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Research Interests: cellular delivery (drugs, sensors, oligonucleotides, proteins, peptides, probes); carrier systems; intracellular sensing; high-throughput screening.

Cellular Delivery

The successful and efficient introduction and delivery of materials into cells is of fundamental importance throughout many areas of biology. It is critical for the analysis of function, the perturbation of specific cellular processes and the development of novel therapeutic strategies.

Recently attention has focused on the development of a diverse range of specific delivery systems in order to enhance transport and uptake at the cellular level. Contemporary examples of delivery vectors include peptides such as those based on fragments derived from the Tat protein, cell penetrating peptides, peptidomimetics such as peptoids, cationic lipids, liposomes, dendrimers, several nanodevices such as nanotubes and polymeric materials such as microspheres.

We have developed chemical based delivery systems for both small molecule (drugs and probes) and macromolecule delivery (PNA, DNA and proteins). Nowadays, we are focused in the synthesis and applications of multifunctionalized polystyrene microspheres.

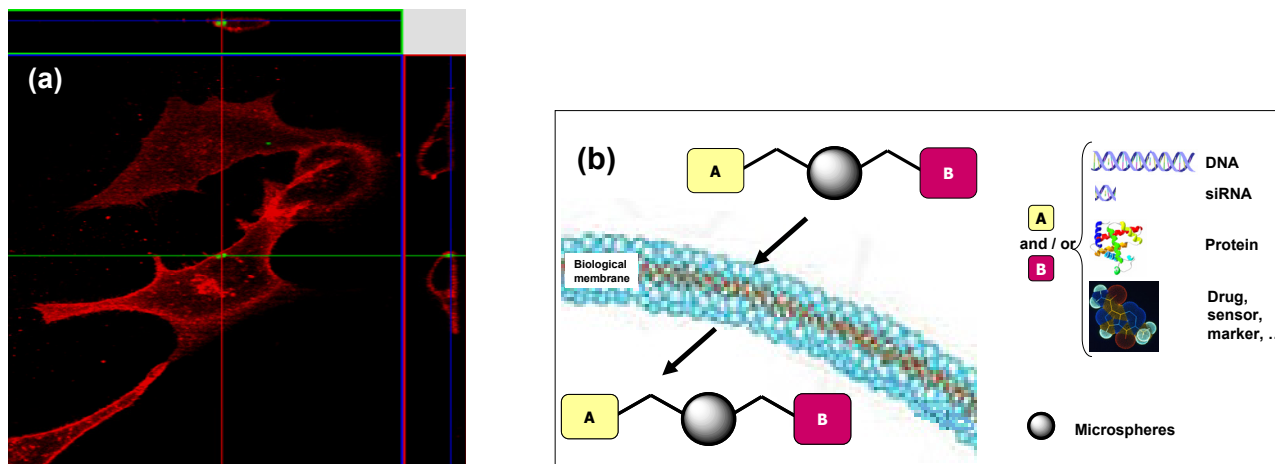


Figure 1. (a) Confocal microscopy image of melanoma cells (B16F10) loaded with fluorescein-labelled microspheres (green circles) after 6 h of incubation at 37 °C. (b) Applications of multifunctionalized polystyrene microspheres.

Intracellular Sensing

In the biochemical and medicinal fields it is becoming increasingly important to be able to monitor the intracellular levels of certain ions. Fluorescent sensors for a variety of ions, such as Ca^{2+} and Na^{+} are among the most useful tools available for studying ion fluxes within the intracellular environment following the modulation or stimulation of a range of complex biological processes. We are working in the development of techniques for intracellular delivery of sensors in which dilution and leakage do not occur. We are also applying this approach for monitoring of enzymatic activity.

SELECTED RECENT PUBLICATIONS

1. Bead-based cellular analysis, sorting and multiplexing. Sanchez-Martín, R. M.; Muzerelle, M.; Chitkul, N.; How, S. E.; Mittoo, S.; Bradley, M. *ChemBioChem* 2005, 6(8), 1341-1345.
2. Synthesis and cellular uptake of cell delivering PNA-peptide conjugates. Diaz-Mochon, J. J.; Bialy, L.; Watson, J.; Sanchez-Martín, R. M.; Bradley, M. *Chem. Comm.* 2005, 3316-3318.
3. Microsphere Based Real-Time, In Situ Calcium Sensing. Sánchez-Martín, R.M.; Cuttle, M.; Mittoo, S.; Bradley, M. *Angew. Chem. Int. Ed.* 2006, 45, 5472-5474.
4. pH sensing in living cells using fluorescent microspheres. Bradley, M.; Alexander, L.; Duncan, K.; Chennaoui, M.; Jones, A. C.; Sánchez-Martín, R.M. *Bioorg. Med. Chem. Lett.*, 2007, doi:10.1016/j.bmcl.2007.10.075.