

Doktorarbeiten im Sci Med Programm

Institute/Clinic: Klinik und Poliklinik für Nuklearmedizin

Research group: Dr. Dr. S. Lütje

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Topic: Adjuvant immune checkpoint inhibition in metastatic prostate cancer to improve long-term efficacy of PSMA-targeted radionuclide therapy

Starting date: October 2019

Project duration: 1 – 3 years

Project description:

Background

Prostate cancer (PCa) represents a major healthcare problem. Approximately 12% of men will be diagnosed with PCa at some point during their lifetime. While curable in early stages, treatments for metastasized PCa are sparse and 5-year relative survival in these patients is <30%. Even new target-specific radionuclide therapies directed against the prostate-specific membrane antigen (PSMA), which is overexpressed in PCa, lack long-term efficacy. Ultimately, recurrences occur and patients die from PCa.

Treating tumors with gamma radiation causes release of tumor-associated antigens, which induces anti-tumor immune responses leading to further tumor destruction. To escape this attack, tumor cells can upregulate the expression of proteins such as programmed-death-ligand-1 (PD-L1). For PSMA-targeted RNT (beta/alpha radiation), the role anti-tumor immune responses and tumor escape strategies is unknown.

Hypotheses

1. PSMA-specific RNT initiates anti-tumor immune responses leading to an increase of PD-1-expressing lymphocytes infiltrating the tumor.
2. PD-L1 expression on PCa cells increases to escape the induced anti-tumor immune responses.
3. The anti-tumor immune escape mechanism can be blocked by adjuvant immune checkpoint inhibition (ICI).

Aim

Developing a strategy for adjuvant ICI to prevent anti-tumor immune escape and thereby improve long-term efficacy of PSMA-targeted RNT.

Methods

Cell culture, radiolabeling of targeting molecules, Lindmo assay, binding- and internalization studies, scatchard analysis, immunohistochemistry, mouse models, biodistribution, Lu-177-PSMA treatments in vitro and in vivo.

Summary:

We offer a structured project with high relevance in the field of nuclear immuno-oncology. Publication of the results in a peer-reviewed journal together with the doctoral student is planned.

Are you interested in joining our team? Don't wait and send a letter of motivation and your CV to Susanne.Luetje@ukbonn.de.