DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

AVVISO DI SEMINARIO

Il giorno venerdì **6 marzo 2020**
alle ore **14:30**
presso l'Aula A, Ex Farmacologia, via Irnerio 48, Bologna

Dott.ssa Isabelle Michaud-Soret, Ph.D.

Research director at the CNRS; Head of the "Biology of Metals" (BioMet) group in the Laboratory of Chemistry and Biology of Metals in Grenoble, France

(ospite Prof. Ciurli)

terrà un seminario dal titolo:

FUR METALLOREGULATOR, THE STORY OF AN IRON RESPONDING TRANSCRIPTION FACTOR

Colleghi e studenti sono cordialmente invitati

Commissione Ricerca e Attività Correlate - FaBiT

ABSTRACT

The ferric uptake regulators (Fur) are bacterial transcriptional regulators responding to iron ions. Fur proteins are found in all proteobacteria and Fur has a role of global regulator in many of them. It controls the transcription of a wide variety of genes involved in iron metabolism, in oxidative stress or in virulence factor synthesis. As a general view, Fur proteins were considered to be dimeric proteins both in solution and when bound to DNA. However, our recent data demonstrate that Fur proteins can be classified into two subfamilies, according to their quaternary structure (1,2) and structural analysis. E. coli and H. pylori Fur are part of the dimer family and the tetramer family contains P. aeruginosa and F. tularensis Fur, which are very stable tetramers in solution. A DNA driven tetramer-splitting mechanism leads to tetramer dissociation with the formation of two Fur dimer-DNA complexes (2). Structural, biophysical, biochemical and modelling studies of both tetrameric and dimeric Fur proteins have been performed and analyzed to decipher their common features, their differences and their interactions with specific and unspecific DNA.
Finally, the critical role of F. tularensis tetrameric Fur in bacterial virulence has been demonstrated. These proteins found only in bacteria and essential for some pathogens, are interesting targets for anti-virulence strategy. In this line, anti-Fur peptides were derived from the peptide aptamers inhibitors found earlier (combinatorial proteins screened from 20.106 molecules). A variety of shorter (6aa) and cyclic mutated peptides were synthesized and assayed on Fur proteins from several pathogens such as Y. pestis, F. tularensis, P. aeruginosa. Modeling studies together with inhibitor-protein interaction studies have been done.

1. Perard J., Coves J., Castellan M., Solard C., Savard M., R. Miras, S. Galop, L. Signor, S. Crouzy, I. Michaud-Soret* and E. de Rosny*, Biochemistry, 2016, 55, 1503-1515.
2. Nader S, Pérard J, Carpentier P, Arnaud L, Crouzy S*, Michaud-Soret I*. Biometals. 2019, 32(3):501-519.
3. Perard J., Nader S., Levert M., Arnaud L., Carpentier P., Siebert C., Blanquet F., Cavazza C., Renesto P., Schneider D., Maurin M., Coves J., Crouzy S.* and Michaud-Soret I.*, Communications biology (Nature group), 2018, 1, 93.
4. - Mathieu S, Cissé C, Vitale S, Ahmadova A, Degardin M, Pérard J, Colas P, Miras R, Boturyn D, Covès J, Crouzy S*, Michaud-Soret I.* ACS Chem Biol. 2016, 11(9):2519-28.

BIOGRAPHICAL SKETCH

Isabelle Michaud-Soret received a BS degree in Biochemistry and a PhD in molecular Pharmacology from the University Pierre and Marie Curie -Parix VI- in the Laboratory of Toxicological and Pharmaciological Chemistry and Biochemistry. Her PhD was devoted to mechanistic studies of non-heme iron enzymes, Lipoxygenases. After a post-doctoral position in the laboratory of Professor Que in the Department of chemistry (Minneapolis, USA), working on mechanistic and spectroscopic studies of non-heme metalloproteins She obtained a full time scientist position in Grenoble. She started there to work on binuclear manganese metalloproteins before focusing her research on metalloregulators such as the Ferric Uptake regulator (Fur) and NikR. She obtained her Habilitation to direct research and became a research director with the CNRS in 2004. Her main scientific interests focus on metalloregulatory proteins able to control gene expression in response to metal ions status in the cell, and the key actors of the metal homeostasis.
Since 2010, her research group is also investigating the mechanistic understanding of interferences between metallic nanoparticles and metal homeostasis.