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Membrane interacting peptides as positron emission tomography (PET) based infection imaging probes

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Abstract

Objective:

Ubiquicidin (UBI) or ribosomal protein S30 (RS30) is a result of post-translational processing of a 133-amino-acid fusion protein Fau, consisting of an N-terminal 74-amino-acid polypeptide FUBI and the C-terminal 59 amino acid RS30 polypeptide also known as Ubiquicidin. Fragments derived from the RS30/ubiquicidin are known to detect bacteria *in-situ*. UBI (29-41) has been labeled with ^{99m}Tc as well as ⁶⁸Ga and ¹⁸F in order to develop single photon emission computed tomography (SPECT) agent and positron emission tomography (PET) based infection imaging agents respectively. A smaller fragment UBI (31-38) is also reported to show uptake in infectious foci. We set out to compare the potential of radiolabeled UBI (29-41) and UBI (31-38) fragments as PET based infection imaging probes with the aim of improving the sensitivity of detection.

To facilitate ⁶⁸Ga labeling, 1,4,7-triazacyclononane-1-glutaric acid-4,7-diacetic acid (NODAGA) conjugated peptide fragments UBI (29-41) and UBI (31-38) were utilized in the current study. Interaction of peptide conjugates was studied with bacterial as well as mammalian membranes models using isothermal titration calorimetry (ITC) and circular dichroism (CD). These peptide conjugates were labeled with ⁶⁸Ga in order to develop PET based infection imaging agent and tested for radiochemical purity (RCP), serum stability and invitro association with bacteria. Bio-distribution of the ⁶⁸Ga labeled peptides was carried out in mice bearing infection to understand the pharmacokinetics of these agents.

Results and discussion:

Both peptides selectively interacted with bacterial membrane model (anionic) and not with mammalian (neutral) membrane models. UBI (29-41) interacted more strongly with bacterial membrane model as compared to the octapeptide UBI (31-38). Stronger interaction of UBI (29-41) with bacterial membrane model could be explained by greater propensity to form helix in a "membrane like environment". Both peptide conjugates could be labelled with ⁶⁸Ga, with high RCP. ⁶⁸Ga labeled peptide conjugates were found to be comparable in terms of in-vitro association with bacteria and bio-distribution in mice bearing infection.

Conclusion: Our results indicate that NODAGA-UBI (29-41) was superior to NODAGA-UBI (31-38) with respect to binding to bacterial membranes.

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