User project report

The absorbed dose – response relationship of Auger electrons from La-135

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

AE therapy is expected to be highly efficient for metastatic disease, leading to lower risks of radiotoxicity in healthy tissues. Several AE-emitting radionuclides are already employed in clinical trials. Most of these radionuclides are however not 'pure' AE emitters but rather emit a combination of Auger, internal conversion (IC) electrons, $\beta_{+/-}$ particles, X-ray and gamma photon emissions. This makes it difficult to discriminate and understand the therapeutic effect especially of the AE's. To this end, La-135 production was recently up-scaled to reach a yield and purity suitable for preclinical research. Its decay radiation emissions and radiochemical properties make it a good candidate to study the basic mechanisms of AE's.

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

Calibration of gamma counter and dose calibrator were difficult due to the high X-ray yield. The upper limit of the linearity of the gamma counter was already reached at ~ 20 kBq. Non-linearity of the dose calibrator was also noted. The radiochemical conversion and purity of the [^{135}La]La-DOTA-TATE was >99% while for [^{135}La]La-DOTA-LM3 the max. conversion and purity was ~97 and 93%, respectively. Qualitative SPECT imaging appeared feasible based on preliminary phantom imaging. The cellular binding pattern of both radioligands corresponds to previous reports with radiolanthanides (Spoormans et al. 2024, JNM) albeit that K_d and B_{max} of [^{135}La]La-DOTA-LM3 were different. The absorbed dose to the nucleus for both radioligands was very low (<0.15 Gy at 25 nM concentration). No statistically significant differences were detected with the CFU and MTS assays.

4. Conclusions (800 characters max. including spaces)

For the internalizing and membrane-bound ligands DOTA-TATE and DOTA-LM3, we conclude that La-135 offers limited therapeutic potential. Also, for diagnostic purposes, the quantification of SPECT images may be challenging and suboptimal. Lanthanum-135 may be interesting to combine with DNA-binding vectors to enable the close-range therapeutic effects of its Auger electrons.

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

The PRISMAP consortium has enabled the study of La-135. As a cyclotron + optimized production method is required, the experiment would not have been feasible otherwise.

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

The application procedure was clear however exclusion for PRISMAP members (PRISMAP members active in different work packages) had to be sorted out last minute. The organization of the nuclear transport for the La-135 from DTU to SCK CEN was quite cumbersome as it involved different radiation protection departments. All communication between the PRISMAP representative and lead application at SCK CEN was clear and satisfactory.

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

A manuscript draft is in preparation.

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."

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