UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Genetics of Development and Differentiation

2122-1-F0601Q076

Aims

Knowledge and understanding
The course aims at familiarizing the students with concepts and experimental approaches concerning modern genetics of transcriptional control in eukaryotic cells in development and cellular differentiation, in the normal and in examples of pathology.

Applying knowledge and understanding
Experimental approaches, the construction of experiments and data interpretation will be the object of particular attention; primary material of the course will be represented by original papers.

Making judgements
The development of critical sense will be pursued, in particular regarding the interpretation of experimental data, and the development of diversified connections between the topics discussed in class.

Communication skills
The understanding of how to present new knowledge, obtained by controlled experiments, will be pursued, by the discussion of original papers, by attending research seminars, and by the presentation and discussion of scientific papers by the students.

Learning skills
Learning will be by direct study and analysis of research results, rather than via textbooks.

Contents

The course will present, through the illustration and analysis of scientific papers, genetic problems related to:

- Transcriptional control in eukaryotic cells;
- Vertebrate embryonic development (hematopoietic system; muscle; nervous system; pluripotent cells of the early embryo);
- Targeted modification of the genome, and its use in mouse genetic models.

Detailed program

A genetic point of view on the regulation of embryonic development and tissue-specific differentiation in vertebrates.

1) Targeted mutations in the mouse genome for the study of gene function.
Transgenesis; gene targeting in embryonic stem cells; in vitro differentiation of stem cells; CRISPR/Cas-based approaches.

2A) Hematopoietic system and its embryogenesis.
Mutants in genes encoding transcription factors and study of their roles in: tissue-specific differentiation programs (e.g. erythroid); cell fate choice and its mechanisms (e.g. granulocyte vs. macrophage); lymphoid destiny by restriction of alternative choices; origin and maintenance of hematopoietic stem cells.

2B) Skeletal muscle and myogenesis.
A “master gene” can activate the whole muscle differentiation program: myoD and myogenic genes. Mouse mutants in myogenic factors; action of genes in muscle differentiation (determination, migration, myogenesis); hyerarchies of regulatory genes; redundancy. Genes controlling muscle stem cells and satellite cells.

2C) Nervous system and its embryogenesis
Neural stem cells, proliferation and neuronal/glial differentiation. Regionalization of the neural tube. Genetic mechanisms in the region-specific differentiation of neurons. The spinal cord example: gradients of signaling molecules and activation of combinations of transcription factors. Genetic mechanisms in the specification of functional areas of the cerebral cortex. Genetic specification of positional identity: homeotic mutants. Genetic control of axon outgrowth and neuronal connectivity development.

2D) Pluripotent cells of the early embryo
Identification of genes that control pluripotency (ability to generate all the cell types of the embryo), and their mechanisms of action. Pluripotency factors and reprogramming of differentiated cells to induced pluripotent (iPS) stem cells.

3) Molecular genetic mechanisms of transcriptional control in eukaryotic cells
Differential gene expression in embryonic development and cell differentiation: methods of study. Levels of regulation of gene expression. Identification and study of transcriptional regulatory sequences: methods and examples (interactions between regulatory proteins and DNA; functional genomics approaches, ENCODE project; functional assays in transgenic animals). Combination of binding sites for transcription factors in programming gene expression in development and differentiation: examples from the regulation of eye development genes in different species. Histone modifications and interactions with transcription factors. Enhancers and insulators.
The different levels of gene regulation in action: the globin genes. Thalassemias caused by deletions and long-range-acting regulatory elements: the “locus control region” and its mechanism of action. 3-D spatial organization and nuclear compartimentalization in gene regulation: “active chromatin hubs” and “transcription factories”. Intergenic transcripts and long noncoding RNAs.
Allosteric modifications in transcription factor function: examples from gene regulation in pituitary development.

Prerequisites

A solid background in general genetics, cellular and molecular biology.

Teaching form

Lessons in class

Textbook and teaching resource

Scientific papers illustrated during the course.
Scott Gilbert, Developmental Biology, Sinauer (the most recent edition available)
Tom Strachan, Andrew Read, Human Molecular Genetics (the most recent edition available)

The transparencies shown during classes are available via elearning.

Semester

First semester

Assessment method

The evaluation will be via an oral examimation, starting with the presentation and discussion of a research paper chosen by the student (among a choice supplied in advance by the teacher), followed by a question on a different aspect of the course, and relative discussion.

Office hours

Meetings can be arranged via email (silvia.nicolis@unimib.it) or personally during class hours