DMP title

Project Name C2 - DMP title
Project Identifier C24M/21/028
Grant Title C24M/21/028
Principal Investigator / Researcher Thomas Voets
Description The project includes preclinical and clinical research aimed at understanding TRP channel-related pain, and at developing novel pain treatments by targeting TRP channel function.
Institution KU Leuven

1. General Information

Name of the project lead (PI)

Prof. Thomas Voets - thomas.voets@kuleuven.be
Prof. Wouter Everaerts - wouter.everaerts@uzleuven.be
Prof. Djalila Mekahli - djalila.mekahli@uzleuven.be
Prof. Rudi Vennekens - rudi.vennekens@kuleuven.be
Prof. Jan de Hoon - jan.dehoon@kuleuven.be

Internal Funds Project number & title

C24M/21/028
TRP - Tackling The Roots of Pain

2. Data description

2.1. Will you generate/collect new data and/or make use of existing data?

- Generate new data

2.2. What data will you collect, generate or reuse? Describe the origin, type and format of the data (per dataset) and its (estimated) volume. This may be easiest in a numbered list or table and per objective of the project.

1. Patient data/material

- Personal data from patients will be stored using REDCap and Formaza, a modified InfoPath (Microsoft) plug-in for electronic Case Report Form (eCRF). These data can be stored/exported as spss, microsoft excel, pdf and csv. Total estimated size: 50 GB.

- Questionnaires (EORTC QLQ- C30, EORTC QLQ-NMIBC24 and BPI-SF) will be collected via MyNexuzhealth-app. This application allows patients to consult their own medical records in a structured way using a smartphone or tablet. These data are then automatically imported into the eCRF (KWS). Total estimated size: 10 GB

-Biopsies will be processed for RNAscope-based in situ hybridisation, immunohistochemistry, WB or qPCR by preserving the tissue in formalin-fixed, paraffin-embedded (FFPE) tissue or by snap freezing in liquid nitrogen at -80°C .

- Some biopsies will be collected in Dulbecco's Modified Eagle Medium (DMEM), penicillin and streptomycin and immediately afterwards processed and cultured to be used for functional experiments in the LICR lab.

All these biopsies will be stored in the UZ Leuven biobank.

2. Preclinical data/material

- Digital images of processed tissue, stored as uncompressed tiff; total estimated size: 500 GB
- Gel scans; stored as uncompressed TIFF; total estimated size: 20 GB.
- Video files of (in vivo and ex vivo) calcium imaging in sensory neurons can be stored as raw data (nd2), exported data (xlsx), analysed data (xlsx, pzfx), Images/figures (tiff png, jpg, avi) with following estimated sizes: 10 GB/file, 10MB/file, 10MB/file, 1MB/file; total estimated size: 10 TB
- Video files from videocystometry, stored as AVI will be stored on an external hard disk in the LICR labo; total estimated size 8 TB.
-single-cell RNA-sequencing data of sensory neurons innervating bladder; stored as .fastq(.gz) files, sequencing alignment data stored as bam, differential expression stored as xlsx. Total estimated size: 10 TB. Sequence alignment data; stored as .bam files; total estimated size: 500

GB.
- RNA scope based in situ hybridisation will be used to determine localisation and image TRP channels. Parafin blocks slide sections and digital slides (czi) will be stored, estimated size: 10MB/file; total estimated size: 500 GB.
- Immunohistochemistry to determine certain TRP channels (fe TRPV4) - Parafin blocks slide sections digital slides will be stored as czi files, estimated size: 2GB/file; total estimated size: 100 GB.
- H&E stainings of tissue (slides) can be stored at room temperature, space is provided in the LICR lab. Digitalised H&E stainings will be stored as czi files when using Zeiss software or nd2 files when using Nikon, total estimated size 100 GB.
- Behavioural assays: videos to study behaviour in animals will be stored as mp4 files, estimated size 200MB/file; total estimated size 40 GB.
- qRT-PCR data to evaluate TRP expression will be analysed via StepOnePlus Software (eds) - 2MB/file, exported raw data (xlsx) - 50 kb/file, analysed data (xlsx, pzfx) - 2 MB/file, Images/figures (tiff, png, jpg) - 100 MB/file; total estimated size 5 GB.
- Filter papers of spotting experiments can be stored in blue boxes until definitive images of these papers are taken, space is provided in the animal hotel (LICR lab). Images of these filter papers are stored as tiff or jpg. files on the KU Leuven servers. Spotting experiments will be analysed with ImageJ.

3. Ethical and legal issues

3.1. Will you use personal data? If so, shortly describe the kind of personal data you will use. Add the reference to the file in KU Leuven's Record of Processing Activities. Be aware that registering the fact that you process personal data is a legal obligation.

Regular personal data will be used: Name and/or address, Contact details (tel. number, e-mail address,...) , Date/year of birth and/or age, Initials, personal identification number assigned to data subjects participating in the study such as EAD number.
Special/sensitive categories of personal data will be used: Health data (e.g. description of characteristics of physical features of the body, medical history and medical test information (such as blood samples results from scans and biopsies).

See S66341

3.2. Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? If so, add the reference to the formal approval by the relevant ethical review committee(s).

Yes. All studies are under revision or approved by the Ethics Committee Research UZ/KU Leuven.

2. The research using human biological material/human data has received formal approval from the UZ/KU Leuven Ethical Committee, with the following reference:

- S66341: The research project using bladder biopsies and cystectomy specimens from included patients entitled "Urinary symptoms in patients undergoing Bacillus Calmette-Guérin (BCG) therapy for non-muscle invasive bladder cancer (NMIBC): the functional role of Transient Receptor Potential (TRP) channels" is approved by the Ethics Committee Research UZ/KU Leuven.

The research using mice described in this project has received formal approval from the KU Leuven Ethical Committee, with the following reference:

- P023/2022: Functionele rol van TRP kanalen in preklinische modellen van inflammatoire blaaspijn: exploratieve experimenten

- Animals are housed in facilities of the Laboratory Animal Center of KU Leuven, which applies Standard Operation Procedures concerning housing, feeding, health monitoring to assure consistent care in accordance with European and national regulations and guidelines. Animal administrative, husbandry and animal welfare data are sensitive data and are stored in the LAIS database according to security procedure of KU Leuven.

3.3. Does your research possibly result in research data with potential for tech transfer and valorisation? Will IP restrictions be claimed for the data you created? If so, for what data and which restrictions will be asserted?

Yes.

Valorisation will be considered in consultation with KU Leuven LRD and VIB Tech Transfer.

3.4. Do existing 3rd party agreements restrict dissemination or exploitation of the data you (re)use? If so, to what data do they relate and what restrictions regarding reuse and sharing are in place?

The project under supervision of prof. Dr. Djalila Mekahli will collaborate with Dr. C. Gimpel in Germany. The anonymized data will be shared with Dr. C. Gimpel in Freiburg, Germany under a signed data transfer agreement for the purpose of data analysis and preparation of a joint publication. Because of the sensitive nature of answers to questionnaires, there are no plans to make source data publicly available and access will stay restricted to the study investigators. The investigators and the University Hospital Leuven will permit access to the source data, if required for the purposes of monitoring, audit, EC review, and/or regulatory inspection.

4. Documentation and metadata

4.1. What documentation will be provided to enable understanding and reuse of the data collected/generated in this project?

-All experiments will be documented using an Electronic Lab Notebook (eLABFTW), which will contain 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, which can be found on the LICR wiki-pages.

4.2. Will a metadata standard be used? If so, describe in detail which standard will be used. If not, state in detail which metadata will be created to make the data easy/easier to find and reuse.

For preclinical data:

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 specific datasets, additional metadata will be associated with the data file as appropriate.

For clinical data:

- Klinisch Werkstation (KWS) is a software package for the management of electronic patient records, developed 25 years ago in UZ Leuven. KWS is now used in different hospitals in Belgium.

- Formasa (UZ): Electronic case report forms (eCRF) will sometimes be collected using Formaza, a modified InfoPath (Microsoft) plug-in for KWS.

- REDCap: REDCap is a secure web application for building and managing online surveys and databases. While REDCap can be used to collect virtually any type of data in any environment (including compliance with 21 CFR Part 11, FISMA, HIPAA, and GDPR), it is specifically geared to support online and offline data capture for research studies and operations.

5. Data storage and backup during the project

5.1. Where will the data be stored?

Clinical data:

Study specific data will be collected from the (e)CRF and REDCap™ Production version 9.5.13 will be used to capture these data. For UZL the REDCap the System Administrator is Gert Goos: gert.goos@kuleuven.be. These databases can be stored on UZ Leuven servers or they can be stored on the REDCap servers for which a fee of 80 euros/database/year needs to be payed.

Electronic case report forms (eCRF) will sometimes also be collected using Formaza, a modified InfoPath (Microsoft) plug-in for KWS. Questionnaires will be collected via MyNexuzHealth, a

secured website and mobile apt allows patients to consult their personal health records in KWS and to input the data from the questionnaires into the KWS.

Laboratory data:

Our data are recorded on the internal and external storage of the computers attached to equipment and is duplicated on the storage facilities of our research unit.

Digital files will be stored on KU Leuven servers, except for private data that will be stored on KU Leuven secure server (digital vault).
- Tissue samples: Tissues will be stored locally in the laboratory. All human tissue samples will be registered with a Belgian biobank, in compliance with the Belgian law on human body material (dd 19-12- 2008).
- Omics data: omics data generated during the project will either be stored on KU Leuven servers or on The Flemish Supercomputer Centre (VSC), initially in the staging area and later in the archive area.
- Videocystometry: videos will be stored as AVI files and immediately stored on an external hard drive in the LICR labo.
- Genetically modified organisms: Mice will be maintained in facilities of the Laboratory Animal Center of KU Leuven, which applies Standard Operation Procedures concerning housing, feeding, health monitoring to assure consistent care in accordance with European and national regulations and guidelines. All animals will be registered in the Leuven Animal Information System (LAIS) database, along with corresponding genotyping information, ethical approval documents and animal provider receipts. Other biological and chemical samples: storage at 4°C and/or as frozen samples in cryovials as appropriate.
- Algorithms, scripts and softwares: All the relevant algorithms, scripts and software code driving the project will be stored in a private online git repository (https://github.com/LICRTV).

5.2. How will the data be backed up?

UZ Leuven - clinical data:
The data will be stored on the university's central servers with automatic daily back-up procedures.

KU Leuven - laboratory data:
KU Leuven drives are backed-up according to the following scheme:
- Data stored on the “L-drive” is 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.
- Data stored on the “J-drive” is backed up hourly, daily (every day at midnight) and weekly (at midnight between Saturday and Sunday); in each case the last 6 backups are kept.
- All omics data stored on the Flemish Supercomputer Centre (VSC) will be transferred on a weekly basis to the archive area which is backed up. Incremental backups are done daily from one 20 TB QNAP NAS to a second 20 TB QNAP NAS.
- Data stored on the digital vault is backed up using snapshot technology, where all incremental changes in respect of the previous version are kept online. As standard, 10% of the requested storage is reserved for backups using the following backup regime: an hourly backup (at 8 a.m., 12 p.m., 4 p.m. and 8 p.m.), the last 6 of which are kept; a daily backup (every day) at midnight, the last 6 of which are kept; and a weekly backup (every week) at midnight between Saturday and Sunday, the last 2 of which are kept.

5.3. 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.

There is sufficient storage and back-up capacity on all KU Leuven servers:
- the “L-drive” is an easily scalable system, built from General Parallel File System (GPFS) cluster with NetApp eseries storage systems, and a CTDB samba cluster in the front-end.
- the “J-drive” is based on a cluster of NetApp FAS8040 controlers with an Ontap 9.1P9 operating system.

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

- Data storage in a REDCAP database costs 80 euros per project per year. As this CA2 project consists of 5 seperate projects, total cost equals 400 euros per year.
- Formaza files are provided by our own PhD researchers, no costs are associated with the

development of these files.
-The costs of digital data storage are as follows: 173,78€/TB/Year for the “L-drive” and 519€/TB/Year for the “J-drive”.
-Maintaining a mouse colony alive costs about 1,200 euro per year (for 6 cages), excluding the costs of genotyping. When no experiment is planned with a particular mouse strain, and in compliance with the 3R’s rule (https://www.nc3rs.org.uk), cryopreservation will thus be used to safeguard the strain, prevent genetic drift, loss of transgene and potential infections or breeding problems. Cryopreservation of sperm/embryos costs about 500 to 700 euro per genotype, plus a minimal annual storage fee (25 euro per strain for 250 to 500 embryos). Frozen specimen are kept in two separate liquid nitrogen tanks at two different sites on campus. When necessary, the costs of revitalization from cryopreserved sperm/embryos are about 1,100/600 euro.
-Electricity costs for the -80° freezers present in the labs are included in general lab costs.
- For backup, the current KU Leuven tariffs are approx. 175 euros per TB per year. Data storage and backup costs are included in general lab costs.

5.5. Data security: how will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

- When using UZ Leuven REDCap, physical access to the data centers is logged and restricted to authorized KU Leuven Information Technology (IT) personnel, using badge identification. At the clinical database level only study team members, monitors and auditors/inspectors for whom the Coordinating or Principal Investigator (as applicable) has requested project-specific eCRF access, are granted data access. Upon successful training completion each user is centrally assigned a user role, associated with predefined system/data privileges, in accordance with CR DM-WI-001.

- Samples will be stored in the archive of O&N1. This room has a separate key to open the door. Access to O&N1 is controlled by electronic badge readers.

- The primary storage location for the data is on password-protected KU Leuven personal computers, with immediate backup to secure network-attached, redundant disk arrays managed by the lab, accessible only to selected members of the lab. Long- term storage for data that does not require repeated fast access is provided by the KU Leuven ICTS' Large Volume Storage service.

- Both the “L-drive” and “J-drive” servers are accessible only by laboratory members, and are mirrored in the second ICTS datacenter for business continuity and disaster recovery so that a copy of the data can be recovered within an hour. Access to the digital vault is possible only through using a KU Leuven user-id and password, and user rights only grant access to the data in their own vault. Sensitive data transfer will be performed according to the best practices for “Copying data to the secure environment” defined by KU Leuven. The operating system of the vault is maintained on a monthly basis, including the application of upgrades and security patches. The server in the vault is managed by ICTS, and only ICTS personnel (bound by the ICT code of conduct for staff) have administrator/root rights. A security service monitors the technical installations continuously, even outside working hours.

- All private data will be rendered anonymous before processing outside the digital vault. Only the PI will be granted access to the server to deposit private data. The PI will be the only responsible for linking patient information, survey data and/or tissue samples, and will strictly respect confidentiality. All de-identified data will be exported from the database by the PI, and stored on KU Leuven servers from where it can be accessed by the research and technical staff from the laboratory.

6. Data preservation after the end of the project

6.1. Which data will be retained for the expected 10 year period after the end of the project? If only a selection of the data can/will be preserved, clearly state why this is the case (legal or contractual restrictions, physical preservation issues, ...).

All data will be retained for at least 10 years after the end of the project.

6.2. Where will these data be archived (= stored for the long term)?

Clinical data:

Clinical data will be stored on the UZ Leuven's central servers with automatic back-up procedures for 25 years, conform the EC guidelines.

Laboratory data:

The data will be stored on the university's central servers (with automatic back-up procedures) for at least 10 years, conform the KU Leuven RDM policy. The costs (€156 per TB per year for “Large volume-storage”) will be covered by funding from the PIs.

Processed samples and data will be archived for at least 10 years in the facilities of LICR (O&N1; 8th floor).

As a general rule, datasets will be made openly accessible, whenever possible via existing platforms that support FAIR data sharing (www.fairsharing.org), at the latest at the time of publication. For all other datasets, long term storage will be ensured as follows:
-Digital datasets: files will be stored on the “L-drive”.
-Tissue samples: Tissues will be stored locally in the laboratory.
-Omics data: datasets will be stored on the “L-drive” or, for larger datasets, on the Vlaams Supercomputer Centrum

6.3. What are the expected costs for data preservation during these 10 years? How will the costs be covered?

In REDCap we pay 80 euros per database-project per year. These costs will be covered by funding of the PIs. Generally, we store the database on the REDCap server as long as the study is ongoing (fe during 2 years for WP 1, during 4 years for WP 2). Afterwards, when the study is terminated, we store these data on the UZ Leuven servers.

The total estimated cost of data storage during 10 years after the end of the project is 22589 €. This estimation is based on the following costs:
-The costs of digital data storage are as follows: 173,78€/TB/Year for the “L-drive” and 519€/TB/Year for the “J-drive”.
- Maintaining a mouse colony alive costs about 1,200 euro per year (for 6 cages), excluding the costs of genotyping. When no experiment is planned with a particular mouse strain, and in compliance with the 3R’s rule (https://www.nc3rs.org.uk), cryopreservation will thus be used to safeguard the strain, prevent genetic drift, loss of transgene and potential infections or breeding problems. Cryopreservation of sperm/embryos costs about 500 to 700 euro per genotype, plus a minimal annual storage fee (25 euro per strain for 250 to 500 embryos). Frozen specimen are kept in two separate liquid nitrogen tanks at two different sites on campus. When necessary, the costs of revitalization from cryopreserved sperm/embryos are about 1,100/600 euro.

Data storage and backup costs are included in general lab costs.

7. Data sharing and re-use

7.1. Are there any factors restricting or preventing the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions or because of IP potential)?

No

7.2. Which data will be made available after the end of the project?

Participants to the present project are committed to publish research results to communicate them to peers and to a wide audience. All research outputs supporting publications will be made openly accessible. Depending on their nature, some data may be made available prior to publication, either on an individual basis to interested researchers and/or potential new collaborators, or publicly via repositories (e.g. negative data).
We aim at communicating our results in journals that require full disclosure upon publication of all included data, either in the main text, in supplementary material or in a data repository if requested by the journal and following deposit advice given by the journal. Depending on the journal, accessibility restrictions may apply.
Biological material will be distributed to other parties upon reasonable request.

7.3. Where/how will the data be made available for reuse?

- In an Open Access repository
- Upon request by mail

Whenever possible, datasets and the appropriate metadata will be made publicly available through
repositories that support FAIR data sharing. As detailed above, metadata will contain sufficient information to support data interpretation and reuse, and will be conform to community norms. These repositories clearly describe their conditions of use (typically under a Creative Commons CC0 1.0 Universal (CC0 1.0) Public Domain Dedication, a Creative Commons Attribution (CC-BY) or an ODC Public Domain Dedication and Licence, with a material transfer agreement when applicable). Interested parties will thereby be allowed to access data directly, and they will give credit to the authors for the data used by citing the corresponding DOI. For data shared directly by the PI, a material transfer agreement (and a nondisclosure agreement if

applicable) will be concluded with the beneficiaries in order to clearly describe the types of reuse that are permitted.

7.4. When will the data be made available?

- Immediately after the end of the project
- Upon publication of the research results

Relevant datasets will be made publicly available with publication.

Results of general interest that will not be published can be made available to other researchers after the end of the project.

7.5. Who will be able to access the data and under what conditions?

Whenever possible, datasets and the appropriate metadata will be made publicly available through
repositories that support FAIR data sharing. As detailed above, metadata will contain sufficient information to support data interpretation and reuse, and will be conform to community norms. These repositories clearly describe their conditions of use (typically under a Creative Commons CC0 1.0 Universal (CC0 1.0) Public Domain Dedication, a Creative Commons Attribution (CC-BY) or an ODC Public Domain Dedication and Licence, with a material transfer agreement when applicable). Interested parties will thereby be allowed to access data directly, and they will give credit to the authors for the data used by citing the corresponding DOI. For data shared directly by the PI, a material transfer agreement (and a nondisclosure agreement if applicable) will be concluded with the beneficiaries in order to clearly describe the types of reuse that are permitted.

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

It is the intention to minimize data management costs by implementing standard procedures e.g. for
metadata collection and file storage and organization from the start of the project, and by using free-to-use data repositories and dissemination facilities whenever possible. Data management costs will be covered by the laboratory budget. A budget for publication costs has been requested in this project.

8. Responsibilities

8.1. Who will be responsible for the data documentation & metadata?

- Clinical research: Clinical trial assistant, Lotte Vanmeerbeek.

- Preclinical research: The research and technical staff will ensure data storage and back up, with support from Dr. Andrei Segal Stanciu for the electronic laboratory notebook (ELN) and KU Leuven drives.

The promotor and co-promotors supervise.

8.2. Who will be responsible for data storage & back up during the project?

The promotor, together with Dr. Andrei Segal Stanciu.

8.3. Who will be responsible for ensuring data preservation and sharing?

The promotor, together with Dr. Andrei Segal Stanciu.

8.4. Who bears the end responsibility for updating & implementing this DMP?

The end responsibility for updating and implementing the DMP is with the supervisor (promotor).

The promotor wishes to stress that the DMP can only be implemented under the condition that the ELN can be used in all experimental rooms. Currently, wifi coverage is lacking in several of the rooms (despite multiple requests to ICTS), making it impossible to use the ELN, and thus to implement a DMP.