Radionuclide therapy for ovarian cancer based on follicle stimulating hormone

Interview with dr. Inês Antunes, Groningen MC

Dr. Inês Antunes (Cartaxo-Portugal, 1976) graduated in Technological Chemistry (Licenciatura, equivalent to MSc) at the University of Science of Lisbon, Portugal. Thereafter, she worked in two research projects as a chemist/radiochemist while obtaining her specialisation in Pharmaceutical and Therapeutical Chemistry at the University of Pharmacy of Lisbon, Portugal in 2006. She then obtained her PhD in Medical Science at the University of Groningen, The Netherlands in 2012 where she is still working as a researcher at the Department of Nuclear Medicine and Molecular Imaging. Since 2017, she has been the R&D laboratory coordinator of this department consisting of three technicians and several PhD, master and baccalaureate students. Currently she is also responsible for setting up the GMP infrastructures to produce ^{177}Lu-based radiopharmaceuticals for clinical use, and co-supervises seven PhD students and one postdoc. She is also a coach in Ethics and Scientific Integrity and Nuclear and Radiochemistry courses from RUG. In her spare time, she likes to cook and bake for friends and family and travels to explore other countries and cultures. In 2023, Inês Antunes received a grant from the Dutch Cancer Society (KWF) to develop a novel type of radionuclide therapy for ovarian cancer.

The title of your project is 'Development of a novel radionuclide therapy for ovarian cancer based on follicle stimulating hormone (FSH)'. What is the clinical problem you address and what are the main research objectives of your project?

Conventional treatments, such as chemotherapy and radiotherapy, are often ineffective in aggressive late-stage (III-IV) ovarian cancer (OC), leading to recurrence of the disease. Therefore, more effective diagnostics and treatment for OC is warranted. Since follicle-stimulating hormone receptors (FSHR) are virtually absent in non-malignant tissues or inflammation but highly expressed in ovarian cancer, we hypothesise that a theragnostic approach targeting the FSHR will yield a new treatment option for ovarian cancer patients. Therefore, the main objective of this project is to develop a new radionuclide based therapy for OC by targeting the FSH receptors.

Which radionuclides did you select for this project and why?

For the diagnostic probe we choose ^{18}F (positron emitter) and for the therapeutic approach we choose ^{177}Lu (beta emitter).

What do you consider the biggest challenge of your project and why?

The biggest challenge of this project is the radiolabelling of the protein since the usual high temperatures used during the radiolabelling are not possible to apply here without degrading the protein.
Therefore, we will need to use indirect labelling which can also be challenging since the conjugation of the protein to the radiolabelled chelator needs to be efficient in a short time. In addition, the use of different chelators for the different isotopes might acquire different biological properties, therefore hampering the comparison of the 18F/177Lu probes.

Who are your main collaborators and what is their role?

The main collaborators of this grant are prof. dr. Erik de Vries, an expert in translational molecular imaging, and dr. Bart Cornelissen, an expert in radiobiology in targeted radionuclide therapy.

Can you also apply this treatment (or the obtained knowledge) to other cancer types?

Since FSHR is also highly expressed by the endothelium of blood vessels in the majority of metastatic tumours,

we believe that we might use this therapy for other cancer types.

What is the most innovative component of your project?

In my opinion, there are two main innovative parts in this project: a) the target itself, because there are not many radioactive probes for this target; subsequently very little is known about how this target behaves and how the therapies affect this target and b) the radiolabelling of proteins which is not very common to do.

If we could look into the future, five years from now, and you look back on your project, what do you hope to have achieved? What would you be most proud of? And what would be the next steps?

Five years from now, I hope that we at least managed to successfully develop a PET diagnostic probe. Then, even if theragnostic can't be applied, we still could get a better understanding of the efficacy of other therapies (monotherapy or combinatorial therapy) and allow the physicians to select those patients that will eventually benefit from an FSH-based therapy. Perhaps most importantly, we would have a diagnostic tool for earlier detection of the cancer that might benefit from conventional treatments as well. If we managed to achieve all of this or even part of it, I would be very proud that at least We were able to hopefully contribute to a better outcome for women who suffer from ovarian cancer. Depending on the outcome of this study we will proceed to further evaluate its potential as a theragnostic target. ♦