BIOTINYLATED AND CHELATED POLY-L-LYSINE AS EFFECTOR FOR PRETARGETING IN CANCER THERAPY AND IMAGING

Abstract:
Objective: The aim of this study was to synthesise and evaluate polylysine-based effectors for pretargeted radioimmunotherapy and imaging. These molecules can readily be size-modified and charge-modified to decrease the renal uptake of radioactivity, which is often a major problem for small radiolabeled molecules. Several chelators and biotin molecules (for antibody-streptavidin-binding in vivo) are also easily incorporated into one structure because of the polylysine. Methods: The effectors were synthesised using poly-L-lysine, NHS-LC-biotin, CHX-A’’-DTPA or p-SCN-Bn-DOTA and succinic anhydride. They were characterised, labelled with 213Bi for targeted α therapy, 68Ga for PET and 111In for SPECT, and evaluated in vitro. A kidney uptake study was performed as well with two different-sized 213Bi-labeled effectors, to evaluate how the difference in size affects the renal filtration. Results: Radiochemical purities between 97.4±0.6 % and 99.6±0.1 % and decay-corrected yields of 80.2±2.4 % after purification were achieved with the radiolabeled molecules, as well as a specific activity of 7.6 × 103GBq/μmol. The avidin binding capacity was 94.4±1.9%. The kidney uptake study demonstrated a reduction of renal absorbed dose by 80% when modifying the molecular size and charge. Conclusion: The synthesised polylysine-based effectors show potential for further in vivo evaluation in pretargeted radioimmunotherapy and imaging.

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Authors:
GUSTAFSSON-LUTZ Anna
BAECK Tom
ANEHEIM Emma
PALM Stig
MORGENSTERN Alfred
BRUCHERTSEIFER Frank
ALBERTSSON Per
LINDEGREN Sture

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