Plan Overview

A Data Management Plan created using DMPonline

Title: Wishing-Table

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Template: UMC Utrecht DMP

Project abstract:

Autologous bone grafts are the current gold standard treatment for large bone defects. However, these grafts often fail to fully heal large defects. After implantation, the viability of the implanted tissue rapidly decreases due to a lack of available nutrients, causing a rapid loss of the living component of these grafts, which is essential for proper bone regeneration, especially in large defects. Therefore, supporting viability and function of the implanted living cells is a key challenge to improve bone regeneration in large defects.
Therefore, the aim of this project is to explore the world’s first self-feeding strategy, which is designed to support cellular metabolism through the innovative use of glycogen. Glycogen is a nanoparticle that naturally occurs inside (human) cells to store and release the nutrient glucose through enzymatic reactions. Surprisingly, we have discovered that cells also secrete the specific enzymes needed to degrade glycogen extracellularly. Thus, we are the first team to identify glycogen incorporation as a controllable and long-term release system for glucose, enabling the exploration of the essential functionality provided by living cells post implantation.
Our consortium converges required expertise on regenerative medicine, bone regeneration, autografting, metabolism, and surgical procedures for maximum synergy. The wishing-table project will deliver new fundamental insights on the use and mechanisms of glycogen supplementation to maintain cell survival and functionality, such as immune-acceptance of xenogeneic glycogens, and osteogenic cell differentiation in oxygen-deprived environments. Additionally, this enables us to explore whether survival of living cells is essential for bone regeneration since glycogen-based cell survival during the pre-vascular phase post-implantation could not be studied ever before. Here, we will explore if cell survival is crucial for implant integration and bone regeneration in a goat model. Finally, a wishing-table formulation, in which a clinically used biomaterial will be enriched with glycogen will be developed to investigate the use of glycogen to improve bone healing in a spinal fusion model in goats to reach end-preclinical stage.

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Wishing-Table

1. General features

1.1. Please fill in the table below. When not applicable (yet), please fill in N/A.

DMP template version	30 (don't change)
ABR number *(only for human-related research)*	N/A
Financial Vidatum number *(only for human-related research)*	V0002561
DEC number *(only for animal-related research)*	AVD11500202216382
Acronym/short study title	Wishing-table
Name Research Folder	n.v.t.
Name Division	DHS
Name Department	Department of orthopaedics
Partner Organization	Twente University
Start date study	1-8-2024
Planned end date study	31-7-2027
Name of datamanager consulted*	DHS datamanagement: Dax Steins/Nivard Koning
Check date by datamanager	24-06-2024

1.2 Select the specifics that are applicable for your research.

- Fundamental / translational study
- Biobank approval needed: "uitgifteprotocol"

Biobank approval needed: "uitgifteprotocol" (from Biobank 08/001) = 24U-1393_Bone Graft as part of the Wishing Table project.

2. Data Collection

2.1 Give a short description of the research data.

Subjects	Volume	Data Source	Data Capture Tool	File Type	Format	Storage space
Cell cultures	2000	08-001/C	Fluorescence/ brightfield microscope	Image	tiff, jpeg, dmc	100-1000GB
Cell cultures	2000	08-001/C	Electronic Lab Journal	Quantitative data	csv	10-100GB
Patients	TBD	08-001/C	Biobank 08-001	Text files, physical samples as highlighted in the biobank protocol	N.A.	N.A.
Goats	TBD	Experimental data	Fluorescence/ brightfield microscope, microCT	image	tiff, jepg, dcm	TBD
Goats	TBD	Experimental data	Electronic Lab Journal	Quantitative data	csv	TBD

The source for primary cells and bone tissue (falls under primary cells) is the biobank of the UMC Utrecht (08/001). New data using the biobank samples will be generated and collected from *in vitro* cell experiments, microscopical studies.

The amount of patients that will be included/ necessary for this project can currently not be estimated, hence the volume is TBD. Once this information is available, the DMP will be updated. The volume of cell cultures is an estimation about all cell cultures that will be performed and does not correlate to the amount of donors that is required, as multiple cell cultures can be performed per donor.

Non-digital (physical) data that is generated includes fixated tissue samples, composite materials and cells. As the cells are sourced from the biobank, these will be stored according to the biobank protocol.

Digital data includes raw and processed measurements from data including cell functionality assays, biochemical assays, qPCRs, pH, histology, immunohistochemistry, DLS and microCT.

During this project, no patient sensitive data will be generated that require any special storage conditions.

All data will remain with the UMCU. The collaboration involves receiving material from Kuros which is defined in the consortium

agreement of the project. Besides that, the University of Twente and Kuros provide expertise for data analysis which is done using DRE.

2.2 Do you reuse existing data?

- Yes, please specify

The proposed work presents a novel technology where new data will be generated. Where possible, historical or pilot data will be re-used in the study design though. Re-use of data for the planned experiments is not possible because experimental settings or applied models will not be the same.

Nonetheless, samples stored within the biobank will be used in combination with the according information. This includes: patient sex, age at sample retrieval and pseudonymized donor number.

In some cases, certain medical predispositions are suspected that can be relevant for our donor selection (e.g. osteoporosis, bone necrosis). In these cases, the person(s) having access to the key linking table will be contacted to check whether the donor indeed had an influential medical pre-disposition. Through the key linking table, the donor is identified and the medical history checked on HIX after which information will be transmitted to the researcher: Was there an influential medical pre-disposition for the study and can the donor be excluded from the donor pool for this specific research.

2.3 Describe who will have access to which data during your study.

Type of data	**Who has access**
Cell culture (goat [model])	Research team, PI, Datamanager
Pseudonymized data (human cell data for cell harvest experiments)	Research team, PI, Datamanager
Key table linking study specific IDs to Patient IDs	PI (with care relationship to patient), Datamanager
Direct identifying personal data	Research team with care relationship to patient, Datamanager

1. The key table linking study specific IDs to patient IDs is available to the datamanager and members of the research team with a care relationship to the patient. Other members of the research team receive a pseudonymized dataset and have no access to direct personal data or the key table.

The University of Twente and Kuros provide expertise for data analysis, which is done using DRE.

2.4 Describe how you will take care of good data quality.

1. Patient data is only accessable within the limitations of the biobank protocol (08/001). All experimental data will be collected using the standard Electronic Lab Notebook (ELN) used within the regenerative medicine center Utrecht (RMCU) using calibrated equipment (performed by RMCU staff). Upon collection, data is frozen and working copies are made to perform analysis with the given data. Versions of the datasets and the full audit trail are recorded in the ELN. Repeated measurements are performed for each experiment/ study based on 80% power to ensure the reliability and reproducibility of the data.
2. Use of software tools now unknown will be registered in eLabJournal. Data will be matched by study subject code.

#	**Question**	**Yes**	**No**	**N/A**
1.	Do you use a certified Data Capture Tool or Electronic Lab Notebook?	x		
2.	Have you built in skips and validation checks?	x		
3.	Do you perform repeated measurements?	x		
4.	Are your devices calibrated?	x		
5.	Are your data (partially) checked by others (4 eyes principle)?	x		
6.	Are your data fully up to date?	x		
7.	Do you lock your raw data (frozen dataset)	x		
8.	Do you keep a logging (audit trail) of all changes?	x		
9.	Do you have a policy for handling missing data?	x		
10.	Do you have a policy for handling outliers?	x		

2.5 Specify data management costs and how you plan to cover these costs.

#	Type of costs	Division ("overhead")	Funder	Other (specify)
1.	Time of datamanager	x		
2.	Software licenses	x	If DM software is required for project	
3.	Data Capture Tool			RMCU labs - benchfee
4.	Storage	x		
5.	Archiving	x	Only where applicable	

Explanation.

2. Standard software licenses (i.e. microsoft office) are provided by the division. In case specialized software is required, the costs will be covered by the funder of the project.

3. Regenerative medicine centre Utrecht, costs for all data capture tools are included within the benchfee paid to work within the RMCU labs

Kuros and Twente are involved in this project but the collaboration does not necessitate datasharing, leading the lack of costs.

2.6 State how ownership of the data and intellectual property rights (IPR) to the data will be managed, and which agreements will be or are made.

UMCU is and remains the owner of all collected data for this study.

Data ownership and IP rights will be agreed upon in the consortium agreement/ research agreement signed by all parties involved.

3. Personal data (Data Protection Impact Assessment (DPIA) light)

Will you be using personal data (direct or indirect identifying) from the Electronic Patient Dossier (EPD), DNA, body material, images or any other form of personal data?

- Yes, go to next question

2. I will process personal data. I have consulted the division datamanager and I do not have to complete a full DPIA. I therefore fill out this DPIA light and proceed to 3.1.

3.1 Describe which personal data you are collecting and why you need them.

1. Our research involves the use of primary cell and tissue samples and therefore includes the gender and age of the patients as described in the biobank protocol.
2. The data received from the biobank is pseudonymized data to which we do not have access and experimental data from the cells, which is not direct identifyable data.

Which personal data?	Why?
Bone samples	The developed technology is anticipated to extend survival of bone tissue, which is a complex tissue that cannot be recreated in vitro.
Primary cells	To test the technology, primary cells will be sourced from the biobank 08/001-K
Gender, age	To describe study population
Medical data	If certain medical predispositions are suspected to be relevant for our donor selection (e.g. osteoporosis, bone necrosis), the person(s) having access to the key linking table will be consulted and HIX will be checked for such medical predispositions by authorized personnel. Afterwards, information will be relayed to the researchers on whether there was such a medical predisposition and if the donor can be excluded from the study.

3.2 What legal right do you have to process personal data?

- Other, please explain

Broad consent, Biobank 08-001/K.
Only relevant for research involving primary, patient derived samples (cells and tissues). The re-use of data is defined in release protocols for the biobank: e.g. Bone_Graft (V1393)

3.3 Describe how you manage your data to comply to the rights of study participants.

1. The data are pseudonymized and the linking table to personal data is saved. An authorized person manages the key linking table linking table that will be stored separately within the Research Folder structure created for each project with restricted access to authorised personnel with a care relationship to patient.

Right	Answers
Right of Access	Research data are coded, but can be linked back to personal data, so we can generate a personal record at the moment the person requires that. This needs to be done by an authorized person.
Right of Rectification	The authorized person will give the code for which data have to be rectified.
Right of Objection	We use broad consents.
Right to be Forgotten	In the broad consent we state that the study participant can stop taking part in the research. Removal of collected data from the research database cannot be granted because this would result in a research bias.

3.4 Describe the tools and procedures that you use to ensure that only authorized persons have access to personal data.

1. We use secured Research Folder Structures for all underlying projects (e.g. Bone_Graft V1393) that ensures that only authorized personnel has access to personal data, including the key table that links personal data to the pseudoID.
2. We make use of an Electronic Lab Notebook (ELN) with build-in Authorization Management

3.5 Describe how you ensure secure transport of personal data and what contracts are in place for doing that.

1. We will not transport any personal data outside the UMCU network drives.
2. In case personal data needs to be transported with colleagues, Surffilesender with encryption will be used.
3. We have a Research Agreement with UTwente and Kuros Biosciences B.V. The agreement is stored at location: TBD (still needs to be signed). No personal data is shared and their involvement is for data analysis purposes only, which will be done using

DRE.
4. In case personal data would have to be transferred to collaborators a Data Transfer Agreement will be signed and stored at the same location as the Research Agreement.

4. Data Storage and Backup

4.1 Describe where you will store your data and documentation during the research.

As data we here define all experimental data obtained from experiments described in the study plan.

1. Data is stored in a standardized format complying with the UMCU research datamanagement policy, GCP and GDPR. (https://intranet.umcutrecht.nl/connect/onderzoek/QualityofResearch/Paginas/Research-Folder-Structure.aspx)
2. All original raw data will be stored in a seperate, write protected research folder (RFS) and analysis are done on copies of frozen datasets.
3. To enable the collaboration with Twente and Kuros on the analysis of generated datasets, data will be stored in DRE, because they assist in the analysis of the data. The results are then transferred to the research maps of the underlying project and developed SOPs are noted in ELN.
4. Final data for publication is stored on the DataverseNL repository.

Storage and documentation of personal data is only required for the biobank. Therefore, the only identifying personal data is stored in key linking tables that are stored in secured separate folders within the research folder structure of each underlying project to which only authorized personnel has access.

4.2 Describe your backup strategy or the automated backup strategy of your storage locations.

1. All (research) data is stored on UMC Utrecht networked drives from which backups are made automatically twice a day by the division IT (dIT). For analysis, data is stored on the data share(s) of one/more DRE workspace(s). DRE data shares are stored on Azure according to LRS standard, ensuring data is replicated thrice in the same Azure data center. Additionally, for version history, DRE takes daily snapshots of the data share, and retains these snapshots for 30 days rolling.
2. The ELN is automatically backed up and contains a full audit trail.
3. The key linking table(s) for the biobank will be will be stored separately within the Research Folder structure created for each project with restricted access to authorised personnel with a care relationship to patient, which is stored on UMC Utrecht networked drives from which backups are made automatically twice a day by the division IT (dIT).

5. Metadata and Documentation

5.1 Describe the metadata that you will collect and which standards you use.

1. Currently there is no metadata standard for all domain specific data. Metadata will be performed under the FAIR principle. All data and metadata will be indentifyable with the exact experiment performed and contain a data dictionary. For each variable, the data dictionary will contain an explanation of the values.
2. The queries of the research will be stored in eLabJournal (under my experiments)

All metadata will include the specific procedure, equipment and chemicals used to perform each individual experiment.

5.2 Describe your version control and file naming standards.

We will distinguish versions by indicating the version in the filename of the master copy by adding a code after each edit, for example V1.1 (first number for major versions, last number for minor versions). The most recent copy at the master location is always used as the source, and before any editing, this file is saved with the new version code in the filename. Also, each version intended for internal distribution will obtain a date of preparation. Older versions are moved to a folder OLD.

6. Data Analysis

6 Describe how you will make the data analysis procedure insightful for peers.

1. For each experiment, analysis steps will be documented in an Electronic Lab Journal. The documentation is shared with other members in the same research group. In future publications, relevant analysis steps will be described and available for everyone.
2. We will be using SPSS, version 29, for statistical analysis of the data. The scripts will contain comments, such that every step in the analysis is documented and peers can read why I made certain decisions during the analysis phase.

7. Data Preservation and Archiving

7.1 Describe which data and documents are needed to reproduce your findings.

1. The data package will contain: the raw data, the study protocol describing the methods and materials, the script to process the data, the scripts leading to tables and figures in the publication, a codebook with explanations on the variable names, and a 'read_me.txt' file with an overview of files included and their content and use.
2. An Electronic Lab Journal will be used and protocols for every step that is needed to reproduce the results. After finishing the project, this documentation will be stored at the UMC Utrecht [path: XXX] and is under the responsibility of the Principal Investigator of the research group.

** 'XXX' in this answer will be updated when available*

7.2 Describe for how long the data and documents needed for reproducibility will be available.

Data and documentation from our studies will be stored for at least 10 years. This may include storage of raw data, processed data and analyses performed on such data, published articles, presentations.

7.3 Describe which archive or repository (include the link!) you will use for long-term archiving of your data and whether the repository is certified.

After finishing the project, the data package will be stored at the UMC Utrecht Research Folder Structure for each underlying project and is under the responsibility of the Principal Investigator of the research group. The UMC Utrecht standard repository is DataverseNL, the data package will be published here.

7.4 Give the Persistent Identifier (PID) that you will use as a permanent link to your published dataset.

DOI-codes of publications will be used. This plan will be updated as soon as codes are available.

8. Data Sharing Statement

8.1 Describe what reuse of your research data you intend or foresee, and what audience will be interested in your data.

The research data can be of interest for other researchers from different groups/institutes in the field or for spin-off projects. And also for new lab members in the research group to join the project at a later stage.

8.2 Are there any reasons to make part of the data NOT publicly available or to restrict access to the data once made publicly available?

- Yes (please specify)

New IP may be developed in this project. IP may cause part of the data to have restricted access.

8.3 Describe which metadata will be available with the data and what methods or software tools are needed to reuse the data.

All data and documents in the data package mentioned in 7.1 will be shared under restrictions. Data underpinning research papers can be made available to other researchers upon request where no IP, legal, commercial or privacy restrictions apply. The guiding principle will be 'as open as possible, as closed as necessary.'

8.4 Describe when and for how long the (meta)data will be available for reuse

- Other (please specify)

Data underpinning research papers will be made available to other researchers at the time of the article’s publication, unless there are valid reasons not to do so. To elaborate, data sharing will be postponed or restricted for example to publish, protect intellectual property, or seek patents.

8.5 Describe where you will make your data findable and available to others.

Data can be requested via contacting the PI who will act as corresponding author on any (open access) published work. Where possible, this will be done via the data repository.