MEDIZINISCHE UNIVERSITÄT
INNSBRUCK

October 2022 – December 2024

MUI-START Report

Forschungsservice und Innovation
Medical University of Innsbruck
October 2022 – December 2024

Content

Disclosure

This annual report was prepared by the Department Forschungsservice und Innovation.

Dr. María Teresa Pérez Mediavilla is responsible for the editorial part concerning the MUI-START Programme. The PIs are responsible for the scientific content of their final reports.

January 2025

1 Background and aim of the programme

MUI-START is the follow-up programme of the MFI (Medizinische Forschungsfonds Innsbruck) which ended in 2011.

The MUI-START programme is devised as a start-up fund for young scientists with the aim to offer them the opportunity of developing new project ideas, within the MUI research focuses, that could serve as basis for a successful subsequent application for external funding (e.g. FWF).

According to the present guidelines, eligible candidates must: 1) have a working contract with the Medical University of Innsbruck for the entire project duration, 2) have completed their doctoral studies, and 3) the applicant´s most recent degree (e.g. PhD/MD) must have been completed no longer than eight years ago. Fully justified career breaks can be taken into account (e.g. parental leave). Professors and PIs of third-party funded (FWF, OeNB, FFG and EU) projects are not eligible. Applicants' track record must be commensurate with their academic age. However, two peer-reviewed international publications as first author are compulsory**.**

The guidelines of the programme have been substantially modified over the years to adapt to the high standards applied by external funding agencies (e.g. FWF). Since 2016, proposals undergo a three-step evaluation procedure: 1) selection of proposals by the MUI-START jury, 2) international peer-review of the pre-selected proposals, and 3) hearing of the shortlisted applicants by the MUI-START jury. Final decisions are based on the reviewers' scores, as well as the outcome of the interviews.

Moreover, since the seventh call (2016) the submission of an external funding proposal before the end of the funding period has become compulsory for all MUI-START grantees. Failure to submit such an application results in the cancellation of the last quarter of the MUI-START grant budget.

2 Overview of MUI-START calls

The first MUI-START call was announced in the summer 2010 and supported 42% of the submitted proposals. Since then, the approval rates have been oscillating from year to year (Table 1) depending on both the available budget and the quality of the submitted proposals. The funded projects from the 13th call will start in December 2022.

Table 1. Overview of all MUI-START calls

Year	Call	Proposals submitted	Proposals gran (Male/Female)	Funding rate	Total fund requested	Total funding granted
2010	1st	31	13 (7M/6F)	42%	€ 2.074.365,7	€ 667.054,8
2011	2nd	11	5 (2M/3F)	45%	€ 629.968,9	€ 173.171,0
2012	3rd	29	9 (4M/5F)	31%	€ 742.808,2	€ 240.000,0
2013	4th	28	14(11M/3F)	50%	€ 713.652,9	€ 323.484,7
2014	5th	31	12(4M/8F)	39%	€ 771.750,5	€ 260.826,6
2015	6th	28	8 (4M/4F)	28%	€ 711.035,4	€ 176.726,0
2016	7th	9	3 (1M/2F)	33%	€ 248.945,0	€ 85.000,0
2017	8th	15	7 (5M/2F)	47%	€ 365.189,3	€ 162.208,8
2018	9th	8	4 (1M/3F)	50%	€ 192.576,2	€ 113.766,3
2019	10th	9	0 (0M/0F)	0%	€ 529.947,8	€ 00000,00
2020	11th	16	3 (1M/2F)	19%	€ 559.657,5	€ 101.454,1
2021	12th	26	7 (6M/1F)	27%	€ 940.979,5	€ 263.885,9
2022	13th	10	3 (1M/2F)	30%	€ 321.140,45	€ 74.421,45
2023	14th	11	5 (3M/2F)	45%	€ 657.415,52	€ 206.243,52
2024		No call open	In the year 2024			

3 MUI-START jury members and reviewers

The MUI START jury members are professors and associate professors at the Medical University of Innsbruck working in both basic as well as in clinical research fields. The jury members are chosen according to their expertise in a specific field of research. The composition of the jury is not fixed, but changes because of the variety of topics covered by the proposals submitted to a particular call.

The following jury members were involved in the selection of the projects **for the last two calls**. We would like to thank them for their help and commitment.

Univ.-Prof. Dr.rer.nat. Christine Bandtlow	*Neurobiochemistry*
Univ.-Prof. Dr. Francesco Ferraguti	*Pharmacology*
Univ.-Prof. Dr.med.univ. Johannes Holfeld	*Cardiac Surgery*
Univ.-Prof. Dr. Markus Reindl	*Neurology*
Univ.-Prof. Dr.med.univ. Barbara Sperner-Unterweger	*Psychiatry II*
Univ.-Prof. Dr.rer.nat. Patrizia Stoitzner	*Dermatology, Venereology and Allergology*
Univ.-Prof. Dr.med.univ. Dominik Wolf	*Internal Medicine V*
Univ.-Prof. Dr.med.univ. Alexandra Lusser	*Molecular Biology*
Assoz.-Prof. Johannes Passecker PhD	*Neurobiochemistry*
Univ.-Prof. Dr.med.univ. Hesso Farhan	*Pathophysiology*

The tasks of the jury members comprise:
1) internal review of the proposals,
2) nomination of the international reviewers, and
3) presentation of proposals during the decision meeting.

The reviewers of the MUI-START projects are international experts active in their field of research. Usually two reviews per proposal are necessary to support the jury members in their decision process.

4 The MUI-START Programm in numbers

- **93 Funded projects/ 84 Projects completed**
- **50 Male PIs / 43 Female PIs**
- **2,85 € Mio granted by the MUI START programme**
- **8,3 € Mio funds acquired by former MUI-START grant holders**

As stated in the first section of this report the aim of the programme is to help young scientists develop new project ideas that could serve as a basis for a subsequent application for third party funding.

So far, (status as of 31.12.2024) 84 MUI-START funded projects have closed. Twenty-six PIs quit the MUI either before the planned end or immediately after the end of the project. Approximately 82 % (48) of the remaining PIs applied for external funding. Given the competitiveness of the current funding landscape, not all applications generated funding.

Additionally, 61 % of PIs of closed projects now have a permanent position at the MUI or at the Tirol Kliniken. Another 14 % of PIs quit the MUI and got positions in other research institutions or at pharmaceutical or high-tech companies. The remaining scientists are still working at the MUI as project collaborators or hold non-permanent positions

5 Summary of all funds acquired based on MUI-START projects

Table 2. FWF/ÖNB funded projects based on MUI-START preliminary data.

Applicant	Project Title	Funding Agency	Duration (Months)	Funds Granted
Manfred Nairz	The iron storage protein ferritin in bacterial infection	FWF - P33062	48	€ 399.430
Bernhard Haubner	Investigating long non-coding RNA regulated pathways driving cardiac regeneration	FWF - I 4161	36	€ 206.892
Sebastian Reinstadler (Co-applicant)	Soluble Neprilysin in ST-elevation Myocardial Infarction	FWF - KLI 772	48	€ 188.118
Michaela Lackner	Intrinsic azole resistance in mucormycetes	FWF - P32329	48	€ 306.517
Markus Keller	Lipid peroxidation as driver of cardiolipin remodeling	FWF–P33333	36	€ 380.963
Kerstin Bellaire-Siegmund	PKCtheta/Coronin 1A Achse in CD4+ T-Zell-Subpopulationen	FWF – M 1636	48	€ 134.540
Natasha Hermann-Kleiter	NR2F6 governs immune defense against microbial pathogens	FWF - P28694	36	€ 317.627
Natasha Hermann-Kleiter	Orphan receptor NR2F6 as a negative regulator of T cell effector functions	FWF - P23537	36	€ 255.859
Galina Apostolova	Role of genome organizer Satb2 in adult brain function	FWF - P25014	36	€ 299.817
Galina Apostolova Co-PI	Function of special AT-rich sequence-Binding Protein 2 (SatB2)	FWF – SFB4416	48	€ 475.755
Birgit Frauscher	Motor activity during sleep in health and disease	FWF - KLI236	36	€ 203.610

Birgit Frauscher	REM sleep without atonia: early sign of neurodegeneration	ÖNB - 15127	30	€ 90.000
Martin Puhr	Functional significance of PIAS1 and BIRC5 in docetaxel resistant prostate cancer	FWF - P25639	30	€ 337.234
Martin Puhr	The Impact of Glucocorticoid Administration on Prostate Cancer Progression and Therapy Resistance	ÖNB - 18280	36	€ 148.000
Markus Theurl	Catestatin for the treatment of myocardial ischemia	FWF - P26251	24	€ 262.731
Rupert Oberhuber	Evaluierung der Leberorganqualität vor Transplantation	ÖNB - 17287	36	€ 110.000
Manfred Nairz	Die Rolle von Innate Response Activator B Zellen bei Sepsis	FWF - J3486	24	€ 69.700
James Wood	Dopamine and NPY signaling in a fear extinction circuit	FWF - M1783	24	€ 157.380
Sebastian Herzog	Molecular regulation of the oncogenic miR-17-92 cluster	FWF - P30194	48	€ 297.305
Sebastian Herzog	Unraveling miR-15 function in health and disease	FWF - P30196	42	€ 364.019
Ramon Tasan	Role of the neurokinin B-expressing neurons in the bed nucleus of the stria terminalis	FWF - P29952	36	€ 399.441
Johanna Gostner	Cellular reactions to low-dose volatile organic compounds (VOC) exposures	FFG - Bridge	36	€ 301.881
Stefan Coassin	Studying a *Lp*(a) mutation in human RNA and liver organoids	FWF - P31458	42	€ 345.914
Antonio Heras-Garvin	Unravelling the pathogenic role of iron dysregulation in MSA	FWF-PAT4208323	36	€ 347.302

Table 3. Additional third party funding acquired by former MUI-START grant holders

Applicant	Project Title	Funding Agency	Duration (Months)	Funds Granted
Wegene Borena	Genital HPV infection among HIV - positive men in West Austria in the Austrian HIV Cohort Study	MFF - Nr.262	18	€ 13.728
Selma Tuzlak	Bcl-2 family	ÖAW - 23949	36	€ 105.000
Christian Ploner	MADI	Land Tirol	51	€ 73.467
Peter Lackner	The role of voltage gated Ca channels for neuroprotection in experimental subarachnoid hemorrhage	Land Tirol	24	€ 75.400
Rupert Oberhuber	Tetrahydrobiopterin as novel therapeutic strategy to improve outcome after the transplantation of organs from brain death donors	TWF-2013-1-17	24	€ 20.000
Sebastian Herzog	Systematic analysis of the miR-26 family in lymphocyte development and cancer	TWF-2014-1-17	24	€ 26.500
Michael Blatzer	Alternative regulatory circuits of secondary metabolite production in *Aspergillus terreus*	TWF-2016-1-1	24	€ 39.500
Beno Cardini	The impact of simvastatin on the ischemia reperfusion injury in the murine heart transplantation model	TWF-2016-1-6	18	€ 32.069
Martin Bodner	Helena's many daughters - Massively parallel sequencing provides highest-resolution insights into the most common West Eurasian mtDNA control region haplotype	TWF-2016-1-2	24	€ 30.122
Lourdes Rocamora	Role of Glucocorticoides on B cell development and function	TWF-2016-1-23	24	€ 37.390
Luca Fava	How do cells count their centrosomes? A mechanistic study	Armenise-Harvard Foundation	60	$1.000.000
Nina Clementi	What makes a Stop codon a Stop codon?	TWF-2017-1-3	24	€ 31.754

Elke Griesmaier	Beurteilung von Secretoneurin als Serum Biomarker der Hirnschädigung bei Frühgeborenen	TWF-2017-1-8	48	€ 18.400
Sebastian Reinstadler	Soluble Neprilysin in ST-elevation myocardial infarction: Release Kinetics, Cardiac Remodeling and Future Cardiovascular Events	Österrichische Kardiologische Gesselschaft	24	€ 48.880
Gamerith Gabriele	Soluble Checkpoints in Vasculitis	NIH	13	€ 35.240
Matteo Cesari	SPRINT Stroke outcome Prediction with aRtificial INTelligence	Land Tirol (AI Call)	10	€ 299.738
Stephan Salcher	Out-FOXOing Chemoresistance in Non-Small Cell Lung Cancer	Fellinger Krebsforschung	24	€ 20.000

6 MUI-START final reports

The principal investigators of the MUI-START funded projects are responsible for the content of their respective final reports.

Tapping unexplored therapeutic opportunities in prostate cancer

Florian Handle PhD
Institute of Pathology, Neuropathology and Molecular Pathology

Project duration: 01.12.2021 – 30.09.2023

Project summary:

Prostate cancer (PCa) is a prevalent malignancy, ranking among the most frequently diagnosed cancers worldwide. Despite advancements in treatment modalities, patients with high-risk PCa often face treatment relapse and metastasis. Metastatic PCa remains incurable and accounts for a significant portion of cancer-related deaths in men, which underscores the urgent need to identify novel therapeutic targets in PCa. To address this, we developed the TUTOR pipeline (tapping unexplored therapeutic opportunities with an R pipeline) for identifying novel therapeutic targets in PCa. By integrating multi-omics data from various sources, we uncovered a wealth of potential therapeutic avenues and established a high-throughput confirmation experiment to validate these candidates. The pipeline's user-friendly web interface will render it a valuable tool for all PCa researchers, independent of their bioinformatics expertise.

In detail, the TUTOR pipeline comprises six prostate tissue datasets encompassing 269 benign, 1506 primary PCa, and 309 metastatic PCa samples. We extracted and harmonized clinical annotation (Gleason score, relapse, tumor stage), gene expression, and copy number aberration data from these datasets to facilitate seamless data integration. Differential gene expression meta-analysis revealed 8,524 significantly deregulated genes in primary PCa samples compared to benign samples, and 5,446 deregulated genes in metastatic samples compared to primary PCa. Additionally, 3,202 genes were found to be significantly deregulated in patients who experienced tumor relapse following radical prostatectomy.

To enrich the pipeline's capabilities for validation experiments, we also incorporated cell line data. Specifically, we extracted gene expression data (19,221 detected genes in 1,406 cell lines) from the cell line encyclopedia dataset and integrated it with CRISPR-KO (17,386 genes/1,086 cell lines) and RNAi (17,023 genes/710 cell lines) based gene perturbation data from the depmap project. This comprehensive dataset encompasses all typical prostate cancer cell lines as well as cell lines from a diverse range of tumor entities, thus fostering generalization. Furthermore, we included bulk and single-cell RNA-seq datasets of enzalutamide-resistant cell lines to identify genes associated with resistance to this important drug. We reprocessed gene expression data from four previously published resistant cell lines. To broaden the scope, we also performed bulk RNA-seq of four additional enzalutamide-resistant cell lines generated here in Innsbruck. We also included single-cell RNA-seq data from two enzalutamide-resistant cell lines generated by a previous collaboration. Due to the heterogeneity observed in these scRNA-seq datasets, we performed our own scRNA-seq experiment with the two most prevalent PCa cell lines (LNCaP and DU145). Remarkably, we observed between 3-6 subpopulations of cells with distinct transcriptomic profiles in all cell lines. We prepared the scRNA-seq data to enable a cell line/subpopulation-specific view of cell cycle progression for identification of potential targets involved in this essential process.

To facilitate user-friendliness, we developed a web application using the R package “shiny” to make this data accessible to prostate cancer researchers without bioinformatics expertise. The initial version of this web app, featuring gene expression data from patient tissue samples, is

available at https://handle-pca.shinyapps.io/pcaviewer/ and is currently undergoing beta testing with selected collaborators. Based on the feedback, we will improve the app and integrate the remaining parts of the TUTOR pipeline, which are currently only usable by a dedicated bioinformatician.

Finally, we set-up a protocol for high-throughput RNAi-based gene perturbation studies using a Cherry-Pick custom siRNA pool library (Dharmacon, Horizon Discovery) coupled to early-barcoding multiplexed RNA-seq (Alithea genomics). This carefully established protocol allows us to screen the functional effect of dozens of genes per week for less than 150 €/gene. For demonstration purposes, we focused on the KRAB zinc finger (KRAB-ZFP) protein family due to their role as transcriptional regulators and the limited literature surrounding many of these genes. We retrieved 361 genes containing both a KRAB and C2H2 ZNF domain from Interpro and used this as input for the PCa TUTOR pipeline. Notably, 34% of these genes were significantly deregulated in PCa tissue, and 10% were correlated with tumor relapse after radical prostatectomy. We shortlisted 21 KRAB-ZFP candidates fulfilling both criteria and performed the aforementioned siRNA-mediated downregulation followed by RNA-seq. Differential gene expression analysis followed by competitive gene set enrichment analysis using limma/camera revealed significant deregulation of proliferation-related pathways in seven candidates, most of which also exhibited deregulation of apoptosis-related signatures. Additionally, we identified deregulation of oxidative phosphorylation (increased in three candidates), EMT (down in one candidate), and ROS (increased in three candidates) pathways.

Taken together, the PCa TUTOR pipeline developed in this project has the potential to accelerate the discovery of novel therapeutic targets by providing this highly relevant multi-omics data to all PCa researchers, independent of their bioinformatics expertise.

External funding

A principal investigator project has been submitted to FWF entitled “Multi-Omics investigation of ZNF695 in prostate cancer” to follow up a very promising target identified in this project. The grant application is currently under consideration by the FWF.

Miscellaneous

In the course of this project an Erasmus+ funded master student from the KU Leuven (Belgium) has successfully performed her master thesis under supervision of the applicant.

Results from this project have been presented at the ESUR23 conference in Basel (Switzerland) in 2023 (title: “Decoding the impact of the stem-cell inhibitor salinomycin on cellular heterogeneity in PCa via scRNA-seq”).

Potentiating chimeric antigen receptor-engineered CD8+ T cell (CAR-T) function by targeting Cblb

Sebastian Peer
Department for Cell Genetics

Project duration: 01.12.2021 – 31.10.2023

Project summary:

Background and objectives
CAR-T immunotherapy is not yet effective against solid cancers. The biggest obstacle in preventing this current CAR-T failure are the immunosuppressive features of the tumor immune microenvironment (TME). Thus, there exists a strong medical need to improve efficacy of CAR-T therapies at the solid tumor site in order to fully unlock the therapeutic potential of CD8+ CAR-T immunotherapy. Mechanistically, a progressive loss of function of infused CAR-T cells within the TME limits their persistence, leading to intrinsic and/or acquired tumor resistance to therapy.

According to our hypothesis, Cbl-b as established anergy-related gene and TCR/CD28 signaling repressor plays a key role in regulating the induction and maintenance of CD8+ T cell exhaustion. Preliminary studies uncover that deficiency of Cbl-b may ameliorate T cell exhaustion.

Specifically, we will determine how Cbl-b-targeting affects the properties and function of CD8+ CAR-T cells. Our goal is to firmly validate as well as define in detail this regulatory role of Cbl-b in solid tumor-induced CAR-T dysfunction.

Results
We were able to show that ablation of *Cblb* leads to increased CAR-T cell activity *in vitro* and *in vivo*. In a subcutaneous mouse tumor model, treatment with CAR T cells lacking *Cblb* leads to reduced tumor growth and longer survival of mice compared to treatment with control CAR T cells (Fig. 1A). This was accompanied by higher CD8+ T cell infiltration in the tumors (Fig. 1B). We were extremely happy with these results, since very few groups at that time could show treatment responses of CAR T cells in solid tumors at all.

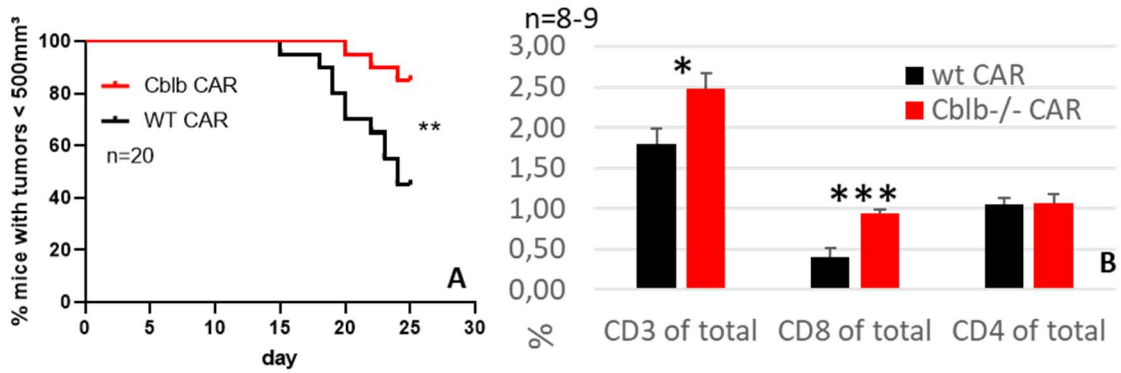

Figure 1: Subcutaneous tumor model: Mice were injected subcutaneously with PanC tumor cells, 500.000 CD8+ CAR T cells were injected intravenously on day 4 after tumor injection. Mice were euthanized and tumor cell suspension analyzed by flow cytometry on day 25 after tumor injection. A) survival curve: cut-off tumor size 500mm³ B) percentage of T cells of whole tumor cell suspension.

Thorough *in vitro* characterization of the *Cblb* ablated CAR T cells demonstrated their superior tumor killing capacity (Figure 2, Figure 3), enhanced IFN□□and GranzymeB production as well as enhanced glycolytic metabolism (not shown). Especially in the presence of TGF□, these in vitro phenotypes were even more profound. Since many tumors show elevated TGF□ secretion, thereby inhibiting immune responses, we hope to verify this relevance of *Cblb* in the human setting as well.

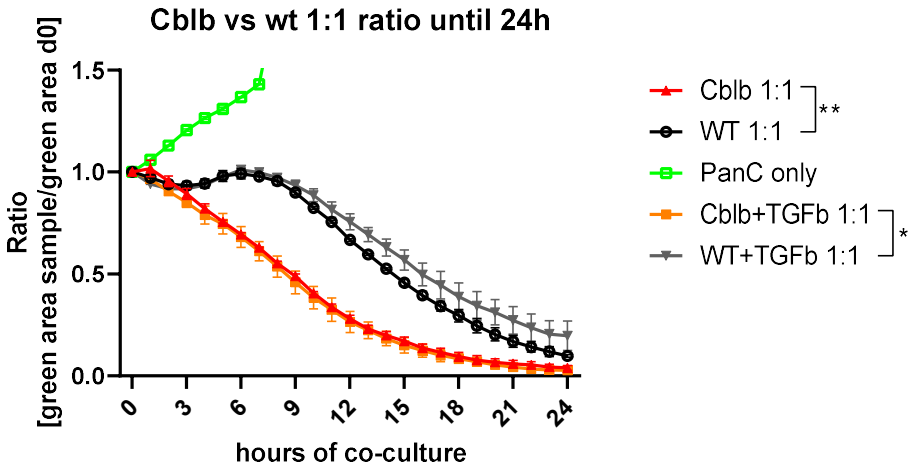

Figure 2 Incucyte measurement: GFP transduced PanC tumor cells were cultured and CAR T cells addedin a 1:1 ratio. Killing is shown by reduction of GFP signal over time

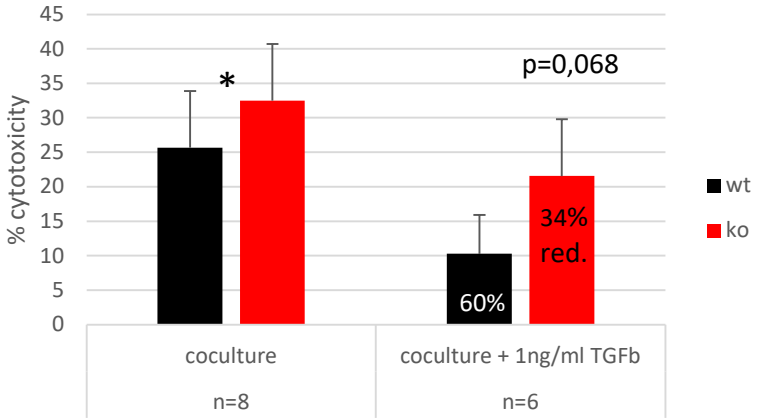

Figure 3 LDH release assay: PanC tumor cells were cocultured with CAR T cells and supernatants taken after one day. LDH release was determined to show the cytotoxic capacity of the CAR T cells.

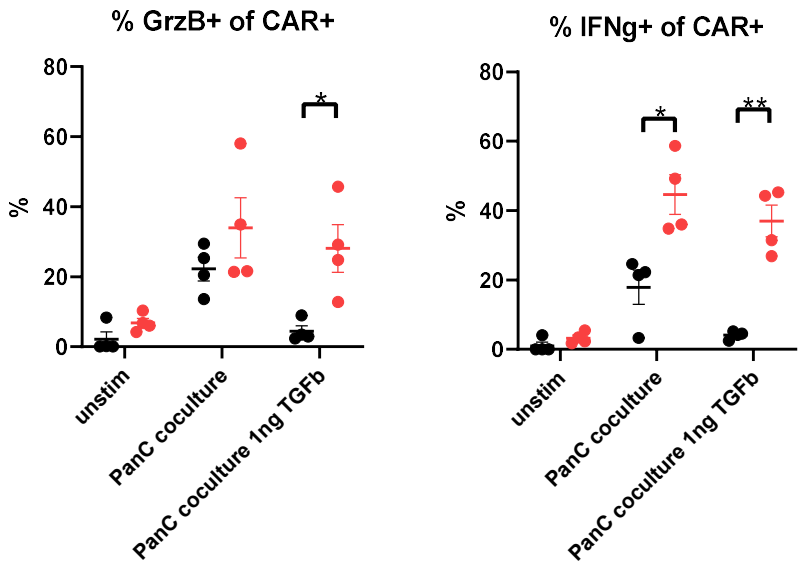

Figure 4 Flow cytometric analysis: CAR T cells were cultured alone or with PanC tumor cells +/- TGF and analyzed after 1 day of culture.

Outlook:

During this project I co-supervised two bachelor students and four project-study students who are now all able to generate CAR-T cells, some of which are continuing on as master students in the institute, helping also in this project. We wrote and received a FFG grant (main author Gottfried Baier, in cooperation with invIOs) to carry on our work in the human setting: We are already able to eliminate *Cblb* via Crispr-Cas9 in human CD8+ T cells and are currently establishing a human CAR T model with the corresponding tumor cell line to characterize these human CAR T cells and, in the long run, take this setting to the clinics. The data shown here will be published soon, along with the human data which are generated at the moment.

Unraveling the pathogenic role of iron dyshomeostasis in multiple system atrophy

Antonio Heras Garvin PhD
Department of Neurology

Project duration: 01.12.2021 - 31.03.2024

Project summary:

Multisystem atrophy (MSA) is a severe neurodegenerative disease classified as a rare disease with no available treatments to mitigate its progression. It is characterized by the abnormal accumulation of α-synuclein (α-syn) in oligodendrocytes, leading to the formation of glial cytoplasmic inclusions (GCIs) and neurodegeneration.

Recent studies have suggested a prion-like behavior of α-syn and shown that MSA-derived α-syn has higher infectivity and pathogenic potential compared to other α-synucleinopathies such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB). Despite various hypotheses, the exact cause and triggering factors of MSA remain largely unknown.

Role of iron dyshomeostasis: Iron is essential for brain function, but its accumulation can lead to oxidative stress. Previous research has shown iron accumulation in both PD and MSA brains, but its role in MSA is not fully understood. Our preliminary data suggest that iron dyshomeostasis is at the heart of MSA pathology, particularly in oligodendrocytes.

Results:

Iron accumulation in the MSA mouse model:

- The PLP-hαSyn transgenic mouse model, which overexpresses human α-syn in oligodendrocytes, mimics MSA pathology. Our studies in these mice show significant iron accumulation in the substantia nigra (SN) in early stages (2 months), preceding dopaminergic neurodegeneration and neuroinflammation.
- We observed an increase in iron levels in the SN of transgenic (TG) mice compared to wild-type (WT) controls.

Gene dysregulation:

- RNA-seq analysis revealed significant dysregulation of iron-related genes in the SN of young (2-month-old) MSA mice, including upregulation of genes related to iron uptake and intracellular transport (Tfrc, Slc11a2) and the downregulation of genes associated with iron storage (Fth1).
- In older (12-month-old) MSA mice, the downregulation of genes associated with iron storage was exacerbated while the upregulation of genes related to iron uptake was less significant, suggesting a progression of iron dysregulation.

Ferritin accumulation:

- Western blot and immunofluorescence analysis showed abnormal accumulation of ferritin (FER) in the SN of MSA mice, mainly in oligodendrocytes and associated with α-syn GCIs. This accumulation was more pronounced in the SN than in the cerebellum (CB), correlating with pathology severity

Microglial iron dyshomeostasis:

- Microglia in MSA mice also showed dysregulation of iron-related genes, characterised by upregulation of genes related to iron uptake and storage and the downregulation of genes associated with iron efflux.

This consistent response across brain regions suggests that microglia are attempting to restore iron balance and possibly mitigate iron-related damage.

Conclusion & Outlook

Our preliminary data show that iron dysregulation is a prominent feature in MSA that occurs early in the disease process and may drive neurodegeneration. Iron dyshomeostasis is significant in the SN compared to other brain regions such as the CB and shows cell-specific variations.

Further research is needed to determine whether iron dysregulation is a primary cause of motor dysfunction and neuronal loss in MSA-like disease progression and to explore its potential as a biomarker for disease progression and as a therapeutic target. Preliminary findings also suggest peripheral iron dysregulation, indicating systemic involvement in MSA pathology

External funding applications:

In a follow-up submitted and approved project (FWF Grant-DOI 10.55776/PAT4208323, Budget: 347.302 Euro), we will fully investigate the link between iron dyshomeostasis and disease progression in MSA mice by completing our characterization of iron accumulation and iron-related molecular changes in different cell types and brain regions at different stages of the disease. We will also explore the association of these changes with behavioral, neurodegeneration and neuroinflammation data. Furthermore, we will explore the cell- and region-specific transcriptional changes associated with iron accumulation. Finally, we will evaluate the amounts of the most promising iron-related molecules in the periphery of MSA mice over the course of the disease. This way, we could identify potential peripheral biomarkers that could be transferred to future clinical studies.

Out-FOXOing therapy-resistant cancer cells

Ass.-Prof. Stefan Salcher PhD
Department of Internal Medicine V, Haematology and Oncology

Project duration: 01.12.2021 - 31.05.2024

Project summary:

Background and objectives
The FOXO3 protein, part of the FOXO family of transcription factors, plays a crucial role in regulating numerous cellular functions and is implicated in several diseases, including cardiovascular conditions, diabetes, neurological disorders, and cancer. FOXO3's activity is modulated by protein kinase B (PKB) and various growth factor- and stress-induced kinases. In the absence of active PKB, FOXO3 localizes to the cell nucleus to control gene transcription, functioning traditionally as a tumor suppressor by inducing cell death and cycle arrest. However, recent studies have revealed its potential oncogenic properties, particularly in advanced and relapsed cancers. The MUI-START funded project: “OutFOXOing Therapy-Resistant Cancer Cells” aimed to investigate the molecular mechanisms of FOXO3 signaling in cancer, specifically its role in chemo-protection and resistance. Additionally, the study sought to evaluate the therapeutic potential of Carbenoxolone (CBX), an FDA-approved compound identified as a putative FOXO3 modulator, in targeting chemo-resistant cancer cells.

Results
Through whole transcriptome single-cell RNA sequencing (scRNAseq), we demonstrated that FOXO3 is expressed in prostate cancer (PCa) and non-small cell lung cancer (NSCLC) tumor cells. A comparative analysis of lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC) revealed that FOXO3 is significantly higher expressed in squamous histology tumors (Figure 1), a subtype associated with poorer overall outcomes. Notably, FOXO3high LUSC tumors correlate with shorter disease-free survival.

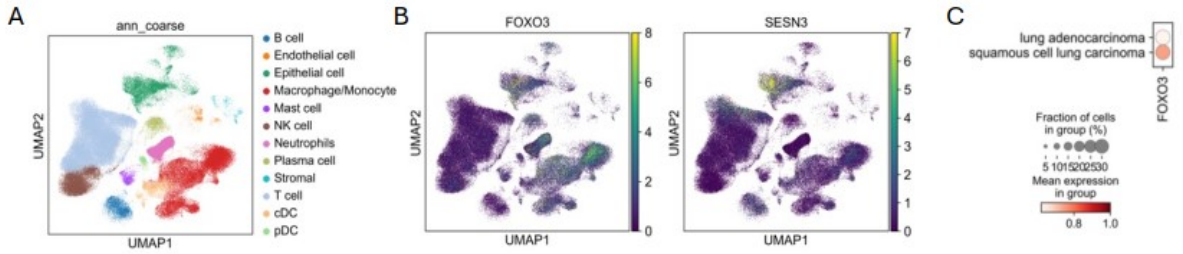

Figure 1: Elevated FOXO3 Expression in NSCLC Tumor Cells Revealed by scRNAseq. A) Overview of the NSCLC scRNAseq dataset (n = 17 patients) showing the epithelial, immune, and stromal/endothelial components depicted using uniform manifold approximation and projection (UMAP) plots. B) UMAP plots demonstrating the expression levels of FOXO3 and SESN3. C) Comparison of FOXO3 expression levels between lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC)

In vitro analysis further supported the role of FOXO3 in mediating chemotherapy resistance. We demonstrated that FOXO3 is highly activated in chemotherapy-resistant
PCa and NSCLC cell lines, inducing its direct transcriptional targets, such as SESN3, ABCB1, and FOXP1, which contribute to the resistant phenotype. To validate the scRNAseq findings, we established chemo-resistant NSCLC cell lines derived from both LUAD and LUSC tumors. Ongoing analysis is focusing on the histology-dependent differences in FOXO3 function.

In chronic myeloid leukemia (CML) cells, we showed that FOXO3 is critical for the persistence of leukemia-initiating stem cells. Additionally, we demonstrated that the putative FOXO3

inhibitor Carbenoxolone (CBX) impairs FOXO3's DNA-binding ability, thereby silencing its transcriptional activity.

Using CBX on chemotherapy-resistant PCa and NSCLC cell lines revealed that CBXmediated FOXO3 silencing abrogates the expression of its target genes SESN3 and ABCB1, effectively overcoming the chemo-resistant phenotype. Hence, our findings propose FOXO3 inhibition as a strategy to specifically target chemotherapy-resistant leukemic cells, as well as PCa and NSCLC tumor cells, offering potential new avenues for therapeutic intervention.

Unexpected results and perspectives
By establishing a single-cell RNA sequencing (scRNAseq) procedure that enabled us to investigate cells with very low mRNA content, we characterized tumor-associated neutrophils (TANs) in lung cancer for the first time (Salcher et al., *Cancer Cell*, 2022; Salcher et al., *Heliyon*, 2024). Remarkably, we discovered that TANs are the major source of VEGFA, a core factor driving tumor angiogenesis, within the tumor microenvironment. This finding identifies pro-tumor TANs as an attractive target for novel therapeutic interventions.

Our in-depth analysis revealed that TANs are primarily found in lung squamous cell carcinoma (LUSC) tumors. Additionally, we observed that FOXO3 is highly expressed not only in tumor cells but also in neutrophils (Figure 1). Recent studies have shown that FOXO3 is a key regulator of the pro-angiogenic switch in neutrophils (Bordbari et al., *IJC*, 2021), suggesting that FOXO3 may contribute to the pro-tumor TAN phenotype in lung cancer. Thus, we established a tumor cell-neutrophil co-cultivation model to study the role of FOXO3 in NSCLC TANs. Ongoing experiments aim to clarify whether FOXO3 silencing is a feasible strategy to reprogram the pro-tumor TAN phenotype. This approach could pave the way for new therapeutic strategies targeting the tumor microenvironment to inhibit cancer progression.

Conclusion & Outlook
In conclusion, the MUI-START funded project demonstrated that FOXO3 plays a crucial role in chemotherapy resistance in PCa, NSCLC, and CML. The putative FOXO3 inhibitor Carbenoxolone (CBX) effectively silences FOXO3's transcriptional activity, overcoming the chemo-resistant phenotype in cancer cells. Additionally, FOXO3 was identified as a putative regulator in TAN, offering new therapeutic targets for combating cancer progression

Publications issued from this project:

At the moment the presented data are not published yet. Two papers are currently under review, and a third publication is in preparation. The MUI Start funding will be acknowledged in these publications.

External funding applications:

"Out-FOXOing Chemoresistance in Non-Small Cell Lung Cancer" Fellinger Krebsforschung 2023; 20,000 €

Miscellaneous:

The therapy-resistant cancer cell lines and established methods developed during the MUI-START funded project enabled the characterization of novel chemo-sensitizers generated in a separate project.

Relationship between Reference Group Identity and Body Dissatisfaction: Comparing Heterosexually-identified Individuals and Sexual and Gender Minority Individuals

Ass.-Prof. Nikola Komlenac PhD
Institute of Diversity in Medicine

Project duration: 01.01.2023 – 18.01.2024

Keywords: body satisfaction, reference group identity, LGBTQ, body modifications, mixedmethods study

Project summary:

Background and objectives:

The project included two research questions. One research question investigated whether identity centrality moderated the link between identifying with a sexual and gender minority group and body appreciation. A second research question tested whether positively or negatively framed information about affirmative action programs for women in academia can increase people's supportive opinions about affirmative action programs.

In gender minority people with high identity centrality the link between belonging to a gender minority group (in comparison to identifying as women) and lower levels of body appreciation was weaker than in gender minority people with low levels of identity centrality. Thus, findings supported the social cure model.

The second part of the project revealed that either positively or negatively framed information can increase men's supportive opinions about affirmative action programs for women in academic careers. Those findings have been published as Original Article in the scientific journal ***Humanities and Social Sciences Communications***. A second manuscript resulting from the project is currently being reviewed for a scientific journal.

Body appreciation

The first part of the project investigated factors that were linked to body appreciation in cis-heterosexual and sexual and gender minority persons. Thereby, the social cure model [1] and the intragroup status and health model [2] were tested. The social cure model predicted that stronger social identification with a (sexual or gender minority group) would result in weaker links between identifying with a minority group and low levels of body appreciation, whereas the intragroup status and health model would predict stronger links with stronger social identification.

The current study focused on people identifying with sexual and gender minority groups (and intersectional identities), because sexual and gender minority people are known to have on average lower levels of body satisfaction and to experience discrimination more often than cis-heterosexual people [3-7]. Study participants were able to choose among many (including intersectional) group identifications (e.g., heterosexual trans* person). As foreseen in the planning of the project many (specific) groups remained underrepresented even though a relatively large sample was recruited (N = 1,680 persons). Thus, some sexual and gender minority subgroups were aggregated to larger (less precise) subgroups. This approach was/is the main point of critics during the review process for the publication in a scientific journal.

Affirmative actions

A second research question could be covered with the available budget. The second research question investigated whether people's supportive opinions about affirmative action programs [8] for the support of women's careers in academia can be increased with the help of two educational texts informing participants about the need for affirmative actions. Thereby, the model of attitudes toward affirmative action programs [9] was used and the effect of positively framed information (i.e., that affirmative action benefits all employees) was compared to the

effect of negatively framed information (i.e., that affirmative action programs replace career development programs that mostly benefit men). In specific, it was tested whether people more favorably perceived affirmative action programs (i.e., perceive career developmental programs offered only to women as having higher levels of fairness and importance) when being presented with positively framed information, in comparison to being presented with negatively framed information or no information about affirmative action programs.

Body appreciation

Overall, 1,680 persons (49.2% cisgender women, 37.7% cisgender men, 9.0% nonbinary, 4.1% transgender) participated in the study. People who identified as gender minority (GM) people reported higher levels of identity centrality than did people who identified as women. People who identified as men, cisgender heterosexual women, cisgender heterosexual men, cisgender SM women, cisgender SM men, or general population reported lower levels of identity centrality than did people who identified as women.

The manifest path model (Figure 2.1) revealed that in comparison to people who identified as women, people who identified as GM people and LGBTQ* people reported lower levels of body appreciation. Found associations in GM people supported the social cure model [1]. Namely, links between having GM people as social group and having low levels of body appreciation was lower in GM people with high levels of identity centrality (IC) compared to people being low in IC. On the other hand, individuals who identified as LGBTQ* people experienced more discrimination and reported lower levels of body appreciation, especially when IC was high. Thus, findings in LGBTQ* people supported the intragroup status and health model [2].

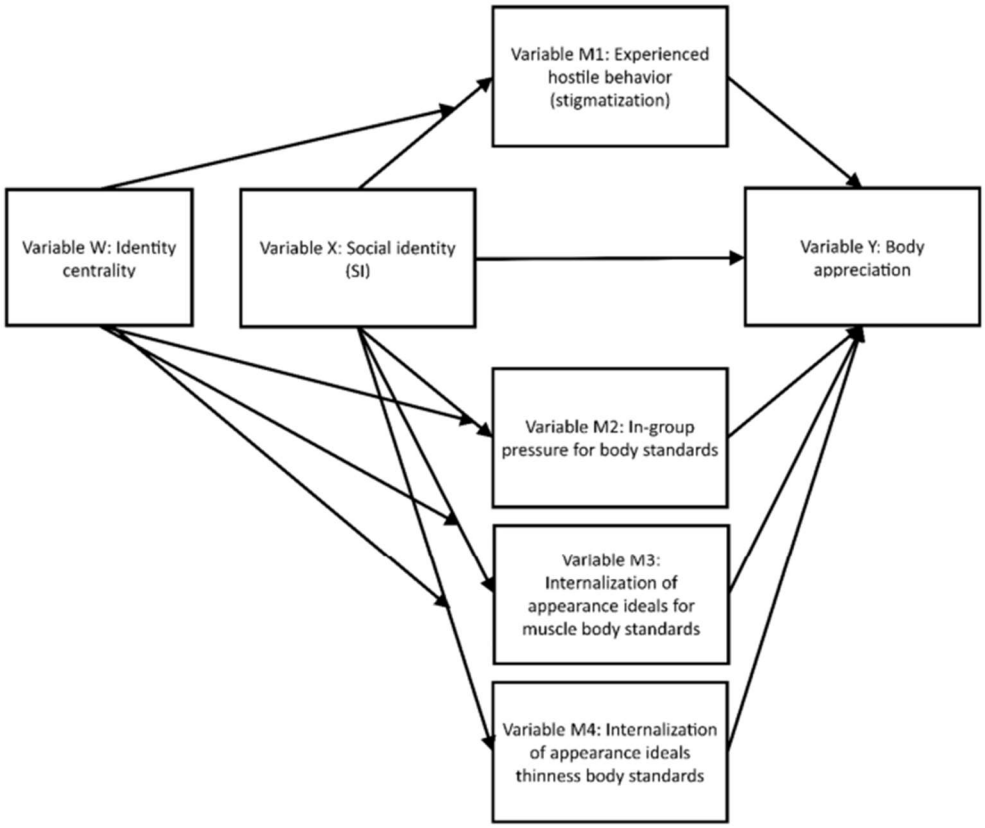

Figure 2.1: Manifest Path Model for Testing the Social Cure Model or the Intragroup Status and Health Model

Affirmative actions

Overall, 510 participants (52.5% cisgender woman and 47.5% cisgender men) took part in the study. Two mixed design analyses of co-variance (ANCOVAs) revealed that career development programs offered to all scientific employees are more favorably perceived, i.e.,

received higher ratings for fairness and importance, than were career development programs offered specifically to women.

The experimental manipulation (offering information with different framing) worked in men in the expected direction (Table 3.1). Namely, men who read that the implementation of affirmative action programs can benefit all employees (positive framing) gave career development programs offered solely to women higher fairness and importance ratings than did men who did not receive any justification for the implementation of affirmative action programs. Finally, men who were informed that some of the currently available career development programs need to be replaced with affirmative action programs (negative framing), because the currently available career development programs are more tailored to help men's job advancement than to help women, gave higher fairness ratings for affirmative action than did men who received no justification for the implementation of affirmative action programs.

Table 2.1

Results from Mixed Design Analyses of Co-variance (ANCOVAs)

Model	Fairness		Importance	
Variables	F(1-2, 498)	η^2	F(1-2, 497)	η^2
Affirmative action (1 = no, 2 = yes)	27.4***	0.05	5.7*	0.01
Text condition	2.8		1.0	
Affirmative action x Text	4.6*[1,2]	0.02	2.0	
Affirmative action x Gender	6.8*[3]	0.01	9.6**[5]	0.02
Affirmative action x Text x Gender	3.2*[4]	0.01	2.9	
Age	0.8		0.1	
Gender	37.3***	0.07	84.9***	0.15
Relationship status	0.4		0.0	
Sexual orientation	2.9		1.1	
Nationality	0.8		0.0	
Education	3.6		0.0	
Employment	0.5		0.0	

[1]Significant contrast between neutral and loss-message condition in ratings of interventions for women ($p < .05$)

[2]Significant contrast between neutral and gain-message condition in ratings of interventions for women ($p < .05$)

[3]Larger difference in mean ratings between women and men when rating interventions for women than when rating interventions for all scientific employees

[4]Significant contrast between neutral and gain-message condition and between neutral and loss-message condition in men's ratings of interventions for women only

[5]Significant contrast between men's ratings of interventions for all scientific employees and interventions for women only

* $p < .05$, *** $p < .001$

Publications issued from this project:

The findings about increasing people's supportive opinions about affirmative action programs for women is published in ***Humanities and Social Sciences Communications*** (https://doi.org/10.1057/s41599-023-02508-x; Impact Factor: 3.5, Rank: 83.2%).

The findings about body appreciation, group identification and identity centrality are currently being reviewed for a scientific journal (Impact Factor: 4.8, Rank: 81.4%).

Findings about people's body appreciation will be presented at the European Congress of Psychiatry (EPA, 6 – 9 April 2024, Abstract accepted, https://epacongress.org/). One more abstract about this study's findings was submitted to the 3. Deutscher Psychotherapie Kongress (11. – 15. June 2024, https://deutscher-psychotherapiekongress.de/). Finally, one abstract about opinions about affirmative action programs was submitted to the International Association for Health Professions Education (AMEE, 24. – 26. August 2024, https://amee.org/).

It is planned to submit the study about body appreciation, group identification and identity centrality to the 17th European Public Health Conference (EPH, 12. – 15. November 2024, https://ephconference.eu/) when Abstract submission starts.

External funding applications:

The PI has applied for third-party funding at the ESSM Research Grant 2022-2023 (RG 22-02) (meanwhile rejected) and Tirol Allgemein (F.49915; currently being reviewed). Furthermore, the PI has applied at the Austrian Science Fund (FWF) for funding (PAT4659723; currently being reviewed) in the amount of € 214,541.12.

Finally, the PI is currently writing a project proposal that can be seen as a follow up to the current project (affirmative action study). The project proposal will be finished and submitted to the FWF for funding in the amount of € 240.317,10 in February 2024.

Fertility Preservation: understanding the effects of low dose ovarian irradiation in a mouse model

Ass.-Prof. Elisabeth Reiser
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Project duration: 09.11.2021 – 31.10.2024

Project summary:

Background and objective:

Survival rates for children, adolescents and young women suffering from cancer continue to improve due to ongoing advances in cancer treatment- giving rise to a special population: adult survivors of childhood cancer that desire to have children after radiotherapy and/or cytotoxic chemotherapy regimens. The human ovary contains a finite pool of primordial oocytes. This fixed number of oocytes is non-renewable and must provide for the entire reproductive needs of the female throughout adult life. Only oocytes which are enclosed by epithelial and stromal cells are able to survive. Therefore, the interaction between oocytes and stromal including immune cells is of utmost importance. A small number of studies assessed the radiation-induced damage of primordial oocytes in animal models. These studies applied high (≥2 Gy) rather than low (0.01-1.0 Gy) radiation doses and did not assess changes in immune cells.

The objective of this study was to assess possible damage to follicles and changes in immune cells after low dose radiation (0.5-1.5Gy). Therefore 144 female C57BL/6J mice were radiated and sacrificed 6 hours, 36 hours, 2 or 5 weeks after radiation. Ovaries were removed and immunohistochemistry staining for follicle count and apoptosis, proliferation, DNA breakage markers as well as FACS analysis for immune cell count was performed.

Results:

After 6h we found no change in follicle numbers, apoptosis or proliferation markers independent from radiation dose. After 36h statistically significant depletion in follicle count concerning all follicle states were detected when radiated with 1.0 Gy and higher. 0.5 Gy did not cause total depletion of follicles. Depletion of follicle count was still verifiable after 2 and 5 weeks after radiation which represents a long-term effect in mice. Markers for DNA breakage were most intense 36h after radiation.

In total, 2% immune cells were detectable within the mouse ovaries and mainly consisted of Natural Killer (NK) and T cells. The immune cell population of the ovaries showed the following composition: NK cells including NK and NKT cells (34%; NKT (10%), T-cells (21%), macrophages (14%), B-cells (11%), dendritic cells (8%). Macrophages were highest 36h after radiation in all dose groups compared to controls and declined after 2 weeks post radiation. NK cells were lowest in controls and highest 36h after radiation in all three dose groups.

Conclusion:

This is the first study to analyze ovarian immune cells following radiation: Already shortly after radiation, NK cells, T-cells and macrophages are increasing dose dependent, whereas B-cells and dendritic cells decreased reflecting a strong immune reaction. In the same manner, follicles depleted after 36h post radiation and were dependent on radiation dose.

Outlook:

As already low dose radiation leads to activation and change of immune cells in the ovary as well as a depletion of the ovarian reserve, fertility preservation counseling is of utmost

importance. Further research will focus on not only follicle numbers dependent on radiation dose but also new markers on follicle and oocyte quality.

Publications issued from this project:

Reiser E, Bazzano MV, Solano ME, Haybaeck J, Schatz C, Mangesius J, Ganswindt U, Toth B. Unlaid Eggs: Ovarian Damage after Low-Dose Radiation. Cells. 2022 Apr 4;11(7):1219. doi: 10.3390/cells11071219

External funding applications:

“Establishment of an in vitro culture system for ovarian tissue to analyze the effect of low doseradiation”:
WF-F.50513/5-2024 - Tiroler Nachwuchsforscher*innenförderung
WF-F.47954/6-2023- Tiroler Nachwuchsforscher*innenförderung

„The role of stromal and immune cells in ovarian damage after low dose radiation:
WF-F.45028/8-2022 Tiroler Wissenschaftsförderun

Miscellaneous:

Effects of low-dose radiation on ovarian immune cells in a mouse model: Posterpresentation at DGGG 2024

Diploma thesis: Jana Clement

Identification of sleep electrophysiological biomarkers of prodromal alpha-synucleinopathies with artificial intelligence

Priv.-Doz. Matteo Cesari MSc PhD
Department of Neurology, Medical University of Innsbruck

Project duration: 01.12.2021 - 31.03.2024

Project summary:

Background and objectives:

Rapid eye movement (REM) sleep behavior disorder (RBD) is a sleep disorder characterized by abnormal muscular tone in REM sleep (REM sleep without atonia – RWA) and dream enactment. Diagnosis of RBD is made in sleep laboratories and based on video-polysomnography (v-PSG), a comprehensive examination where several electrophysiological signals are recorded. Isolated RBD (iRBD) refers to the condition when RBD is not associated to any overt neurodegenerative disease or sign. Several independent longitudinal studies have shown that up to 90% of patients with iRBD progress to an overt alpha-synuclein neurodegenerative disease (i.e., Parkinson's disease (PD), dementia with Lewy bodies (DLB) or multiple system atrophy (MSA)) within years or decades. These findings made researchers realize that patients with iRBD are in the early stages of alpha-synucleinopathies and therefore they constitute the most promising cohort to test disease-modifying and neuroprotective therapies. To design such clinical studies, there is the high need of having biomarkers that could serve either for 1) selecting subpopulations of iRBD patients that have high risk of converting to an overt alpha-synucleinopathy, or 2) tracking reliably the evolution of the alpha-synuclein pathology. Despite several biomarkers have been investigated and proposed in several studies, none is still accepted by the scientific community as the best one to be used in the context of clinical trials.

As v-PSG is required to diagnose RBD, biomarkers of progression and/or conversion derived from v-PSG might be unexpensive and easy-to-obtain. Despite v-PSG data are available for each patient with iRBD, only a limited number of studies have investigated such biomarkers, with increased amounts of RWA and sleep instability being the most investigated ones. Furthermore, these studies employed univariate statistical approaches, thus lacking proper validation and combination of several biomarkers. In recent years, artificial intelligence (AI) algorithms have emerged as a powerful tool to analyze sleep. Classical machine learning (ML) algorithms employ features derived from input data to perform a specified task. Deep learning (DL) algorithms usually an end-to-end approach, without the need for extracting features from input data.The main aim of this project was to employ novel AI algorithms for the identification of sleep biomarkers of disease progression and/or conversion in patients with iRBD.

Methods and results:

Database definition: The first step of the project consisted of the creation of a retrospective database of patients with iRBD and age- and sex-matched controls by considering the patients admitted at the Sleep Disorder Unit, Department of Neurology, Medical University of Innsbruck. Two databases were created: the "conversion database" (to evaluate the conversion to overt alpha-synucleinopathies) and the "progression database" (to evaluate biomarkers of disease progression). The first database included a total of 66 patients with iRBD, for which a baseline v-PSG was available, and of which 18 converted to an overt alpha-synucleinopathy after 2.7±1.0 years (13 to PD, 4 to DLB and 1 to MSA). The second one consisted of 23 patients with iRBD and 23 sex- and age-matched controls, who underwent two v-PSGs with distance of 4.0±2.5 years. None of the iRBD patients converted to an overt alpha-synucleinopathy at the second v-PSG.

Machine learning algorithm for prediction of conversion: The aim of this part of the project was to develop a ML algorithm that could predict conversion to an overt alpha-synucleinopathy in patients with iRBD from v-PSG data. The v-PSGs of the 66 iRBD patients of the “conversion database” were considered. Sleep stages were scored with a previously validated AI algorithm and several features were then extracted from electroencephalography (EEG) and electromyography (EMG) in both REM and non-REM (NREM) sleep. These features included both time-domain features (i.e., describing signal properties in the time domain), as well as frequency-domain features (i.e., features derived from spectral analyses of the signals). Random survival forest algorithms were employed to predict the time to phenoconversion, by testing several combinations of features. The best test performances were obtained when considering EEG features in REM sleep only (Harrel’s C-index: 0.723±0.113, Uno’s C-index: 0.741±0.11, integrated Brier score: 0.174±0.06). Features describing EEG slowing had high importance for the ML model.

Biomarkers of disease progression: To evaluate biomarkers of disease progression, the “progression database” was considered. For each baseline and follow-up v-PSG, previously validated AI algorithms were employed to score sleep stages and identify sleep spindles in N2 sleep (i.e., sporadic cortical oscillatory events with a frequency of 11 16 Hz and duration of 0.5-2 seconds, which have been found to be altered in patients with iRBD in previous studies). Furthermore, an automatic algorithm was employed to calculate relative powers in different frequency bands in the EEG in both REM and NREM sleep. The results showed that, while patients with iRBD showed slowing of EEG at the baseline v-PSG, no further progression of this phenomenon was observed at follow-up. On the other hand, relative EEG power in the gamma band (30-40 Hz) significantly increased over time in patients with iRBD compared to controls, and sleep spindles showed a significant reduction of frequency and relative power compared to controls over time.

Preliminary analyses for employing deep learning for prediction of conversion: The objective of this part of the project was to evaluate whether DL algorithms could be useful for the prediction of conversion in patients with iRBD. In particular, it was hypothesized, based on previous research, that sleep structure alterations could be a potential useful biomarker in this context. As a preliminary analysis, it was evaluated whether DL algorithms could differentiate iRBD patients from controls based on sleep structure. A database specific for this purpose was created and it included 86 patients with iRBD and 81 controls, who all underwent one v-PSG. A validated AI algorithm was employed to obtain a total of 16 hypnodensities from each v-PSG. A hypnodensity is a probabilistic representation of sleep structure, where each 30-s sleep epoch is represented a mixture of probabilities of different stages. The hypnodensities were obtained by considering different combinations of EEG and EMG channels. A Res-Net-18 DL model was trained to discriminate patients with iRBD from controls. The validation results showed that the algorithm could differentiate the groups with F1-score of 0.717±0.04.

Conclusions:

This project aimed to investigate v-PSG biomarkers of conversion to neurodegeneration and progression of the disease in patients with iRBD, by employing novel AI algorithms. The main findings are the following: i) EEG slowing in REM sleep may be an important biomarker of phenoconversion; ii) power and frequency in sleep spindles, as well as power in the high frequency in the EEG could be a biomarker of progression of the neurodegeneration and iii) sleep structure described with a hypnodensity representation can be helpful to discriminate patients with iRBD from controls, thus opening the floor to future investigations to evaluate whether it could also be useful as a biomarker of progression and/or conversion. The findings are innovative and show that signals recorded during v-PSG, when analyzed with AI algorithms, hold promise to track the ongoing neurodegeneration.

Outlook:

Future studies should validate the findings in larger and multi-centric cohorts, as well as evaluate whether a combination of these biomarkers with other easy-to-obtain biomarkers (e.g. clinical biomarkers) might be useful to better understand the progression of neurodegeneration in patients with iRBD. AI algorithms will play an important role in this context, as they will allow to combine such biomarkers efficiently. Future studies should also evaluate whether the biomarkers investigated in this project could be obtained with novel wearable technologies.

Publications:

Accepted:

- Feuerstein S., Stefani A., Angerbauer R., Egger K., Ibrahim A., Holzknecht E., Högl B., Rodriguez-Sanchez A., Cesari M. Sleep structure discriminates patients with isolated REM sleep behavior disorder: a deep learning approach. Proceedings of the IEEE EMBC Annual Conference 2024

Submitted/In preparation:

- Cesari M., Portscher A., Stefani A., Angerbauer R., Ibrahim A., Brandauer E., Feuerstein S., Egger K., Högl B., Rodriguez-Sanchez, A., Machine learning models predict phenocoversion in isolated REM sleep behavior disorder from polysomnography
- Angerbauer R., Stefani A., Zitser J., Ibrahim A., Egger K., Brandauer E., Högl B., Cesari M. Temporal progression of sleep electroencephanography features in isolated REM sleep behaviour disorder.

External funding applications:

- FWF ESPRIT grant with title “Mortality prediction with novel automatic sleep measures” (rejected)

Miscellaneous:

The findings of the project have been/will be presented at the following conferences:

- World Sleep Congress 2023 (Rio de Janeiro, Brazil):
  - Talk with title “A machine learning algorithm to predict short-term phenoconversion from polysomnography in isolated REM sleep behavior disorder” – presented by Matteo Cesari
- International RBD Study Group Meeting 2024 (Oxford, UK):
  - Talk with title “Discrimination of patients with REM sleep behavior disorder with deep learning” – presented by Matteo Cesari
  - Talk with title “Progression of sleep electroencephalography markers in isolated REM sleep behaviour disorder” – presented by Matteo Cesari
- Engineering in Medicine and Biology Conference 2024 (Orlando, US)
  - Talk with title “Sleep structure discriminates patients with isolated REM sleep behavior disorder: a deep learning approach” – presented by Simon Feuerstein
- Congress of the European Sleep Research society 2024 (Seville, Spain)
  - Poster with title “Progression of sleep electroencephalography markers in isolated REM sleep behaviour disorder”
  - Poster with title “Discrimination of patients with REM sleep behavior disorder with deep learning”

The PI of the project co-supervised with Assoz-Prof. Antonio Rodriguez Sanchez (Department of Computer Science, University of Innsbruck) the M.Sc. thesis projects of Andrea Portscher and Simon Feuerstein.