DMP title

Project Name DMP_FWO_G090922N - DMP title

Grant Title G090922N

Principal Investigator / Researcher Prof Dr Laurens Ceulemans

Project Data Contact laurens.ceulemans@kuleuven.be

Description As ultimate therapy for patients suffering from end-stage lung disease, LTx prolongs survival and improves quality of life. However, LTx has a poor long-term outcome. Severe primary graft dysfunction (PGD) at any time point during the first three days after LTx is found in 30% of patients and is associated with increased morbidity (length of mechanical ventilation, intensive care) and both, early (90 days) and late (1-, 5-, 10-year) mortality. But in clinical practice, treatment for PGD is limited. Ex-vivo lung perfusion (EVLP) is a platform that maintains lung grafts in a physiologic and metabolic active state through perfusion and ventilation. EVLP was designed to enable evaluation of lung grafts with questionable quality before LTx. By reducing the cell injury and immune activation with targeted therapies before LTx, EVLP offers a unique platform to treat the lung and prevent PGD to occur, without potentially harming other organs. The rat EVLP and LTx model is an excellent starting point for development of new treatment strategies. In this project we focus on the clinical potential of new treatments for PGD supported by data with a strong translational value towards PGD in clinics. The effect of our PGD treatment strategy will be assessed based on lung graft function and imaging: gas exchange, lung compliance and computed tomography (CT) imaging. These are the same tools that clinicians use to follow-up LTx recipients and that are used to determine severity of PGD. The project consists of three objectives: 1. Create a model of rat PGD after EVLP and LTx with lung imaging/function quantifying PGD 2. Show that an AAV vector can enable transgene expression during rat EVLP and after LTx 3. Show that a CRISPR encoding AAV vector reduces the severity of PGD after rat EVLP and LTx Combining EVLP and LTx models is a novel approach that increases the translational value. AAV vectors encoding reporter genes allow us to measure transgene expression with bioluminescence and histological staining. This has never been performed after rat EVLP or LTx. And CRISPR gene therapy during rat EVLP and LTx will be an innovative step in LTx research.

Institution KU Leuven

1. General Information

Name applicant

Prof Dr Laurens Ceulemans

FWO Project Number & Title

Project Number: G090922N

GENE THERAPY DURING EX-VIVO LUNG PERFUSION FOR TREATMENT OF PRIMARY GRAFT DYSFUNCTION AFTER LUNG TRANSPLANTATION

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).

WP1:

- type: computed tomography (CT) images; format: .tif; volume: 450 GB; origin: chest CT of rats
- type: microscopy; format: .tif; volume: 15 GB; origin: histology rat lungs
- type: physiological parameters; format: .xls; volume: 10 MB; origin: ex-vivo perfusion circuit, ventilator, arterial blood gas, wet/dry ratio
- type: interleukin ELISA; format: .xls; volume: 10 MB: origin: ELISA bronchoalveolar lavage

and serum rat

WP2A:

- type: microscopy; format: .tif; volume: 21 GB; origin: histology rat lungs
- type: physiological parameters; format: .xls; volume: 10 MB; origin: ex-vivo perfusion circuit and ventilator
- type: bioluminescence; format: .tif; volume: 4.2 GB; origin: IVIS bioluminescence measurement of rat

WP2B:

- type: computed tomography (CT) images; format: .tif; volume: 90 GB; origin: chest CT of rats
- type: microscopy; format: .tif; volume: 3 GB; origin: histology rat lungs
- type: physiological parameters; format: .xls; volume: 10 MB; origin: ex-vivo lung perfusion circuit and lung ventilator
- type: bioluminescence; format: .tif; volume: 600 MB; origin: IVIS bioluminescence measurement of rat

WP3A:

- type: interleukin RNA polymerase chain reaction (PCR): format: .xls; volume: 25 GB; origin: PCR rat serum
- type: interleukin Western blot: format: .tif; volume: 5 GB; origin: Western blot rat serum

WP3B:

- type: computed tomography (CT) images; format: .tif; volume: 150 GB; origin: chest CT of rats
- type: microscopy; format: .tif; volume: 5 GB; origin: histology rat lungs
- type: physiological parameters; format: .xls; volume: 10 MB; origin: ex-vivo perfusion circuit, ventilator, arterial blood gas, wet/dry ratio
- type: bioluminescence; format: .tif; volume: 1 GB; origin: IVIS bioluminescence measurement of rat

- type: interleukin RNA polymerase chain reaction (PCR): format: .xls; volume: 25 GB; origin: PCR rat serum
- type: interleukin Western blot: format: .tif; volume: 5 GB; origin: Western blot rat serum

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

Privacy Registry Reference:
Short description of the kind of personal data that will be used:

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

Ethical committee approval: P064/2021

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?

- No

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 the experimental procedures and analyses of the end points a detailed description of the data will be provided.

A standard operating procedure for every step of the experimental process will be registered in an electronic lab notebook.

The collection of data and the type of data with necessary annotations will be stored and saved for multiple years on the laboratory server.

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.

- No

5. Data storage and backup during the FWO project

Where will the data be stored?

The physical data will be stored in appropriate storage places including histology rooms, fridges, freezers and cryotanks.

Digital data will be stored on our dataservers:

GBW-0076_LTx is a smaller (0.5Tb) server but faster server on which each fellow stored analyzed/processed data.

GBW-0017_LTx is a larger (15Tb) server but slower on which we store all raw data for long time. The annual costs are 156,6 euro.

Copies of the raw data and unanalyzed data are made and kept on personal devices only by members of our research group.

How is backup of the data provided?

Snapshots:

Backups of project data on faculty network shares are made using “snapshot” technology, which is the online storage of incremental data changes. The standard backup regime is as follows:

- An hourly backup (at 8 AM, 12 PM, 4 PM and 8 PM) the last 6 of which are stored on our servers
- A daily backup, at midnight, the last 6 of which are stored on our servers
- A weekly backup, Saturday night at midnight, the last 12 of which are stored on our servers

The end user can use his own Windows PC to restore files to an older version using the “previous versions” function. According to the above backup scheme, it is possible to go back in time up to 12 weeks (~3 months).

Mirror:

For the purpose of “business continuity” or “disaster recovery”, a mirror (exact copy) of all data is created in a second datacenter. The data are copied every hour to the second datacenter. In the event that the primary storage unit is corrupted, the ICTS team can get this copy online within the hour.

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

Yes and this is still expandable:

Our data will be stored at the KUL university's secure environment, of which daily backups are made by the ICT to secure the data. Our dataservers are:

GBW-0076_LTx (a smaller but faster server on which each fellow stored analyzed/processed data).

GBW-0017_LTx (a larger server but slower on which we stored all raw data for long time).

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

For GBW-0076_LTx the annual cost is 519 euro/terrabyte. We will use 500 GB storage on this sever, resulting in an annual cost of 259.5 euro/year.

For GBW-0017_LTx the annual costs are 156,6 euro/terrabyte. We will reserve 1 TB for this project resulting is a yearly cost of 156.6 euro/year.

The overall currently yearly cost for both servers will be 416.1 euro. The total budget needed for the 4 years of the project is about 1664 euro.

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

The data are secured on both servers by the university ICT. All ICT solutions at KU Leuven are subject to the university-wide ICT information security standards. The group ICT service organizes the raw network storage, it procures from central ICT services in such a way that access permissions are limited, fixed, delegated to and audited by data managers who do not need to have an IT background.

Access to these servers are restricted to the research group members. The lab manager (Karen Maes) and the PI of the project control who has access to the servers.

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, ...).

Certainly, raw data will be stored for a longer period.

Big dataset that impact on the need of server space are datasets of computed tomogrpahy scans, microscopy, bioluminescence and molecular analyses (PCR, Western blot). Physiological parameter data in excel do not impact server space.

Raw digital data of scans, slide picture and molecular profiles are stored on the large volume server. Analyzed subdatasets and clinical and end-analytical excel data stored at the smaller server by the individual researchers are always evaluated at the end of the PhD. The excess of data is removed and valuable data remain at the large volume server under the name the fellow in a folder ‘old fellows”. Currently this concept is permanent storage but this can be reconsidered in the future. A minimum of 5 years is considered which allows us to reanalyze all published work if needed.

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

Data will remain on the servers mentioned before. The large volume server (GBW-0076_LTx) is more used for the raw data and long-time storage.

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

Considering the currently yearly cost we expect costs for data preservation (156.6 EUR/TB/year) to be about 783 euro. The department CHROMETA reserves for each separate group per year a small budget which is enough to cover these annual (and total) cost of basic storage

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?

No data will be made available, only upon request to the principal investigator.

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

Data will be available upon request to the principal investigator.

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?

All data will be available upon request to the prinicpal investigator.

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

No cost expected.

8. Responsibilities

Who will be responsible for data documentation & metadata?

Data documentation and metadata will be organized by the PIs and fellows organizing the laboratory and project.

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

Both servers are dedicated to the PI of the project and access is managed by the PI and the lab manager. ICT (Gert Goos as contact person and PI) is handling back-up and if needed expansion of storage capacity.

Who will be responsible for ensuring data preservation and reuse ?

All persons mentioned before being the PI and fellows.

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

The PI, Prof Dr Laurens Ceulemans, bears the end responsibility of updating & implementing this DMP.