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Conferencia:

Imaging quadruplex DNA with small molecules

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03/05/17

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Imaging quadruplex DNA with small molecules

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Abstract

With the mounting evidence that non-canonical DNA structures play key biological roles,[1] there is considerable interest in developing optical probes that can selectively detect and image specific DNA structures and topologies. In particular, over the past few years there has been increasing interest in studying guanine-quadruplex DNA. These quadruply-stranded nucleic acids have been proposed to play important biological roles as well as being potential targets for the development of anticancer drugs.[2]

This lecture will discuss the development of a series of organic and metal-organic probes that can be successfully used to target and image quadruplex DNA. Our initial studies centred around platinum-based probes that 'switch on' their emission upon interaction with DNA.[3,4] More recently we have developed a series of polyaromatic molecules which have the ability to discriminate between different DNA topologies by time resolved emission studies.[5] The ability of one of these optical probes to act as a live cell fluorescent probe has been explored by confocal microscopy and fluorescence lifetime imaging (FLIM). These studies have provided important insights into the presence of G-quadruplexes DNA in life cells and their targeting by small molecules.

References

[1]Regina Z. Cer, Kevin H. Bruce, Uma S. Mudunuri, Ming Yi, Natalia Volfovsky, Brian T. Luke, Albino Bacolla, Jack R. Collins, Robert M. Stephens, *Nucleic Acid Res*. **2011**, *39*, D383

[2]Balasubramanian, S.; Hurley, L. H.; Neidle, S. *Nat. Rev. Drug. Discov*., **2011**, *10*, 261

[3]K. Suntharalingam, A. Łęczkowska, M.A. Furrer, Y. Wu, M.K. Kuimova, B. Therrien, A.J.P. White, R. Vilar, *Chem. Eur. J.* **2012**, *18*, 16277

[4]N. H. Abd Karim, O. Mendoza, A. Shivalingam, A.J. Thompson, S. Ghosh, M.K. Kuimova and R. Vilar,
RSC Adv., **2014**, *4*, 3355

[5]Shivalingam, M. A. Izquierdo, A. Le Marois, A. Vyšniauskas, K. Suhling, M. K. Kuimova and R Vilar, *Nature Comm*. **2015**, 6, 8178

Curriculum Vitae — Prof. Ramón Vilar

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Employment history:

Since 08/2011:	*Professor in Medicinal Inorganic Chemistry*	Dep. of Chemistry, Imperial College, UK
10/2007 to 07/2011:	*Reader in Chemistry*	Dep. of Chemistry, Imperial College, UK
01/2006 to 09/2007:	*Senior Lecturer*	Dep. of Chemistry, Imperial College, UK
04/2004 to 12/2005:	*Group Leader*	Inst. of Chemical Research of Catalonia, Spain
10/2003 to 03/2004:	*Senior Lecturer*	Dep. of Chemistry, Imperial College, UK
04/1999 to 09/2003:	*Lecturer*	Dep. of Chemistry, Imperial College, UK
10/1996 to 03/1999:	*Temporary Lecturer*	Dep. of Chemistry, Imperial College, UK
09/1992 to 09/1993:	*Research Assistant*	Univ. Nacional Autónoma de Mexico, Mexico

Higher Education:

10/1993 to 10/1996:	Department of Chemistry, Imperial College PhD. in Chemistry. Supervisor: Prof. D.M.P. Mingos, FRS
09/1987 to 06/1992:	Universidad Nacional Autónoma de México (UNAM) MSci Chemistry – Final Grade: 99/100

Honours and Awards

- President's Award for Excellence in Teaching (2016)
- Imperial College Award for Excellence in Teaching (2010)
- EPSRC Leadership Fellowship (2009-2015)
- Gabino Barreda Medal (top student), UNAM (1992)

Teaching Activities:

- Head of Inorganic Teaching Section (09/2006-09/2009)
- Director of MRes in Bioimaging Sciences (09/2006-09/2015)
- Undergraduate courses taught over the past 5 years: Molecular Structure (UG-1), Bio-inorganic Chemistry (UG-3), Molecular Imaging (UG-4), Metals in Medicine (UG-4)"
- Current postgraduate teaching: Design of molecular probes
- Current supervision of research students: 4 Master's and 10 PhD students
- Number of PhD students graduated under Prof Vilar's supervision: 30

Academic Administrative Activities:

- Deputy Head of Chemistry Department (since 01/2015)
- Director of Research – Chemistry Department (since 01/2015)
- Head of the Chemical Biology research section – Imperial College London (08/2013-12/2015)
- Member of the Executive and Research Board Committees of the Institute of Chemical Biology – Imperial College London (since 10/2012)
- Member of the Research Committee of the Faculty of Natural Sciences (since 01/2015)

- Member of the Research Committee of the Institute of Molecular Sciences and Engineering, Imperial College London (since 10/2015)
- Member of Editorial Board of *Scientific Reports* (from Nature Publishing Group)
- Member of Editorial Board *of Journal of Chemical Biology*

Funding: Over the past 10 years, our research has been funded by EPSRC, BBSRC, NERC, Leverhulme Trust, British Heart Foundation, EC, Lowe Syndrome Trust, Newton-fellowships. Total amount of funding over the past 10 years: *ca*. **£ 7 M**

Other Activities:

- Member of Professional Bodies: *Royal Society of Chemistry, American Chemical Society*

- Invited visiting positions in other universities:
    - *Institute of Advanced Studies* (CINVESTAV, Mexico). Funded by: Royal Society (04/2007)
    - *University of Oviedo* (Spain). Funded by the Spanish Ministry of Science (07/2008)
    - *Nanyang Technological University / Institute of Education* (Singapore) (02/2010)
    - *Institute of Advanced Studies* (CINVESTAV, Mexico) (12/ 2011)

- Invited lectures at international conferences (selected examples in the past 10 years):
    - 5th Latin American Biological Inorganic Chemistry Conference (Mexico, 10/2016)
    - COST meeting – Nucleic Acids (Portugal, 09/2015)
    - 13th International Symposium on Applied Bioinorganic Chemistry (Ireland, 07/2015)
    - IC3EM 2014 (Portugal, 09/2014)
    - EuroBIC-12 (Switzerland, 08/2014)
    - ICIQ 10th Anniversary Symposium (Spain, 07/2014)
    - 12th International Symposium on Applied Bioinorganic Chemistry (China, 12/2013)
    - RSC Macrocyclic and Supramolecular Chemistry Meeting (London, UK, 12/2012)
    - 2nd Supramolecular Chemistry in Water meeting – Plenary Speaker (Portugal, 11/2012)
    - 40th International Conference of Coordination Chemistry (Spain, 09/2012)
    - 5th EuCheMS Conference on Nitrogen Ligands (Spain, 09/2011)
    - CRUK-EPSRC Imaging Conference, (Oxford, UK, 25th March 2010)
    - 2nd International Symposium on Bioinorganic Chemistry, (Japan, 07/ 2009)
    - 1st Quadruplex DNA Symposium (London, UK, 09/2008)
    - 4th EuCheMS Conference on Nitrogen Ligands (Germany, 08/2008)
    - American Chemical Society-Nat Meetings (Boston, 08/2007)

Research interests: The work carried out in my group covers various aspects of chemical biology, supramolecular chemistry and bioinorganic chemistry (see the group's webpage at: (http://www3.imperial.ac.uk/people/r.vilar).

Publications: Published over 125 scientific papers in international journals (H index: 40; full list of publications can be found at: https://www.imperial.ac.uk/people/r.vilar/publications.html)