Mesoporous Silica Nanoparticles for Combined ^{19}F MRI Imaging and Boron Neutron Capture Therapy (BNCT)

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Melanoma is one of the most aggressive cancers, known for its ability to develop resistance to conventional therapies. Most melanoma cells exhibit radio- and chemoresistance and rapidly acquire resistance to targeted therapies. Despite advances in understanding melanoma biology and continuous improvements in treatment strategies, the prognosis remains poor for advanced cases.**[1]** Boron Neutron Capture Therapy (BNCT) presents a promising approach for melanoma treatment. This therapy involves the administration of molecules containing the ^{10}B isotope, which can absorb irradiated neutrons and release short-range ionizing radiation, selectively damaging cancer cells that have previously accumulated the boron compound. However, due to the low intratumoral concentration of currently approved compounds, there is a need to develop trackable boron-based drugs that can achieve higher tumor accumulation.**[2]**

To address these challenges, we propose a nanoplatform (NP) based on mesoporous silica nanoparticles (MSN) with a core-shell structure encapsulating a perfluoro-crown ether (PFCE) emulsion, which provides a ^{19}F MRI quantitative signal. The NP is tailored for BNCT through its functionalization with borocaptate (BSH) modified organosilane synthesized in our laboratory. The optimized nanoparticles are stabilized by a polyethylene glycol (PEG) coating, which enhances their stability in physiological fluids and culture media while preventing premature elimination by mononuclear phagocytic cells in vivo.

The nanoparticles' physicochemical properties were characterized using various techniques, including dynamic light scattering (DLS), transmission electron microscopy (TEM), ^{1}H and ^{19}F NMR/MRI, inductively coupled plasma (ICP) analysis, Thermogravimetric analysis (TGA) and Fourier-transform infrared (FT-IR) spectroscopy. The cytotoxicity of the NP was evaluated using MTT assays on the A375 melanoma cell line.

To enhance their specificity, the nanoparticles will be functionalized with an RGD peptide targeting integrins, which are frequently overexpressed on cancer cells.**[3]** The next steps of the project include in vitro studies of nanoparticle internalization pathways and accumulation in 2D and 3D melanoma (A375) and fibroblast (HDF) cell models, followed by in vitro neutron irradiation tests and in vivo biodistribution analysis in murine models.

In summary, this project aims to demonstrate the feasibility of using our nanoparticles for BNCT, offering a promising approach to cancer treatment by enabling quantifiable intratumoral boron accumulation with reduced side effects.

[1] : PDQ Adult Treatment Editorial Board. *Melanoma Treatment (PDQ®). Health Professional Version*; National Cancer Institute (US): Bethesda, MD, USA, 2002.
[2] : International Atomic Energy Agency. *Advances in Boron Neutron Capture Therapy*; IAEA: Vienna, 2023.
[3] : Gu, Y.; Dong, B.; He, X.; Qiu, Z.; Zhang, J.; Zhang, M.; Liu, M.; Pang, X.; Cui, Y. The Challenges and Opportunities of αvβ3-Based Therapeutics in Cancer: From Bench to Clinical Trials. *Pharmacol. Res.* 2023, *189*.