Development of cancer-targeting radioconjugates for precision imaging of squamous cell carcinoma

Location:
Dept of Radiopharmacy, Karolinska University Hospital / Dept of Clinical Neuroscience, Karolinska Institutet, Stockholm

Background:
CD44v6 is an antigen overexpressed in squamous cell carcinomas, especially in the head & neck region. We have previously assessed several targeting molecules towards this antigen for molecular imaging using PET (Positron emission tomography) with promising results. Recently, two scFv's (single chain fragments) towards CD44v6 were selected and affinity matured in a collaboration between UU, KI and KTH, demonstrating the best properties for molecular imaging that we have achieved so far.
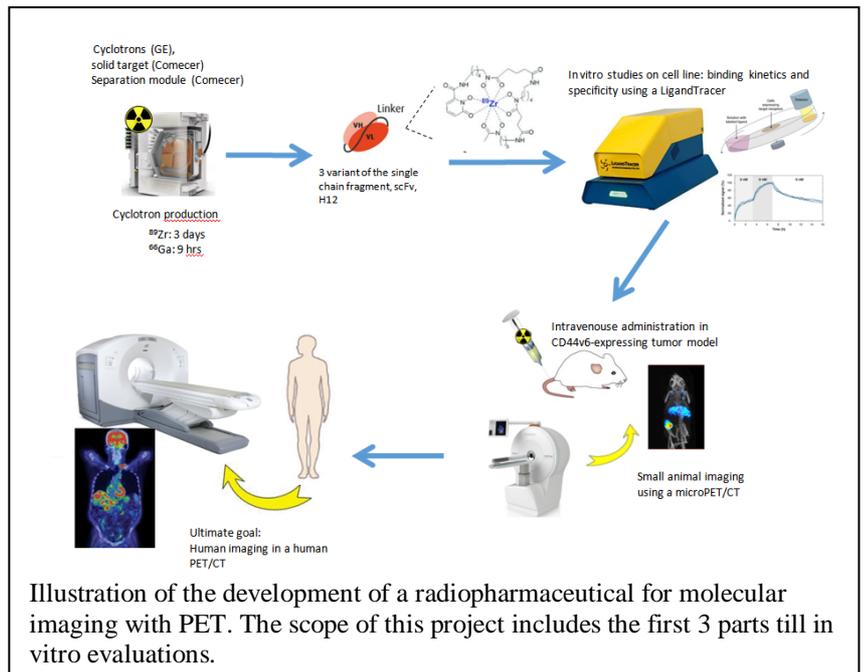

Illustration of the development of a radiopharmaceutical for molecular imaging with PET. The scope of this project includes the first 3 parts till in vitro evaluations.

We now want to take this project further by optimizing and evaluating the top candidate for potential in molecular imaging of squamous cell carcinoma.

Aim: To assess the CD44v6-targeting molecule H12 and two modified H12-variants 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), 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.

Workplan: 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 radiolabeling of 3 variants of the single chain fragment, H12 with 89Zr.
3) Evaluating labelling yield, stability and the in vitro binding specificity of the conjugates.
The student will be involved in and get familiar with all steps: radionuclide/isotope production on a cyclotron, conjugation and radiolabeling of molecules, handling of cells, running a Ligandtracer for cell studies. All necessary safety and radiation protection courses will be given to the student before start of work.

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.

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