Evaluation of radiolabelled PD-L1 targeting molecules for PET (Positron Emission Tomography) imaging

Background

Programmed death ligand 1 (PD-L1) is an immune regulatory ligand that binds to the T-cell immune check point programmed death 1. Blockade of PD-1/PD-L1 has shown to be effective in patients in several tumor types. PD-L1 might be possible predictive and prognostic biomarker (Heskamp et al).

The $^{18}$F-labelled Z PD-L1 affibody molecule has been evaluated in vitro and in vivo (Gonzalez et al), showing rapid and specific uptake of tracer in a PD-L1 positive xenograft in mice. The $^{89}$Zr-labelled antibody atezolizumab has recently been clinically evaluated in a number of cancer patients for detecting the PD-L1 expression (Bensch et al).

Aim: To in vitro assess the PD-L1-targeting molecules 68Ga-affibody and/or 89Zr-atezolizumab for potential in molecular imaging of PD-L1 expression in different cancer cell lines, primarily in breast cancer, lung cancer and melanoma cell lines.

Methods:
This will be done as illustrated in figure above by 1) labeling the targeting molecules with radioisotopes (68Ga with half-life of 68 min and/or 89Zr with half-life of 3 days) and 2) evaluating e.g. labeling yield, stability and specific activity of the conjugates, as well as 3) characterizing antigen binding of the conjugates in vitro in PD-L1-expressing cell lines. The part of animal studies and clinical transalional imaging is not part of the student’s work. The student will be involved in and get familiar with all steps: radiolabelling 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 noninvasively visualize PD-L1 expression in cancer patients to predict response to PD-L1 targeted therapy.

References

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