Title Development of CD44v6-targeted radioconjugates for precision imaging of squamous cell carcinoma

Background (including references): CD44v6 is an antigen overexpressed in squamous cell carcinomas, especially in the head & neck region (1). We have previously assessed several targeting molecules towards this antigen for molecular imaging using PET (Positron emission tomography) with promising results (see for example refs 2, 3). Recently, two scFv's (single chain fragments) towards CD44v6 were selected and affinity maturated in collaboration with KI/KTH, demonstrating the best properties for molecular imaging that we have achieved so far (See ref 4). We now want to take this project further by optimizing and evaluating the two top candidate A11 and H12 for potential in molecular imaging of squamous cell carcinoma.

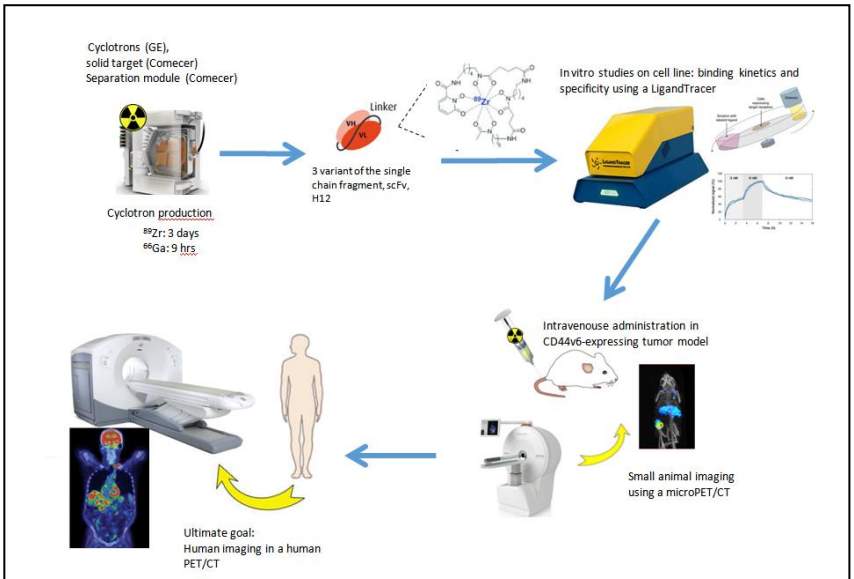

Illustration of the development of a radiopharmaceutical for molecular imaging with PET. The scope of this project includes the first 3 parts till in vitro evaluations.

Aim: To assess the CD44v6-targeting molecule H12 and/or A11 for potential in molecular imaging. This will be done by labeling the molecules with 89Zr (a radionuclide with a half-life of 3.3 days) (see ref 5, 6), and evaluating e.g. labeling yield, stability and specific activity of the conjugates, as well as characterizing antigen binding of the conjugates in vitro in CD44v6-expressing cell lines.

Methods: The project is going to be performed in 3 steps
1) Production and separation of 89Zr using the solid target on a cyclotron
2) Chelator conjugation and radiolabelling of three variants of the single chain fragment, H12 with 89Zr.
3) Evaluating labelling yield, stability and the in vitro binding specificity of the 89Zr-labelled H12 conjugates.

Significance
The long-term aim of this project is to find the optimal candidate for visualization of squamous cell carcinoma in the clinic, as a more cancer specific alternative to FDG-PET. This is needed especially in head & neck squamous cell carcinoma, where current methods are not good enough to separate local recurrence from tissue affected from radiotherapy. Furthermore, this technique can be used to detect occult tumors, metastases as well as monitoring treatment response. In the long run, we hope it will contribute to prolonged cancer patient survival.
Ethical approval is not needed for this project.

References

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2) Haylock et al Int J Oncol. 2016 Feb;48(2):461-70
3) Haylock et al: EJNMMI Res. 2014 Mar 6;4(1):11
4) Haylock AK, et al. Oncotarget. 2017 May 18;8(39):65152-65170
5) JP Holland et al. Nucl Med Biol. 2009 Oct; 36(7):729-739.

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