Development of nanomedicines for boron neutron capture therapy

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Boron Neutron Capture Therapy (BNCT) is a binary approach to cancer therapy based on the ability of Boron-10 (^{10}B) to capture thermal neutrons, which results in the $^{10}B(n, \alpha, \gamma)^{7}Li$ nuclear reaction. Alpha particles and ^{7}Li recoil ions have high linear energy transfer properties and path lengths in the range of the diameter of a single cell. Hence, if cancer cells selectively take up a sufficient amount of ^{10}B and are irradiated with thermal neutrons, the alpha particles and ^{7}Li ions result in cellular damage and trigger cell death, while sparing healthy surrounding tissue.

During decades, different molecular modalities have been proposed as BCNT drug candidates, including boronated carbohydrates, amino acids, peptides, nucleic acids and immunoconjugates [1]. However, and in spite of huge efforts, only two compounds, i.e. sodium borocaptate (BSH) and p-boronophenylalanine (BPA), are currently approved for clinical trials, and they show low specificity. The recent emergence of nanotechnology has opened new avenues to achieve preferential delivery of boron atoms in tumours taking advantage of the well-known enhanced permeability and retention (EPR) effect, which is based on the presence of leaky vasculature and deficient lymphatic drainage in the vicinity of tumours. This, ultimately, results in a passive accumulation of non-targeted nanosized materials in tumour tissue after intravenous administration. In the last years, a plethora of nanostructured materials have been assayed as boron delivery agents, including liposomes, carbon nanotubes, boron nitride nanotubes, magnetic nanoparticles, boron carbide nanoparticles, borosilicates and functionalized gold nanoparticles.

Here, we will present our recent advances in the development of different boron-rich nanosized materials that could be used for BNCT, including functionalized gold nanoparticles and micelles. The preparation methods will be described and discussed. Additionally, radiolabelling strategies to assess the capacity of the novel nanosystems to reach different tumor types by means of in vivo positron emission tomography will be presented. In vivo data could not only predict the therapeutic efficacy of novel BNCT agents, but also identify the optimal time window for neutron irradiation application.

References

[1] V. I. Bregadze, I. B. Sivaev, in Boron Science: New Technologies and Applications (2016) 181-207

Figures

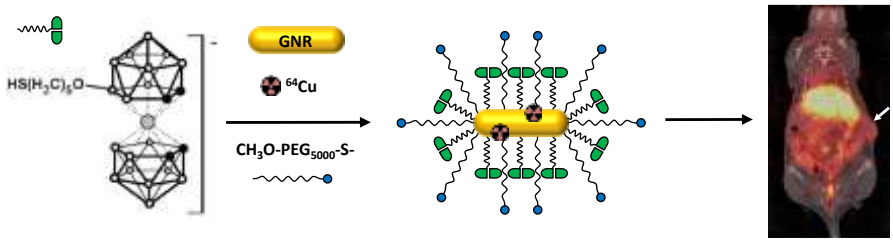

Figure 1: Schematic representation of the synthesis/radiolabelling of boron-rich gold nanorods (GNRs) and their in vivo evaluation in a mouse model using Positron Emission Tomography.