DMP title

Project Name Development of a mouse model for Multiple System Atrophy based on peripheral triggers of a-synuclein aggregation and propagation - DMP title

Project Identifier 3M190532

Grant Title 1SE8922N

Principal Investigator / Researcher Anna Barber Janer

Project Data Contact Anna Barber Janer, anna.barberjaner@kuleuven.be

Description Multiple system atrophy (MSA) is a rare neurodegenerative disease characterized by a rapid and aggressive decline in motor and autonomic functions. Currently there are no symptomatic or disease modifying treatments for MSA patients. The major neuropathological hallmark are alpha-synuclein (aSYN) protein aggregates, which are mostly found in oligodendrocytes. Most studies have focused on the central nervous system (CNS), but recent evidence has shown aSYN aggregates in the urinary tract of MSA patients, which correlates with urinary dysfunction being one of the earliest symptoms. aSYNâ€™s ability to propagate like a prion supports the hypothesis that the disease may start in the periphery and later advance to the brain when the motor deficits appear. We hypothesize that peripheral inflammatory insults, such as infections, could act as triggers of MSA in susceptible individuals. To develop disease-modifying therapies for MSA we rely on limited understanding of the disease aetiology. In this project we aim to develop a novel MSA model to study aSYN propagation from the urinary tract to the CNS as a potential contributor to disease pathogenesis. Additionally, we aim to elucidate the role of infections as triggers or modifiers of disease progression. This project will provide new insight into pathogenic mechanisms leading to MSA together with the development of tools that can be used for prospective modelling or therapeutic approaches.

Institution KU Leuven

1. General Information

Name applicant

Anna Barber Janer

FWO Project Number & Title

1SE8922N

"Development of a mouse model for Multiple System Atrophy based on peripheral triggers of a-synuclein aggregation and propagation"

Affiliation

- KU Leuven

2. Data description

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

- Generate new data

Describe in detail the origin, type and format of the data (per dataset) and its (estimated) volume. This may be easiest in a table (see example) or as a data flow and per WP or objective of the project. If you reuse existing data, specify the source of these data. Distinguish data types (the kind of content) from data formats (the technical format).

Type of Data	Format	Volume	How created
Analysis of microscopy data	.xls, .pzfx	200-500MB	Quantification of microscopy image data performed using Fiji, QuPath and cloud-based Aiforia, in microsoft excel and GraphPad prism
Analysis of qRT-PCR data	.xls, .pzfx	50-100 MB	Analysis of qRT-PCR data using CFX Maestro software (bio-rad). Compilation of data in microsoft excel and GraphPad prism

Analysis of western blot images	.xls, .pzfx	50-100 MB	Compilation and quantification of western blot images performed using Fiji, in microsoft excel and GraphPad prism
Analysis of motor behaviour	.Avchd (video recordings), paper/.xlsx, .pzfx	150 GB	- .docx for protocol on how to perform the tests - Video recordings of animal behaviour - Measures associated with motor performance on paper records will be transferred to digital .xlsx format as soon as possible - Quantification with statistical analysis will be performed in GraphPad prism
Figures of data for publication	.ai	50 GB	Figures of amalgamated data produced during the project, created using adobe illustrator
DNA plasmids	Tubes containing DNA plasmids stored at -20C	NA	DNA plasmids produced during the project, derived from existing DNA plasmids provided by commercial and non-commercial suppliers
DNA sequencing files	.abi	100 MB	Sequencing of plasmids, sequencing of PCR products performed by LGC genomics
Lab Book and protocols	Paper notes, OneNote	NA	Dated written notes about everyday tasks associated with carrying out experimental procedures. Protocols
Manuscript	.docx, .pdf	50 MB	Compilation of data to disseminate project results
Microscopy images	.tiff, .lif, .svs, .jpg, .ome-tiff	1000 GB	Transmitted-light microscopy, epifluorescent microscopy and confocal microscopy of mouse brain, spinal cord and urinary bladder
Microscopy slides	Glass microscopy slides	1000-5000 slides	Microscopy slides used during imaging, consisting of formaldehyde-fixed tissue immunostained or dyed using chemicals
Mouse urine samples	Tubes containing mice urine	100-500	Tubes of mouse urine collected during the project
PCR gel images	.tiff, .ome-tiff	50 MB	Images of ultraviolet irradiated DNA samples run on agarose gels. Images collected using BioDoc-It imaging system

Plasmid maps	.dna	50 MB	*In silico* reprocessing of existing data from papers and online databases, data derived from DNA sequencing files
Presentations of data	.pptx	500 MB	Presentations compiling analysed data and images to disseminate project results
Protein samples	Tubes containing protein	100-500	Samples of denatured or undenatured proteins extracted from tissue or cells using detergents
qRT-PCR raw data	.eds, .xls	500 MB	Raw qRT-PCR data collected using CFX Opus 96 thermocycler and CFX Maestro software (bio-rad)
Recombinant viral vectors	Tubes containing recombinant viral vectors stored at -80C	NA	Viral vectors produced during the project with the support of the Leuven Viral Vector Core
RNA and cDNA samples	Tubes containing RNA or derived cDNA	100-500	RNA/cDNA samples extracted from tissue or cells
Western blot images	.gel, .tiff, .ometiff	500 MB	Tif images of chemiluminiscent signal taken using ImageQuant LAS 4000 instrument

3. Legal and ethical issues

Will you use personal data? If so, shortly describe the kind of personal data you will use. Add the reference to your file in KU Leuven's Register of Data Processing for Research and Public Service Purposes (PRET application). Be aware that registering the fact that you process personal data is a legal obligation.

- No

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

We will perform experiments on mice. All necessary safety measures for laboratory and animal work will be taken. The animal experiments will comply with the relevant ethical principles and applicable international, EU, and national law EU Directives 2010/63/EU and 86/609/EEC. The permission to perform the animal experiments covered by this project has been approved by the Animal Ethics Committee at KU Leuven. Ethical permission for animal work was given for following ECDs: P008/2021.

Does your work 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

The project largely contains fundamental research that could result in data with potential for tech transfer and valorisation. It holds a potential to medical translation or application in the clinic but only in the long run. There might be IP depending on the obtained results. This may

involve the development of animal models that would be attractive for biotech companies to perform their drug discovery programs. In case our findings are promising for clinical application, IP protection will be ensured in collaboration with KU Leuven Research & Development (LRD). Our IOF fellow, Dr. Veronique Daniëls, will coordinate all dissemination and exploitation efforts. However, the IP protection does not withhold the research data from being made public. In case a decision is taken to file a patent application it will be planned so that publications need not be delayed.

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 are in place?

- No

4. Documentation and metadata

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

For every WP we will have an index file/read me file (.txt file), linking the name, location (folder and subfolder on server) and description of experimental files. Each individual file with experimental data will contain information on the study design and date, the origin of the samples, storage, and all necessary information for an independent analyst to use or reuse the data accurately and efficiently.

Digital data:

- For microscopy images the following information will be noted: dimensions, image type, bit-depth, pixel sizes and microscope settings. The methodology and protocol will be described in detail in the lab book. A ReadMe file of the image collection will be written. We will also keep a record of the date of the experiments and slides used in the lab book and the excel file relating to that experiment together with detailed steps involved in data analysis and relevant analysis scripts (Fiji, QuPath).

- For molecular work, the methodology and protocols will be described in detail in the lab book. We will also keep a record of the date of the experiments, origin of samples used, storage and results in the lab book and the excel file relating to that experiment.

- For behavioural data, a protocol will detail how to perform the test and how the videos will be analysed, including software used (if any), readouts and observations in an excel document. We will also keep a record of the date of the experiments, animals used and staff in the lab book and the excel file relating to that experiment.

Physical data:
Samples taken from experiments will be documented and stored for up to three years after the end of the project. Storage will be in fixative or in freezers depending on the kind of sample. Immunohistological stained slides will be stored in approriate boxes in a dry place or fridge.

Will a metadata standard be used? If so, describe in detail which standard will be used. If no, state in detail which metadata will be created to make the data easy/easier to find and reuse.

- Yes
- No

The OME-TIFF metadata standard will be used for imaging data from microscopy, western blot, PCR gel experiments.

Where no metadatastandard exists, metadata will be stored based on the Dublin core standard (http://www.dcc.ac.uk/resources/metadata-standards/dublin-core).

5. Data storage and backup during the FWO project

Where will the data be stored?

All digital data will be stored on servers centrally managed by ICTS KU Leuven and with back-up capacities (Large Volume-storage). During the project we will also use KU Leuven OneDrive for Business for active use of the data.

The physcial data, consisting of engineered recombinant viral vectors,(immuno)histologically stained tissue sections, biochemical samples (protein extracts, mRNA), western blots, etc. will be

stored in freezers/fridges. Also unstained paraffin/cryo sections will be stored at a dry/cold place for possible future use. Bacterial stocks are stored in -80C in glycerol stocks and a second vial will be available for backup.

AI models (AIforia) for automated image and pathology detection will be stored in Aiforia Cloud and is accessible to a restricted number of researchers in the lab.

How is backup of the data provided?

We will use the back-up facilities of KU Leuven ICTS with automatic daily back-up procedures that allow for disaster recovery.

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

KU Leuven drive servers allows for sufficient (unlimited) data storage.

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

Data storage and backup costs are included in general lab costs. Our lab has a yearly subscription to an an online backup service paid from the general budget of the laboratory and a second online cloud service via Aiforia. The yearly cost of the service is 10.000 euros. This cost includes unlimited data storage, not only the data belonging to the present project.

Electricity costs for the -80° and -20° freezers and refrigerators present in the labs as well as the cost of liquid nitrogen cryostorage are included in general lab costs.

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

All network storage is hosted in the KU Leuven ICTS data center, with a mirror in the second ICTS center, to provide disaster recovery and additional back-up capacity, thus guaranteeing long-term data availability. Access to data is conditioned by KU Leuven security groups. All notebooks and physical data are stored in the labs. Entry to the lab requires ID-card and key. Access to the digital data is u-number and password controlled.

6. Data preservation after the FWO project

Which data will be retained for the expected 5 year period after the end of the project? In case only a selection of the data can/will be preserved, clearly state the reasons for this (legal or contractual restrictions, physical preservation issues, ...).

After the end of the project, all data will be retained for the 5-year period expected by KU Leuven.

Where will the data be archived (= stored for the longer term)?

As a general rule, datasets will be made openly accessible, whenever possible at the latest at the time of publication. For all other datasets, long term storage will be ensured as follows:

- Digital datasets will be stored on storage space of an online data-backup service for at least 10 years, conform the KU Leuven RDM policy.

- Physical samples, such as viral vectors or microscopy slides, will be stored appropriately for potential future use.

What are the expected costs for data preservation during the retention period of 5 years? How will the costs be covered?

Electricity costs for the -80° freezers in the labs are included in general lab costs. The cost of the laboratory's professional subscription to the online data backup service is 10.000 Euros per year (50.000 Euros for 5 years). This cost includes unlimited data storage, not only the data belonging to the present project. Data storage and backup costs are included in general lab costs.

7. Data sharing and reuse

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)?

- No

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

Data will only be made available in case of publications that require the publication/disclosure of the dataset.

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 top 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. Physical data (e.g. cell lines) will be distributed to other parties if requested.

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

- Upon request by mail

When will the data be made available?

- Upon publication of the research results

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

As stated above, only requests via mail will be answered. Privacy and legal experts will be consulted when sharing data with researchers outside of the research group.

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

NA

8. Responsibilities

Who will be responsible for data documentation & metadata?

The day-to-day data documentation and metadata will be managed by the PhD student working on this project Anna Barber Janer (anna.barberjaner@kuleuven.be).

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

The supervisors of the project (Prof. Veerle Baekelandt and Dr. Wouter Peelaerts) and the day-to-day manager of the project PhD student Anna Barber Janer.

Who will be responsible for ensuring data preservation and reuse ?

The supervisors of the project (Prof. Veerle Baekelandt and Dr. Wouter Peelaerts).

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

The PI (Prof. Veerle Baekelandt) bears the end responsibility of updating and implementing this DMP.