Functionalized multi-responsive protein nanoparticles for cancer theranostics

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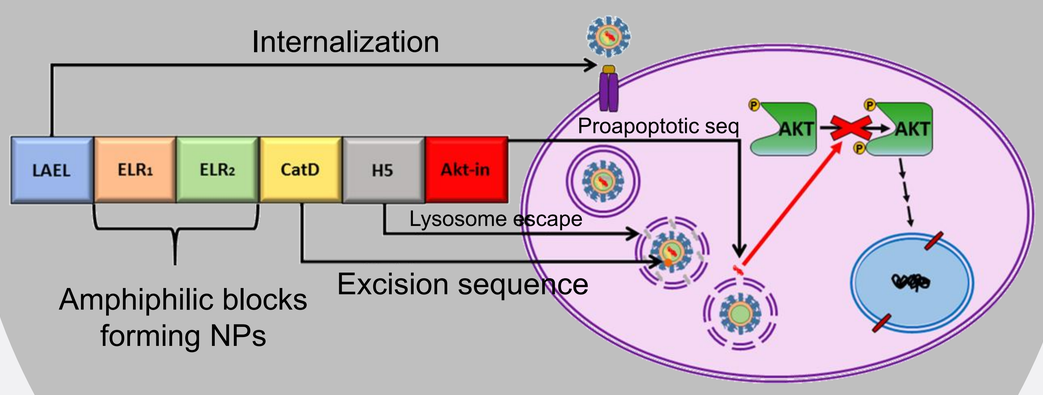
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INTRODUCTION

Cancer causes 19.3 million newly diagnosed cases and nearly one in six deaths worldwide. Therefore, prevention, early diagnosis, screening, and management are hard challenges for a longer life expectancy globally. Despite the promising results of chemotherapeutic drugs and personalized immunotherapy, **groundbreaking strategies** are **still needed**. Biomaterials are promising agents for improving disease imaging and targeted drug delivery. Among this wide variety of biomaterials, Elastin-like recombinamers (**ELR**s) highlight due to their unique excellent **biocompatibility**, **multi-responsive behavior,** and **self-assembling**. In this work, we explore radiolabeled ELR nanoparticles carrying an inhibitor of Akt kinase for tumor imaging and treatment.

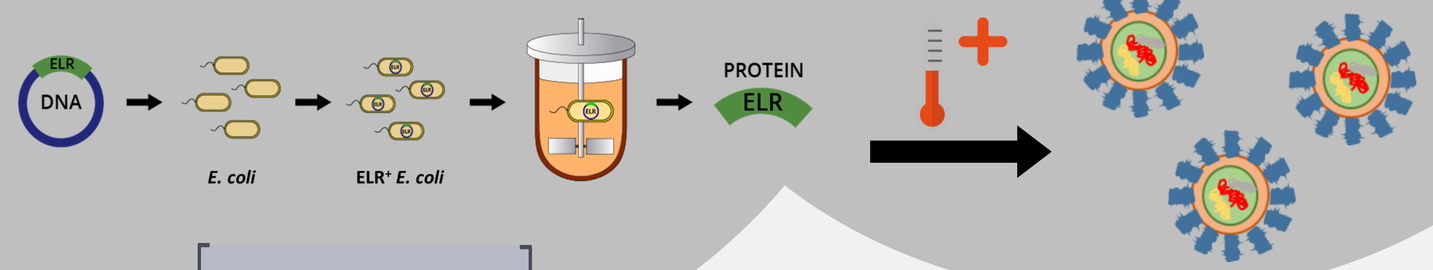
Design of multi-stimuli responsive nanoparticles



Control LAEL | E50 | I60

Akt-in LAEL | E50 | I60 | CatD | H5 | Akt-in

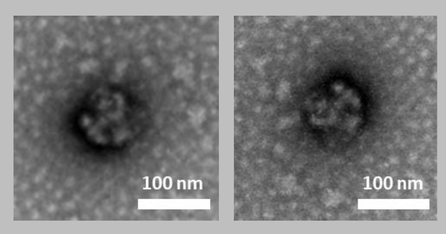
Bioproduction

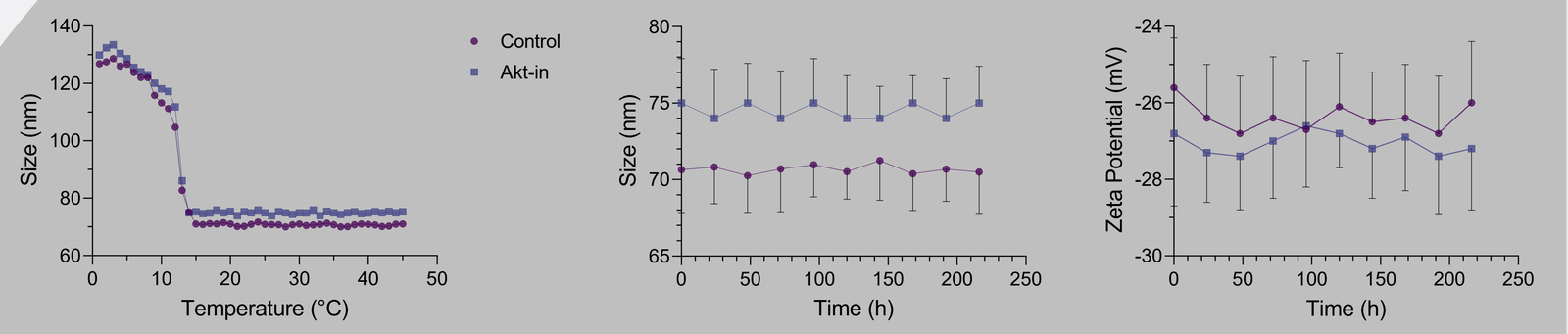


RESULTS

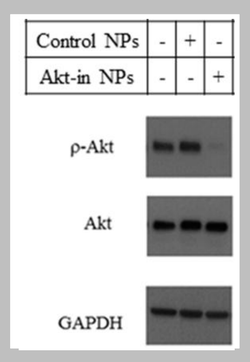
Nanoparticles characterization

Nanoparticles **self-assemble** above **15ºC** and present high stability over time, with **70-75 nm size** and negative surface charge (**-27 mV**).

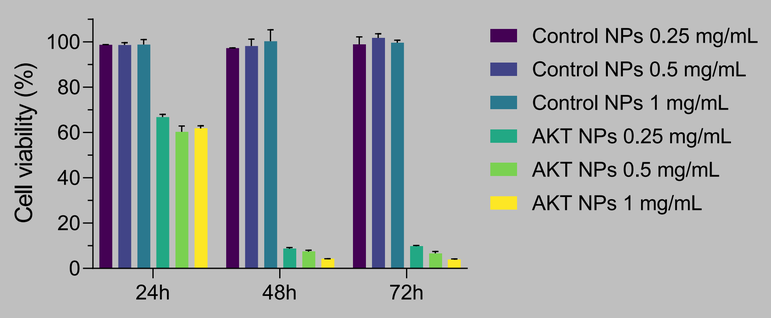




In vitro inhibition of Akt phosphorylation and cytotoxicity

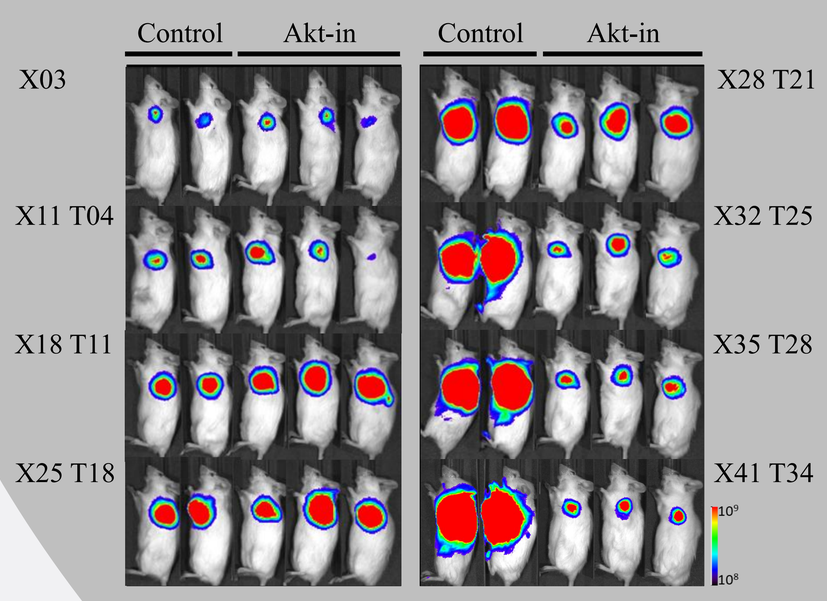


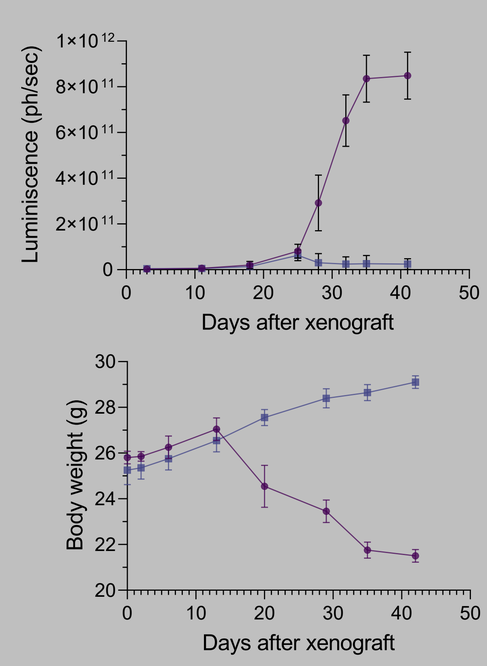
Akt phosphorylation in GBM248 cells is markedly **diminished** after incubation **with Akt-in nanoparticles**.



Control nanoparticles don't affect **cell viability** of GBM248 cells, whereas therapeutic nanocarriers carrying the **Akt inhibitor** show **dose-dependent effect**.

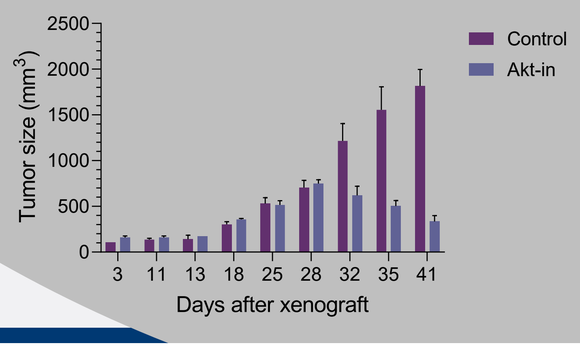
In vivo biodistribution and anti-tumor effect

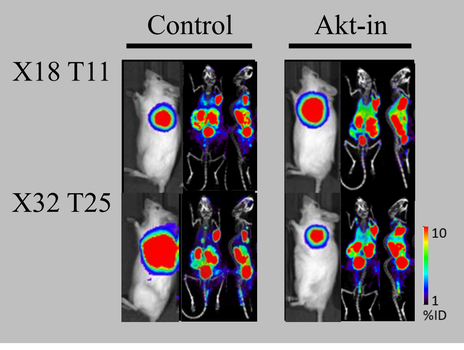




Therapeutic nanoparticles reduce tumor growth in mice.

Radiolabeled nanoparticles with ^{18}F are **localized in** the **tumor** with minimum uptake in healthy tissues.





METHODS

- ELR polymers are designed by **recombinant DNA technology**, based on an amphiphilic backbone with multiple bioactive sequences.
- Nanoparticles are characterized by **DLS** and **TEM**. ***In vitro*** **citotoxicity** is evaluated in GBM248 cells.
- ***In vivo*** biodistribution is determined by **IVIS** and **PET/CT scanning**.

CONCLUSIONS

- Our complex nanosystem allows us to achieve selective **controlled release** of Akt inhibitor in cancer cells and **reduced tumor growth** in an animal model.
- These smart nanoparticles could lead to the development of **more effective theranostic options** against cancer focused on Akt inhibition.

References

1. https://www.iarc.who.int/
2. Shi *et al*., *Nat. Rev. Cancer* (2017)
3. Gonzalez-Valdivieso *et al*., *ACS Appl. Mater. Interfaces* (2021)
4. Gonzalez-Valdivieso *et al*., *Biomacromolecules* (2019)

Acknowledgements

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