Tackling SLC1A3 in tumor-associated macrophages to overcome anti-PD1 immunotherapy resistance in breast cancer

A Data Management Plan created using DMPonline.be

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Project abstract:

Tumor-associated macrophages (TAMs) are the most abundant cells in the TME and promote tumor growth by helping the establishment of an immunosuppressive environment. In fact, higher numbers of TAMs in the TME are associated with resistance to immune checkpoint blockade (ICB). Despite this association, the molecular mechanism leading to compromised cytotoxic T cell function and poor response to therapy, remain unclear. Analyzing sequencing results from paired pre- and on- ICB treatment breast cancer patients, we observed that SLC1A3 is the most abundant glutamate transporter expressed in TAMs where it becomes strongly upregulated in non-responding patients. Despite the growing number of studies proving the central role of metabolism on cell activity and phenotype, the role of glutamate metabolism in the tumor context is understudied. My unpublished results show that selective deletion of Slc1a3 in TAMs is sufficient to increase ICB treatment susceptibility. Following to this, I aim to understand the roles of SLC1A3 in immune cell's biology and whether and how its targeting can be proved beneficial against ICB resistance onset by using in vitro systems, mouse models and ex vivo breast cancer explants. Ultimately, this work will advance the current immunotherapeutic options in breast cancer and in the long term, the acquired knowledge could result in the discovery of new drugs and combination therapies for the treatment of breast cancer and other refractory cancer types.

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DPIA

DPIA

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

- No

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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
Sequencing	scRNA-seq	New	digital	Experimenta	.bam	<10TB	
	Flow Cytometry	New	digital	Experimenta	fcs	<5TB	
	Murine organ	New	Physical	Experimenta			10 boxes
	Microscopy	New	digital	Experimenta	.lsm, .tif	<1TB	
Functional assays	Phagocytosis Cytotoxicity Antigen presentation T cell suppression Glutamate / glutamine / aspartate uptake	New	digital	Experimenta	.xlsx .pfz .fcs	<1GB	
	Lentiviral vectors	New					10 boxes
	Mouse strains	New					
	SOPs	New	digital	Experimenta	.pdf	<1GB	
	DNA RNA Proteins	New					
	qRT-PCR	New	digital	Experimenta	.xlsx, .pfz	<1GB	
	Metabolomics	New	digital	Experimenta	raw, .pmd	<10GB	
	Tumor growth, volume, metastasis	New	digital	Experimenta	.xlsx, .pfz	<1GB	
	Illustration	New	digital	Experimenta	.ai .pdf .tiff	<5GB	
	Publication	New	digital	Experimenta	.pdf	<5GB	
	Spatial transcriptomics	New	digital	Experimenta		<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:

NA

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

ECD reference number: P059/2021

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

Intellectual property arising from this work will be managed based on the framework agreement between VIB (VIB Tech Transfer) and KU Leuven.

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

As above, dissemination or exploitation of the data will be managed according to the framework agreement between VIB, KULeuven and UZ 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.

- 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).

Protocols and details related to data collection and processing will be recorded in physical lab books and transcribed to Word or Excel files by the applicants. Long-term storage of the lab books is supervised by the lab manager. The lab book describes in detail the experimental setting and any deviation from the original experimental design. Experiments are organized by date and therefore fully searchable. Data folders containing raw and processed data will be hierarchically organized and labelled based on the source of the data, the type of experiment, the date of data generation and the different experimental conditions analysed. Data analysis methods and particularities (including metadata) will be described in text documents and Excel files included in these folders. Standard operating procedures (SOP) are constantly updated and safely stored as PDF to ensure proper replication of the biological experiments. SOPs are backed up to the J-drive once per month, where they are available for all members of the lab. Similarly, all the experimental data (raw and processed data), are safely stored in dedicated drives.

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

If no, please specify (where appropriate per dataset or data type) which metadata will be created:
Text documents and Excel files stored within each experiment folder will respectively 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. Experiments are organized by date so they can be compared with lab books for additional information. References of reagents used are listed on an excel table together with the reference and the dilution used.

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

Where will the data be stored?

Storage options: (1) J-Drive (Minimum 100Gb, Expandable, Unlimited Size, Stored data can be modified); (2) L-Drive (Minimum 5Tb, Unlimited Size, Stored data can be modified); (3) K- Drive (Archive storage, Minimum 100Gb, Expandable, Unlimited Size, Stored data can NOT be modified or deleted).

How will the data be backed up?

Data storage and backup is managed by KU Leuven IT services. Specifically, mirror copies of the stored data are made immediately upon upload, for safety backup purposes. Data storage and backup is based on a combination of internal servers and external storage with commercial providers such as Microsoft, and with public databases and repositories. Long- term storage, is ensured by the L-drive (stored data can NOT be modified or deleted. This, will guarantee the preservation of data over the minimum term of 10 years. Regular computer backups through the inSync platform (unlimited storage) secure the recovery of unsaved data.

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 institutes (KU Leuven and VIB) have sufficient and scalable storage capacity available, both during the research and during at least 10 years after the end of the research.

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

Non-public data are login-protected (2FA) and accessible to designated staff members only. Network security is ensured by the KULeuven IT services.

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

The annual cost of storage is approximately 569.2 € per 5TB of storage space per year. This cost and capacity include the performance of mirror copies of the stored data, for safety backup purposes. We expect that 15 TB will be sufficient to store all data generated as part of the project. These costs will be covered by the budget of the project leader.

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...).

Biologicals will be retained when possible. The storage will be at (1) room temperature, (2) 4°C, (3) -20°C, (4) -80°C, (5) -150°C, according to

the type of biological material. As a general rule, data will be preserved for a minimum term of 10 years. Datasets collected in the context of clinical research, which fall under the scope of the Belgian Law of 7 May 2004, will be archived for 25 years, in agreement with the University Hospital policies and the European Regulation 536/2014 on clinical trials of medicinal products for human use.

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

Physical space in the lab will be provided to store the biological material (refrigerators, cold rooms as well as cupboards for non-degradable materials). Digital data will be stored on KU Leuven storage space: the KU Leuven L-Drive (virtually unlimited size) has sufficient storage capacity for the outlined project.

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

The annual cost of storage is approximately 569.2 € per 5TB of storage space per year. This cost and capacity include the performance of mirror copies of the stored data, for safety backup purposes. We expect that 15 TB will be sufficient to store all data generated as part of the project. These costs will be covered by the budget of the project leader.

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.

- Other, please specify:

The key findings of the project and their interpretation will be made available through publication of journal articles in established, peer-reviewed (non-predatory) academic journals. Relevant raw data will be made publicly available through upload to well-established open-access data repositories

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

Data may be shared externally upon reasonable requests from collaborating scientists, which will be reviewed and approved on a case-by-case basis by the project leaders. We do not exclude that the proposed work could result in research data with the potential for tech transfer and valorization. The partner institutes have a policy to actively monitor research data for such potential. If there is substantial potential, the invention will be thoroughly assessed, and in a number of cases, the invention will be IP protected (mostly patent protection or copyright protection). As such the IP protection does not withhold the research data from being made public. In the case a decision is taken to file a patent application it will be planned so that any delay to publication is minimal.

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, Other

We do not exclude that the proposed work could result in research data with the potential for tech transfer and valorization. If there is substantial potential, the invention will be thoroughly assessed, and in a number of cases, the invention will be IP-protected (mostly patent protection or copyright protection). As such the IP protection does not withhold the research data from being made public. In the case a decision is taken to file a patent application it will be planned so that any delay to publication is minimal.

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

Depending on the nature of the dataset both open-access and restricted-access repositories will be used to store data. All requests and approvals for reuse of data other than those deposited in open-access repositories will be assessed on a case-by-case basis by the project leaders.

When will the data be made available?

As study leader, Prof. Massimiliano Mazzone will monitor data sharing requests. Data will be automatically made available after the publication of results to any requestor using the data for non-commercial purposes. Commercial use of the data will be negotiated through the VIB tech transfer office.

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

Data not deposited in open-access repositories will in principle only be accessible to members of the lab. Other collaborations and sharing are possible with staff and students within the VIB–KU Leuven Center for Cancer Biology, as well as within the KU Leuven Department of Oncology, upon reasonable request. Any user can place reasonable requests data for non-commercial purposes, and these requests will be assessed on a case-by-case basis by the project leaders. Commercial- based requests will be navigated in coordination between KU Leuven/VIB Tech Transfer team.

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

When relevant PID/DOI/accession numbers will be added to datasets

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

Mainly publication fees and other costs for data sharing will be discussed with collaborators on a case-by-case basis.

6. Responsibilities

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

Data documentation, and metadata acquisition and storage will be performed by the students and postdocs associated with this project. Prof. Massimiliano Mazzone and Sarah Trusso Cafarello (Lab Manager) will monitor.

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

Data management, storage and back up will be performed by the PhD student (Iris Nikoletta Charatsidou) associated with this project. Prof. Massimiliano Mazzone and Sarah Trusso Cafarello will monitor.

Who will manage data preservation and sharing?

As study leader, Prof. Massimiliano Mazzone will be responsible for data preservation. He will also monitor data sharing requests. Data will be automatically made available after the publication of results to any requestor using the data for non-commercial purposes. Commercial use of the data will be negotiated through the VIB tech transfer office.

Who will update and implement this DMP?

The lab manager (Sarah Trusso Cafarello, lab of Tumor Inflammation and Angiogenesis), staff scientist (Dr. Marcello Delfini, lab of Tumor Inflammation and Angiogenesis) and the PI (Prof. Massimiliano Mazzone) will share the responsibility of updating & implementing this DMP.