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IN THE HELMHOLTZ ASSOCIATION

Contribution ID: **39** Type: **POSTER**

Evaluation of EpCAM Peptide Binding and Internalization for Breast Cancer Radiotheranostic Applications

Breast cancer is a heterogeneous disease and remains one of the most prevalent cancers among women worldwide, highlighting the urgent need for more effective diagnostic and therapeutic approaches. Epithelial Cell Adhesion Molecule (EpCAM) is a transmembrane glycoprotein involved in cell adhesion, proliferation and differentiation and is overexpressed in several types of cancer including breast, gastric, prostate, ovarian and colorectal. EpCAM expression demonstrates a context-dependent impact on cancer prognosis, correlating with tumor progression, metastasis and poor prognosis in breast and ovarian cancers, but with favorable outcomes in colorectal and gastric cancers. Due to its position on the cell surface, EpCAM presents a promising target for molecular imaging and targeted radionuclide therapies. We successfully synthesized two peptides EpCAM-1 (SNFYMPL) and EpCAM-2 (EHLHCLGSLCWP) via automated solid-phase peptide synthesis at high chemical purity and conjugated with DOTA chelator and Alexa Fluor-488. The aim of this study is to evaluate the specific binding and internalization of the peptides [177Lu]Lu-EpCAM-1 and [177Lu]Lu-EpCAM-2 in breast cancer cell lines using internalization assays and flow cytometry with EpCAM-1 Alexa-Fluor-488 and EpCAM-2 Alexa-Fluor-488 conjugates. For internalization assays, these peptides will be radiolabeled with [177Lu]LuCl3 (~5 MBq) in 0.4 M NaOAc (pH 5), at 95℃, for 30 min. Cells will be seeded in 24-well plates 24 h before the experiment. The cells will be incubated with 20 and 100nM [177Lu]Lu-EpCAM-1 or [177Lu]Lu-EpCAM-2 in 150 µL Opti-MEM for 1 h at 37℃. For flow cytometry studies, cells will be incubated with different concentrations of EpCAM-1 Alexa-Fluor-488 and EpCAM-2 Alexa-Fluor-488 conjugates for 60 min at 4 and 37℃. These results will allow us to determine the potential of EpCAM for prospective radiotheranostic applications in breast cancer.

Research type

Translational research

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Session Classification: Poster presentation