Degradation of CDK1 and HDACs as a strategy to treat T-cell malignancies

A Data Management Plan created using DMPonline.be

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Project abstract:

Our recent studies in peripheral T-cell lymphoma (PTCL) have identified an important role for EZH2 as a transcriptional co-factor of NMYC. Our data show that this is independent of the methyltransfersase activity of EZH2 and that phosphorylation of EZH2 by CDK1 is required to stabilize NMYC and MYB. To further investigate the clinical value of these findings for T-cell leukemia and lymphoma, we have investigated EZH2 degradation and CDK1 inhibition together with the FDA-approved histone deacetylase (HDAC) inhibitors on the survival of lymphoma/leukemia cells. Our data show strong synergy between HDAC inhibitors and EZH2 degraders or CDK1 inhibitors, both in direct effect on NMYC and MYB protein levels, and on cell viability. For EZH2 we use protein degraders, because the enzymatic activity of EZH2 is not required for its transcriptional function. To target CDK1 or HDACs we used enzymatic inhibitors, but also for these targets protein degraders (PROTACs) could be of interest, as these could be more potent and less affected by resistance mutations.

In this CELSA project, we aim to convert inhibitors of CDK1 and HDAC into PROTACs. We will test the activity of these PROTACs to inhibit our cell models of T-cell malignancies alone or in combination with EZH2 degraders. Moreover, we will compare the potency and specificity of these PROTACs with the enzymatic inhibitors. The results of this project will contribute to the development of more effective and less toxic treatments for T-cell malignancies.

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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.

Dataset name / ID	Description	New or reuse	Digital or Physical data	Data Type	File format	Data volume	Physical volume
		Indicate: ***N****(ew data) or* ***E****(xisting data)*	Indicate: **D**(igital) or **P**(hysical)	Indicate: **A**udiovisual **I**mages **S**ound **N**umerical **T**extual **M**odel **SO**ftware Other (specify)		Indicate: <1GB <100GB <1TB <5TB >5TB NA	
Protein degradation	Protein levels of target proteins and control proteins	N	D	I, N	tiff, excel tables	<1TB	J drive
Cell viability	Cell viability of cell lines treated with the drugs	N	D	I, N	excel tables	<1TB	J drive

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:

N/A

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, refer to specific datasets or data types when appropriate and provide the relevant ethical approval number.

- No

only commercial cell lines are used.

Will you process personal data? If so, please refer to specific datasets or data types when appropriate and provide the KU Leuven or UZ Leuven privacy register number (G or S number).

- No

N/A

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

Our results can lead to the identification of interesting lead compounds for drug development. We will closely follow up with LRD and VIB tech transfer office.

Do existing 3rd party agreements restrict exploitation or dissemination of the data you (re)use (e.g. Material or 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

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).

The excel files with the data will contain the detailed description of the experiments: cell lines used, drugs used, concentrations used, time points used, detection methods used. In addition, the protocol and exact reagents used will be documented in a separate file.

Will a metadata standard be used to make it easier to find and reuse the data?
If so, please specify which metadata standard will be used.

If not, please specify which metadata will be created to make the data easier to find and reuse.

- No

Each experiment has its own control (untreated cells) and there is no metadata standard needed here.

Data Storage & Back-up during the Research Project

Where will the data be stored?

- Shared network drive (J-drive)
- Other (specify below)

additional backup on 2 external hard drives.

How will the data be backed up?

- Standard back-up provided by KU Leuven ICTS for my storage solution
- Other (specify below)

additional backup on 2 external hard drives.

Is there currently sufficient storage & backup capacity during the project?

If no or insufficient storage or backup capacities are available, explain how this will be taken care of.

- Yes

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

J drive is only accessible to lab members ; external hard drives are securely stored in an office room

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

no extra costs.

Data Preservation after the end of the Research Project

Which data will be retained for 10 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 data will be preserved for 10 years according to KU Leuven RDM policy

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

- Other (specify below)
- Large Volume Storage (longterm for large volumes)

additional backup on 2 external hard drives.

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

regular storage, these are relatively small files and will not require extra investment above the usual needs we have.

Data Sharing and Reuse

Will the data (or part of the data) be made available for reuse after/during the project?
Please explain per dataset or data type which data will be made available.

- Other (specify below)

The data will be made available as soon as a publication can be completed. The data will remain private until publication is possible. Before publication we will discuss with LRD and VIB tech transfer office to determine how IP should be protected.

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

N/A

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 per dataset or data type where appropriate.

- Yes, intellectual property rights
- Yes, other

Publication plans and IP protection are important factors that will prevent sharing of the data.

Where will the data be made available?

If already known, please provide a repository per dataset or data type.

- KU Leuven RDR (Research Data Repository)

When will the data be made available?

- Upon publication of research results

Which data usage licenses are you going to provide?

If none, please explain why.

- CC-BY 4.0 (data)

Do you intend to add a persistent identifier (PID) to your dataset(s), e.g. a DOI or accession number? If already available, please provide it here.

- No

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

none

Responsibilities

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

Jan Cools

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

Jan Cools

Who will manage data preservation and sharing?

Jan Cools

Who will update and implement this DMP?

Jan Cools