

## Recent therapeutic advances using polystyrene microspheres as delivery systems

Rosario M. Sánchez-Martín

University of Granada, Department of Medicinal and Organic Chemistry, Faculty of Pharmacy, Campus Cartuja, s/n, 18071, Granada, Spain  
GENYO. Centre for Genomics and Oncological Research: Pfizer / University of Granada / Andalusian Regional Government, Av. de la Ilustración, 114 – PTS, 18016, Granada, Spain

[rmsanchez@ugr.es](mailto:rmsanchez@ugr.es), [rosario.sanchez@genyo.es](mailto:rosario.sanchez@genyo.es)

### Abstract

The search for efficient and safe carrier systems to achieve better availability of therapeutic cargoes at the target site has been a challenging yet exciting area of research. Nowadays many research teams are focused in the development of approaches based in the use of nanodevices as tool to achieve novel therapeutic strategies.

We have developed a simple technique for the synthesis of a range of robust and biocompatible functionalized polymer microspheres of highly defined size (100 nm – 500 nm) and loading (Figure 1).<sup>[1-2]</sup> A range of bioactive cargoes have been conjugated to these particles following a multifunctional strategy and they have been effectively taken up by different type of cells included primary cells and embryonic, neuronal and mesenchymal stem cells (Figure 2).<sup>[3]</sup>

We have demonstrated that these microspheres can efficiently deliver various small molecules (e.g. biosensors) and macromolecules (e.g. proteins).<sup>[4-5]</sup> We also show that microsphere internalization does not affect ES cell pluripotency as bead-treated ES cells could be used to generate high contribution chimeric embryos.<sup>[6]</sup> We have developed several chemical strategies to use these devices as transfection agents (delivery of oligonucleotides such as pDNA and siRNA).<sup>[7-10]</sup> These devices have been for in vivo cell tracking.<sup>[11]</sup> Recently we have successfully developed micro heterogeneous catalysts by immobilising palladium nanoparticles on these microspheres and employed them to do chemistry in living systems.<sup>[12]</sup>

These microspheres are inherently attractive as a delivery system due to their lack of toxicity and highly controllable cellular loading.

### References

- [1] Sanchez-Martin, R.M.; Muzerelle, M.; Chitkul, N.; How, S.E.; Mittoo, S.; Bradley, M., *ChemBioChem*, **6** (2005) 1341-1345.
- [2] Unciti-Broceta, A.; Johansson, E. M.V.; Yusop, M.; Sánchez-Martín, R. M.; Bradley. M., *Nature Protocols*, **7** (2012) 1207–1218.
- [3] Sánchez-Martín, R. M., \* Alexander, L.; Cardenas-Maestre, J.M.; Bradley, M., *Strategies for Microsphere-Mediated Cellular Delivery*, Book: *Ideas in Chemistry and Molecular Sciences: Where Chemistry meets Life*, Wiley-VCH Ed. Pignataro, B. (2010) 117–140.

[4] Sanchez-Martin, R.M.; Cuttle, M.; Mittoo, S.; Bradley, M. *Angew. Chem. Int. Ed.*, **45** (2006) 5472-5474.

[5] Sanchez-Martin, R. M.\*; Alexander, L.; Muzerelle, M.; Cardenas-Maestre, J. M. ; Tsakiridis, A.; Brickman, J. M.; Bradley, M. *ChemBioChem*, **10** (2009) 1453-1456.

[6] Tsakiridis, A.; Alexander, L.; Gennet, N.; Sanchez-Martin, R. M.; Livigni, A.; Li, M.; Bradley, M.; Brickman, J. M., *Biomaterials*, **30** (2009) 5853-5861.

[7] Alexander, L.; Sanchez-Martin, R. M.; Bradley, M. *Bioconjugate Chem*, **20** (2009) 422-426.

[8] Borger, J.G.; Cardenas-Maestre, J.M.; Zamoyska, R.; Sanchez-Martin, R.M.\* *Bioconjugate Chem.*, **22** (2011) 1904-1908.

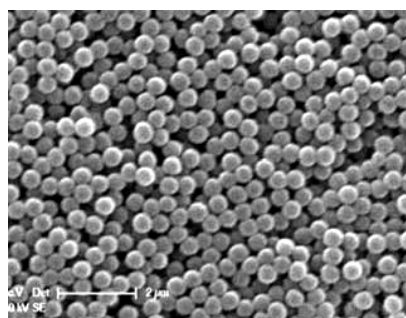
[9] Cardenas-Maestre, J.M.; Panadero-Fajardo, S.; Perez-Lopez, A.M.; Sanchez-Martin, R.M.\* *J. Mater. Chem.*, **21** (2011) 12735-12743.

[10] - Unciti-Broceta, A.; Díaz-Mochón, J. J.; Sánchez-Martín, R. M.\* and Bradley, M.\* *Accounts Chem. Res.*, **45(7)** (2012) 1140-1152.

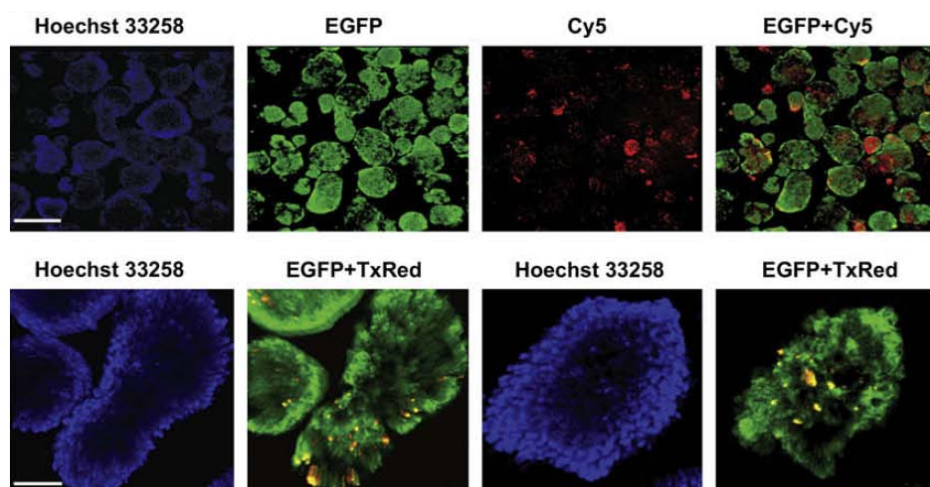
[11] - Dhaliwal, K.; Alexander, L.; Escher, G.; Unciti-Broceta, A.; Jansena, M.; Mcdonalda, N.; Cardenas-Maestre, J.M.; Sanchez-Martin, R.; Simpson, J.; Hasletta, C.; Bradley, M. *Faraday Discuss.*, **149** (2011) 107-114.

[12] - Yusop, M.; Unciti-Broceta, A.; Johansson, E. M.V.; Sánchez-Martín, R. M.; Bradley, M. *Nature Chemistry*, **3** (2011) 239-243.

## Figures



**Figure 1.** SEM images of cross linked microspheres



**Figure 2.** Microsphere-mediated delivery in differentiating Embryonic Stem (ES) cells. Confocal microscopy images of day 7 EBs derived from aEGFP cells