanisms has the potential to create morphological diversity between different species. Morphogenesis of the vertebrate thyroid gland is unique in that the primordium relocates from its site of origin, the epithelium of the primitive pharynx, to a final position in the anterior neck region in amniotes or to a similar area ventral to the pharynx in fishes, respectively. Comparison between species reveals naturally occurring variation of primordial relocation, and in position and shape of the mature gland. This review gives an overview about functional studies in different model species that provide insight into the molecular mechanisms required for thyroid relocation. Based on these data and comparative studies, I present a model that could explain species-specific variation of thyroid position and shape. Furthermore, I refer to congenital defects in humans that can be related to abnormalities in thyroid relocation.

Guillaume E. Desanti (France), Julien Y. Bertrand (USA), Rachel Golub (France) Fetal Spleen Development, the Ride toward Multiple Functions (pp 78-90)

ABSTRACT

Invited Review: The aim of this review is to clarify the different steps of fetal and neonatal spleen development that lead to the formation of a functional adult immune organ. The adult spleen harbors a highly organized architecture directly correlated with its roles in the innate and adaptive immune system. Before achieving these immune functions, the spleen undergoes two important steps: the acquisition of the hematopoietic capacities during the fetal period followed by the implant of distinct organ areas during the neonatal phase. It is first a site of hematopoiesis, producing cells that will then be segregated into different areas. The spleen primordium appears around embryonic day E11.5 and is colonized early by several hematopoietic progenitors, via blood circulation. The interactions between the stromal microenvironment and the hematopoietic progenitors constitute a key step to understand spleen organogenesis. We discuss herein all the data concerning fetal spleen hematopoiesis characteristics that will provide the main cell subsets involved in its organogenesis. We actually highlight the relationship between these different hematopoietic compartments, the acquisition of architecture complexity and the gain of organ functions that take place at the neonatal period. We also report several models of aberrant murine spleen development, which constitute important tools to study the specificities of the fetal spleen microenvironment.

Nobuyoshi Shiojiri (Japan) Cell Lineages in Hepatic Development and Molecular Mechanisms of Cell-Cell Interactions Underlying Hepatoblast Differentiation into Mature Hepatocytes and Biliary Epithelial Cells (pp 91-98)

ABSTRACT

Invited Mini-Review: The endodermal epithelium in the mammalian liver consists of hepatocytes and biliary epithelial cells. Both cell types originate from hepatoblasts, which may be hepatic stem cells in fetal stages. When hepatoblasts are located around the portal veins, they give rise to biliary epithelial cells under an inductive action by portal connective tissues. Nonperiportal hepatoblasts differentiate into mature hepatocytes. Recent studies on naturally mutated or genetically engineered animals have highlighted several new aspects of the hepatoblast differentiation. Mosaic analysis using random inactivation of either paternal or maternal X-chromosome carrying a *sp^{fl/sh}* mutation in the heterozygous females has demonstrated that hepatoblasts may be bipotential for their differentiation potency into hepatocytes and biliary epithelial cells. This idea is strongly supported by the observation that hepatoblasts in *C/EBP α* -knockout mouse livers abundantly develop pseudoglandular structures, which resemble precursor structures for intrahepatic bile ducts (pearl-like structures or ductal plates). The data have also shown that the suppression of *C/EBP α* expression in periportal hepatoblasts is a key for biliary cell differentiation, which leads to elevation of *HNF6* and *HNF1 β* expression. In this review article, molecular mechanisms for bile duct formation are discussed, including roles of the suppression of *C/EBP α* expression and Jagged1/Notch2 or activin/TGF β signaling. For hepatocyte maturation and growth, cell-cell interactions such as hepatoblast-stellate or endothelial cell interactions are also required. Our present understanding of their molecular mechanisms is summarized with cell lineages and roles of nonparenchymal cells in liver development.