COURSE SYLLABUS

Genetica dello Sviluppo e del Differenziamento

1718-1-F0601Q076

Aims

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. 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.

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

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.

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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 through the teacher. We will try to make them available also via elearning (overcoming present technical problems).

Semester

First year, first semester

Assessment method

Oral exam; in 30-40 minutes, the student will be asked in general 3 questions, pertinent to different subjects of the course, to ascertain the knowledge of basic information, the familiarity with the experimental approaches and the understanding of the experiments involved in acquiring the described knowledge.
Office hours

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