Contribution ID: **27** Type: **Poster**

Orthogonal Click Chemistry for Synthesis of Dual-targeting Agents Towards αvβ3 Integrin and Folate Receptors for Molecular Imaging

Thursday, 2 May 2019 17:26 (6 minutes)

Folate-based radiopharmaceuticals were applied for targeting the folate receptor (FR) positive malignant tissue while cyclic Arg-Gly-Asp (c(RGD)) peptides were used to target αvβ3 integrin which is overexpressed during tumor angiogenesis. Combination of these two different targeting motifs in one molecule could be utilizable for dual-targeting. Here, we present the introduction of folate and c(RGD) motifs to chelator fusarinine C (FSC) in a "one-pot"employing orthogonal "click"reactions. All heterobivalent compounds were then evaluated for dual-targeting of FR and αvβ3 integrin.
Starting with [Fe]FSC functionalized with alkyne and maleimide, thiol-maleimide click reaction with c(RGDfK)-(PEG)4-SH was performed, followed by Cu(I) catalyzed azide-alkyne cycloaddition (CuAAC) with folate-(PEG)3-N3 and subsequent iron removal. Stability, binding affinity (IC50), distribution coefficient (logD) and protein binding were investigated. Internalization assays were performed in FR-positive cancer cells (KB) and human melanoma αvβ3-positive cells (M21).
Orthogonal click reactions were successfully applied for a one-pot synthesis of heterobivalent conjugates. Products were obtained in moderate yields and could be radiolabeled with [68Ga] in quantitative radiochemical yields. All conjugates revealed high hydrophilicity (logD = -3.46 to -3.83) and low protein binding. Dimeric c(RGDfK) and dimeric (folate) conjugates showed higher specific uptake in vitro than monomeric counterparts. Biodistribution studies and microPET/CT imaging in tumor-bearing mice are ongoing.
This study shows the possibility of applying orthogonal click reactions for introducing different targeting vectors to one chelator scaffold in a one-pot synthesis with high selectivity and without purification in each step. This finding may stimulate new strategies for designing the dual-targeting agents for diagnostic, therapeutic, and theranostic applications.

Primary author: Mrs KAEOPOOKUM, Piriya (Dept. Nuclear Medicine, Medical University Innsbruck)

Co-authors: Dr SUMMER, Dominik (Dept. Nuclear Medicine, Medical University Innsbruck); Prof. ROSS, Tobias (Department of Nuclear Medicine, Radiopharmaceutical Chemistry, Hannover Medical School); Dr REFFERT, Laura (Department of Nuclear Medicine, Radiopharmaceutical Chemistry, Hannover Medical School); Dr RANGGER, Christine (Department of Nuclear Medicine, Medical University Innsbruck); Dr HAUBNER, Roland (Department of Nuclear Medicine, Medical University Innsbruck); Prof. HAAS, Hubertus (Division of Molecular Biology, Biocenter, Medical University Innsbruck); Prof. DECRISTOFORO, Clemens (Department of Nuclear Medicine, Medical University Innsbruck)

Presenter: Mrs KAEOPOOKUM, Piriya (Dept. Nuclear Medicine, Medical University Innsbruck)

Session Classification: Posters Session

Track Classification: Preclinical research and development of new radiopharmaceuticals