Self-reporting Nanoparticles for Cancer Immunotherapy

Milene Costa da Silva[a]
Cátia Vieira Rocha[a], Cátia Martins[b], Susana P. G. Costa[b], Manuela M. Raposo[b], Manuel Bañobre-López[a] and Juan Gallo[a]
[a]Advanced (magnetic) Theranostics Nanostructures Lab, International Iberian Nanotechnology Laboratory, Avenida Mestre José Veiga s/n, 4715-330 Braga, Portugal; [b]Centro de Química, Universidade do Minho, Campus de Gualtar, 4710-057, Braga, Portugal
milene.silva@inl.int

The tumor microenvironment (TME) is composed of infiltrating immune cells that can dictate the progression of the primary tumor. Usually, the immune response is suppressed in the TME but with the aid of immunostimulating (IS) drugs, the immune system can be reprogrammed to fight cancer. Current cancer therapies are often non-specific, inefficient and result in severe side effects. Taking advantage of the characteristics of the TME and nanotechnology, we have designed magnetic pNIPAM nanocarriers that respond to temperature (T) (induced by magnetic hyperthermia) in order to release a cocktail of IS drugs in the TME, resulting in a targeted, more specific cancer therapy. Temperature-responsive magnetic pNIPAM nanoparticles of 250nm in size were synthesized through wet chemistry approach. An IS drug was efficiently encapsulated into the polymeric shell and the final pNIPAM formulations were characterized using spectroscopic techniques, TEM, and magnetometry. The responsiveness of the pNIPAM nanoparticles to changes in temperature was confirmed via UV-Vis. Cell-mediated cytotoxicity assays were established to test the capacity of the nanocarriers to promote tumor cell death. We co-cultured HT-29 cells (colorectal cancer cell line) with NK92CI cells (NK cell line) at different ratios and in the presence of IS drug. The viability of the tumor cells was measured using a fluorescence redox indicator for cell viability. Initial results show that free IS drug and unloaded pNIPAM have no direct effect on the cell viability of immune cells or tumor cells, but in the cell-mediated cytotoxicity assay, the tumor cell killing is enhanced when NK cells are stimulated with IS drugs. The final formulation (pNIPAM-IS drug) induced NK cell activation and tumor cell killing, which was enhanced after magnetic hyperthermia. Future work includes the synthesis and characterization of a self-reporting probe activated by immune cells. The final goal is to develop a new and efficient nanoparticle-based system to be applied in colorectal cancer theranostics.

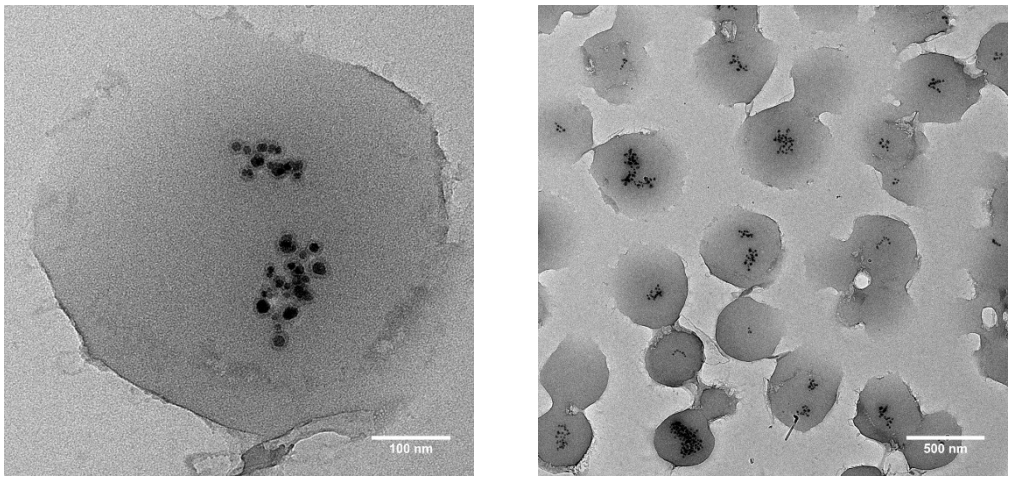

Figure 1: Image of the pNIPAM nanoparticles by transmission electron microscopy