CH-415

Chemistry of small biological molecules

Goun Elena

Cursus	Sem.	Type
Chimiste	MA1, MA3	Opt.

Language of teaching	English
Credits	2
Session	Winter
Semester	Fall
Exam	Written
Workload	60h
Weeks	14
Hours	**2 weekly**
Courses	2 weekly
Number of positions	

Summary

The main goal of the course is to provide students with relevant background on available chemical tools (predominantly small molecules) that are used to solve important problems in biology and medicine.

Content

1. Short overview: Chemical synthesis of biological molecules such as proteins, DNA, RNA, peptides, lipids, carbohydrates, and antibodies.
2. Methods to chemically modify, recognize, and modulate proteins, DNA, RNA, peptides, lipids, carbohydrates, and antibodies with small molecules.
2.1 Protein modification methods:
- modifications of N- and C-terminus
- cysteine and lysine modification methods
- tyrosine and tryptophan modifications
2.2 Native chemical ligation reactions:
- ligation of two peptides
- protein trans-splicing
- expressed protein ligation
2.3 Bioorthogonal Chemistry based on unique amino acid sequences
- bisboronic fluorogenic acid reagents
- enzyme modifications of peptide tags
- using transition metals to detect peptide tags through chelation
2.4 Studies of biomolecules that are not genetically encoded (glycans, lipids, metabolites)
- requirements for bioorthogonal reactions
- condensation methods of amine nucleophiles with ketones and aldehydes
- Staudinger ligation of triarylphosphines and azides
- the [3+2] cycloaddition of alkynes and azides
- bioorthogonal ligation with alkenes
2.5 Bioorthogonal group incorporation into various biomolecules
- proteins: labeling via residue specific modification, site-specific modifications (genetic method), combination of bioorthogonal chemical reporter strategy and activity based protein profiling.
2.6 Labeling of and imaging glycans
2.7 Labeling of and imaging of lipids
2.8 Labeling of and imaging of nucleic acids
2.9 Labeling and detection of other small metabolites
3. Basic principles of successful probe design
- solubility, pharmacokinetics, brightness, photo-stability
4. Optical in vitro and in vivo imaging and its applications to study molecular signatures of targeted tissues. Bioluminescent and fluorescent imaging.
5. Applications of PET and MIR imaging as a new tool to visualize biological processes of medicinal significance.
6. Other imaging modalities and their applications in medicine and biology - optoacoustic, ultrasound, DNP.
7. Case studies: successful applications of chemical biology approaches in the area of oligonucleotide therapeutics, synthetic vaccines, DNA-encoded libraries, and antibody drug conjugates, proteomics, stem cells and regenerative

medicine.

Assessment methods

Written exam

Resources

Websites

- http://scgc.epfl.ch/telechargement_cours_chimie