

Responsive polymers in diagnostics and therapeutics

Cameron Alexander,¹ Amanda Pearce,¹ Patricia Monteiro,¹ Nishant Singh,¹ Vincenzo Taresco,¹ Arwyn T. Jones,² Stefano Salmaso,³ Paolo Caliceti³

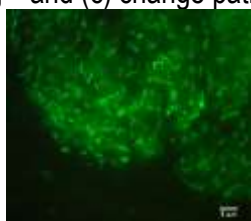
CAMERON.ALEXANDER@NOTTINGHAM.AC.UK

¹ School of Pharmacy, University of Nottingham, Nottingham, UK.

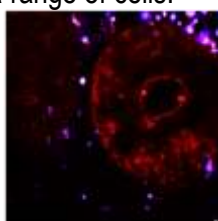
² SCHOOL OF PHARMACY AND PHARMACEUTICAL SCIENCES, CARDIFF UNIVERSITY, CARDIFF, UK.

³- DEPT. OF PHARMACEUTICAL AND PHARMACOLOGICAL SCIENCES, UNIVERSITY OF PADOVA, PADOVA, ITALY

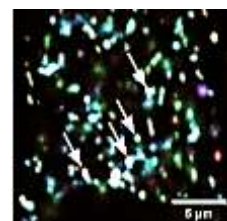
Responsive biomaterials have many applications ranging from anti-infectives, drug delivery and tissue engineering. However, the processes and mechanisms by which synthetic polymers and particles bind to bacterial and mammalian cells, and how they transport within, are not always analogous to their natural analogues. We have been working on materials which can probe cell surface binding and intracellular transport phenomena through a range of (bio)responsive functionality. These include polymers which can reversibly change from a chain-extended to a chain-collapsed state in response to temperature, pH, ionic strength or redox potential. The responses of these polymers can lead to a hydrophilic/hydrophobic switch at a surface, the unveiling of a ligand to bind to a receptor, or a release of a therapeutic payload at a target site. Recent studies have shown that even relatively simple 'model' polymer systems can behave in unexpected ways in varying cell types and populations. The talk will accordingly focus on polymers that can (a) bind to cell surfaces and interfere with bacterial Quorum Sensing (QS)^[1] and redox systems^[2] (b) selectively enter cancer cells by a polymer-mediated ligand switch,^[3] and (c) change pathways inside a range of cells.^[4]



Polymer-bacteria interactions



Selective cell entry



Pathway switching

We will show that new synthetic polymers can exhibit a variety of intriguing properties in the presence of a range of cell types, and that the knowledge gained from these studies can give useful insights into disease processes and new therapies.

Acknowledgments: The UK Engineering and Physical Sciences Research Council (EPSRC) for grants EP/G042462/1, EP/H005625/1, EP/I01375X/1, EP/N03371X/1, EP/N006615/1 and the Royal Society (Wolfson Research Merit Award WM150086) for funding.

[1] L. T. Lui, X. Xue, C. Sui, Brown, Alan, D. I. Pritchard, N. Halliday, K. Winzer, S. M. Howdle, F. Fernández Trillo, N. Krasnogor, C. Alexander, *Nature Chemistry* **2013**, 5, 1058–1065.

[2] E. P. Magennis, F. Fernandez-Trillo, C. Sui, S. G. Spain, D. J. Bradshaw, D. Churchley, G. Mantovani, K. Winzer, C. Alexander, *Nature Materials* **2014**, 13, 748-755.

[3] (a) E. Sayers, J. P. Magnusson, P. Moody, F. Mastrotto, C. Conte, C. Brazzale, P. Borri, P. Caliceti, P. Watson, G. Mantovani, J. W. Aylott, S. Salmaso, A. T. Jones, C. Alexander, *Bioconjugate Chemistry* **2018**; (b) C. Brazzale, F. Mastrotto, P. Moody, P. D. Watson, A. Balasso, A. Malfanti, G. Mantovani, P. Caliceti, C. Alexander, A. T. Jones, S. Salmaso, *Nanoscale* **2017**, 9, 11137-11147.

[4] (a) P. R. Moody, E. J. Sayers, J. P. Magnusson, C. Alexander, P. Borri, P. Watson, A. T. Jones, *Molecular Therapy* **2015**, 23, 1888-1898; (b) L. Purdie, C. Alexander, S. G. Spain, J. P. Magnusson, *Molecular Pharmaceutics* **2017**; (c) L. Purdie, C. Alexander, S. G. Spain, J. P. Magnusson, *Bioconjugate Chemistry* **2016**, 27, 1244-1252.