UNIVERSITÄT LEIPZIG

Selective BB_2 Receptor Agonist for BNCT

Carborane Conjugates for Boron Neutron Capture Therapy (BNCT) of Breast, Prostate and Small-cell Lung Cancer

IDEA

Selective cell-targeting of breast, prostate and small-cell lung tumors for BNCT by combining a specifically peptidic human BB_2 receptor agonist bearing carboranes for high boron loading

DEMONSTRATOR

Activation of the human BB_2 receptor, resulting in internalization of the receptor into HEK293 cells transfected with the human BB_2 receptor

PROTOTYPE

In preparation

BACKGROUND/ MEDICAL PROBLEM

Since cancers of the breast, prostate and the lung are amongst the most common cancers in women and men worldwide, there is a substantial need for treatment and boron neutron capture therapy (BNCT) could be an alternative to the traditional radiation-, chemo-therapy or surgery. BNCT allows the non-invasive treatment of cancer on a cellular level by cell specific elimination of malignant cells. Requirement for this binary approach is the administration of a tumor-seeking drug containing a non-radioactive isotope with a high neutron cross section. Following this, the tumor will be irradiated locally with low energy neutrons that induce a nuclear fission reaction. The excited $^{11}B^*$ nuclides are instable and decompose in high linear energy transfer (LET) ^4He and ^7Li particles. Due to limited path lengths of the particles in tissue (5-9 µm), the destructive effects of those is limited to boron containing cells. To achieve sufficient results, a very selective boron accumulation of 5 – 20 µg/g tumor is needed.

POTENTIAL APPLICATION

- Non-invasive BNCT treatment of prostate-, breast- and small-cell lung cancer

ADVANTAGES

- Highly specific peptidic BB_2 receptor agonists (up to sixteen carborane units per peptide unit)
- High accumulation of boron in BB_2 receptor expressing cells
- Compounds can be converted to pharmaceutically acceptable salts

Project 19001

TECHNOLOGY OFFER

Picture: Colourbox

TECHNOLOGY/SOLUTION

One very promising receptor to be addressed is the gastrin releasing peptide receptor (BB_2, GRPR). It is part of the bombesin receptor family consisting of three G protein-coupled receptors (BB_1; BB_2; BB_3) widely expressed in brain and peripheral tissues. BB_2-receptor is significantly overexpressed in prostate- and breast cancer tissues.

We therefore generated highly selective peptide drug conjugates, which are modified with carboranes. Carboranes are boron clusters that consist of ten boron and two carbon atoms. They are stable under biological conditions. All compounds showed great receptor activation efficacy. Even the compounds with the highest boron loading (up to sixteen carborane units per peptide unit) were effectively internalized into HEK293 cells expressing the BB_2 receptor.

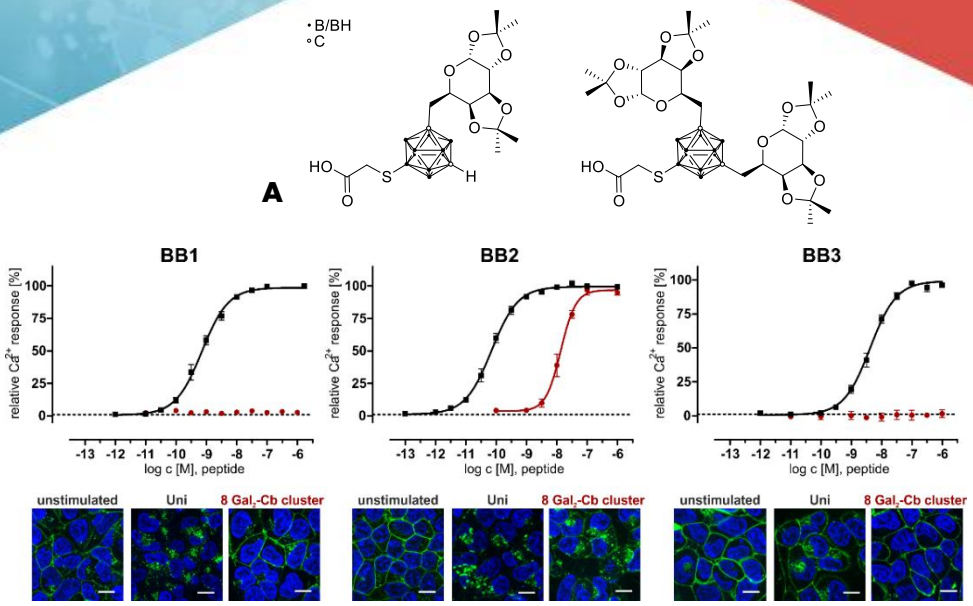

Figure
A Saccharide functionalized *meta*-carborane derivatives as boron-rich coupling partners for the selective BB_2 receptor agonist.
B Selective signal transduction and internalization of a selective bombesin derivative modified with eigth Gal_2-Cb clusters.

FURTHER READING:

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Frank et al., *Polyhedron 2012, 39, 9-13*

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Frank et al., *J. Organomet. Chem. 2015, 798, 46-50*

(DOI: 10.1016/j.jorganchem.2015.08.011)

STATUS OF PROPRIETARY RIGHTS

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COOPERATION OPTIONS

- R&D Agreement
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