UNIVERSITÀ
DEGLI STUDI DI MILANO-BICOCCA

# COURSE SYLLABUS

# Advanced Cellular Models in Pre-Clinical Research and Personalized Medicine

**2526-1-F0803Q082**

## Aims

This course addresses the challenges of (re)constructing multicellular systems that can reproduce various aspects of tissue heterogeneity and variability. Understanding these complexities requires a multidisciplinary approach, integrating techniques from biochemistry, cell biology, and molecular biology with advanced methodologies such as microfluidics, microscopy, image analysis, and spatially resolved omics.

Such an approach enables integrated studies of fundamental biological processes, providing tools not only for generating and structuring knowledge but also for developing in vitro replicas of tissue and organ portions from individual patients, with the goal of identifying personalized pharmacological treatments.

Learning Outcomes

1. Knowledge and understanding: by the end of the course, students will learn and understand the potential of various advanced cellular models in both basic and pre-clinical research, as well as in diagnostic and therapeutic applications, with a particular focus on precision medicine.

2. Knowledge application: students will be able to apply the knowledge acquired (as described in point 1) to scientific, methodological, and practical problems beyond those explicitly covered during the course.

3. Critical thinking and problem solving: students will be capable of reworking the principles and methodologies learned, enabling them to independently consult scientific literature to keep their expertise up to date and to identify the most relevant fields of application. The development of these skills will be possible thanks to the analysis of scientific articles that will be conducted interactively in the classroom and thanks to journal clubs in which the students themselves will have to analyze in detail a scientific article provided by the teachers.

4. Communication skills: at the end of the course, students will be able to communicate the topics covered with appropriate terminology and confidence, both in Italian (for native speakers) and in English (for all

students).

5. Learning Skills: students will be able to analyze, apply, integrate, and connect the knowledge acquired, along with that gained from literature review and related courses, to solve scientific problems in both basic and applied biochemistry.

## Contents

Preclinical studies of multifactorial diseases such as cancer and neurodegenerative disorders require increasingly complex cellular models capable of more effectively recapitulating the characteristics of the pathology under investigation compared to conventional two-dimensional cell cultures.
The course will describe and compare the formation methods of various models and the main analytical technologies, with particular focus on techniques that allow for the analysis of properties related to the nature and spatial positioning of cells, using advanced imaging methods and single-cell and spatial omics technologies. Finally, the potential role of some of these cellular models in personalized medicine will be discussed. Most of the topics will be addressed through a multidisciplinary analysis of specific case studies.

## Detailed program

1. Spheroids: three-dimensional cellular aggregates derived from a single cell type (homotypic) or from two or more different cell types (heterotypic).
   Organoids: Structures derived from one or a few cells of a tissue, embryonic stem cells, or induced pluripotent stem cells, capable of self-organizing in three-dimensional cultures thanks to their self-renewal and differentiation capacities.

2. Organ-on-chip: systems containing engineered or natural miniature tissues grown within microfluidic chips. To better mimic human physiology, these chips are designed to control cellular microenvironments and maintain specific tissue functions

3. Patient-Derived Xenografts (PDX): tumor models in which tissue or cells from a patient’s tumor are implanted into an immunodeficient or humanized mouse to reconstruct an environment that supports natural tumor growth, monitoring, and evaluation of patient-specific treatment responses.

4. Analytical technologies, including quantitative approaches: imaging, morphometric analysis, autofluorescence, Seahorse assays, and specific fluorescent probes.

## Prerequisites

Prerequisites: none. However, the course builds upon concepts and methodologies covered in introductory courses in Biochemistry and Molecular Biology. In particular, it is useful a basic understanding of fundamental aspects of cellular biochemistry in complex eukaryotes, including metabolism, signal transduction, the cell cycle, and cell death. Basic knowledge of statistics is also appreciated.

## Teaching form

The course consists of 14 lectures of 2 hours each, including:

8–10 lectures in a traditional format (content-delivery teaching, Didattica Erogativa, DE), focused on the presentation and explanation of scientific concepts, content, and principles;
4–6 interactive lectures (Didattica Interattiva, DI), which involve:
Interactive discussion of scientific articles led by the students;
Student presentations of scientific papers in formats similar to scientific conference data presentations (oral presentations or posters, i.e., Journal Club or Poster sessions).
The exact distribution between DE and DI will also depend on the number of students enrolled in the course.

In addition, the course includes 20 hours of laboratory activities focused on the preparation and biochemical and image-based analysis of advanced cellular models—particularly homotypic and heterotypic spheroids, both with and without matrix support—and their morphometric and biochemical characterization.

All activities are conducted in person.

The course is taught in Italian, but can be switched to English upon request by international students.

## Textbook and teaching resource

Specialized articles, review papers, and/or book chapters will be recommended during the course.
Specific experimental protocols for the practicals will be provided.
Video recordings of classroom lectures will also be made available to students.

## Semester

First semester

## Assessment method

There are no midterm assignments.

The final examination is oral and will assess the acquisition of core concepts related to the development and use of advanced cellular models and their applications, including the in-depth discussion of specific scientific articles previously agreed upon with the students.

The exam consists of three parts:

- Assessment of knowledge acquired on advanced cellular models.
- Assessment of knowledge regarding analytical methodologies.
- Evaluation of laboratory skills and the quality of the written laboratory report.

The final grade will reflect performance across all of the above components.

## Office hours

By appointment via email

## Sustainable Development Goals

GOOD HEALTH AND WELL-BEING | QUALITY EDUCATION