Development of new compounds to define the potential of TRPM4 inhibition for prevention and suppression of Ca2+ dependent cardiac arrhythmias.

A Data Management Plan created using DMPonline.be

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Template: FWO DMP (Flemish Standard DMP)

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Project Administrator: Rudi Vennekens

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Project abstract:

Ca2+ dependent arrhythmias are a critical feature of conditions such as CPVT, ischemia and atrial fibrillation. TRPM4 is a Ca activated cation channel and an interesting drug target for the prevention and suppression of this type of arrhythmias. To date, the only in vivo applicable blockers of TRPM4 are meclofenamate and glibenclamide, which have obviously other prominent targets and have a relatively low efficacy to block TRPM4. Therefore, we aim to design a new class of high-affinity TRPM4 blockers, and determine the role of TRPM4 in tissue with high-translational value. Specifically, we aim to: i) to define the binding site for meclofenamate by CryoEM, in order to delineate the binding pocket for inhibitors on the TRPM4 protein. Based on this information we will create an in silico model that will be used to ii) identify new compounds with high affinity using a ultra-large scale virtual screen and structure-activity relation optimisation of meclofenamate through medicinal chemistry, and iii) test the effect of novel compounds and meclofenamate in human iPSC derived cardiomyocytes , and in living guinea pigs. Taken together, this project will deliver new insight in the mechanism of block of TRPM4, and the translational potential of TRPM4 targeting as a strategy to prevent cardiac arrhythmias.

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DPIA

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

- Not applicable

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GDPR

GDPR

Have you registered personal data processing activities for this project?

- No

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FWO DMP (Flemish Standard DMP)

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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
		Please choose from the following options: • Generate new data • Reuse existing data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Observational • Experimental • Compiled/aggregated data • Simulation data • Software • Other • NA	*Please choose from the following options:* • .por, .xml, .tab, .csv,.pdf, .txt, .rtf, .dwg, .gml, … • NA	*Please choose from the following options:* • <100MB • <1GB • <100GB • <1TB • <5TB • <10TB • <50TB • >50TB • NA	
Calcium Imaging	Calcium imaging of cardiomyocytes	Generate new data	digital	Experimental	.tif .nd2	<1TB	
Patch Clamp	Patch clamp recordings of cardiomyocytes	Generate new data	digital	Experimental	.csv	<100GB	
ECG recording	ECG recordings of laboratory animals	Generate new data	digital	Experimental	.csv	<1TB	

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:

not applicable

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, animal data

The use of laboratory animals in this proposal is covered by already approved ECD projects.

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

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).

-All experiments will be documented using an Electronic Lab Notebook (eLABFTW), which willcontain all the details of the experimental protocols and procedures along with the reference to the relevant data files, and which will be time-stamped.
- All preclinical experiments are performed according to protocols of LICR (Lab of Ion channel research), which are embedded into eLABFTW.

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.

- Yes

Metadata will include the following elements:
• Title: free text
• Creator: Last name, first name, organization
• Date and time reference
• Subject: Choice of keywords and classifications
• Description: Text explaining the content of the data set and other contextual information
needed for the correct interpretation of the data, the software(s) (including version number) used to produce and to read the data, the purpose of the experiment, etc.
• Format: Details of the file format
• Resource Type: data set, image, audio, etc.
• Identifier: DOI (when applicable)

• Access rights: closed access, embargoed access, restricted access, open access.
Additionally, we will closely monitor MIBBI (Minimum Information for Biological and Biomedical Investigations) for metadata standards more specific to our data type. For datasets, additional metadata will be associated with the data file as appropriate.

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

Where will the data be stored?

During the project: Digital files will be stored on KU Leuven servers. Metadata and notes are stored via ELN. After the project: Digital files and meta data will be stored on MaNGO.

How will the data be backed up?

Data stored on the KU Leuven servers are backed up daily using snapshot technology, where all incremental changes in respect of the previous version are kept online; the last 14 backups are kept.

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

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

Raw data are stored on the KU Leuven Large Volume Storage service and secured by KU Leuven security groups. Analyzed data are stored on password-protected KU Leuven personal computers and hard drives.

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

Expected costs for data storage are estimated at 4500 euro/3 years. These costs will be covered by the host labs

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 digital data (raw, processed and metadata) will be retained for at least 5 years after the end of the project in a safe, secure & sustainable way for purposes of reproducibility, verification, and potential reuse.

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

After processing and publication, data and metadata will be saved in the KU Leuven ManGO: active data management platform.

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

The costs for preservation on ManGO after ending the project will be covered by the host labs. Estimated costs are 1000 Euro/year.

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.

- Yes, in a restricted access repository (after approval, institutional access only, …)

All the virtual data will be made available for members of the host lab. The decision to share the content and/or reuse of the data by external researchers will be made by the supervisor of the project.
After publication of the research results, data will be fully available upon request.

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

Access will be provided by the promotor of the project: Rudi Vennekens

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.

- No

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

Following publication, data will be made available via established depositories, depending on the type of data and the requirement of publishers or other agencies.

When will the data be made available?

-Data is made available to members of the host laboratory during the project.
-For external researchers/groups, data will be made fully available upon publication of the research results.

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

Data from the project that can be shared will be made available under a creative common's attribution license (cc-by 4.0), so that users have to give credit to the original data creators.

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.

- No

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

Minimal/no costs are expected.

6. Responsibilities

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

Rudi Vennekens

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

Andrei Segal Stanciu and Andy Pironet

Who will manage data preservation and sharing?

Andrei Segal Stanciu is responsible for data preservation. Rudi Vennekens responsible for data reuse/sharing.

Who will update and implement this DMP?

Rudi Vennekens