NANOTECHNOLOGIES

UTAustin Portugal

Targeted and externally controlled nanotheranostics of triple-negative-breast-cancer

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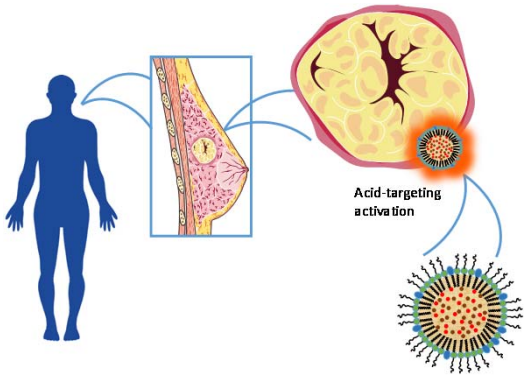
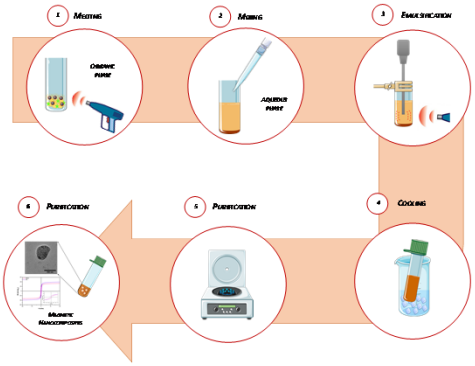
Background

Triple-negative breast cancer (TNBC) is often among the highest-grade and poorer prognosis breast cancers, mainly because targeted therapy is not available. Therefore, there is an urgent demand to discover specific targets and develop novel targeted therapies as well as early diagnostic methods. The main objective of this project is to ameliorate the prognosis of TNBC through the preparation and preclinical validation (in vitro plus in vivo) of a targeted theranostic nanoparticle/probe that is able to specifically recognize tumor-associated macrophages (TAMs), offering a non-invasive imaging capability by MRI together with a synergic magnetic hyperthermia (MH) and chemotherapy treatment against TNBC.



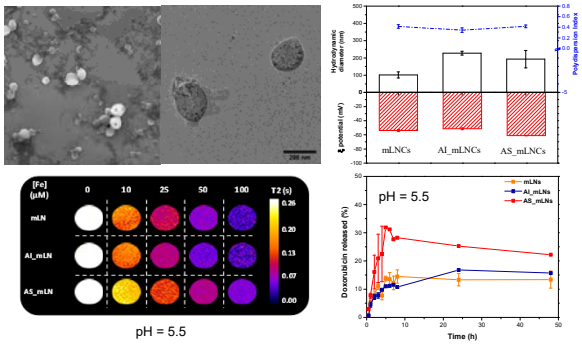
Methodology

At this point of the project, water colloidally stable targeted drug-loaded magnetic hybrid lipid nanocomposites (mLNCs) were prepared by a simple, versatile and scalable melt-emulsification method. Doxorubicin (DOX)-loaded magnetic hybrid nanocomposites (mLNCs-DOX) have been developed, fully characterized and functional validated (i.e. MRI, MH and drug release). In order to promote the active targeting of the theranostic probe in the tumor area, a strategy based on the functionalization of the hybrid nanoparticles with a mixture of responsive ligands is followed to target TAMs. In vitro and in vivo studies are also planned to validate the potential of these formulations as theranostic drugs.



Results

mLNCs were successfully prepared using a mixture of responsive ligands showing a size, polydispersity index and stability suitable for biomedical applications. Their encapsulation and loading efficiency of DOX (EE >95%, LE >80%) and magnetic nanoparticles (EE >99%, LE~15%) were optimized to allow a combined use as diagnostic and therapeutic probes. Increased drug release levels and high values of relaxivity (~500 $mM^{-1}s^{-1}$) confirm the high potential of these acidic-sensitive functionalized formulations as localized theranostic agents at the tumor site.



pH = 5.5

Impact

At the end of the funding period, we expect to have an in vitro and in vivo validated theranostic probe showing imaging and multi-treatment capabilities against TNBC. These expected results will enable future translational research and will be the key in the advance towards an adequate and timely therapeutic intervention in patients with TNBC, being also a step forward on the way to targeted, image-guided therapies of cancer.

Conclusions

Targeted lipid-based nanoparticles were loaded simultaneously with magnetic nanoparticles and an anticancer drug. A strategy based on the functionalization of the hybrid nanoparticles with a mixture of responsive ligands was followed to target tumor associated macrophages (TAMs). Final formulations showed excellent properties in terms of drug encapsulation and delivery and as T_2-contrast agents in MRI. In vitro and in vivo validations are ongoing.

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