

CiQUS Lecture



Prof. Michael J. Hannon

Supramolecular recognition of DNA and RNA junction structures for anti-viral and anti-cancer therapy



UNIVERSITY OF
BIRMINGHAM

FONDO EUROPEO DE DESENVOLVEMENTO REXIONAL
PO FEDER Galicia 2014-202 - Unha maneira de facer Europa

Thursday, July 13, 2023
CiQUS Seminar Room

Physical Sciences for Health Centre & School of Chemistry, University of Birmingham, Edgbaston,
Birmingham B15 2TT, UK

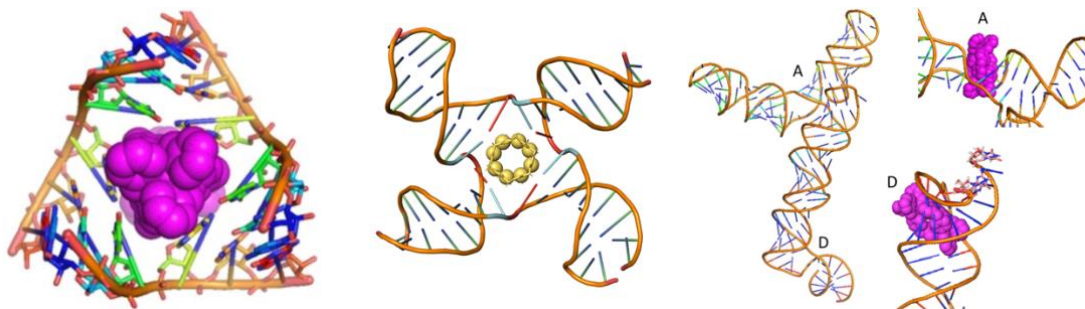
m.j.hannon@bham.ac.uk

<https://research.birmingham.ac.uk/en/persons/mike-hannon>

Abstract:

E Metallo-supramolecular cylinders (helicates) bind strongly to DNA and RNA Y-shaped junctions, forks and bulges, and prevent DNA transactions. They enter cells and rapidly localise in cell nuclei, where the fork-binding agents interfere with the processing of DNA leading to cell cycle arrest followed by apoptosis, without inducing genotoxicity or mutagenicity.^[1] As a route to control the activity of these agents, we encapsulate them in a cucurbituril ring to create a rotaxane structure, with release from the rotaxane switching on the junction-binding activity.^[2] We also extended our junction recognition approach to organometallic agents that recognise the cavities of DNA 4-way Holliday junctions.^[3]

Recognition of a specific nucleic acid shape is a powerful approach: In RNA-viruses the ends of the genome are non-coding parts which fold into specific structures and regulate viral replication. The same structures are common to many different viruses and an exciting new anti-viral target. We have shown that some of our agents can bind junction and bulge structures (Fig 1) in the untranslated regions of both SARS-CoV-2 and HIV-1 and show potent anti-viral activities at concentration levels where they are not cytotoxic to mammalian cells.^[4]



References

- [1] L. Cardo, M. J. Hannon, *Metal Ions Life Sci.*, 2018, 18, 303-324.
- [2] C.A.J. Hooper, L. Cardo, J.S. Craig, L. Melidis, A. Garai, R.T. Egan, V. Sadovnikova, F. Burkert, L. Male, N.J. Hodges, D.F. Browning, R. Rosas, F. Liu, F.V. Rocha, M.A. Lima, S. Liu, D. Bardelang, M.J. Hannon, *J. Am. Chem. Soc.*, 2020, 142, 20651–20660.
- [3] J.S. Craig, L. Melidis, H.D. Williams, S.J. Dettmer, A.A. Heidecker, P.J. Altmann, S. Guan, C. Campbell, D.F. Browning, R.K.O. Sigel, S. Johannsen, R.T. Egan, B. Aikman, A. Casini, A. Pöthig, M.J. Hannon, *J. Am. Chem. Soc.*, 2023, doi.org/10.1021/jacs.3c00118.
- [4] L. Melidis, H.J. Hill, N.J. Colman, S.P. Davies, K. Winczura, T. Chauhan, J.S. Craig, A. Garai, C.A.J. Hooper, R.T. Egan, J.A. McKeating, N.J. Hodges, Z. Stamataki, P. Grzechnik, M.J. Hannon, *Angew. Chem. Int. Ed.*, 2021, 60, 18144-51; L. Melidis, I.B. Styles, M.J. Hannon, *Chem. Sci.*, 2021, 12, 7174-7184.

Biosketch:

Mike Hannon holds the Chair of Chemical Biology at the University of Birmingham and is the Director of the EPSRC Research and Training Centre in Physical Sciences for Health. He is a member of the Board of Trustees of the Institute of Advanced Study at TU Munich and the Scientific Advisory Board of Zukunftskolleg at University of Konstanz.

Mike's research lies at the interface between chemistry and the life sciences and is focused on metal complexes in biology and medicine as both imaging agents and therapeutics. He has expertise in synthetic chemistry (organic, supramolecular, nanoscale) and in applying biophysical methods to recognition of different DNA structures. In particular his work on the non-covalent recognition of DNA Y-shaped junctions has transformed the field of study and prompted a sudden and growing international activity in exploring the use of metallo-supramolecular structures in DNA recognition and as anti-cancer drugs.

Mike is the immediate past President of The Society of Biological Inorganic Chemistry (SBIC), the international learned society. He chaired the prestigious Gordon Research Conference 'Metals in Medicine' in 2014 and was the chair of the 14th European conference on Biological Inorganic Chemistry which he hosted at the University of Birmingham in 2018.

Mike was Director of Birmingham's Institute of Advanced Studies from 2015-19, and co-organiser of the Intercontinental Academia 'Laws Rigidity and Dynamics' jointly with NTU Singapore in 2018-19. (<https://www.icalaws.com>).