Constructing ^{68}Ga-DOTA-TATE analogues for improving the molecular imaging of the Somatostatin receptor subtype 2 (sst_2)

A prospective feasibility study into the design, synthesis, purification and validation of a novel tumour imaging peptide marker , targeting neuroendocrine tumours (NETs)

Conventional imaging of NETs is performed with 18-Fluorine-Fluoro-Deoxyglucose (18F-FDG), however this imaging can be non specific, and has greater value in showing the spread of the cancer, see Figure 1.
Somatostatin receptors are expressed in a variety of tumours, especially NETs. Somatostatin analogues, with DOTA-tags at the N-terminus have been used together with a radioactive 68-Gallium ligand to image these receptors and hence the tumours.
These DOTA peptides have variable binding efficacies to the tumour receptor subtypes, specifically DOTA-TATE has a bindings affinity for receptor subtypes 2 & 5. The ^{68}Ga-DOTA-TATE is also taken up to different extents, depending on the differentiation state of the NET.
We wish to evaluate the potential of improved binding to these receptor subtypes by subtle variations in the molecular structure of the DOTA-TATE, see Figure 2.
Providing we are successful in obtaining such peptides, further animal studies will be performed for clinical validation.

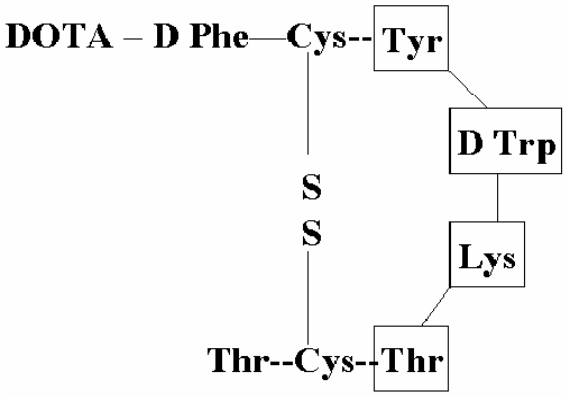

Figure 1: Schematic of the DOTA-TATE construct. The radioactive 68-Gallium is chelated by the DOTA molecule.

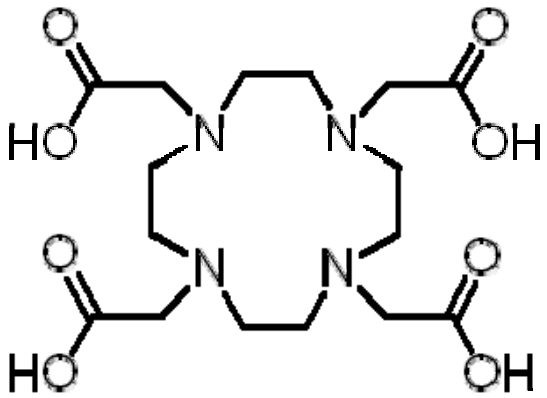

Figure 2: DOTA: 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid.

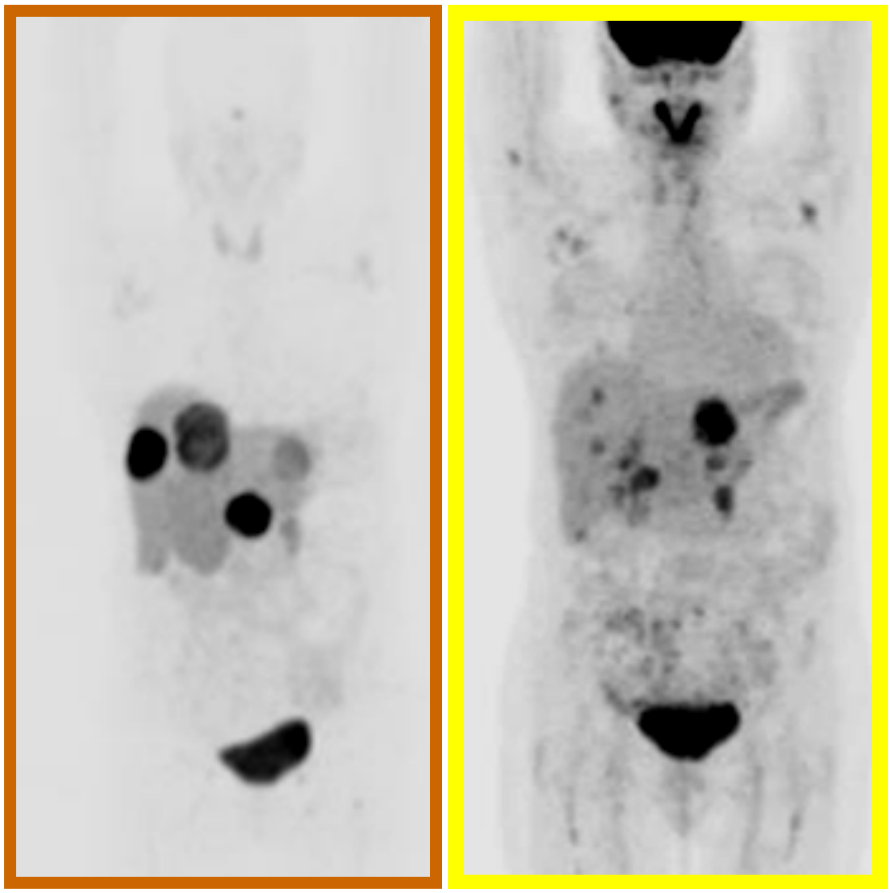

Figure 3: Images of the same patient subjected to Left image 68Ga-DOTATATE, the tumour metastases are demonstrated in the liver and paraaortic lymph nodes. Right image 18F-FDG, only a solitary liver metastasis is seen. Well differentiated NET show greater avidity for ^{68}Ga DOTATATE and poorly differentiated NET show greater avidity for ^{18}F-FDG

Project Content

The project will take place within the presently established collaboration between the departments of:
Physics and Nanotechnology (AAU),
Chemistry,
Environmental engineering and Biotechnology (AAU),
Nuclearmedicine Aalborg sygehuse Syd.

The project will involve peptide :
Design (2 to start with),
Purification using HPLC,
Validation using mass determination by matrix assisted laser desorption ionisation - time of flight (MALDI-TOF) mass spectrometry, and possibly Tandem mass spectrometry.

Student learning objectives

- Learn to operate a Fmoc based synthesis of peptides.
- Learn to purify peptides using reverse phase C-18 and C-8 High Pressure Liquid Chromatography (HPLC).
- Learn to validate peptide masses using MALDI-TOF mass spectroscopy.

Project collaborators

Department of Physics and Nanotechnology AAU
Lektor Eva Maria Petersen
Lektor Peter Fojan

Department of Chemistry, Environmental engineering and Biotechnology AAU
Lektor Allan Stensballe

Department of Nuclear Medicine Aalborg Sygehuse Syd
Ledende Overlæge Ivan Noer
Overlæge Vineet Prakash
Overlæge Victor Iyer
Ingeniør Rune Wiik Andersen