

# Multifunctional Nanoplatform for Biomedical Applications

R. Piñol<sup>1</sup>, L.M.A. Ali<sup>1</sup>, R. Bustamante<sup>1</sup>, C. Brites<sup>2</sup>, L. Gabilondo<sup>1</sup>,  
J.L. Murillo<sup>1</sup>, N.J.O. Silva<sup>2</sup>, V. Sorribas<sup>3</sup>, M. Gutierrez<sup>4</sup>, R. Cornudella<sup>4</sup>, L. Carlos<sup>2</sup>,  
F. Palacio<sup>1</sup>, A. Lascialfari<sup>5</sup>, J. Carrey<sup>6</sup>, M. Respaud<sup>6</sup>, G. C. Sanmartí<sup>7</sup>, J.-P. Salvador<sup>7</sup>, M.-P. Marco<sup>7</sup>, J.  
Criado<sup>8</sup>, M. Fuentes<sup>8</sup>, A. Millan<sup>1</sup>

<sup>1</sup> Instituto de Ciencia de Materiales de Aragón (ICMA), CSIC–University of Zaragoza, C/ Pedro Cerbuna 10, 50009 Zaragoza, Spain.

<sup>2</sup> Departamento de Física and CICECO. University of Aveiro, 3810-193 Aveiro, Portugal.

<sup>3</sup> Laboratory of Molecular Toxicology, Faculty of Veterinary Medicine, University of Zaragoza, 50009 Zaragoza, Spain.

<sup>4</sup> Department of Hematology, Faculty of Medicine, University of Zaragoza, 50009 Zaragoza, Spain.

<sup>5</sup> Department of Physics “A. Volta”, University of Pavia, 27100 Pavia, Italy.

<sup>6</sup> Laboratoire de Physique et Chimie des Nano-Objets (LPCNO), INSA-University of Toulouse, 135, av. de Rangueil, F-31077 Toulouse, France.

<sup>7</sup> Instituto de Química Avanzada de Cataluña (IQAC), CSIC, Jordi Girona, 18-26, 08034, Barcelona, Spain.

<sup>8</sup> Centro de Investigación del Cáncer (CIC), CSIC-University of Salamanca, Campus Miguel de Unamuno, 37007 Salamanca, Spain.

[pinol@unizar.es](mailto:pinol@unizar.es), [amillan@unizar.es](mailto:amillan@unizar.es), [palacio@unizar.es](mailto:palacio@unizar.es)

## Abstract

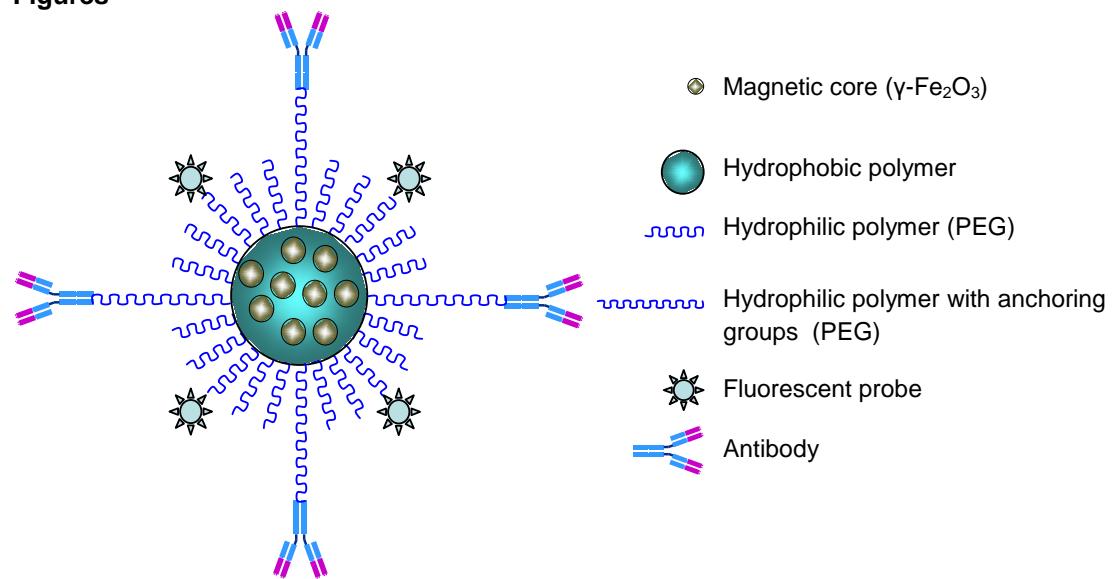
After a period of intense research, nanoparticles incorporating a biological functionality have already found several punctual applications in biotechnological and clinical practices. Nowadays, the development of functionalization techniques with a high versatility permits to aspire to a more general use of nanoparticles in nanomedicine. In this direction, the concept behind this work pretends to use nanoparticles as a platform for assembling multiple interchangeable pieces each of them incorporating a physical or biological functionality. The nanoplatform presented here shows that it is possible to combine physical, chemical and biological functionalities in a single particle and simultaneously. It consists on a hydrophobic polymer core having a surface with multiple equal anchoring groups for the covalent bonding of the functionalised pieces. This core in itself may also incorporate several functionalities in the form of smaller inorganic nanoparticles. The functionalised pieces consists of hydrophilic chains ending on a reactive group that fits on the core surface and holds at the other end a biological or physical functionality. The coupling system is a Michael addition from a Michael-donor (amine, thiol, etc) to a Michael acceptor (acrylate) [1]. This system has the advantages of a clean synthesis (no by-products), mild conditions, and an easy and controlled multifunctionalization. The nanoplatform has been functionalized with radiochemical tracers (In111), luminescent dyes (fluorescein, rhodamine, lanthanide compounds), and magnetic nanoparticles, and therefore it can be a powerful tool in imaging. Besides, it has also been functionalized with a therapeutic drug, an antibody, and an optical thermometer made of lanthanide complexes [2]. Health safety of the system has been tested in cellular and in vivo assays. The nanoplatform is highly stable in biological fluids, shows low cell toxicity [3], high capacity of cell internalization, no *in vivo* damage for tissues and organs, excellent hematocompatibility, and anticoagulation properties [4]. It is shown that magnetic properties can be tuned up in the whole superparamagnetic range [5]. Moreover, the system has shown excellent performance in magnetic resonance imaging [6] and hyperthermia.

## References

- [1] R. Piñol, A. Millán, F. Palacio, L. Gabilondo, Spanish Patent no. P201031493 submitted to the Spanish Patent and Trademark Office (07-10-2010).
- [2] C. D. S. Brites, P. P. Lima, N. J. O. Silva, A. Millán, V. S. Amaral, F. Palacio, L. D. Carlos, Advanced Materials, **22** (2010) 4499-4504.
- [3] R. Villa-Bellosta, G. Ibarz, A. Millan, R. Piñol, A. Ferrer-Dufol, F. Palacio, V. Sorribas, Toxicology Letters, **180**, (2008) S221-S221.
- [4] Lamiaa M.A. Ali, M. Gutiérrez, R. Cornudella, J.A. Moreno, R. Piñol, L. Gabilondo, A. Millán and F. Palacio, J. Biomed. Nanotechn. (in press) (2013).
- [5] A. Millan, F. Palacio, A. Falqui, E. Snoeck, V. Serin, A. Bhattacharjee, V. Ksenofontov, P. Gütlich and I. Gilbert, Acta Materialia, **55**, (2007), 2201-2209.

[6] H. Amiri, P. Arosio, M. Corti, A. Lascialfari, R. Bustamante, A. Millán, N.J.O. Silva and F. Palacio, Magn. Res. in Medicine, **66**, (2011) 1715-1721.

## Figures



Scheme of core-shell multifunctional nanoplatform containing magnetic nanoparticles