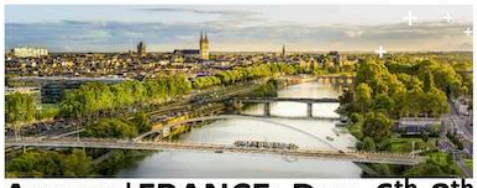

Targeting strategy for a high selective accumulation and therapeutic efficiency of dendronized nanoparticles in head and neck cancer cells

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A major challenge in nanomedicine is to design nanoplatforms able to selectively target abnormal cells to ensure early diagnosis and/or targeted therapy of diseases. However if nanoparticles developed for biomedical applications such as iron oxide nanoparticles (IONPs) have been optimized for combining imaging and therapy, their selective accumulation in diseased organs to enable precise diagnosis and targeted therapy remains an important issue. Most of developed IONPs accumulate, after intravenous injection, in eliminatory organs and only low amounts are seen accumulating in tumours. For a precise treatment, active targeting with affinity ligands to achieve tumor specificity is crucial.
We have developed IONPs coated with original dendron molecule which have demonstrated in several *in vitro* and *in vivo* studies to display antifouling properties. With their favourable biodistribution and bioelimination profile, they are very well adapted for investigating affinity targeting. In that context, we have studied the targeting of head and neck cancer (HNC) cells by coupling selected targeting ligands on IONPs' surface with an adapted carbodiimidation method. We selected cRGD to target the integrin and a peptide derived from GE11 to target epidermal growth factor receptor (EGFR). The grafting was successfully assessed by combining different techniques such as zeta potential and hydrodynamic size measurements and HR-MAS spectroscopy. After the control of the cytotoxicity of different samples (MTT, Crystal Violet), targeting specificity on two HNC cell lines surexpressing EGFR (FaDu, 93-VU) and a control cell line (MM074) was checked via internalization studies (iron dosage in cells, immunofluorescence imaging). They demonstrated the strong specificity of GE11-like peptide for internalizing high amount of IONPs.
We have then studied the effect of magnetic and photo-hyperthermia and protontherapy on cells with internalized IONPs. These studies showed that IONPs size has a great effect on the different therapeutic modes and dendronized IONPs are promising theranostic nanoplatforms for combining targeting, imaging and therapeutic properties inside one nano-object.