UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

COURSE SYLLABUS

Protein Biochemistry

2223-1-F0601Q060

Aims

This course aims to deepen concepts related to the relationships between the structure and function of proteins within a pathway that, starting from physiological and evolutionary aspects, considers pathological implications of certain dysfunctions and projects towards the biotechnological application of certain natural phenomena. Some biophysical and biochemical techniques suitable for studying the structure, function and modification of individual proteins or biochemical circuits will be described. By emphasising the need for a multidisciplinary approach, the course aims to offer not only cognitive but also methodological tools useful for the study, control and biotechnological exploitation of complex biological phenomena involving proteins. The general objectives are as follows:

Knowledge and understanding
By the end of the course, students will have acquired knowledge about the mechanisms of protein folding, the relevance of structural flexibility and functional promiscuity, conformational and functional transitions, natural evolution and *directed-evolution* of proteins, conformational transitions often associated with the establishment of protein-protein interactions, under both physiological and pathological conditions. Students will acquire knowledge of some techniques for structural and functional studies of some classes of proteins.

Ability to apply knowledge and understanding
The examples illustrated during the lectures bring out the main mechanisms of (mal)functioning of proteins, associated with their structural peculiarities and interaction with the environment. It is expected that they can be recognised in contexts other than those exemplified and are potentially applied, for example, to design new 'synthetic' proteins. It is expected that students learn to recognise the various contexts in which the techniques outlined in the course are profitably applicable.

Autonomy of judgment
Students will be stimulated to recognise the relationships between protein structure and function and to predict the effects of certain environmental contexts on both these aspects.
Students will be encouraged to personally identify the wealth of connections between the disciplinary content and the thematic blocks into which this teaching is divided. The identification of complex biological problems and the

development of original solutions increasingly requires the use of knowledge from different and complementary disciplinary fields - from cell biology to chemistry to physics. Grasping relationships between different phenomena (e.g. molecular and biophysical) and exploiting the complementarity of different investigative techniques creates the prerequisites for proposing new visions, developing a critical sense and offering new solutions.

Communication skills
By the end of the course, students will have acquired the appropriate vocabulary and language skills to describe the biochemical and molecular phenomena covered in the course and of interest to this subject area.

Learning skills
Students will be able to deal with teaching in the field of *Protein science*, functional and structural studies of proteins and, more generally, to understand the scientific literature in these subject areas.

Contents

1. Structure of proteins and methods for their study.

2. *In-vitro* and *in-vivo* studies on protein folding.

3. Protein-protein interactions; separation and phase transition of biomolecules.

4. Mechanisms of protein turnover.

5. Principles of natural and biotechnological evolution of proteins.

Detailed program

1. Structure of proteins and methods for their study.
Structural order and disorder; Structural elements and motifs;
Methods for the structural study of proteins: X-ray crystallography, Electro-cryo microscopy, NMR spectroscopy
How to meeasure protein similarity;
Similarity and divergence in protein structure analysed through case studies.

2. *In-vitro* and *in-vivo* studies on protein folding
Thermodynamic and kinetic aspects of protein folding;
Protein folding theories;
Protein folding *in vivo*;
Importance of translation events on protein folding (codon bias and translation rate);
Biotechnological implications of translation rate control.

3. Protein-protein interactions; separation and phase transition of biomolecules
Methods for studying protein-protein interactions (microcalorimetry; surface plasmon resonance);
Chemical-physical phenomena underlying molecular condensates;
Examples of biological relevance of bio-molecular condensates;
From liquid condensates to solid aggregates: physiological and pathological aspects of phase transition;
Types of protein aggregates;
Amyloid fibrils and prion proteins. Hallmarks of amyloid aggregation;
From propagation mechanisms to diagnostic devices of amyloid pathologies.

4. Mechanisms of protein turnover
Overview of cellular mechanisms of protein turnover;
Protein degradation by the ubiquitin-proteasome system (UPS);
Pharmacological potential of natural UPS mechanisms and dual target degrader drugs. Case studies.

5. Principles of natural and biotechnological evolution of proteins
General concepts of natural evolution and evolvability from the perspective of biotechnological protein design;
Protein evolution rate and fitness landscape;
Role of phenotypic variation and neutral drift in protein evolution;
Various protein engineering approaches and techniques of protein directed evolution.
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Prerequisites

Prerequisiti: Basic knowledge in the fields of Biochemistry and Cellular biology.

Teaching form

Classroom lectures supported by PowerPoint slides, videos, discussions of scientific papers.

Textbook and teaching resource

PPT slides and videos published on the Moodle website (http://elearning.unimib.it/).

Articles referred/described in the lessons

Semester

First semester

Assessment method

Oral examination: this consists of an interview lasting approx. 30 minutes, with questions on the content of the lectures (from at least two thematic blocks) and the related scientific articles (pointed out during the lectures and available on the website). The degree of comprehension of the topics covered, the ability to understand the difficulties and technical-scientific solutions for the study of structural/functional aspects, the ability to identify connections between thematic blocks and individual topics covered, as well as the acquisition of language property and clarity of exposition will be assessed.

Office hours

On demand, by mail to stefania.brocca@unimib.it

Sustainable Development Goals

QUALITY EDUCATION