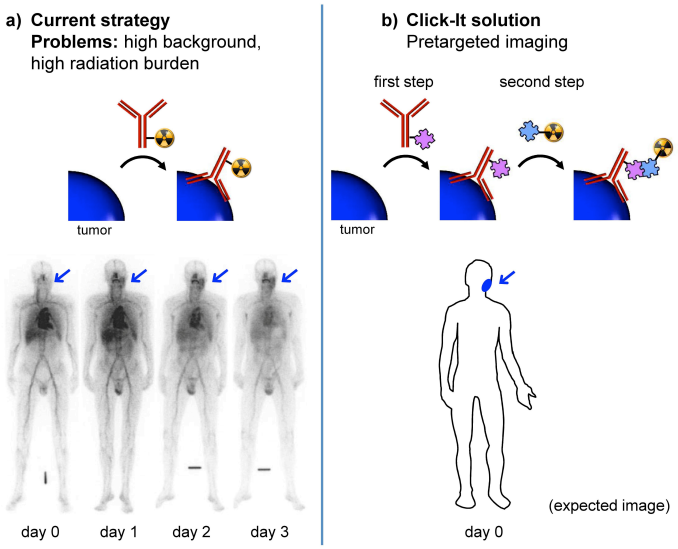
Pretargeted chemistry: Organic chemistry in man

Positron emission tomography (PET) companion diagnostic imaging can be used to select patients and monitor therapy. To date, there are **no technologies available** that allow **for the direct in vivo monitoring of slow clearing targeting vectors** as antibodies. These targeting vectors are crucial to diagnose or treat patients. Therefore, a possibility to follow the fate of these particles would help clinicians to tailor treatment.

This project aims to develop a technology that closes the aforementioned gap and develop a method for the direct in vivo monitoring of slow clearing targeting vectors. In this regard, a pretargeting approach will be applied that separates the targeting from the actual monitoring process. As a result, clinical acceptable patient radiation burden and a higher image quality will be achieved (Figure 1).

Pretargeted Chemistry Concept: A tagged nanomedicine such as a mAb is administered and allowed to bind to the target as the first step. Subsequently, a fast-clearing, short-lived radiolabeled imaging probe is administered. The imaging probe binds then to target-bound mAbs, **enabling pretargeted imaging** (Figure 1b). PET scan snapshots at multiple time points provide long-term imaging information. This strategy reduces the absorbed radiation dose resulting in a boost in target-blood ratios, as the nanomedicine can be imaged at a time point when the blood concentration of unbound nanomedicine has lowered to an acceptable level.



Requested qualifications:

- **Organic chemistry basics**
- **Interest in evaluation studies**
- **Basics in pharmacokinetics**
- **Fun at interdisciplinary studies**

This work is a part of a greater EU H2020 project located in Vienna, Mainz, Eindhoven and Copenhagen. The suitable candidate may have the possibility to stay abroad for a short timeframe.

Figure 1: a) Single-photon emission computed tomography (SPECT) images of a patient with a carcinoma in the left parotic region after the administration of a radiolabeled mAb (^{186}Re-bivatuzumab). The dark background and the contrast in the heart and in major blood vessels demonstrate the effect of a large amount of radioactivity circulating in blood up to 3 days post-mAb injection. This results in high patient radiation burden, which is limiting for approval by regulatory agencies[1]. **b)** General scheme of a pretargeting in vivo click imaging approach. First step tumor pretargeting (days); second step pretargeted chemistry (hours)[2]. This approach circumvents the radionuclide dilemma, ultimately resulting in acceptable patient radiation doses and in a superior imaging contrast.

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References: 1. Postema, E. J. et al. J Nucl Med 44, 1690 (2003) 2. Rossin, R. et al.. Angew Chem Int Ed Engl 49, 3375 (2010)