KALOT-1: Aza-BODIPY: a new vector for enhanced theranostic Boron Neutron Capture Therapy applications

Ghadir Kalot [1‡], Amélie Godard [2‡], Benoît Busser [1,3], Jacques Pliquett [2], Mans Broekgaarden [1], Vincent Motto-Ros [4], Ulli Köster [5], Franck Denat [2], Jean-Luc Coll [1], Ewen Bodio [2*], Christine Goze [2,*] and Lucie Sancey [1,*]

1 *Institute for Advanced Biosciences, UGA INSERM U1209 CNRS UMR5309, 38700 La Tronche, France; Ghadir.kalot@univ-grenoble-alpes.fr; mans.broekgaarden@univ-grenoble-alpes.fr; jean-luc.coll@univ-grenoble-alpes.fr;*

Corresponding author: *lucie.sancey@univ-grenoble-alpes.fr*

[2] *Institut de Chimie Moléculaire de l'Université de Bourgogne, UMR 6302, CNRS, Université Bourgogne Franche-Comté, 21078 Dijon, France; amelie_godard@etu.u-bourgogne.fr; jacques.pliquett@googlemail.com; franck.denat@u-bourgogne.fr; ewen.bodio@u-bourgogne.fr; Christine.goze@u-bourgogne.fr*

[3] *Grenoble Alpes University Hospital 38043 Grenoble, France; bbusser@chu-grenoble.fr*

[4] *Institut Lumière Matière UMR 5306, Université Lyon 1 - CNRS, Université de Lyon 69622 Villeurbanne, France; vincent.motto-ros@univ-lyon1.fr*

[5] *Institut Laue Langevin 38042 Grenoble, France; koester@ill.fr*

Abstract: Boron Neutron Capture Therapy (BNCT) is a radiotherapeutic modality based on the nuclear capture of slow neutrons on stable ^{10}B atoms followed by charged particle emission inducing extensive damage on a very localized level (<10 µm). To be efficient, a sufficient amount of ^{10}B should accumulate in the tumor area, while it should be almost cleared from the normal surroundings. A water-soluble aza-BODIPY fluorophore was reported to strongly accumulate in the tumor area with high and BNCT compatible Tumor/Healthy Tissue ratios. We coupled the clinically used ^{10}B-BSH to the water-soluble aza-BODIPY platform for enhanced ^{10}B-BSH tumor vectorization. We demonstrated a strong uptake of the compound in tumor cells, and we determined its biodistribution in mice-bearing tumors. We developed a model of chorioallantoic membrane-bearing glioblastoma xenograft to evidence the BNCT potential of such compound, by subjecting it to slow neutrons. We demonstrated the tumor accumulation of the compound in real-time using optical imaging, and *ex vivo* using elemental imaging based on laser-induced breakdown spectroscopy. We reduced significantly tumor growth as compared to BNCT with ^{10}B-BSH. Altogether, the fluorescent aza-BODIPY/^{10}B-BSH compound is able to vectorize and image the ^{10}B-BSH in the tumor area, increasing its theranostic potential for efficient approach of BNCT.