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*TM22_DIP_FAR*

# *Teach Mob – Visiting Professors*
# *Academic year 2015/2016*

| **2nd term** |
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| **COURSE TITLE**<br>**Protein Crystallography and Drug Discovery** |
| **Scientific area**<br>**Medicinal Chemistry** |
| **Department of Medicine Science and Technology** |
| **Language used to teach**<br>**ENGLISH** |
| **Course summary**<br>BASIC PRINCIPLES AND METHODS OF PROTEIN CRYSTALLOGRAPHY<br>Protein structure and function, including aspects of structural bio-IT.<br>Basic principles of protein structure such as secondary structure elements, domains and folds, databases. Relationships between protein amino acid sequence and the three-dimensional structure.<br>Homology modelling. Basics of protein crystallization and protein crystallography. Descriptions of protein crystals. Crystallization methods and technologies. Crystallization of protein–ligand complexes. Data collection. From diffraction intensities to a molecular structure. The diffraction of X-rays by crystals. The phase problem. Model building and refinement. Most used types of electron-density maps. Use of PDB and CCDB data bank. Information content and limitations of crystal structures.<br>PRACTICAL APPLICATIONS Target identification, selection and validation. Hit/lead generation. Structure-based drug design (SBDD). Structure-based virtual screening approaches. Fragment-based screening. Lead optimization. |
| **Learning objectives**<br>The aim of this course is to provide an outline of the basic principles and methods of protein crystallography, learning how crystallographic data can contribute today to the different phases of pharmaceutical research. The objective of this course is to show how the different stages of drug discovery research can benefit from the already available structural knowledge; to point out how experimental structure determination by X-ray analysis can be integrated into the hit/lead finding, triaging, validation and optimization phases inside Structure-based drug design (SBDD). It will emphasize the strengths, usefulness and application of protein crystallography, so that any medicinal chemist engaging in a new research program and having access to a structural biology group, can gauge if, and how, his project could potentially benefit from this technology. Medicinal chemists, in particular those working in the industry, have access to large, public as well as proprietary, depositories of refined crystal structures. To make proper use of these data, it is essential for them to be well aware of the limitations and potential uncertainties associated with X-ray |
| **Tutorship activities**<br>2-3 Students attending the lab work to prepare their experimental thesis as well as 3 PhD students should be tutored by the visiting professor. The aim of their research is to generate a structure-based pharmacophore model of human as well as plasmodium falciparum DHODH to identify structurally diverse lead hits. The skills of the visiting professors will be critical to identify hits that might be the starting point for developing novel and potent inhibitors selective for human or for Plasmodium Falciparum DHODH enzyme respectively. |

**Other activities besides the course: i.e. seminars and conferences addressed to PhD students and research fellows, dissemination conferences**

Visiting professor will give seminars and conferences addressed to the students of the PhD course in Pharmaceutical and Biomolecular Sciences, as well as to research fellows of the Department of Chemistry and Pharmaceutical Technology of the Turin University.

**Visiting Professor Profile**

The visiting professor should have a long research experience in the field of structural biology, bioinformatics protein crystallography as well as in Drug Discovery. Primary methodological focus on structural biology using biophysical methods like X-ray crystallography, single particle electron microscopy and small-angle scattering of X-rays (SAXS). Due to the intermediate level of the background of the students (3rd year of a five-year course), visiting professor should combine the rigorous presentation of the topics with the ability to give the basic information, when required. In tutoring undergraduate and PhD students to generate structure-based pharmacophore models an expertise in Structure-based drug design, Structure-based virtual screening approaches, Fragment-based screening, Lead optimization will be highly appreciated.

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