| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **5CI407** | **Molecules, Metal Ions and Metal Complexes in Biology and Medicine**<br>Inorganic Medicinal Chemistry, Chemical Biology, Fluorescent Probes, Photodynamic Therapy, Bioorganometallic Chemistry, Metalloproteins, Metallomics, Dioxygen Activation, Bio-orthogonal Chemistry, Chemistry in Cell | | | | | | | | |
| Responsable | Gilles Gasser, Group Leader, Laboratory for Inorganic Chemical Biology, Chimie ParisTech, PSL Research University | | | | | | | | |
| *ECTS* | *Cours (h)* | *TD (h)* | *TP (h)* | *Tutorat (h)* | *Ecrit (%)* | *CC (%)* | *TP (%)* | *Oral (%)* | *Eval. répartie* |
| 6 | 48 | | | 12 | 75 | | | 25 | non |

*Descriptif de l'UE*

Living beings are chemical systems. As such, they are prone to interactions and reactions with chemical actors such as organic molecules and metal-containing species. Both these species are endogenously used with mechanisms important to decipher. Specific chemical systems can also be designed to study living matter and to rescue physiologically healthy states of living beings. These features have found extensive applications in biology and in medicine. The purpose of this series of courses is precisely to provide an overview on this modern and fast developing area in which chemists presently play a key role.

*Objectifs d'apprentissage*

Outline and explain the specific use and reactivity of metal ions in a complex biological environment
Outline the mechanisms of metalloproteins and define the design of artificial metalloenzymes
Describe the mechanism of action of important metal-based drugs
Predict potential targets of a random metal-based drug candidate
Design a probe reporting on a molecule or on the physicochemical properties of a complex medium
Critically present a research article from the literature during an oral presentation
Based on literature, propose a molecular design fulfilling a function upon obeying constraints

*Prérequis*

The students following this course are expected to have solid knowledge in both organic, inorganic and general chemistry with insights in photochemistry. It is expected that they have some basic knowledge in biology and biochemistry.

| *Langue*(1) | *Cours, TD, TP* | *Documents* | *Bibliographie* |
|---|---|---|---|
| | English | English | English |

(1) D'une manière générale, les documents de cours sont à rédiger en anglais. Les sujets d'examen sont en anglais ou accompagnés d'une explication en anglais s'il y a des étudiants non francophones.

## *Fonctionnement de l'UE*

Living beings are chemical systems. As such, they are prone to interactions and reactions with chemical actors such as organic molecules and metal-containing species. Both these species are endogenously used with mechanisms important to decipher. Specific chemical systems can also be designed to study living matter and to rescue physiologically healthy states of living beings. These features have found extensive applications in biology and in medicine. The purpose of this series of courses is precisely to provide an overview on this modern and fast developing area in which chemists presently play a key role.

Firstly, we intend to illustrate that metal-containing species play a great role in biology. Indeed nature uses metal ions to accomplish essential biological functions. Due to their different kinetic, geometric and electronic properties, metal complexes can undergo reactions which are not possible with organic agents, providing nature with a wider chemical repertoire. We therefore intend to describe a variety of endogenous metallobiomolecules and metalloproteins and detail their mechanism at the molecular level. As we will show, metal ions play a crucial role in dioxygen

metabolism and the course will have a special focus on dioxygen activation and protection against harmfull species derived from $O_2$. In parallel, we will show how chemists mimic metalloproteins' structure and function and how artificial metalloproteins can be designed to accomplish abiotic functions. Moreover, we will also show how specially designed metal catalysts can now be used to carry out reactions in living environments with selected applications in labelling and medicinal chemistry. In addition, metal-containing species have a great potential as therapeutic agents. With the exception of cisplatin and its derivatives, metal-containing drugs, particularly organometallics, have been, until very recently, largely neglected by both the pharmaceutical industry and academia. Over the last few years, however, things have changed, and significantly! Indeed, "inorganic drug candidates" are beginning to enter clinical trials, with more promising lead structures in the pipeline. We will point out the latest advances in the field of medicinal inorganic chemistry with an emphasis on the discovery of new inorganic compounds with proven anti-cancer activity, enzyme inhibition or anti-malarial properties. Moreover, the specific mechanism of action of the metal-based drugs will be presented in detail.
We will show how chemicals can be used to interrogate living cells and acquire a rich body of information by exploring the concept of molecular probe. The chemists have developed numerous tags and techniques to evidence and quantify molecular components, to image their location and their motion, to control their release or action, etc... More generally, there is a great interest to probe physicochemical properties of complex media such as pH, redox potential, temperature, viscosity, etc... and molecular probes are often at the forefront to obtain this information as it will be illustrated in this course.