G081723N Unravelling the versatile transcriptionally repressive effects of the vitamin D receptor, highlighting the regulation of calcium and energy homeostasis

A Data Management Plan created using DMPonline.be

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Project abstract:

The vitamin D receptor (VDR) is a well-known regulator of calcium and bone homeostasis. However, the mechanisms responsible for VDR-mediated signalling in different tissues remain incompletely understood, potentially because previous studies neglected the transcriptionally repressive effects of the VDR. In the current project, we will therefore investigate transgenic mouse models in which only transcriptional repression can take place (Vdr-delta-AF2 and Cyp27b1 knockout mice). This approach allows us not only to answer long-standing questions on the mechanisms of transcriptional repression (Aim 1), but also to gain novel insights in VDR-regulated transcriptional networks. Notwithstanding the fact that vitamin D is a major stimulator of intestinal and renal calcium (re)absorption, not all proteins involved in this process have been identified. Interestingly, previously performed transcriptome analyses in intestine and kidney of Vdr-delta-AF2 mice showed differential regulation of genes that function in mineral (re)absorption. We will evaluate whether these transporters are implicated in vitamin D-induced calcium (re)absorption (Aim 2). Our transcriptome analysis also revealed
multiple differentially regulated genes involved in energy
homeostasis, which is interesting in view of the lean phenotype of mice with defective VDR signaling. We will therefore investigate whether VDR-mediated alterations in intestinal and skeletal nutrient handling contribute to this phenotype (Aim3).

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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
Naping assay	Mapping of coregulator interactions	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .cvs, .xlsx, .jpg	*Please choose from the following options:* • <1TB	
VDR-ChIP sequencing	ChIP sequencing on renal tissue of transgenic mice strains	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .bcl, .gz, .sam, .bam	*Please choose from the following options:* • <100GB	Input material will be stored at -80°C in CEE
RXR-ChIP sequencing	ChIP sequencing on renal tissue of transgenic mice strains	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .bcl, .gz, .sam, .bam	*Please choose from the following options:* • <100GB	Input material will be stored at -80°C in CEE
Corepressor-ChIP sequencing	ChIP sequencing on renal tissue of transgenic mice strains	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .bcl, .gz, .sam, .bam	*Please choose from the following options:* • <100GB	Input material will be stored at -80°C in CEE
ChIP coupled to mass spectrometry	Identification of novel VDR interacting proteins	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .cvs, .xlsx, .jpg	*Please choose from the following options:* • <100MB • <1GB • <100GB • <1TB • <5TB • <10TB • <50TB • >50TB • NA	
Selection of primary vitamin D target genes	qPCR analysis to evaluate RNA levels of vitamin D-regulated genes, Western blotting	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .cvs,.xls	*Please choose from the following options:* • <1GB	RNA will be stored at -80°C in CEE
Stable cell lines with silencing of vitamin D-regulated transporters	Intestinal and renal cell lines	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • NA	*Please choose from the following options:* • NA	Stable cell lines will be physically stored in the cryotheque and submitted to the biobank

Transgenic mice with tissue-selective deletion of vitamin D-regulated transport proteins		*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Physical	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • NA	*Please choose from the following options:* • NA	Mice will be bred in the animal facility and cryopreserved in case of an interesting phenotype
Phenotypic characterization of tissue-selective deletion of vitamin D-regulated transport proteins	Serum and urine biochemistry, echoMRI, qPCR analysis of tissues, µCT analysis, immunohisto-chemistry and bone histomorphometry	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital	*Please choose from the following options:* • Observational • Experimental	*Please choose from the following options:* • .tif, .tiff, .jpg, .jpg2, .pdf, .bmp, .csv, .tab, .txt, .xlsx	*Please choose from the following options:* • <10TB	
Role of VDR-mediated signaling in intestinal lipid handling	qPCR analysis, Western blotting	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital	*Please choose from the following options:* • Experimental	*Please choose from the following options:* • .cvs,.xls	*Please choose from the following options:* • <1GB	
Phenotypic characterization of in vivo lipid handling in Vdr transgenic mice	Analysis of in vivo lipid handling, oral lipid tolerance test, fatty acid oxidation, glucose and lipid biodistribution	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital • Physical	*Please choose from the following options:* • Observational • Experimental	*Please choose from the following options:* • .tif, .tiff, .jpg, .jpg2, .pdf, .bmp, .csv, .tab, .txt, .xlsx	*Please choose from the following options:* • <5TB	RNA will be stored at -80°C in CEE
Evaluation of high fat diet in Vdr transgenic mice	Serum and urine biochemistry, echoMRI, qPCR analysis of tissues, µCT analysis, immunohisto-chemistry and bone histomorphometry	*Please choose from the following options:* • Generate new data	*Please choose from the following options:* • Digital	*Please choose from the following options:* • Observational • Experimental	*Please choose from the following options:* • .tif, .tiff, .jpg, .jpg2, .pdf, .bmp, .csv, .tab, .txt, .xlsx	*Please choose from the following options:* • <10TB	

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:

In this project, we will reuse existing data (RNAseq datasets performed in FWO project GD4217N) and 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, animal data

Yes, animal data. Ethics approval will be obtained from the Ethical Committee for Animal Experimentation.

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

We do not exclude that the proposed work could result in research data with potential for teach transfer and valorization. The KU Leuven has 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 protected (mostly patent application or copyright protection). As such the IP protection does not withhold the research 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 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.

- No

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).

1. Cell culture experiments.

Page-numbered laboratory notebooks will be maintained to document cell line, culture media, experimental treatments, timing and end-point analyses. All data derived from 1 experiment will be stored in 1 folder of which the name carries at least the name of the used cell type and the date. End-point-specific files will be stored within this folder and file names will include cell type, date, time point, and end-point analysis. The experimental folder will also contain a text file in which the experimental procedure is explained in such detail that it can easily be repeated. Standard experimental procedures (SOPs) and practices will be fully documented (as MS Word and PDF files) and stored on the J drive

2. Phenotypic analyses of transgenic mice.

Notes on breeding and genotyping (protocol & results) are stored in dedicated files on a shared network drive. In-depth phenotyping results will be stored in folders containing a least the strain name. Within this folder, different end-point analyses will be stored in subfolders of which the name contains at least the name of the transgenic line, animal age and sex, and the name of the end-point analysis.

3. All experimental RNA and cDNA samples are catalogued in dedicated MS Excel files, which will contain information on the physical storage of all samples.

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.

- Yes

Sequencing data types require particular metadata, such as data submitted to EGA, GEO, SRA, ArrayExpress, or ENA. Local data that is not (yet) submitted to these resources will be based on generalized metadata schema such as Dublin Core or DataCite, including the following elements:

- Title: free text
- Creator: Last name, first name, organization
- Date and time reference
- Subject: Choice of keywords and classifications
- Description: Text explaining the content of the data set and other contextual information needed for the correct interpretation of the data, the software(s) (including version number) used to produce and to read the data, the purpose of the experiment, etc.
- Format: Details of the file format,
- Resource Type: data set, image, audio, etc.
- Identifier: DOI (when applicable)Access rights: closed access, embargoed access, restricted access, open access.

When depositing data in a local or public repository, the final dataset will be accompanied by this information under the form of a README.txt document. This file will be located in the top level directory of the dataset and will also list the contents of the other files and outline the file-naming convention used (see section 7 below). This will allow the data to be understood by other members of the laboratory and add contextual value to the dataset for future reuse.
Further, we will store metadata from experiments in a searchable database format. These will include the following search parameters: date, investigator name, type of study, and strain name in case of animal studies.

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

Where will the data be stored?

Digital files will be stored on KU Leuven servers:

Omics data: omics data generated during the project will either be stored on KU Leuven servers.
Other data files (digital images, µCT data, equipment-generated data) will be stored on local KU Leuven servers and PI computers. Large data volumes will be back-up at local hard disks.
Paper lab notebooks will be kept in lockable closets in the lab of the PI.

How will the data be backed up?

KU Leuven drives are backed-up according to the following scheme:
Data stored on the “L-drive” is backed up daily using snapshot technology, where all incremental changes in respect of the previous version are kept online; the last 14 backups are kept.
Data stored on the “J-drive” is backed up hourly, daily (every day at midnight) and weekly (at midnight between Saturday and Sunday); in each case the last 6 backups are kept.

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

There is sufficient storage and back-up capacity on all KU Leuven servers:
The “L-drive” is an easily scalable system, built from General Parallel File System (GPFS) cluster with NetApp eseries storage systems, and a CTDB samba cluster in the front-end.
The “J-drive” is based on a cluster of NetApp FAS8040 controlers with an Ontap 9.1P9 operating system.

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

For digital files: all data will be stored at the university's secure environment and access to these sites is password-protected.
For paper notebooks and experimental samples: will be stored within the laboratory and office rooms, which will be inaccessible after office hours.

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

The total estimated cost of data storage during the project is €2000. This estimation is based on the following costs: The costs of digital data storage are as follows:

- One drive (2 TB): free
- J-drive: €519/TB/Y
- K-drive: €56.9/TB/Y
- L-drive: €284.6/TB/Y

The costs will be covered by internal funding.

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...).

In accordance to the KU Leuven policy we will retain all data for at least 5 years after the end of the research project, after the publication data, or after the end of a PhD dissertation.
For biological samples, it is not always feasible to store the samples for a time frame of 5 years as sample quality deteriorates over time.

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

Digital data will be stored at KU Leuven's archive (K:\) and large vulume storages (L:\) drives. Team and personal hard disks will provide local back-up and will be stored in lockable closets within the laboratory of the PI.
Paper lab notebooks and experimental samples will be stored within the laboratory of the PI.
Manuscripts will be deposited in KU Leuven repository (LIRIAS).

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

The total estimated cost of data storage during the 5 years after the end of the FWO project is €1000. This estimation is based on €70/Tb/Y.
The costs will be covered by internal funding.

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 a restricted access repository (after approval, institutional access only, ...)
- Yes, in an Open Access repository

The PI in the present project is 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).

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

Data could be reused by other members of the CEE team, after consultation and approval of the head of the research team (Prof A. Verstuyf).
Data can be made accessible to a third party after signing a data sharing agreement and approval of the head of the research team (Prof A. Verstuyf). An appropriate DTA and/or MTA will be put in place. Access will be considered after a request is submitted explaining the planned reuse. Only uses for research purposes will be allowed and commercial reuse will be excluded. Exceptions are to be submitted to the head of the research team (Prof A Verstuyf).

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.

- No

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

Sharing policies for specific research outputs are detailed below:

- Omics datasets will be deposited in open access repositories such as the EMBL-EBI platform for genomics and epigenomics data, or the NCBI Gene Expression Omnibus (GEO), the EBI ArrayExpress databases for functional genomics data or the EBI European Genome-phenome Archive (EGA) for personally identifiable genetic and phenotypic data.
- Other digital datasets that support publications (including image, µCT data) will be made publicly available via an open research data platform such as Mendeley Data or Zenodo.
- Research documentation: All protocols used to generate published data will be described in the corresponding manuscript(s), and the related documentation will be included as supplementary information.
- Manuscripts: Publications will be automatically added to our institutional repository, Lirias 2.0, based on the authors name and ORCID ID (the metadata will be added, not the full manuscripts).

When will the data be made available?

Upon publication of the research results
As a general rule all research outputs will be made openly accessible at the latest at the time of publication. No embargo will be foreseen unless imposed e.g. by pending publications, potential IP requirements.

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

Data usage licenses will be discussed with LRD before any licenses are granted. Similarly, when DTAs or MTAs are discussed, this will always be after consulting and collaborating with LRD.

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

Depending on the data repository and the type of data that would be made available, a unique identifier will be added to the data set.

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

It is the intention to minimize data management costs by implementing standard procedures (internally generated operational procedures (https://en.wikipedia.org/wiki/Standard_operating_procedure)) e.g. for metadata collection and file storage and organization from the start of the project, and by using free-to-use data repositories and dissemination facilities whenever possible. Data management costs will be covered by internal funding.
If shipment of data or material is required, the costs will be covered by the researcher requesting the materials after DTAs and/or MTAs are put in place.

6. Responsibilities

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

The PI (Prof A Verstuyf) and Co-PI (Lieve Verlinden) will be responsible for documentation of data and metadata. Post-docs, PhDs and technicians will have the daily responsibility of record keeping of all data (digital, paper and biological samples). They will also be responsible for a correct and accurate data entry and recording of metadata.

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

Post-docs, PhDs and technicians will have the daily responsibility of record keeping of all data (digital, paper and biological samples). They will also be responsible for a correct and accurate data entry and recording of metadata. The PI (Prof A Verstuyf) and Co- PI (Lieve Verlinden) will be responsible for data storage and back-up during the project.

Who will manage data preservation and sharing?

The PI (Prof A Verstuyf) and Co-PI (Lieve Verlinden) will be resposible for data preservation and reuse.

Who will update and implement this DMP?

The PI (Prof A Verstuyf) is ultimately responsible for all data management during and after data collection, including implementing and updating the DMP.

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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)

In this project, we will reuse existing data (RNAseq datasets performed in FWO project GD4217N) and generate new data. Personal data will not be generated or collected.

Research data		
Observational data	.csv/ .tab/ .txt/ .xlsx	up to 1 GB
qPCR analysis	.csv/ .tab/ .txt/ .xlsx	up to 1 GB
Immunohistochemistry & histomorphometric analysis	.tif/ .jpg/ .czi/ . bmp/ .csv/ .tab/ .txt/ .xlsx	up to 1 TB
ELISA assays	.csv/ .tab/ .txt/ .xlsx	up to 1 GB
Chemistry analyzer	.csv/ .tab/ .txt/ .xlsx	up to 1 GB
Western blotting	.tif/ .jpg/ . bmp/ .csv/ .tab/ .txt/ .xlsx	up to 10 GB
Microcomputed tomography data	.tif/ .jpg/ .czi/ . bmp/ .csv/ .tab/ .txt/ .xlsx	up to 5 TB
EchoMRI data	.csv/ .tab/ .txt/ .xlsx	up to 1 GB
RNAseq data	.bcl/ .fastq/ .sam/ .bam	up to 2 GB
ChIPseq data	.bcl/ .fastq/ .sam/ .bam	up to 2 GB
Research documentation		
Ethical approval documents	.txt/ .doc/ .docx	up to 1 GB
Laboratory notes	.txt/ .doc/ .docx	up to 1 GB
Protocols	.txt/ .doc/ .docx	up to 1 GB
Databases	.xlsx	up to 1 GB
Manuscripts	.doc/ .docx/ .tif/ .jpg/ .jp2/ .pdf/ .pzfx	up to 50 GB

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)

Designation of responsible person
Annemieke Verstuyf: Mieke.Verstuyf@kuleuven.be
Lieve Verlinden: Lieve.Verlinden@kuleuven.be
Storage capacity/repository - during and after the research
Digital data files will be stored at KU Leuven servers:

- Omics data: omics data generated during the project will be stored on KU Leuven servers
- Other data files (digital images, µCT data, equipment-generated data) will be stored on local KU Leuven servers and PI computers. Large data volumes will be backed up on local hard disks
- There is sufficient storage and back-up capacity on all KU Leuven servers:
  - the L-drive in an easily scalable system, built from General Parallel File System (GPFS) cluster with NetApp eseries storage systems, and a CTDB samba cluster in the front end.
  - the J-drive is based on a cluster of NetApp FAS8040 controlers with an Ontap 9.1P9 operating system

Biological samples will be stored in -20°C and -80°C freezers. Lab books and electronic files will be maintained to keep track of the content of these freezers so that biological samples can be easily retrieved.
In accordance to the KU Leuven policy we will retain all data for at least 5 years after the end of the research project, after the publication date, or after the end of a PhD dissertation.

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)

Digital data will be maintained for a minimum of 5 years.
For biological samples it is not always feasible to store the samples for a time frame of 5 years as sample quality deteriorates over time.

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)

Yes, animal data. Ethics approval will be obtained from the Ethical Committee for Animal Experimentation.

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

None

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DPIA

DPIA

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

- Not applicable

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GDPR

GDPR

Have you registered personal data processing activities for this project?

- Not applicable