Polymer-grafted gold nanoparticles for cancer treatment: synthesis and evaluation of their radiosensitizing properties

Marine Le Goas, B. Cambien, Aurélie Paquirissamy, Manon Boul, Anne Xu, Valérie Geertsen, T Pourcher, J-P Renault, Géraldine Carrot

Polymer-grafted gold nanoparticles for cancer treatment: synthesis and evaluation of their radiosensitizing properties

M. Le Goas[1], B. Cambien[2], A. Paquirissamy[1], M. Boul[1], A. Xu[1], V.Geertsen[1], T. Pourcher[2], J-P. Renault[1], G. Carrot[1]

(1) *NIMBE UMR 3685, CEA, CNRS, Université Paris-Saclay, Gif-sur-Yvette, France*
(2) *TIRO, UMRE 4320, iBEB, DSV, CEA, Université de Nice-Sophia Antipolis, Nice, France*

Today, even though treatments have much improved, cancer is still a leading cause of death in the world, being responsible for 1 death out of 6. Radiotherapy is widely used for tumor treatment, but suffers from side effects due to the irradiation of healthy surrounding tissues. Another issue is the radioresistance developed by some tumor cells, which implies to increase the involved doses. The challenge remains to deliver curative doses to tumor tissues while sparing sound ones. Hence the use of tumor-located radiosensitizers is a promising way to improve the efficacy of radiotherapy[1]. High-Z materials have been known for several decades to amplify the damaging effects of both photon and ion radiations[2]. Various nanoparticles have already been developed to take advantage of this property: gold, platinum and gadolinium are amongst the most investigated elements[3].

A well-controlled synthesis is key to obtain stable and scalable nano-objects. Here, various polymers were grafted onto metallic nanoparticles to improve stability and biocompatibility and to facilitate subsequent functionalization. Advanced methods of characterization attested both robustness and reproducibility of the synthesis procedure. Moreover, promising results were obtained regarding the radioenhancing properties of these hybrid nanocompounds. Therefore, special attention has been given to the underlying mechanisms of the assessed radiosensitization, since they are not fully understood yet.

Synthesis of polymer-grafted gold nanoparticles was performed through an *in situ* method, *via* the reduction of gold salts in the presence of polymeric ligands mainly prepared using controlled radical polymerization. The resulting nano-objects were fully characterized by thermogravimetric analysis, inductively coupled plasma mass spectrometry (ICP-MS), transmission electronic microscopy and small-angle x-ray and neutron scattering.

Interactions between our nanocompounds and biological systems were studied in order to better understand the mechanisms at play. At the cellular scale, three aspects were examined for each type of nanoparticles: cellular uptake, cytotoxicity and radiosensitizing properties, through ICP-MS measurements, cell proliferation assays and clonogenic assays respectively. All irradiations were performed while keeping the delivered doses to low values (under 30 Gy) that are typical of clinic reality. Different types of radiations were tested, in order to compare their effects and their synergy with the nanocompounds.

The synthesized nano-objects have shown great potential to enhance radiation cancer treatment. Their stability and controlled surface chemistry have allowed to develop multiple strategies in order to optimize their radiosensitizing effect and *in vitro* behavior.

References

1. Kwatra, D., Venugopal, A. & Anant, S. Nanoparticles in radiation therapy: a summary of various approaches to enhance radiosensitization in cancer. Transl. Cancer Res. **2**, 330–342 (2013).
2. Kobayashi, K., Usami, N., Porcel, E., Lacombe, S. & Le Sech, C. Enhancement of radiation effect by heavy elements. Mutat. Res. Mutat. Res. **704**, 123–131 (2010).
3. Schlathölter, T. et al. Improving proton therapy by metal-containing nanoparticles: nanoscale insights. Int. J. Nanomedicine **11**, 1549–1556 (2016).

Corresponding author email: marine.le-goas@cea.fr