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Host: Dr. Jordi Llop

A pre-targeting approach to boron neutron capture therapy: towards multipurpose boron-enriched therapeutic agents

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Boron neutron capture therapy (BNCT) is a binary approach for cancer treatment in which boron-10 atoms and thermal neutrons need to colocalize to become effective. Recent research in the development of BNCT drug candidates focuses increasingly on nanomaterials, with the advantages of high boron loadings and passive targeting due to the enhanced permeability and retention (EPR) effect. The use of small nanoparticles (NPs), such as gold nanoparticles (AuNPs) and boron carbon dots (B-CDs), in combination with a pretargeting approach is proposed. The particles were synthesized, boron loaded and functionalized with tetrazine. To enable *in vivo* tracking of the NPs by positron emission tomography (PET), labelling with either ^{64}Cu (AuNPs) or ^{18}F (B-CDs) was performed. For the pretargeting approach, the monoclonal antibody Trastuzumab was functionalized with trans-cyclooctene-N-hydroxysuccinimide ester (TCO-NHS). The boron delivery system was evaluated *in vivo* using breast cancer xenograft bearing mice and PET imaging. For the AuNPs tumor uptake due to the EPR effect could be witnessed with $\approx 5\% \text{ID cm}^{-3}$ at 24 h postinjection, but no increased retention could be observed using the pretargeting strategy. For B-CDs instead, fast clearance from tumor tissue could be witnessed in the control group, but enhanced tumour accumulation was achieved when using the pretargeting approach.