S12-FP06

LUMINESCENT TEMPERATURE PROBES FOR REAL-TIME INTRACELLULAR THERMOMETRY AND MAGNETIC HYPERTERMIA

R. PIÑOL,[a] Y. GU,[a] R. MORENO-LOSHUERTOS,[b] C.D.S. BRITES,[c] J. ZELER,[c] A. MARTINEZ,[d] G. MAURIN,[a] P. FERNANDEZ-SILVA,[b] J. MARCO-BRUALLA,[b] R. NAVARRO, L.D. CARLOS,[c] A. MILLAN[a]

[a]*INMA Institute of Nanoscience and Materials of Aragon. CSIC-University of Zaragoza,* Zaragoza, Spain.

[b] *Departamento de Bioquímica, Biología Molecular y Celular, and Instituto de Biocomputación y Física de Sistemas Complejos. University of Zaragoza, Zaragoza, Spain.*

[c] *CICECO-Aveiro Institute of Materials, Department of Physics, University of Aveiro, Aveiro, Portugal.*

[d] Departamento de Electrónica de Potencia. I3A. *University of Zaragoza, Zaragoza, Spain.*

e-mail: pinol@unizar.es

Keywords: *luminescence, nanothermometry, magnetic hyperthermia,*

Exogenous and endogenous heat generation inside cells is a subject of intense debate in recent times. Most of the thermometric systems proposed for intracellular thermometry are noncontact luminescent nanothermometer (LNT) capable of acquiring local temperatures with spatial and temporal resolution at the nanoscale. LNT must operate at the physiological temperature range and show an outstanding thermometric performance response. Nevertheless, the main and most difficult requirement that LNT has to meet for intracellular mapping is the stability in the intracellular environment. Accurate and noninvasive monitoring of subcellular temperature changes in individual cells might help to clarify intricate cellular processes and led to development of novel diagnostic and therapeutic technologies. For example, Magnetic induction heating of nanoparticles can be a powerful non-invasive technique for hyperthermia therapy of cancer.[1] However, controversy has been established between those who theoretically predict that it is not physically possible to achieve substantial temperature increments between the heat source and those who measured temperature gradients. The capacity and efficiency of such local heating systems should require of an adequate local temperature control of magnetic nanoheaters (MNHs). Therefore, single nanoparticles integrating both functions, magnetic heating and luminescent thermometry (MNH-LT), should be the best option. [2]

Here, we present a system for intracellular mapping and able of measuring local temperature gradients in intracellular magnetic hyperthermia using a ratiometric luminescent thermometer based on Lanthanide complexes (Ln= Sm^{3+}/Eu^{3+}). The Eu^{3+} and Sm^{3+}-based complexes can covalently bonded on amphiphilic block copolymers (ABCP). The adequate selection of the lanthanide complexes combined with the protection provided by the polymer coating have made it possible to obtain new MNH-LNT and polymeric Ln doped Nanoparticles that are robust measurement systems that retain their thermometric properties inside the intracellular environment. Making use of these luminescent probes, we have been able to record two-dimensional (2D) thermal images showing subcellular gradients of ~5 degrees between the nucleolus and the rest of the cell [3] and measuring temperature increases of around 11°C at the MNH surface without any appreciable temperature increase in the cell membrane during the application of intracellular magnetic hyperthermia.

This work was supported by the Spanish Ministry of Science Innovation and Universities [Grant No: PGC2018_095795_B_I00] and Diputación General de Aragón [E11/17R]. The support of the European Union's Horizon 2020 FET Open program under grant agreements No. 801305 (NanoTBTech) and 829162 (Hotzymes) is also acknowledged.

References

[1] R. Piñol, C. D. S. Brites, N. J. O. Silva, L. D. Carlos. A. Millán Chapter 6 - Nanoscale Thermometry for Hyperthermia Applications. In Nanomaterials for Magnetic and Optical Hyperthermia Applications, Eds. Elsevier: **2019**.

[2] R. Piñol C. D. S. Brites, R. Bustamante, A. Martinez, N. J. O. Silva, J. L. Murillo, J, Carrey, C. Estepa, C. Sosa, F. Palacio, L. D. Carlos, A. Millán *Acs Nano* **2015,** ***9***, 3134-3142

[3] R. Piñol, J. Zeler, C.D. S. Brites, Y. Gu, P Téllez, A. N, Carneiro, T. E. da Silva, R. Moreno-Loshuertos, P. Fernandez-Silva, A. I. Gallego, L. Martinez-Lostao, A. Martinez, L. D. Carlos, A, Millán, *Nano Letters* **2020,** *20*, 6466-6472.