## Chlorotoxin

Chlorotoxin (CTX) is a small, 36 amino acid neurotoxin isolated from the venom of the Giant Yellow Israeli scorpion Leiurus Quinquestriatus.

Chlorotoxin-tagged cells isolated by flow cytometry and cultured up to two passages exhibit positive labeling for GFAP and vimentin, but not for prolyl 4-hydroxylase (fibroblast), A2B5 (O2A progenitor), or OX-42 (microglia). Expression of a novel chlorotoxin-sensitive Cl(Ca) channel in a morphologically distinct subpopulation of NRAs distinguishes these cells as a new subtype of reactive astrocyte <sup>1)</sup>.

Interestingly, the peptide has been found to preferentially bind to a variety of human malignancies, but shows little or no binding to normal human tissues. A synthetic version of this peptide (TM-601) has been manufactured and covalently linked to iodine 131 (131I-TM-601) as a means of targeting radiation to tumor cells. Preclinical studies and Phase I clinical trials have been completed in patients with recurrent glioma, a type of malignant brain tumor. These studies demonstrated that intracavitary dosing of 131I-TM-601 appears safe, minimally toxic, and binds malignant glioma with high affinity and for long durations. A Phase II trial of this agent using higher doses of radioactivity and repeated local administrations is underway. In addition, enrolment has begun in a Phase I trial evaluating whether systemically delivered 131I-TM-601 can be used to image metastatic solid tumors and primary gliomas. Due to its small size, selective tumor binding properties, minimal toxicity and relative ease of manipulation, CTX represents a potentially important targeting agent for many cancers<sup>2</sup>.

Further modification of this radiopeptide with other better imaging isotopes may provide an important tool for determining tumor extent and differentiating regions of viable tumor from necrosis <sup>3)</sup>.

Superparamagnetic iron oxide nanoparticle (SPIO)-fluorescein isothiocyanate (FITC)-chlorotoxin (SPIOFC) is suitable for the specific and efficient targeting of glioma cells. MRI and optical imaging in conjunction with SPIOFC can differentiate glioma cells from normal brain tissue cells <sup>4</sup>.

Tumor Paint BLZ-100, a tumor ligand chlorotoxin (CTX) conjugated to indocyanine Green (ICG), has shown potential to be a targeted contrast agent. There are many infrared imaging systems (NIR) in use, but they are not optimized to the low concentration and amount of ICG

BLZ-100 has a very high affinity toward human gliomas. They also describe a small, cost-effective, and sensitive NIR system for visualizing brain tumors tagged using BLZ-100. Butte et al. hope that the use of BLZ-100 along with NIR imaging will be useful to delineate the brain tumors in real-time and assist surgeons in near-complete tumor removal to increase survival and reduce neurological deficits <sup>5)</sup>.

## 1)

Dalton S, Gerzanich V, Chen M, Dong Y, Shuba Y, Simard JM. Chlorotoxin-sensitive Ca2+-activated Clchannel in type R2 reactive astrocytes from adult rat brain. Glia. 2003 Jun;42(4):325-39. PubMed PMID: 12730953.

Mamelak AN, Jacoby DB. Targeted delivery of antitumoral therapy to glioma and other malignancies with synthetic chlorotoxin (TM-601). Expert Opin Drug Deliv. 2007 Mar;4(2):175-86. Review. PubMed PMID: 17335414.

Hockaday DC, Shen S, Fiveash J, Raubitschek A, Colcher D, Liu A, Alvarez V, Mamelak AN. Imaging glioma extent with 131I-TM-601. J Nucl Med. 2005 Apr;46(4):580-6. PubMed PMID: 15809479.

## 4)

Meng XX, Wan JQ, Jing M, Zhao SG, Cai W, Liu EZ. Specific targeting of gliomas with multifunctional superparamagnetic iron oxide nanoparticle optical and magnetic resonance imaging contrast agents. Acta Pharmacol Sin. 2007 Dec;28(12):2019-26. Erratum in: Acta Pharmacol Sin. 2008 Feb;29(2):176. PubMed PMID: 18031618.

Butte PV, Mamelak A, Parrish-Novak J, Drazin D, Shweikeh F, Gangalum PR, et al: Near-infrared imaging of brain tumors using the Tumor Paint BLZ-100 to achieve near-complete resection of brain tumors. Neurosurg Focus 36(2):E1, 2014

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