TARGETING CELL SURFACE RECEPTORS TO INHIBIT METASTATIC GROWTH

A Data Management Plan created using DMPonline.be

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Project abstract:
Breast cancer is the most prevalent cancer and Belgium has the highest incidence rate in Europe. At early-stage disease survival of patients is more than 90%. However, once cancer cells spread to other organs and metastases arise, this drops to less than 25%, resulting in over 685,000 deaths per year. Thus, there is an urgent need to define novel therapeutic strategies against metastatic breast cancers.
We have found that patients with metastatic breast cancer often have a genome amplification in their tumor specific to a cell surface protein called NMDA receptor. This receptor is activated by molecules including one called aspartate. We find that aspartate is elevated in organs of mice and patients with breast cancer, increasing the growth of metastases. Thus, we hypothesize that targeting the activation of the NMDA receptor by aspartate inhibits breast cancer metastases. We will 1. define how aspartate activates the NMDA receptor in metastases; 2. identify how an active NMDA receptor promotes metastases; and 3. target the NMDA receptor to inhibit metastases growth. We will exploit biochemical assays, multi-omics analysis, bioinformatics and clinical approved drugs in breast cancer cells, mice and patient samples.
In summary, we will dissect the function of the NMDA receptor in metastases. We expect to contribute in the long-term to the use of NMDA receptor inhibitors against metastases in the clinic.

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DPIA

DPIA

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

- Yes

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GDPR

GDPR

Have you registered personal data processing activities for this project?

- Not applicable as patients are deceased upon collection of tissue samples

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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)

Data will be initially collected in a variety of file formats which allows import into e.g. Microsoft Excel. These files will also be stored in Open Document Format or as CSV files. Digital images will be saved as TIFF files with an estimated volume of 500 GB.
Detailed lab notes and a digital lab book will be used, which will contain information on the experimental setup, sampling methodology, and all information necessary to use the data accurately and effectively. The main outcome of the research will be in terms of manuscripts, which will be made publicly available via open access. These articles (and their supporting information) will also describe the analyzed samples in detail.

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 data will be stored on the university's central servers with automatic daily back-up procedures. These provisions are already in place (current capacity 3 TB).
The responsibilities are as follows:
• Data documentation: Researchers working on the project (lead Ms Doglioni supported by Dr. Ferreira Campos and Dr. Fernandez-Garcia)
• Storage & back up during the project: Researchers working on the project (lead Ms Doglioni, Dr. Ferreira Campos and Dr. Fernandez-Garcia) and Prof. Fendt
• Data preservation and reuse: Prof. Fendt
• Updating & implementing this data management plan: Prof. Fendt

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)

All data will be retained for the expected 5 year period after the end of the project. The data will be stored on the university's central servers (with automatic back-up procedures), conforming with the KU Leuven research data management policy.

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)

The data do not require additional security measures. Patient data will be accessed through the UZ Leuven UPTIDER consortium and will contain no information that can allow the identification of the identity of the patients.

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

Data sharing and reuse: Upon publication of the research results, the full datasets will be made available upon request and adhering to GDPR law.

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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
Cell lines	Cell lines (mouse 4T1 and EMT6.5 lines; human MDA-MB-231, HCC70 and MCF10A-HRASV12 lines) will be stored in liquid nitrogen tanks	Generate new data and reuse existing data	Physical	/	/	/	1-2 boxes for 81 samples in the LN tank
Mouse tissues	primary breast tumor and metastatic lung tissue of Balb/c, nude and PDX mouse models	Generate new data	Physical	/	/	/	1 big storage box for FPPE imbedded tissue blocks on room temperat

							ure, 8 small storage box for snapfrozen tissues in the -80 freezer (half a rack)
Human samples	Interstitial fluid of multiple metastatic organs as well as metastatic tissue of multiple organs will be stored in -80 freezer	Generate new data/reuse existing data	Physical	/	/	/	3 full racks in the -80 freezer (48 small storage boxes)
Plasmids	Overexpression and knockdown plasmids will be stored in -20 degrees freezer	Generate new data/reuse existing data	Physical	/	/	/	1 storage box for eppendorf tubes in -20 freezer
Viral vectors	Viral vectors will be stored in -80 degrees freezer	Generate new data	Physical	/	/	/	1 storage box for eppendorf tubes in the -80 freezer
Primers	Oligonucleotide primers for qPCR will be stored at -20 degrees.	Generate new data/reuse existing data	Physical	/	/	/	1 storage box fer eppendorf tubes in -20 freezer
Chemicals	13C tracers, pharmacological drugs, ... will be stored at the required temperature (room temperature, -20 degrees or -80 degrees)	Generate new data/reuse existing data	Physical	/	/	/	Storage in chemical cabinet or appropriate freezer
Antibodies/fluorescent probes	Antibodies used for multiplex immunohistochemistry, western blotting, Cellular thermal shift assay and live imaging	Generate new data/reuse existing data	Physical	/	/	/	1 storage box fer eppendorf tubes in -20 freezer
Inventory files	Inventory files containing detailed information about cell lines, chemicals, oligonucleotides,	Generate new data	Digital	Other	.xlsx	<1GB	/

	plasmids, lentiviral vectors, antibodies, mouse tissues and pseudonymized human samples and their storage location						
Microscopy images	Microscopy images of cell cultures	Generate new data	Digital	Experimental	.jpg/.tiff	<100GB	/
H&E and multiplex immunohistochemistry stainings	High quality scans of H&E or multiplex immunohistochemistry stainings of primary tumor and lung metastases, analysis using QuPath software	Generate new data	Digital	Experimental	.qptiff/.xlsx	<100GB	/
Digital photographs	Images of mouse tissues/metastasis will be taken with a digital camera	Generate new data	Digital	Observational	.jpg	5GB	/
Bioluminescence images	Bioluminescence imaging will be performed to measure the luciferin flux using the IVIS Spectrum system. Bioluminescence will be analyzed using the LivingImage processing software.	Generate new data	Digital	Experimental	.txt/.xlsx/ .tiff/.jpg	<1GB	/
MRI images	PDX tumors will be monitored with small animal magnetic resonance imaging	Generate new data	Digital	Experimental	.tiff	<1GB	/
RNA sequencing/polysome profiling	Sequencing data file (.fastq), count matrix (.mtx) and genome-aligned (.bam) files will be generated. Data analysis will be conducted in R, generating R script files (.R) with analysis output (.RData, and .txt). Gene set enrichment analysis (GSEA) will be conducted,	Generate new data	Digital	Experimental	.fastq/.mtx /.bam/.R/ .Rdata/.txt /.gmt/.rnk /.bedGraph/ .tdf/.html/.xlsx/.png	100GB	/

	requiring libraries of pathways (.gmt) and normalized transcriptome reads in a ranked format (.rnk). The data will be will visualized in .bedGraph and .tdf files. Output files are produced in various formats (.html, .xlsx, .png images).						
Proteomics	Peptides will be injected for LC-MS/MS analysis on an Ultimate 3000 RSLCnano system in-line connected to a Q Exactive HF BioPharma mass spectrometer (Thermo). Proteomics data files will be processed using the Maxquant software and the Uniprot Mus Musculus database.	Generate new data	Digital	Experimental	.raw/.csv /.mstune/ .mscal/.txt /.xlsx/ .pdf	100GB	/
Mass spectrometry data of bulk metabolomics, 13C tracing and chiral LC-MS	Tissue and plasma samples will be measured using the GC-MS and LC-MS systems, resulting in the generation of raw data files (.ms and .d files, respectively). The .ms and .d files will be integrated using the Agilent ChemStation (compatible with the .ms files) and Agilent MassHunter software (compatible with the .d files). The integrated data will subsequently be exported as excel files (.xlsx)	Generate new data	Digital	Experimental	.ms/.d/.xlsx /.m/ .mat/.png /.pdf	5GB	/

	and further analyzed in MATLAB, leading to the generation of data analysis scripts (.m) and data files (.mat). The output of the data analysis will be exported in excel files (.xlsx) and figure files (.png or .pdf).						
Spatial metabolomics	Mass spectrometry imaging data will be obtained from the mouse and human tissues with Matrix-Assisted Laser Desorption Ionization (MALDI) and processed using MetaboScape from Bruker to perform non-targeted analyses. The raw data files (.d) are stored on the acquisition computer and on the lab server after data processing. Additional files created during the acquisition are .txt files, containing the sample information and metadata and .mis file for data visualization in the Scils lab software from Bruker. A metaboscape compound annotations .mca file is created with MetaboScape and allows the visualization of the identified metabolites in Scils Lab, leading to the generation of .slx files, that	Generate new data	Digital	Experimental	.d/.txt/.slx/.png	250GB	/

	can be exported to .png images.						
Western blotting images	Protein expression analysis using the LAS4000 imager and ImageQuant software	Generate new data	Digital	Experimental	.gel/.tiff/.jpg	5GB	/
Protein quantification	Quantification using BCA	Generate new data	Digital	Experimental	.xlsx	<1GB	/
RT-qPCR	Gene expression analysis from cells/tissues using QuantStudio3	Generate new data	Digital	Experimental	.xlsx	<1GB	/
Statistical and graphical analysis	GraphPad Prism9 will be used for all statistical analyses and graphical designs	Generate new data	Digital	Experimental	.pdf/ .png/ .wmf / .svg	5GB	/
Electronic lab book	Experimental and computational protocols, as well as details related to collection and processing of data (both documentation and metadata) will be stored on the electronic lab book platform Benchling	Generate new data	Digital	Observational and Other	.pdf	<1GB	/

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, we will reuse research material to generate new data.

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, human subject data
- Yes, animal data

Clinical data from patients will be accessed through the UZ Leuven biobanks and will only contain information on the age of the patient, initials and a personal identification number as well as 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)). GDPR approval was obtained before applying for ethical approval at the KU/UZ Leuven EC by Prof. Christine Desmedt. The approval is available and outlined in EC S64410.
Animal experiments will be performed during this project. All experiments have been approved by the Ethical Committee for Animal Experimentation (ECD) at KU Leuven and are available and outlined in ECD #P025-2020.

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.

- Yes

Clinical data from patients will be accessed through the UZ Leuven biobanks and will only contain information on the age of the patient, initials and a personal identification number as well as 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)). GDPR approval was obtained before applying for ethical approval at the KU/UZ Leuven EC by Prof. Christine Desmedt. The approval is available and outlined in EC S64410.

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

Intellectual Property arising from this work is managed as per the framework agreement between the VIB (VIB Tech Transfer) and the KU Leuven, the two participating institutes in this study.

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.

- Yes

Yes, as above, dissemination or exploitation of the data is managed according to the framework agreement between the VIB and the KU Leuven.

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.

- Yes

Intellectual Property arising from this work is managed as per the framework agreement between the VIB (VIB Tech Transfer) and the KU Leuven.

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).

Protocols and details related to data collection and processing will be recorded in electronic lab books (Benchling) by the lead PhD scientist (Ms. Ginevra Doglioni) and lab technician (Ms. Ines Vermeire). Data folders containing raw and processed data will be hierarchically organized and labeled based on the source of the data, the type of experiment, the date of data generation, and the different experimental conditions analyzed. Data analysis methods and particularities (including metadata) will be described in README.txt and Excel files included in these folders. All files will be stored in the KU Leuven Large Volume Storage space (L-Drive), with sharing possibilities via One Drive (managed by the KU Leuven IT department).

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

Text documents and Excel files stored within each experiment folder in the L-Drive will contain guidelines describing data collection/analysis methods and all relevant metadata (including experimental conditions, sample keys, computational analysis pipelines and their parameters) to ensure the reusability of the data and the reproducibility of any further data generation.

3. DATA STORAGE & BACK-UP DURING THE RESEARCH PROJECT

Where will the data be stored?

Upon data collection/preprocessing, temporary copies of the data will primarily be stored in the KU Leuven-managed personal OneDrive account of the lead PhD scientist (Ms. Ginevra Doglioni) and lab technician (Ms. Ines Vermeire). A copy of the data will be immediately uploaded to the KU Leuven Large Volume Storage space (L-Drive) for long-term preservation and backup.

How will the data be backed up?

Data stored on the KU Leuven L-Drive is managed, maintained, and backed up by KU Leuven IT services.

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

The KU Leuven L-drive has sufficient storage capacity for the outlined project. We estimate that 1-2TB of data storage space will be sufficient for long-term storage of all data generated as part of this project.

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

Data stored intermediately on personal KU Leuven OneDrive accounts that are protected via password access set up by KU Leuven IT. Off-site access to L-drive data is available by KU Leuven data access points and is password protected. Access to modify these files are limited to lab members with access to the Fendt Lab L-Drive folders.

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

The annual cost of KU Leuven L-Drive storage is 569.2 euro/5TB/year. This cost and capacity include the performance of mirror copies of the stored data, for safety backup purposes. We expect that 5TB will be more than sufficient to store all data generated as part of the project. These costs will be covered by the budget of the project lead (Prof. Sarah-Maria Fendt).

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 raw data will be retained for 5 years on the KU Leuven L/K-Drive. Initially, all data will be saved on the L-drive. Upon publication, all published data will be further organized and catalogued by figure for future reference to the raw datasets used for each figure and archived on the KU Leuven K-drive archive storage.

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

All raw data will be stored on the KU Leuven L-Drive until publication, upon which the data will be transferred to the KU Leuven K-drive Archive storage.

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

The annual cost of L-Drive storage is 569.2 € per 5TB of storage space per year. We expect that 5 TB will be more than sufficient for long-term storage of all data generated as part of the project. Upon publication, the data will be reorganized by figure and stored on the KU Leuven Archive K-drive. The annual cost of the K-drive is around 60€ per 1TB. We believe 1-2TB should be sufficient to for the archiving of all data related to the project. These costs will be covered by the budget of the project lead (Prof. Sarah-Maria Fendt).

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 an Open Access repository
- Yes, in a restricted access repository (after approval, institutional access only, …)
- Other, please specify:

Datasets will be made publicly available, if possible, through repositories to support FAIR data sharing. Mouse sequencing and proteomics data will be made available on the GEO and PreoteomeXchange websites, respectively. All patient data will be made available in repositories with appropriate access control (e.g. images in OMERO) upon de-identification of the personal data. Access to these data will be made available to any individuals making a specific request and this request will be handled by the institutional data access committee (DAC) in consultation with UZ/KU Leuven and the project lead, Prof. Sarah-Maria Fendt. The remaining data can be approved for reuse upon request and will be assessed for approval on a case-by-case basis by the project lead (Prof. Sarah-Maria Fendt).

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

Patient data will be made available in restricted access repositories. Requests for access to the patient data will be assessed on a case-by-case basis by the Data Access Committee, KU/UZ Leuven and the project lead (Prof. Sarah-Maria Fendt).

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
- Yes, Ethical aspects

Intellectual Property arising from this work is managed as per the framework agreement between the VIB (VIB Tech Transfer) and the KU Leuven, the two participating institutes in this study.
Patient data will be made available in restricted access repositories. Requests for access to the patient data will be assessed on a case-by-case basis by the Data Access Committee, KU/UZ Leuven and the project lead (Prof. Sarah-Maria Fendt).

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

All sequencing data generated from non-patient material will be made available on the open access repository, GEO. Patient data will be made available in restricted access repositories.

When will the data be made available?

Data will be made available upon publication of the research results.

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

Mouse sequencing and proteomics data will be available in open access under the standard open data license. The remaining data can be approved for reuse upon request and will be assessed for data usage license on a case-by-case basis by the project lead (Prof. Sarah-Maria Fendt).

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

All data that will be deposited in open and restricted access will receive a persistent identifier (e.g, GEO data will receive a GSE accession number, EGA data will receive a EGA accession number,...). Moreover, the manuscript will receive a DOI number upon publication in a peer-reviewed academic journal.

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

Costs for data sharing will be discussed with collaborators on a case-by-case basis. To minimize data management costs, free-to-use data repositories will be used when possible. Data management will be covered by own funding.

6. RESPONSIBILITIES

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

Prof. Sarah-Maria Fendt accepts all responsibility for data documentation and metadata. Ms. Ginevra Doglioni and Ms. Ines Vermeire will be responsible for experimental data. Dr. Margarida Campos (mass spectrometry specialist) will be responsible for mass spectrometry data.

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

The lead postdoctoral scientist (Ms. Ginevra Doglioni) and lab technician (Ms. Ines Vermeire) will be primarily responsible for collecting/generating data, and for correct documentation and upload onto the L-Drive storage space. The KU Leuven IT department will be responsible for maintenance and back up of the L-Drive data storage space.

Who will manage data preservation and sharing?

Prof. Sarah-Maria Fendt will be responsible for ensuring data preservation, sharing and reuse.

Who will update and implement this DMP?

Prof. Sarah-Maria Fendt bears the end responsibility of updating & implementing this DMP.