SUBJECT:	**DEVELOPMENTAL BIOLOGY**				
CREDITS:	Total:	**4.5**	Theory:	**2.5**	Practical: **2**

GENERAL OBJECTIVES

The course in Developmental Biology is an introduction to animal development and places special emphasis on mammalian and human development. Students have a basic knowledge of biochemistry and cell biology and begin to study the multicellular level of biological organization. The principal objective is to introduce students to the developmental processes that lead to the establishment of the body plan of vertebrates and the corresponding cellular and genetic mechanisms. This will allow students, at a later stage, to understand organogenesis and histogenesis, as well as pathology related to mechanisms of development and differentiation.

SPECIFIC LEARNING OBJECTIVES

The course is divided into five parts:

–Introduction to development

–Gametogenesis and fertilization

–Segmentation, gastrulation and neurulation

–Mammalian development

–Cellular and molecular foundations of development.

Each part consists of theory lessons, practical sessions (P) and seminars (S) which are planned according to the corresponding subject. The practical material allows students to work principally with three developmental models: amphibians, birds and mammals. Through observation and comparison, students can identify the common and differential features and grasp the complexity of development beyond the rigid structures of textbooks and theory lessons. In the part dealing with mammals, students study in greater detail the first stages of development focusing mainly on the human model. Finally, the course covers some aspects of the genetic and cellular mechanisms of development.

In accordance with these subject areas, students will be required to understand the different points of the theory and practical programme at a level that corresponds the content of the basic bibliography, theory and practical classes and seminars.

Students should be able to:

- Indicate the principal historical stages and methodological approaches to the study of embryonic development and the characteristics of the principal experimental models.
- Identify embryonic structures in preparations, photographs and diagrams.
- Arrange sequences in developmental processes in order.
- Identify the homologies, similarities and differences between structures and processes in the developmental models studied.
- Indicate the derivatives of embryonic structures.
- Attain a basic conceptual knowledge of the principal cellular mechanisms of development and identify the genetic and molecular elements that are involved.
- Explain the clinical implications of development and the mechanisms that intervene in developmental alterations.

Programme

The programme encompasses both theory and practice: practical sessions (P) and seminars (S) are planned to correspond to the lessons of the theory programme.

Introduction to development

1. Historical elements. What is developmental biology? Origins in Ancient Greece. Renaissance of developmental biology. Preformation and mechanicism. Epigenesis and vitalism. Embryology, cell biology and genetics at the turn of the century. 20th Century: experimental embryology and molecular biology.

2. Stages. The sex cycle, somatic cells and germinal cells. Polarity of the egg, radial symmetry. Principal characteristics of segmentation. Principal characteristics of gastrulation. Principal characteristics of organogenesis and differentiation, metamorphosis.

3. Models. Types of egg according to the content and distribution of the vitellus. Types of segmentation. Comparative embryology, Baer's law. The most commonly studied experimental models, principal use and main interest of each model. Evolutionary conservation of developmental genes.

4. Mechanisms and basic concepts. Proliferation and programmed cell death. Morphogenetic movements, cell aggregation, disgregation and migration. Cell determination and differentiation, conservation of genetic information: classic blastomere separation experiments, nuclear transplant experiments. Stem cells and cytoplasmic determinants. Intercellular signalling, induction. Pattern formation, positional information. Mosaic and regulation.

P1. Developmental models. Microscopic observation of eggs, embryos and larvae from different models (starfish / sea urchin, nemertine, drosofila, frog, chick). Interpretation of sections on the sagittal/parasagittal, transverse and frontal (coronal) planes. Video on developmental models, *A dozen eggs*.

Gametogenesis and fertilization

5. Germinal cells. Identification of primordial germinal cells (PGC), germinal plasma. PGC migration and colonization of genital crests. Proliferation and death of oogonia and spermatogonia in the embryo. Common and differential characteristics of the processes of oogenesis and spermatogenesis.

6. Oogenesis. Nuclear and cytoplasmic changes during the growth of oocytes and vitellogenesis, amphibian model. Oogenesis in mammals, role of follicular cells, follicle development, Graafian follicle. Hormonal control of oogenesis.

7. Spermatogenesis. Structural and functional characteristics of the sperm cell. Spermatogenesis and spermiogenesis, position of the different cells in the seminiferous tubule, processes of cell differentiation, role of Sertoli cells. Maturation of the sperm cell, capacitation.

8. Fertilization. Approximation, capacitation and penetration of the corona radiata. Adhesion to the zona pellucida. Acrosomal reaction and penetration of the zona pellucida. Cell fusion and cortical reaction. Egg activation, end of meiosis and formation of the diploid nucleus of the zygote.

Segmentation, gastrulation and neurulation

9. Segmentation. Polarity of the egg and polarities of the embryo, dorsalization and establishment of the plane of bilateral symmetry in amphibians. Structural and functional characteristics of segmentation in amphibians, structure of the blastula. Segmentation in birds, structure of the blastodisc.

10. Gastrulation. Gastrulation in amphibians, cell movements, fate map of presumptive territory. Blastopore, archenteron and formation of germinal layers. Gastrulation in birds, cell movements, similarities to gastrulation in mammals. Primitive streak and Hensen's node, homology with the blastopore.

11. Neurulation. Neurulation and initial organogenesis in vertebrates, morphogenetic movements of the ectoderm. Development of the ectoderm, mesoderm and endoderm, establishment of body plan, amphibian model. Neurulation in birds.

12. Derivatives of germinal layers. Ectoderm: epiectoderm. Neuroectoderm, neural tube and neural crests. Mesoderm: notochord. Prechordal plate. Somite, sclerotome, myotome and dermatome. Gononephrotome. Splanchnopleura. Somatopleura. Endoderm. Germinal cells. Extraembryonic derivatives in amniotes, embryonic annexes in birds.

P2. *Xenopus,* a developmental model for vertebrates. Observation of preparations of ovary and testicle from *Xenopus.* Video on ovulation and fertilization. Microscopic observation of preparations of eggs and embryos from *Xenopus:* unfertilized eggs, blastulae, gastrulae, neurulae and larvae at different stages. Developmental

alterations. Observation through stereoscopic lens (whole samples) and with transmission microscope (sections).

P3. Chick, a developmental model of amniotes. Poster and video of chick development. Video on obtaining chick embryos. Observation of preparations of chick embryos at different stages with stereoscopic lens (whole samples) and transmission microscope (sections). Observation of embryos and extraembryonic membranes after 9 to 12 days of incubation.

Mammalian development

13. Preparation for pregnancy. Structural elements of the female reproductive apparatus. Hormonal control of the reproductive cycle in women, ovarian and endometrial cycles. Hormonal control related to reproduction in men.

14. Gamete transport and fertilization. Ovulation. Ovular transport. Formation and function of the corpus luteum, ovulation and pregnancy. Sperm transport. Fertilization. Treatment of infertility via in vitro fertilization and embryo transfer.

15. Segmentation and implantation. First and second weeks of human development. Characteristics of segmentation in mammals, morula, blastocyst, embryoblast and trophoblast. Tubular transport of embryo. Implantation of embryo, cytrophoblast and syncitiotrophoblast. Decidual cells and decidual reaction. Bilaminar germinal disc stage, second week.

16. Formation of the three germinal layers. Third week of human development, gastrulation. Formation of the primitive streak and primitive or Hensen's node, origin of the embryonic mesoderm, trilaminar germinal disc. Regression of the primitive streak. Notochord and prechordal plate, notochordial process, neurenteric canal, oropharyngeal membrane.

17. Development of the ectodermal germinal layer. Fourth week of human development, establishment of the body plan. External morphology of the embryo during the fourth week. Neurulation, formation and segmentation of the neural tube, neural crests, sensory placodes.

18. Development of the mesodermal and endodermal germinal layers. Paraxial mesoderm, somitogenesis. Intermediate mesoderm. Parietal and visceral mesodermal layers, coelom. Formation of blood and vessels. Development of the endoderm.

19. Placenta and extraembryonic membranes. Amnion. Vitelline sac. Allantoid. Chorion and placenta. Formation of chorionic villi. Relation between the chorionic and decidual tissues. Structure of the placenta and placental circulation. Functions of the placenta.

20. Developmental alterations. Frequency and importance of malformations. General principles. Risk periods. Patterns of abnormal development. Causes of malformations, genetic factors and background factors. Disruption of developmental processes that determine malformations.

P4. Mammalian development. Microscopic observation of preparations of mammal ovary and testicle. Observation of electronic micrographs of mammalian ovarian follicles and sperm cells. Microscopic observation of sections of rat embryo. Dissecting and obtaining female foetuses from pregnant rats (the animals supplied will be killed previously and will be studied fresh without fixation). Observation of human developmental models and of fixed human placenta and foetus.

S1. Clinical correlations. Meiotic disorders. Determination of pregnancy data. Sterility, in vitro fertilization and embryo transfer. Pregnancy with twins. Ectopic pregnancy. Diagnosis of congenital malformations and innate metabolic errors, ecography, amniocentesis and chorionic villus sampling.

Cellular and molecular foundations of development.

21. Determination and regulation. Genetic expression during the first phases of development, parental imprint, X chromosome inactivation. Capacity of regulation in early mammalian embryos. Transgenic embryos. Cloning.

22. Mesodermal and neural induction. Neural or primary induction in amphibians, the Spemann organizer. Generalization in other vertebrates. Molecular basis for neural induction. Anteroposterior regionalization of neural induction. Mesoderm induction.

23. Genetic control mechanisms I. The drosophila as a model of genetic control of development, maternal effect genes or egg-polarity genes, segmentation genes and homeotic genes. positional information, morphogen gradients, the case of the *bicoid*.

24. Genetic control mechanisms II. Evolutionary conservation of the genetic control of development, principal functional categories of regulatory molecules and their role in vertebrate development.

25. Programmed cell death, morphogenetic movements and cell migration. Role of programmed cell death (*apoptosis*) in development, examples. Morphogenetic movements, cell shape change and cell adhesiveness. Cell migrations, importance and examples.

S2. Determination of pattern. Video *The Royal Institution Christmas Lectures, Prof. Lewis Wolpert*. Discussion of a scientific article distributed and analyzed previously on the determination of the vertebrate limb pattern.

S3. Current techniques in developmental biology. Discussion of a scientific article distributed and analyzed previously on the genetic control of development.

LEARNING RESOURCES AND TEACHING METHODOLOGIES

All aspects of the programme are covered in the theory classes, practical classes and seminars. The teaching material employed in these sessions includes videos, preparations of eggs and whole embryos and sections of different models, histological preparations, 3D models, embryonated hens´ eggs, fixed material of mammalian embryology, scientific articles to be analyzed, transparencies and slides. Each month students will be provided with a basic and an extended bibliography, as well as compact discs and references of websites with additional information (see bibliography*******) and Guides to practical classes and seminars which indicate the material to be used for each session, the plan for the practical class or seminar and the questions that should be answered based on the observations made. These guides will also contain additional notes to give students a better understanding of each activity.

For the practical classes, students will be expected to have read the corresponding guide in advance and should carry out the activity according to the instructions given. The teaching staff will discuss observations with students in relation to different materials and will ask for answers to the questions set out in the corresponding guide.

For the seminars, students will be expected to have prepared the session in advance and should actively participate, providing answers to the questions set out in relation to different aspects of clinical correlation or the analysis of a scientific article.

A session will be held prior to the exam to clarify doubts about any aspect of the programme.