

**Titre de votre intervention :** Thermo-responsive core/shell SPION and their drug release properties

**Auteurs :**

Zied Ferjaoui, Raphaël Schneider, Lina Bezdetnaya, Eric Gaffet, Halima Alem,

**Résumé**

Due to their ability to carry anticancer drugs and generate localized heat when exposed to an alternating magnetic field, superparamagnetic iron oxide (SPIO) nanoparticles (NPs) can be used as multimodal cancer therapy agent by combining chemotherapy and hyperthermia<sup>1</sup>. Core/shell Fe<sub>3</sub>O<sub>4</sub>@copolymer nanoparticles were synthesized with covalent grafting of a thermos-responsive biocompatible copolymer based on 2-(2-methoxy) ethyl methacrylate (MEO2MA) and oligo (ethyleneglycol) methacrylate (OEGMA) on a superparamagnetic NPs surfaces. The lower critical solution temperature (LCST) of grafted copolymer was tuned in physiological media in order to release the cancer drug at controlled temperatures. The 41-42°C LCST was obtained with a copolymer composed with 60% MEO2MA and 40% OEGMA. Another class of responsive NPs was obtained by the functionalization the Fe<sub>3</sub>O<sub>4</sub>@copolymer by folic acid (FA) which led to the Fe<sub>3</sub>O<sub>4</sub>@copolymer-FA, a biological cancer targeting molecule. Both types of NPs (Fe<sub>3</sub>O<sub>4</sub>@copolymer and Fe<sub>3</sub>O<sub>4</sub>@copolymer-FA) were loaded with the anticancer agent doxorubicin (DOX). In vitro, DOX release kinetics was investigated at 42°C: 25% at 5h, 50% at 24h and 100% at 56h of DOX release were measured for both types of NP. At 37°C, NPs were found stable until 24h (<10% DOX release)<sup>2-4</sup>.

Further, the viability of human ovarian cancer cells (Skov3) exposed to NPs, free DOX or DOX-NPs for 24h at 41°C or 37°C for control cells, was assessed by measuring cell metabolic activity (MTT test). Results showed that NPs (without DOX) preserved cell viability ( $> 78.44 \pm 9.48 \%$ ) irrespective of the temperature and the NP concentration.

This study demonstrates the potential of Fe<sub>3</sub>O<sub>4</sub>@P(MEO2MA60-co-OEGMA40) nanoparticles for cancer treatment combining chemotherapy and hyperthermia.

- (1) Xie, J.; Huang, J.; Li, X.; Sun, S.; Chen, X. *Curr. Med. Chem.* **2009**, *16* (10), 1278–1294.
- (2) Jamal Al Dine, E. ; Ferjaoui, Z.; Roques-Carnes, T.; Schejn, A.; Meftah, A.; Hamieh, T.; Toufaily, J.; Schneider, R.; Gaffet, E.; Alem, H. *Nanotechnology* **2017**.
- (3) Ferjaoui, Z.; Meftah, A.; Gaffet, E.; Alem, H.; Schneider, R. . *RSC Adv.* **2017**, *7*, 26243–26249.
- (4) Jamal Al Dine, E.; Ferjaoui, Z.; Ghanbaja, J.; Roques-Carnes, T.; Meftah, A.; Hamieh, T.; Toufaily, J.; Schneider, R.; Marchal, S.; Gaffet, E.; et al. *Int. J. Pharm.* **2017**, *532* (2), 738–747.