Development of Small-Molecule Inhibitors of FabV Effective in Gram-negative Bacteria

A Data Management Plan created using DMPonline.be

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Project abstract:

The rapid spread of antimicrobial resistance poses a major threat to human health. The World Health Organization (WHO) estimates that currently more than 700,000 patients die each year due to infections with multidrug-resistant pathogens. This number is predicted to rise dramatically, with 10 million deaths annually by 2050, if no actions are taken. In order to avoid the looming prospect of a post-antibiotic age within the next few decades, a continuous development of not just new antibiotics, but more importantly, new classes of antibiotics, is imperative. An attractive yet underexplored target for antibiotic drug development in bacteria is the fatty acid biosynthetic pathway (FasII). Fatty acids are essential components of cellular membranes. Most bacteria are unable to scavenge fatty acids from host organisms and therefore rely on de novo production. The FasII enzyme responsible for the final step in the fatty acid elongation cycle, differs significantly from the FasI pathway of mammals, plants and fungi. These enzymes, known as enoyl-acyl carrier protein reductases (ENR), have thus been recognized as an interesting target for new antibacterials with a novel mode of action. Triclosan, one of the most common additives to consumer products worldwide, is a well-known inhibitor of the ENR enzyme FabI in a wide range of bacteria. While triclosan was found to be unsuitable as an antibiotic due to its toxicity, multiple FabI inhibitors with improved bioavailability and toxicity profiles have been reported in recent years as a potential new class of antibiotics. However, several notorious and highly pathogenic Gram-negative bacteria, including the opportunistic WHO priority I pathogen P. aeruginosa, have been shown to be resistant to FabI inhibitors. This resistance stems from the expression of FabV, an ENR isoenzyme. The goal of this project is the development of novel FabV inhibitors, in order to re-sensitize these pathogens to antibiotics.

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DPIA

DPIA

Have you performed a DPIA for the personal data processing activities for this project?

- Not applicable

Development of Small-Molecule Inhibitors of FabV Effective in Gram-negative Bacteria
GDPR

GDPR

Have you registered personal data processing activities for this project?

- Not applicable

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Application DMP

Questionnaire

Describe the datatypes (surveys, sequences, manuscripts, objects …) the research will collect and/or generate and /or (re)use. (use up to 700 characters)

The protein structures used for rational drug design will be gathered from PDB web collections as .mol2 or .pdb files.
Laboratory notes will be stored and archived using the ELN, including a PDF version to ensure data availability at all times, in case licences would expire.
Experimental data and results will be saved by Office software and Graphpad Prism.
Characterization with NMR and MS will be done with .fid files and proprietary data files, respectively.
A PDF version will be stored to ensure data availability at all times.
Compounds synthesized in the course of the project will be appropriately stored and indexed in a searchable catalog, using the open-source .dwar format.

Specify in which way the following provisions are in place in order to preserve the data during and at least 5 years after the end of the research? Motivate your answer. (use up to 700 characters)

The promotor, Peter Verwilst, will be responsible for the preservation of the data during and at least 5 years after the end of the research.
During the research, as copy of the data will be stored on a shared folder, to allow all collaborators to access the data, to ensure a smooth collaboration.
Experimental data and results will be documented on an electronic lab notebook and a backup of these data will be made on an external hard drive. Furthermore, data will be stored on a server maintained by the KU Leuven central IT service.
These data will be preserved at a minimum of 5 years after the end of the research.

What's the reason why you wish to deviate from the principle of preservation of data and of the minimum preservation term of 5 years? (max. 700 characters)

N/A

Are there issues concerning research data indicated in the ethics questionnaire of this application form? Which specific security measures do those data require? (use up to 700 characters)

N/A

Which other issues related to the data management are relevant to mention? (use up to 700 characters)

N/A

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FWO DMP (Flemish Standard DMP)

1. Research Data Summary

List and describe all datasets or research materials that you plan to generate/collect or reuse during your research project. For each dataset or data type (observational, experimental etc.), provide a short name & description (sufficient for yourself to know what data it is about), indicate whether the data are newly generated/collected or reused, digital or physical, also indicate the type of the data (the kind of content), its technical format (file extension), and an estimate of the upper limit of the volume of the data.

				Only for digital data	Only for digital data	Only for digital data	Only for physical data
Dataset Name	Description	New or reused	Digital or Physical	Digital Data Type	Digital Data format	Digital data volume (MB/GB/TB)	Physical volume
Synthetic procedures	Experimental conditions leading to molecules	New Data	Physical				Up to 10 notebooks
Structured synthetic details	A fully written out version of the experiment, with an interpretation of the main analytical results	New Data	Digital	Compiled	.docx and .pdf	<1GB	
NMR data	Raw and processed NMR data	New Data	Digital	Experimental	.fid	<1GB	
Mass data	Processed Mass data	New Data	Digital	Experimental	.pdf	<1GB	
Flash column	Processed Flash column purification profiles	New Data	Digital	Experimental	.pdf	<1GB	
In vitro inhibition	Enzymatic substrate depletion assay data and processed IC50 calculations	New Data	Digital	Experimental	Raw data: .xlsx or .txt Processed: .pzfx or .prism	<100MB	
In vivo bacterial inhibition	Bacterial survival in the presence of selected congeners	New Data	Digital	Experimental	.xlsx	<100MB	
Toxicity assays	Toxicity of compounds in human cell lines	New Data	Digital	Experimental	.xlsx	<100MB	
SPR data	Processed SPR data	New Data	Digital	Experimental	.pptx	<1GB	
Dockings	Docking poses of commercial and newly synthesized molecules	Reusing existing data and generating new data	Digital	Simulation data	.pdbqt, .csv and .xlsx	<100GB	
Stardrop analyses	Prediction of physicochemical properties and hypotesis formulations	New Data	Digital	Simulation Data	.sdproj	<100MB	
Monthly progress meetings	Slides used during monthly individual progress meetings	New Data	Digital	Compiled Data	.pptx	<1GB	
Compound Index	Index of available intermediate and final molecules with indications of physical locations	New Data	Digital	Compiled Data	.dwar	<100MB	

If you reuse existing data, please specify the source, preferably by using a persistent identifier (e.g. DOI, Handle, URL etc.) per dataset or data type:

Data of gene and protein sequences, as well as structural information from online databanks will be used, such as ncbi (https://www.ncbi.nlm.nih.gov/), uniprot (https://www.uniprot.org/) and PDB (https://www.rcsb.org/).

For docking, commercial compound libraries are used and all molecules are converted to .pdbqt files. These libraries are provided by companies (BLD Pharm, Enamine, Pharma Block, ...)

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? Describe these issues in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes, dual use

In the project, a research stay at the research lab of Prof. Eshwar Mahenthiralingam in planned during the second half of 2026, providing the research has progressed enough to enable this.
During this stay, the goal would be to characterize the capability of our newly developed antimicrobials to prevent the growth of Burkholderia species, including B. mallei and B. pseudomallei. These two species are classified by The Centers for Disease Control and Prevention as category B bioterrorism agents, given the previous use of B. mallei (the causative agent of the equid disease glanders) as a biological weapon during World War I.
Bacterial strains will only be used to assess the capacity of our FabV inhibitors to incapacitate the above mentioned pathogens. No research regarding the pathogens themselves will be conducted and thus no data will be gathered beyond the microbial activity of our congeners. The research will be conducted in an academic research lab, following the appropriate security and person safety measures.
The research proposal, received a positive advice from the EC DMM, with approval number D-20231114.f

Will you process personal data? If so, briefly describe the kind of personal data you will use in the comment section. Please refer to specific datasets or data types when appropriate.

- No

Does your work have potential for commercial valorization (e.g. tech transfer, for example spin-offs, commercial exploitation, …)? If so, please comment per dataset or data type where appropriate.

- Yes

The project may lead to novel compound development, for which IP rights may be exploited in the future. LRD will be consulted.

Do existing 3rd party agreements restrict exploitation or dissemination of the data you (re)use (e.g. Material/Data transfer agreements/ research collaboration agreements)? If so, please explain in the comment section to what data they relate and what restrictions are in place.

- No

Are there any other legal issues, such as intellectual property rights and ownership, to be managed related to the data you (re)use? If so, please explain in the comment section to what data they relate and which restrictions will be asserted.

- No

2. Documentation and Metadata

Clearly describe what approach will be followed to capture the accompanying information necessary to keep data understandable and usable, for yourself and others, now and in the future (e.g., in terms of documentation levels and types required, procedures used, Electronic Lab Notebooks, README.txt files, Codebook.tsv etc. where this information is recorded).

Notebooks will contain information on research methods, protocols and experimental results.
NMR and Mass data are named according to a traceable numbering system, clearly indicated in the lab notebooks. All other data will be preserved similarly, where if appropriate a short explanatory note will be introduced to describe the data in the corresponding folders.

Will a metadata standard be used to make it easier to find and reuse the data? If so, please specify (where appropriate per dataset or data type) which metadata standard will be used. If not, please specify (where appropriate per dataset or data type) which metadata will be created to make the data easier to find and reuse.

- No

3. Data storage & back-up during the research project

Where will the data be stored?

During the project the data will be stored on the researcher's computer. A backup is made on a shared drive with automatic back-up procedures, maintained by the ICTS.

How will the data be backed up?

During the project the data will be stored on the researcher's computer. A backup is made on a shared drive with automatic back-up procedures, maintained by ICTS managers.
Our shared drive also contains backup procedures and is managed by the ICTS.

Is there currently sufficient storage & backup capacity during the project? If yes, specify concisely.
If no or insufficient storage or backup capacities are available, then explain how this will be taken care of.

- Yes

Our shared drive has enough capacity to host the volume needed (estimated at 20 GB).

How will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

The shared drive is also very well secured by the ICTS managers of the Rega Institute. The folder is not accessible to non-KU Leuven staff, and permission must be given to each staff member that can access the data.

What are the expected costs for data storage and backup during the research project? How will these costs be covered?

The costs for the shared drive is covered by the division/institute. A laptop with a 512 GB hard disk was purchased for the student with the FWO bench fee.

4. Data preservation after the end of the research project

Which data will be retained for at least five years (or longer, in agreement with other retention policies that are applicable) after the end of the project? In case some data cannot be preserved, clearly state the reasons for this (e.g. legal or contractual restrictions, storage/budget issues, institutional policies...).

All research data will be retained for 5 years after the end of the project on a KUL long-term storage server. A copy will also be stored on an external hard drive for 10 years.

Where will these data be archived (stored and curated for the long-term)?

All research data will be retained for 5 years after the end of the project on a KUL long-term storage server. A copy will also be stored on an external hard drive for 10 years.

What are the expected costs for data preservation during the expected retention period? How will these costs be covered?

5 Years storage, up to 5TB (Large volume storage) at KU Leuven server: 475.7 euro*
1 External Hard drive up to 1TB (SSD): approx. 200 euro
Costs for this storage are covered by an FWO research grant (G053122N), of which this PhD project is a part of the research.
*At the end of the project, all options will be assessed once more, given that the estimated data size is significantly smaller than the minimum amount of 5TB.

5. Data sharing and reuse

Will the data (or part of the data) be made available for reuse after/during the project? In the comment section please explain per dataset or data type which data will be made available.

- Other, please specify:

Yes all generated data will be used in published articles and the fellow's PhD thesis. Access to raw experimental data of published articles can be made available upon reasonable request to the supervisor.

If access is restricted, please specify who will be able to access the data and under what conditions.

Access may be restricted for some unpublished data such as the structure of compounds that have not yet been published. Access may be restricted to anyone who hasn't signed a non disclosure agreement.

Are there any factors that restrict or prevent the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)? Please explain in the comment section per dataset or data type where appropriate.

- Yes, Intellectual Property Rights

Access may be restricted for some unpublished data such as the structure of compounds that have not yet been published. Access may be restricted to anyone who hasn't signed a non disclosure agreement.

Where will the data be made available? If already known, please provide a repository per dataset or data type.

Data will be made available via the RDR, the KU Leuven institutional repository. However, repository depositions will only be used in case of a direct request for raw data to the supervisor.

When will the data be made available?

After publication of research results, upon request to the supervisor.

Which data usage licenses are you going to provide? If none, please explain why.

The use of specific data usage licenses is not yet known.

Do you intend to add a PID/DOI/accession number to your dataset(s)? If already available, you have the option to provide it in the comment section.

- Yes

If data sets are shared a DOI will be available through RDR

What are the expected costs for data sharing? How will these costs be covered?

The costs of data sharing are expected to be very small as the RDR is covered for KU Leuven staff.

6. Responsibilities

Who will manage data documentation and metadata during the research project?

The fellow (Radu Bulai)

Who will manage data storage and backup during the research project?

The supervisor (Peter Verwilst) in close collaboration with the fellow (Radu Bulai)

Who will manage data preservation and sharing?

The supervisor (Peter Verwilst)

Who will update and implement this DMP?

The supervisor (Peter Verwilst) in close collaboration with the fellow (Radu Bulai)