Advanced Molecular Biology

2017 - 2018

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Advanced Molecular Biology

2017 - 2018

Stint 1 – March 7 – March 22:	M De Bortoli
Stint 2 – March 26 – April 13:	V Perissi
Stint 3 – April 16 – May 4:	M De Bortoli
Stint 4 – May 7 - May 31:	S Cutrupi

Michele De Bortoli

Full Professor, Molecular Biology (BIO/11)

1980-83 Post-Doc – RBM Institute Biomedical Research (Ivrea)

1983-85 Visiting Associate, National Cancer Institute, Bethesda, USA

1986-90 Research Assistant – Biochemistry – UniTo

1991 Visiting Scientist. Friedrich Miescher Institute, Basel, Switzerland

1992-97 Research Assistant – Molecular Biology, UniTo

1998-06 Associate Professor, Inst. Cancer Research & Treatment, Candiolo

1999 Visiting Scientist, UCSD – Rosenfeld Lab, La Jolla, USA

2007- Director, Center for Molecular Systems Biology, Unito

2010- Full Professor UniTo, Dept. Clinical & Biological Sciences @ San Luigi Hospital

2016- Coordinator, PhD programme in Complex Systems for Life Sciences

Research

- Steroid hormone receptors and cAMP-binding proteins as prognostic marker for Breast Cancer
- Ras and ERBB2/HER2 oncogenes drive BC development and progression in combination with estrogen
- Tyrosine kinase receptor expression is finely regulated by estrogen in BC
- Gene expression profiling in breast cancer
- Estrogen and antiestrogen effects on gene expression in breast cancer
- Gene signatures as predictive markers in BC
- Estrogen Receptor controls a network of coding and noncoding genes through an extensive cistrome.
- Genomic action of unliganded Estrogen Receptor alpha
- Estrogen Receptor acts through long noncoding RNAs and circRNAs

CMB Master - AMB

Advanced Molecular Biology

The main focus of this course is **regulatory genomics**

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- The functional organization of Genomes
- Regulatory mechanisms and motifs
- Regulatory networks
- Genome regulation and Human diseases

Course Structure

ca. 14 hours lectures (MDB)

Ca. 24 hours lectures (VP)

(2 x 4 hrs hands-on databases & browsers)

ca. 10 hours reports (MDB)

ca. 20 hours lectures (SC)

Course objectives

Students will acquire an advanced level of knowledge on the activity of genes and genomes and the mechanisms of genome regulation at the transcriptional and post-transcriptional level, in the contexts of development, differentiation, cellular homeostasis and cancer.

In the **first part** of the course Students will understand how the modern global methods (microarrays, Next Generation Sequencing, epigenomics, protein-DNA, protein-RNA, proteomics), make it possible to represent the organization and control of most evolved genomes.

In the **second part** of the course, Students will acquire the ability to use their theoretical knowledge in solving applicative problems, with special regard to biomedical issues, through the study of literature. In particular, Students will learn how to associate the genomic variants and dysfunction with possible regulatory events and with disease states.

Specific objectives are:

- To make the point on how Molecular Biology has evolved since the end of the Human Genome Project and the advent of high throughput genome sequencing technologies
- To discuss advancements in regulatory Biology thanks to Genomics, with specific regard on the regulation of gene expression and gene interaction at the network level
- To introduce Students to understand Molecular Biology at the systems level
- To guide Students to the reading and interpretation of research articles in the field of regulatory molecular biology
- To make Students understanding the applications of genomics in the fields of medicine and neurobiology.

Expected outcomes

Knowledge

- the most common analytical methods in Genomics and transcriptomics, comprising the fundamentals of bioinformatics analysis of results
- the most important modalities of transcriptional regulation in higher Eukaryotes.
- the mechanisms of alternative RNA transcript generation, including non-coding RNAs and associated functions.
- the constitutive principles of gene regulatory networks
- the involvement and dysfunction of components of these networks in human disease

Expected outcomes

Ability

- to do literature searches on the course topics
- to search for information and expose a summary of the main methods of genomics and functional genomics
- to analyze, interpret and report publicly on a recent scientific article, including the methodology used, concerning one of the course topics
- to interpret results and diagrams relating to the main issues discussed
- to expose briefly one of the topics of the course, with specific reference to genomics and methodology

Expected outcomes

Understanding

- how a systems molecular biology study is planned and conducted; how results are presented and discussed in a primary scientific journal; and finally how results must be evaluated in the framework of current knowledge.
- which methodological approach (among those studied) should be used to answer a specific scientific question.
- what information can be obtained from genomic analysis to understand the molecular mechanisms associated with diseases;
- how to use this knowledge to develop a potential therapeutic strategy

EXAM

Students are expected to show:

1. Knowledge of **basic** concepts
2. Understanding of **specific** concepts
3. Comprehension of experimental **methodology**

<u>Evaluation</u> steps:

Within the course:

1) Students' activity on the Moodle website is monitored
2) Selecting, analysing and reporting to the class a scientific paper on specific themes is evaluated

33/30

After the course:

1) Moodle test with scoring and open questions — 33/30
2) Oral discussion on course subjects — 33/30

average

Due to the structure of proficiency evaluation,

Students are strongly encuraged to follow the activities step-by-step, doing all complementary activities on Moodle, and

→ Sustaining the EXAM in the first sessions (summer).

In the international contexts, repetitive and delayed exam sessions - as we use in Italy -

is **an absolute anomaly**

First part

There will be 5 Chapters

For each Chapter, one Review and one Scientific Paper is assigned **in advance**

Students should read the material before the lectures, since this will enormously help their understanding

Lecture workflow:

- Discussion of the assigned paper
- refreshing basic knowledge (first level)
- Concepts, questions , experimental approach and conclusions (slides)
- Other scientific papers contributing knowledge to the subject

What you will find on the **Moodle** website:

1. Lecture PDFs: the slides we used during the class
2. Textbook: *reviews* that you will use for studying the subjects
3. Research Papers: articles that we will analyze in detail
4. Bibliography: scientific literature concerning the subject
5. Exercises & tasks: utilities to help comprehension
6. Background help: materials for those of you who do not have sufficient basic knowledge

http://cmb.i-learn.unito.it/course/view.php?id=124

Lecture PDFs

Slides used during class hours

are **NOT** a textbook !!!

Students should NOT limit their study to reiterated contemplation of teachers' PDFs !!

Textbook

One ore more Reviews that Students should read carefully, since they contain most of the essential knowledge on the specific subject.

If anyone has difficulty in deciphering terms, there are good friends online: first, NCBI-EMBL; second, Wikipedia is OK for Molecular Biology, 99% guaranteed. Do not leave words floating empty !!!

Another excellent solution is to use Moodle Forum to post your question and obtain help from other Students.

Research papers

These are original scientific articles that Students **should read and study very carefully**: they are paradigmatic in this field and teach us methodology, background and new conclusion

Analysis of results and methodology of these papers will be part of the final exam.

(Again, you may use Wikipedia and Students' Forum for help).

Bibliography

This is the collection of articles that your Profs have read to set up the lectures.

These articles are available if, for any reason, Students need or wish to access to the original information.

Tasks & exercises (called Activities)

These are Moodle activities intended to **help** comprehension of different subjects.

There will be also Technical Forums, Wiki based, where groups of Students will build up description pages on specific technical aspects.

Students' participation in Moodle activities will be evaluated.

Exercises and tasks on the Moodle site are part of your work !

Do it as soon as possible → acquire important knowledge →

→ improved comprehension at next classes →

→ everything will be easier !!!

Background Help

This is a tutorial activity.

Students participating in this course have different backgrounds and also they have taken different courses during the first semester

We will assess the major background weakness and set up Tutorial help to recover missing information

Small green spots like the following may appear in the slides:

Mechanisms of DNA Replication

These refer to basic knowledge revision at **your charge**

Important.

Reading of the assigned Research Papers should **precede** discussion in the classroom

Papers will be made available one week before the cognate lecture

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Advanced Molecular Biology

Introduction

Genomes are extraordinarily complex

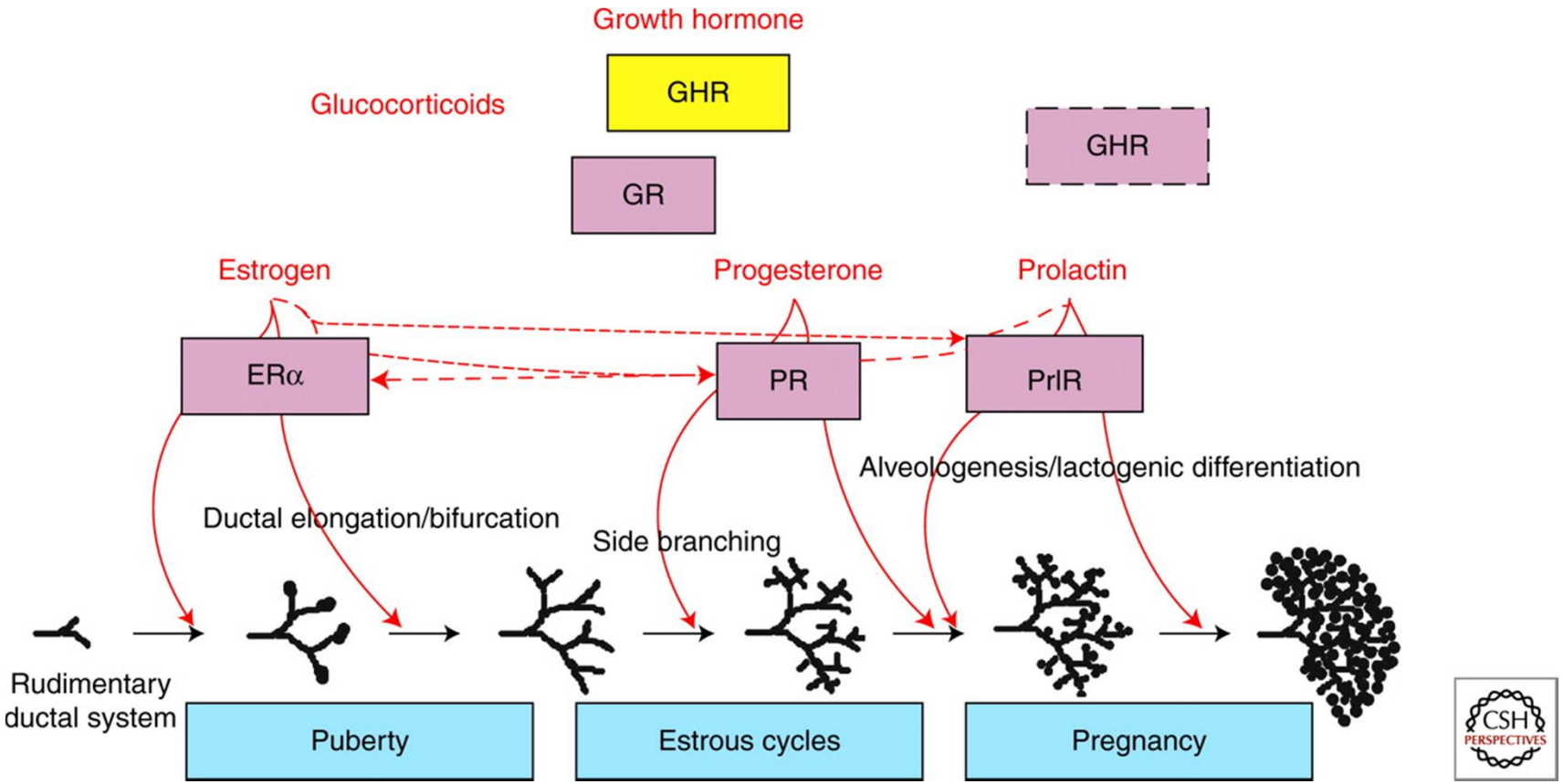
- Large number of protein-encoding genes
- Large number of non-protein coding genes
- Wide intergenic spaces
- Repetitive and transposable elements

Genomes contain information for all the functions needed by an organism

- Cell division and Development
- Cellular differentiation, tissues orgaization
- Cell-to-cell communication
- Response to stimuli
- Response to environment
- Death
- …


HHMI

Control of mammary gland development by hormones.



Cathrin Brisken, and Bert O'Malley Cold Spring Harb Perspect Biol 2010;2:a003178

Cells activate timely specific **genetic programs** to give diversified functions.

A genetic program is the sum of gene products necessary to perform a function

We say «**gene expression**» to indicate the fact that the cell contains a functional product encoded by a gene:

- transcription → RNA
- processing and localization
- (translation and post-translation if protein)

The expression of genes is carefully controlled (gene regulation)

In Humans, we know more than 2,500 proteins employed to control gene expression only concerning the level of gene transcription. 10% of our Genome is dedicated to this activity.

The genome **Regulatory Network** is very complex. It is devised to fullfill a number of requirements:

- Which genes ?
- When ?
- How much ?
- For how long ?

How does the Regulatory Network «sense» the needs ?

Remeber:

Read: Textboox G – Levine's review

+

Moodle - Activity 1