User project report

Radioligand Development for the Gastrin Releasing Peptide Receptor Targeting using the Theranostic Pair 44/47Sc

PD Dr Eleni Gourni

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP). This document reflects only the view of the author(s). The Agency is not responsible for any use that may be made of the information it contains.

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2. Context of the project (800 characters max. including spaces)

The gastrin-releasing peptide receptor (GRPr) is overexpressed in prostate, breast, small cell lung cancers, as well as gastrointestinal stromal tumors and urinary cancer vessels. This has led to the development of GRPr-based radiopharmaceuticals. Various GRPr-peptide radiotracers have been created using SPECT (^{99m}Tc, ^{111}In) and PET (^{68}Ga, ^{64}Cu, ^{18}F) radionuclides, with GRPr-radioantagonists showing superior pharmacokinetics. PET/SPECT imaging at later time points with long half-life radionuclides enhances tumor visualization, reducing background activity and improving contrast for detecting primary and metastatic tumors. In this project, we developed and preclinically evaluated a **^{47}Sc-labeled** GRPr radioantagonist using small animal SPECT/CT and targeted radionuclide therapy studies.

3. Results and discussion (1000 characters max. including spaces)

[^{47}Sc]Sc-LF1 was prepared with high radiochemical purity and molar activities up to 40 MBq/nmol. It exhibited affinity for PC3 and T47D cells, with K_d values of 7±2.3 nM and 10.6±3.0 nM, respectively. [^{47}Sc]Sc-LF1 exhibited a low internalization rate (<10%) relative to total cell-bound activity for both cell lines. Metabolite analysis identified three hydrophilic metabolites. In PC3 xenografts, [^{47}Sc]Sc-LF1 achieved high, sustained, and specific tumor uptake, with values of 24.1±2.1% and 4.8±1.6% % I.A./g at 1 and 72 h p.i., respectively. The lower GRPR density in T47D xenografts resulted in tumor uptake of 9.5±2.5% and 0.7±0.1% I.A./g at 1 and 72 h p.i., respectively. In both models, radioactivity cleared significantly faster from the pancreas compared to the tumor (Fig 1). Tumor volume reduction and extended survival were observed, particularly in groups treated with 20 MBq. Untreated groups displayed rapid tumor progression, emphasizing the therapeutic potential of [^{47}Sc]Sc-LF1.

4. Conclusions (800 characters max. including spaces)

The strong and prolonged tumor uptake seen in prostate and breast cancer models, combined with a clear tumor response—evidenced by reduced tumor size and improved survival—demonstrates the high potential of [^{47}Sc]Sc-LF1. This dual-purpose agent offers both precise SPECT imaging and effective targeted therapy, making it a promising tool for cancer diagnosis and treatment. Its ability to localize tumors accurately while delivering therapeutic effects underscores its versatility and clinical value, paving the way for improved patient outcomes in oncology.

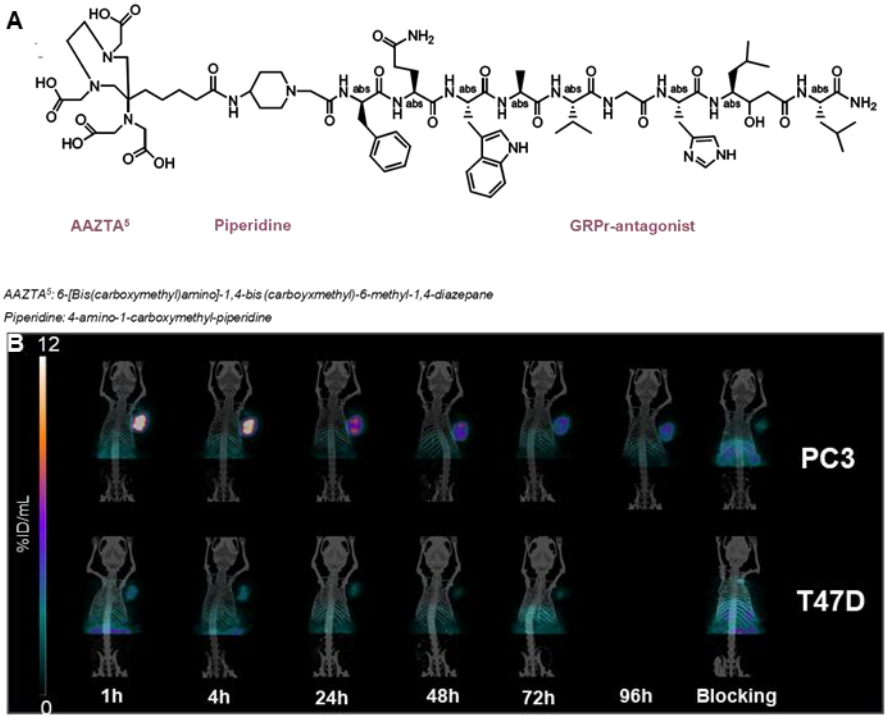

Figure 1. (A) Structure of LF1; (B) SPECT/CT images of [^{47}Sc]Sc-LF1 in PC3 and T47D mice.

5. Involvement of the PRISMAP services (600 characters max. including spaces)

Our project used 47Sc, focusing on radiolabeling optimization, in vitro evaluation, and SPECT/CT imaging. While 44Sc is established in Switzerland, 47Sc is still emerging. Given the absence of a nuclear reactor in Switzerland, securing its availability poses a challenge. Thanks to PRISMAP and our well-established collaboration with POLATOM (NCBJ, Otwock-Swierk, Poland), we secured high-quality 47Sc for our research, enabling our project's successful completion.

6. Feedback to PRISMAP (600 characters max. including spaces)

The communication with POLATOM (NCBJ, Otwock-Świerk, Poland) was excellent. They ensured smooth coordination as they took over the production of 47Sc. The received 47Sc was of great quality, meeting our expectations. Logistics for delivery were well-organized, and all shipments arrived on time. We appreciate the professionalism and efficiency demonstrated throughout the process. Thank you for the outstanding service.

7. Publications and other dissemination activities (conferences etc.)

Part of the results of this project have been present to the following conference:

- European Association of Nuclear Medicine (EANM) annual congress, 2024, Hamburg, Germany (oral talk). The results of this work were mentioned in highlight lecture during the opening ceremony of the conference.

A 47Sc-labeled GRPR Antagonist with Superior SPECT Imaging Characteristics Compared to its 177Lu-labeled Counterpart

T. Läppchen[1], E. Pilatis[1], E. Menéndez[1], A. Bilinska[1], A. D'Onofrio[1], E. Moon[2], M. Zoltowska[3], D. Pawlak[3], I. Cieszykowska[3], R. Mikolajczak[3], F. Rösch[2], A. Rominger[1], E. Gourni[1]

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[3]Radioisotope Centre POLATOM, National Centre for Nuclear Research, Otwock, POLAND.

Part of the results of this project will be presented to the following conference:

- 26th International Symposium on Radiopharmaceutical Sciences, Gold Coast, Australia (poster)

Advancing Cancer Imaging and Therapy: Evaluation of a ^{47}Sc-Labeled Gastrin Releasing Peptide Radiotracer, [^{47}Sc]Sc-LF1, for Prostate and Breast Tumors

Naveen Kumar[1], Tilman Läppchen[1], Adrianna Biliska[1], Elena Menéndez[1], Euy Sung Moon[2], Malgorzata Zoltowska[3], Dariusz Pawlak[3], Izabela Cieszykowska[3], Renata Mikolajczak[3], Frank Rösch[2], Axel Rominger[1], Eleni Gourni[1]

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- All the results acquired from the project will be summarized in a manuscript which is already in preparation. We intent to submit this manuscript by the end of August 2025.

Appendix 1. Dissemination guidelines for user projects as agreed in the signed User Agreement

Dissemination rules

Only user groups that are allowed to disseminate the results which they have generated under the project may benefit from the access, unless they are working for SMEs.

For each user group project, a publishable project summary and a publishable summary of the results will be published on the European Union Horizon 2020 PRISMAP project website www.prismap.eu. The publication of results in journals or at conferences is strongly encouraged.

To ensure the long-term sustainability of the PRISMAP initiative, proper recognition of the contributing facilities, their services and the involved persons is necessary. All participating PRISMAP facilities shall be acknowledged in the publication. Acknowledgement and co-authorship of PRISMAP staff members who participated in the experiment shall be considered according to the research field best practices and verified with the PRISMAP Technical Manager before any publication.

The user group shall contact the PRISMAP Technical Manager 30 days prior to submission of publications or other communications of results that were obtained by making use of services provided by PRISMAP (radionuclides delivered or medical services provided). The Technical Manager will communicate to the user group the list of PRISMAP facilities and persons that have contributed to each specific project and the way this contribution must be acknowledged in the publication/communication or where co-authorship is required to reflect specific scientific contributions.

Users must comply with Horizon 2020 dissemination rules (i.e. acknowledge that their work was financially supported by the European Union's Horizon 2020 Research and Innovation Programme by including the following acknowledgement: "This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP)"), and grant open access to resulting publications and related data.

Dissemination shall take place only once legitimate interests regarding intellectual property have been safeguarded. A maximum publication delay of 90 days may be granted for this purpose.

Acknowledgements

The list of name(s) to be mentioned in the acknowledgment section is sent to the technical manager by the main contact of the involved facilities.

A general sentence will be added by the corresponding author of the article (user side):

"The authors would like to thank the members of the PRISMAP consortium and of the PRISMAP user selection panel, coordination and management team for their advice and support."

Funding acknowledgement

"This work was supported by the European Union's Horizon 2020 research and innovation programme as a user project of PRISMAP – The European medical radionuclides programme (GA 101008571)".