

Comparative preclinical evaluation of ⁶⁸Ga-labelled Neuromedin N and B for targeting glioblastoma malignant tissues

Neuromedin N is a hexapeptide that shares the 4 amino acid Pro-Tyr-Ile-Leu homology with neurotensin and exhibits neurotensin-like effects in malignant glioma cells. Neuromedin B is a bombesin-like peptide which specifically binds to BN receptors widely expressed in central nervous system and in peripheral tissue and organs. This study was aimed to select and characterize the most effective Neuromedin peptide to target glioblastoma U87MG cancer cells.

DOTA-Neuromedin N and B were labelled with ⁶⁸Ga obtained from a ⁶⁸Ge/⁶⁸Zn generator, in order to quantify their ability to bind to their specific receptors expressed on glioblastoma U87MG cancer cells. The selective binding of peptides was characterized and their binding capacity towards NT receptors and BN receptors previously reported on U87MG cell line was tested. The influence of synthesis parameters like reaction time, evaporation time and pH upon overall process indicators and quality parameters of the final product were studied. The synthesis method has been translated to an automated synthesis module, which lead to a shortening of the process time, consistent high yields (>85%) and radiochemical purity greater than 90% for both radiotracers. The stability of the radiolabelled peptides was assessed up to 4h post-synthesis. Comparative preclinical in vitro assay of the cellular uptake-retention curves on U87MG cancer cells was performed in order to determine the time from incubation and peptide concentration at which the receptors are saturated, and to evaluate the retention profile over time. Specific binding of both peptides was characterized by selectively antagonized receptors blocking with SR 142948/48692 and NTRC 824 antagonists for neurotensin receptors and PD 176252/ML18 for bombesin receptors respectively. The results showed over 60% retention of ⁶⁸Ga-DOTA-Neuromedin B stable up to 80 minutes from incubation and more than 50% retention for ⁶⁸Ga-DOTA-Neuromedin N. The preliminary in vivo investigations (biodistribution and ¹⁸F-PET imaging) using both ⁶⁸Ga-DOTA-Neuromedin B and ⁶⁸Ga-DOTA-Neuromedin N on glioblastoma bearing mice, at 30 min and 60 minutes post-injection, have shown promising results for glioma malignant tissues imaging.

This work was supported by a grant of the Romanian Ministry of Research and Innovation UEFISCDI project number 64PCCDI/2018.

Primary authors: Ms CHILUG, E. Livia (1 Horia Hulubei National Institute for R&D in Physics and Nuclear Engineering, Radiopharmaceutical Research Center, 2 University Politehnica of Bucharest, Faculty of Applied Chemistry and Materials Science); Dr NICULAE, Dana (Horia Hulubei National Institute for R&D in Physics and Nuclear Engineering, Radiopharmaceutical Research Center)

Co-authors: Dr LEONTE, Radu Anton (Horia Hulubei National Institute for R&D in Physics and Nuclear Engineering, Radiopharmaceutical Research Center); Dr MANDA, Gina ("Victor Babes" National Institute of Pathology); Mr MUSTACIOSU, Cosmin (1 Horia Hulubei National Institute for R&D in Physics and Nuclear Engineering, Radiopharmaceutical Research Center, 2 University Politehnica of Bucharest, Faculty of Applied Chemistry and Materials Science); Prof. LAVRIC, Vasile (University Politehnica of Bucharest, Faculty of Applied Chemistry and Materials Science)

Presenter: Ms CHILUG, E. Livia (1 Horia Hulubei National Institute for R&D in Physics and Nuclear Engineering, Radiopharmaceutical Research Center, 2 University Politehnica of Bucharest, Faculty of Applied Chemistry and Materials Science)

Session Classification: Poster Session