In vitro study of dendronized nanoparticles designed for theranostics in breast cancer context

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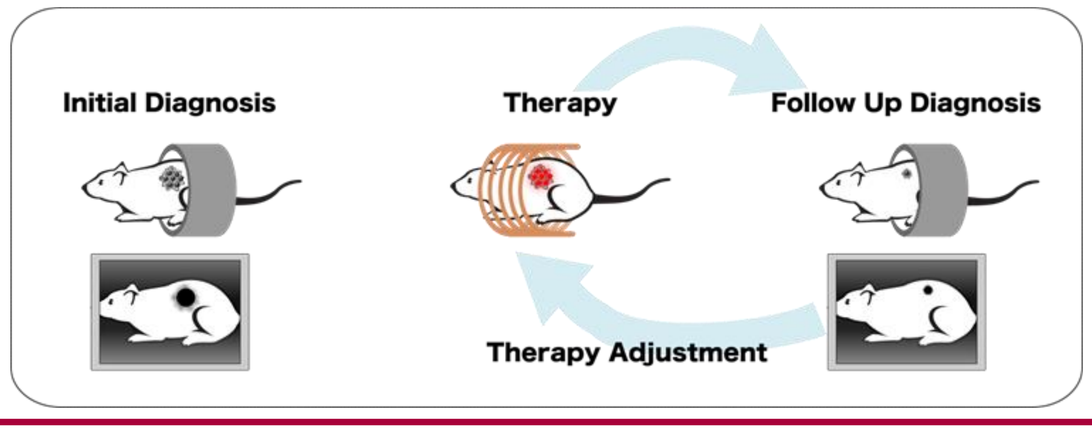
Introduction

The aim of ***Theraget*** **project** is to develop **targeted multifunctional nanoplatforms** that allow diagnosis, therapy (theranostic) and follow up diagnosis in **breast and ovarian cancer** context.

Theranostic :

- Diagnostic with MRI (iron oxide nanoparticles IONPs)
- Therapy using magnetic hyperthermia, a local elevation of temperature (alternative magnetic field)[1]

In vitro experiments must be done first, such as **cytotoxicity** tests and evaluation of IONPs **internalization**.



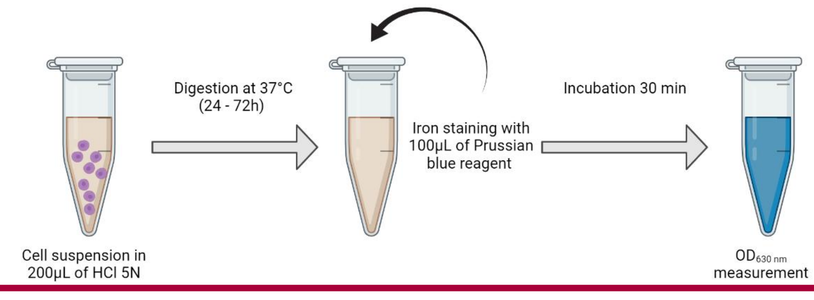
Material & methods

IONPs are

- Synthesis : thermal decomposition + **coated with dendrons**[2]
- Conjugated to targeting ligands : **cRGD and peptide 22** (which are recognize by integrin $\alpha V\beta_3$ and EGFR)

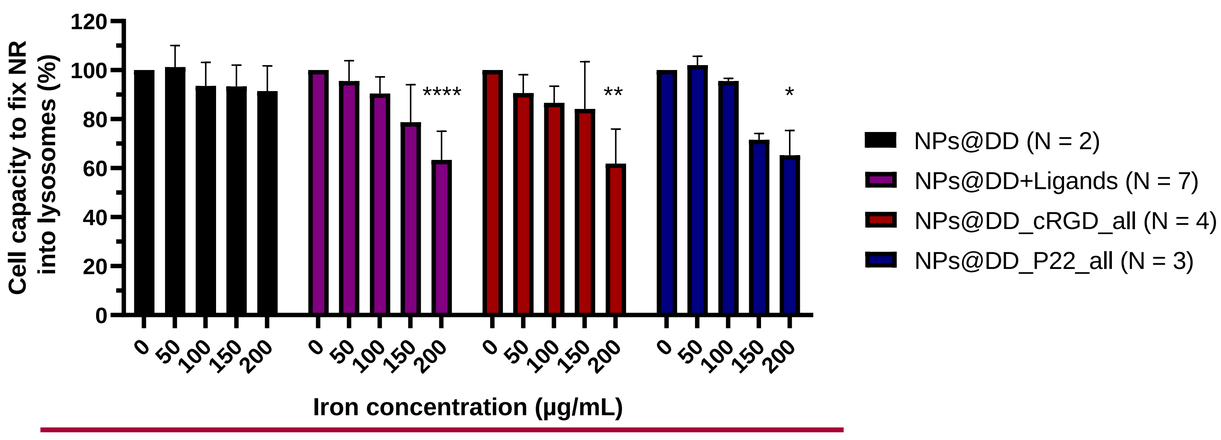
Integrins $\alpha V\beta_3$ ➔ overexpressed in tumoral environment for **neovascularization**[3,4].
Peptide 22 ➔ promising **EGFR specific** triple negative breast cancer cell binding peptide [5].

LDH Release : unviable cells will release LDH in the extracellular medium. This extracellular LDH is quantified.
Neutral red : viable cells internalize the neutral red dye into lysosomes and keep it even after washing.
Internalization : measured using iron quantification in biological matrix method[6]

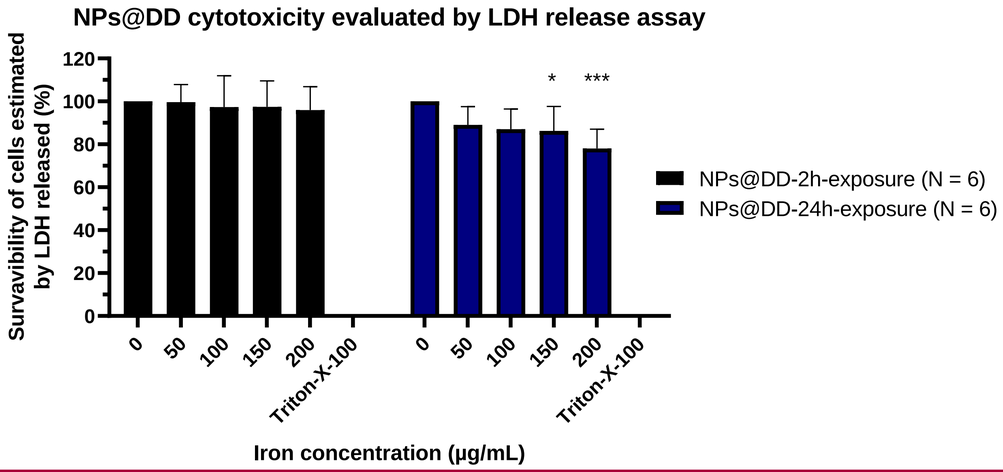


Cytotoxicity

NPs cytotoxicity evaluated by neutral red assay (2 hours of exposure)

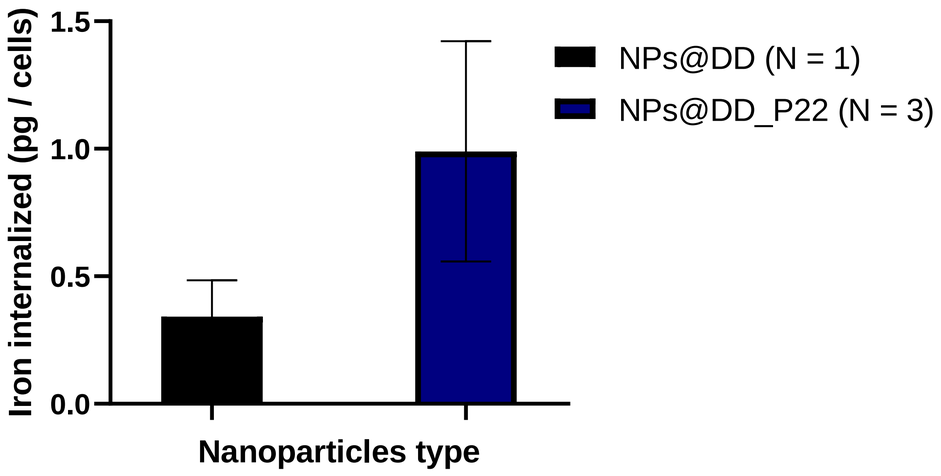


NPs@DD cytotoxicity evaluated by LDH release assay



Internalization study

Iron internalized by MDA-MB-231 cells after 24h exposure of 50 µg/mL nanoparticles



After 24 hours exposure to 50 µg/mL iron, MDA-MB-231 cells have internalized :

- IONPs@DD_P22 : 1,72 ± 0,08 pg_{iron} / cell
- IONPs@DD : 0,34 ± 0,14 pg_{iron} / cell

Discussion

Considering the number of replicates, it seems that :

- Peptide 22 is a good candidate to increase IONPs internalization into MDA-MB-231. However, this value could be greater as compared to litterature.
- IONPs synthesis will be modified in order to increase the number of targeting ligands on the NPs surface.
- Our IONPs are not toxic below 150 µg/mL, after 2 hours of incubation.
- For next steps, we won't use more concentrated solutions.
- More measurements must be done at exposure times up to 24h.

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References

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