Catarina Oliveira Silva

CBIOS - ULHT, Campo Grande, 376, 1749-024 Lisboa, Portugal; Faculty of Pharmacy, University of Alcalá, Ctra. Universidad Complutense, 28871 Alcalá de Henares, Spain.

catarina.m.oliveira.silva@gmail.com

Advances and current approaches of photoactivated functionalized nanoparticles in cancer targeting treatment

Cancer is one of the leading causes of mortality worldwide, and is foreseen that its incidence will continue to rise, as a result of the population aging and increasing risk factors [1]. Over the last decades, scientific research and medical care are focused on finding more effective and safer solutions to reduce the burden of cancer and improve patients' survival and quality of life. In this context, precision medicine has evolve, improving the access to innovative technologies, which offer early diagnosis and better treatment options. While contributing greatly to this recent progress, the Nanotechnology field provide multiple functionalities and a promising role in targeted tumor therapy. For instance, hybrid nanoparticles, made of polymers, metallic or bioactive compounds, have been developed to mitigate limitations associated with tumor targeting, safety issues and multiple resistance to conventional treatments. Amongst all the available nanostructures, gold nanoparticles have been widely studied for light-based applications, due to high absorption coefficient, potential versatility and functionalization [2]. Photothermal therapy, using targeted gold nanoparticles and laser irradiation with near-infrared light (NIR, 700-1200 nm), is a technique that enhance tumor cell death, penetrating deeper into the tumor tissue and preventing its growth. Currently, some of these nanosystems moved forward in clinical trials, combining both diagnostic and therapeutic approaches and photothermal chemotherapy. Hence, we have developed multifunctional nanoparticles with the potential to destroy melanoma cells at their initial stage [3, 4]. Briefly, two strategies were appraised: 1) polymeric nanoparticles with a core-shell structure, loaded with Parvifloron D (cytotoxic drug); 2) gold nanoparticles functionalized with the ligand Epidermal Growth Factor (EGF) and photoactivated by NIR laser irradiation. Overall, nanoparticles with a size of 100 nm and spherical morphology were successfully coated with hyaluronic and oleic acids, maintaining their long-term stability (Figure 1). Functionalization was achieved with multiple targeting moieties, by electrostatic interactions. Both nanosystems were able to internalize the cells overexpressing specific cancer receptors, decrease melanoma cells viability and showed a safe *in vitro* cytotoxic profile over normal-like cells. In preliminary *in vivo* studies, these therapeutic approaches promoted extensive necrosis of human cutaneous melanoma A375 cells and reduced tumor growth (up to 80%), without damage of the surrounding tissue.

Acknowledgments

Financial support was provided by the Portuguese Foundation for Science and Technology (PTDC/BBB-BMC/0611/2012) and Universidad de Alcalá and CBIOS/ULHT under the EHEA Doctorate Programme in Health Sciences.

References

[1] Ferlay J., et al., Int J Cancer, 5 (2016) E359-86.
[2] Abdeer N.S., Murphy C.J., J Phys Chem C 120 (2016), 4691–4716.
[3] Silva C.O., et al., Ther Deliv, 7 (2016), 521-44.
[4] Silva C.O., et al., PLoS ONE 11 (2016), e0165419.

Figures

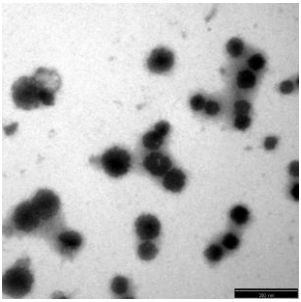

Figure 1: TEM image of EGF conjugated hybrid gold nanoparticles for photothermal therapy (at scale bar of 250 nm).