DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

AVVISO DI SEMINARIO

il giorno **venerdì 21 Giugno 2019**
alle ore **14:30**
presso Aula A (Ex Farmacologia) via Irnerio 48, Bologna

il **Prof. Mauro Freccero, PhD**
Department of Chemistry, University of Pavia
(ospite Prof. Giovanni Capranico)

terrà un seminario dal titolo:

ENGINEERING ORGANIC LIGANDS FOR SENSING AND TARGETING OF G-QUARDRUPLEX NUCLEIC ACID STRUCTURES

Colleghi e studenti sono cordialmente invitati

Commissione Ricerca e Attività Correlate - FaBiT

ABSTRACT

DNA and/or RNA guanine-rich sequences can fold into four stranded G-quadruplex supramolecular structures (G4s). There are more than 7x105 putative G4s in the human genome, which are highly enriched in telomeres, gene promoters, RNA hexanucleotide repeats (G4C2)n related to amyotrophic lateral sclerosis (ALS), without mentioning those in viral and parasite genomes. G4 nucleic acids are the subject of widespread investigation as targets for small molecule intervention in biological studies. Several organic molecules acting as reversible ligands are capable to recognize and stabilize G4s. On the contrary, G4 targeting by reactive ligands has seldom been described, despite the potential applications in: (i) targeted anticancer and ALS therapies, (ii) selective tagging, (iii) G4 pull-down for extraction and purification and (iv) G4 degradation. Our group has engineered different classes of ligands with enhanced selectivity such as: naphthalene diimides, squaraines and polyheteroaryls. These small ligands have been conjugated to Peptide Nucleic Acids (PNAs), transient electrophiles (i.e. quinone methides and oxiranes), ROS (reactive oxygen species) catalysts, and RED-NIR fluorescent tags. Their synthesis, properties and reactivity toward G4s will be described.

Author's Key References

1. "Carbohydrate-naphthalene diimide conjugates as potential antiparasitic drugs: Synthesis, evaluation and structure-activity studies" Zuffo, M.; Stucchi, A.; Campos-Salinas, J.; Cabello-Donayre, M.; Martinez-Garcia, M.; Belmonte-Reche, E.; Perez-Victoria, J. M.; Mergny, J. L.; Freccero, M.; Morales, J. C.; Doria F. Eur. J. Med. Chem. 2019, 163, 54.
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3. "More is not always better: finding the right trade-off between affinity and selectivity of a G-quadruplex ligand". Zuffo M.; Guedin A.; Leriche E.-D.; Doria F.; Pirota V.; Gabelica V.; Mergny J.-L.; Freccero M. Nucleic Acids Res., 2018, 46, e115
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5. Doria, F.; Nadai, M.; Zuffo, M.; Perrone, R.; Freccero, M.; Richter, S. N. Chem. Comm. 2017, 53, 2268.
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7. Doria, F.; Oppi, A.; Manoli, F.; Botti, S.; Kandoth, N.; Grande, V.; Manet, I.; Freccero, M. Chem. Comm. 2015, 51, 9105.
8. Nadai, M.; Doria, F.; Germani, L.; Richter, S. N.; Freccero, M. Chem. Eur. J. 2015, 21, 2330.
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BIOGRAPHICAL SKETCH

Full Professor in Organic Chemistry. P.I. of an Organic Synthesis Unit at Pavia University, Italy, since 2002. Head of the Ph.D. School in Chemical and Pharmaceutical Sciences at Pavia University, since 2013. **Professional career**:

- 4-2016; present. Professor at Pavia University
- 10-2008; 2-2017. Adjunct Professor at Vita-Salute San Raffaele University
- 10-2002; 3-2016. Associate Professor at Pavia University.
- 9-1996; 9-2002. Assistant Professor at Pavia University.
- 1-1996; 9-1996. Post-doctorate at the Dept. of Organic Chemistry, Pavia University
- 8-1994; 12-1995. Post-doctorate at the Dept. of Chemistry, Dublin City University (DCU), Dublin (Ireland).
- Beginning of 1994. R&D Chemist, at ACS Dobfar S.p.A., fine chemicals, MI (Italy).
- 3-1993; 10-1993. Visiting Scientist, Dep. of Chemistry & Biochemistry, University of Maryland USA.
- 1990-1993. Ph.D in Chemistry, at the Dept. of Chemistry, Pavia University.
- 1990. Degree in Chemistry (110/110 cum laude) at the University of Pavia.

Prof. Freccero authored 114 publications, 108 in peer review international journals, 4 book chapters and 2 international patents [H-index 35, citations 3502, https://scholar.google.it/citations?user=hIzA26cAAAAJ&hl=it&oi=ao; H-index 33, citations 2920 (Web of Science); H-index 32, citations 3072 (Scopus)]. Freccero's research interest is focused on organic synthesis and binding properties of selective ligands, targeting G-quadruplex in human telomeres and oncogene promoters for theranostic applications (i.e.: targeted anticancer therapy, and fluorescence emission diagnostic). Currently, he is developing selective ligands targeting G-quadruplex in the HIV-1 genome as conceptually new antiviral drugs. In parallel, he is developing effective transient and activatable reactants [quinone metide and reactive oxygen species (ROS)] targeting DNA secondary structures. **Most important financed projects:**

1) 2007-2009. Project: AIRC IG2007-5049: "Novel irreversible protein kinase inhibitors targeting a conserved active site cysteine" Local Coordinator of the Organic Synthesis research unit (Funding: 20 K€)

2) 2009-2015. Project: FIRB-IDEA RBID082ATK 003: "New drug for anticancer targeted therapy" Unit coordinator: (Funding: € 480 K€).

2011-2013. Project: PRIN 2009MFRKZ8. "Selective Molecular Devices Targeting "GQuadruplexes" P.I. and National Coordinator. (Total funding € 250.6 K€; Funding to the PV unit: 88.4 K€).

3) 2013-2016. Project: AIRC IG2013-14708: "Photoactive molecules targeting telomeric Gquadruplex as multimodal agents in anticancer therapy" Project P.I. (Funding € 265 K€).

4) 2014-2019. Project within the 7th FRAMEWORK PROGRAMME, HIV LTR G-4 (Consolidator Grant, no: 615879): "G-quadruplexes in the HIV-1 genome: novel targets for the development of selective antiviral drugs". Second beneficiary of a "Two-beneficiary contract". (PV Funding: 659.6 K€).

Teaching experiences. Organic Chemistry III and Laboratory for chemists (an advanced course, since 2001). Organic Chemistry for Biotechnology (since 2001), both at Pavia University. Organic Chemistry for Biotecnology, and Chemistry for the International MD Program (in English) at UniSR (Università Vita-Salute San Raffaele), Milan, Italy, from 2008 to 2016.