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D7.2 Report on the status of co-developed screening technologies

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1. Introduction

EU-OPENSCREEN (EU-OS),[1] is the European Research Infrastructure Consortium (ERIC) for Chemical Biology and early Drug Discovery, which was established in 2018 and offers access to state-of-the-art high-capacity screening and medicinal chemistry services throughout Europe for the development of small molecule tools and lead compounds. EU-OS services are currently provided by >30 partner sites in 10 member countries across Europe (CZ, DK, ES, FI, LV, NO, PL, PT, SE and DE as host country). It operates an open-access database, the European Chemical Biology Database (ECBD),[2] hosted in Prague at IMG, and a central compound management facility (CCMF) in Berlin, Germany which stores quality-controls and manages the jointly-used EU-OPENSCREEN compound collection.[3] The latter is comprised of about 100,000 commercially (European Chemical Biology Library (ECBL)), and a growing number of academically sourced compounds (European Academic Compound Library (EACL)), which are used in high-throughput screening assays at screening partner sites.

In 2019, EU-OPENSCREEN-DRIVE started as a European Union HORIZON 2020 project to ensure long-term sustainability of EU-OS operations by promoting measures for i) widening awareness of academia and industry for its services and data, ii) growing capacity and competence in its field across Europe, and iii) completing the management processes needed for a large, distributed infrastructure. As outlined in the EU-OPENSCREEN-DRIVE project proposal, ensuring the long-term sustainability of EU-OS necessitates more than just serving as a service-oriented infrastructure. Instead, active engagement with industry stakeholders becomes imperative. In this regard, the EC encourages ERICs to proactively identify the requirements of the industry and customize user policies and practices to meet these demands. This strategic approach involves the attraction of high-tech companies and specialized facilities, effectively establishing innovation hubs within each region. These local hubs serve the dual purpose of enhancing the skills of research infrastructure personnel and fostering the growth of user communities.[4] Thus, within the framework of EU-OPENSCREEN-DRIVE, a Work Package (WP7) was dedicated to primarily setting up a permanent communication channel with the pharmaceutical industry and biotech companies, followed by the identification and execution of several joint innovative assay- and drug development projects. Thus, as part of the EU-OPENSCREEN-DRIVE project, EU-OPENSCREEN has

[1] https://www.eu-openscreen.eu/

[2] https://ecbd.eu/

[3] https://www.eu-openscreen.eu/services/compound-collection.html

[4] see https://ec.europa.eu/research/infrastructures/pdf/swd-infrastructures_323-2017.pdf and https://ec.europa.eu/research/infrastructures/pdf/esfri/publications/esfri_scripta_vol2.pdf.

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positioned itself as a prominent innovation hub in the European pharmaceutical and biotech sector, particularly within the realm of early drug discovery.

2. Aims of WP7

The overarching goal of industry engagement in the framework of the EU-OPENSCREEN-DRIVE project was divided into the following objectives:

1. Foster communication and engagement with industry.
2. Establish continuous exchange with industry stakeholders.
3. Enhance EU-OS' innovation management.
4. Communicate best practices in knowledge transfer.
5. Promote joint projects with industry on specific scientific developments.

3. Innovation strategy & deliverable report

Our approach is rooted in open innovation, which drives the generation of business opportunities. To establish this innovation hub, we established an 'Industry Liaison Office' (ILO) composed of multiple EU-OS partner sites and industry representatives (Figure 1). The primary goal of the ILO is to create a seamless and permanent communication channel with industry partners, thereby facilitating the achievement of all five above-mentioned objectives. Through collaborations with industry stakeholders, we have aligned public and private interests, fostering an open innovation ecosystem in drug discovery. This approach created a new generation of knowledge and technology that supports efficient models of public-private partnerships (PPPs). Furthermore, the valuable insights provided by representatives from the industrial organizations within the ILO have been instrumental in shaping the new ERIC business plan for 2023-2027. This report focuses on objective 5, the accomplishment of joint projects with industry on specific scientific developments. Six co-development projects with five different companies (Aquarray, GSK, Promega, REVVITY, and InnoME) were defined and agreed upon with the ILO members during

Figure 1: EU-OPENSCREEN industry boards (picture taken from the "Building Innovation in Drug Discovery" brochure available at https://www.eu-openscreen.eu/fileadmin/user_upload/newsroom_and_downloads/EU-OPENSCREEN__Industry_Collaboration__26_10_2022_web.pdf.)

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the lifetime of EU-OPENSCREEN-DRIVE and subsequently implemented.

3.1 Company profiles of co-development partners

3.1.1 AQUARRAY

Aquarray is a privately held German biotech company developing a proprietary technology platform, the Droplet Microarray (DMA), which enables highly miniaturized assays, screenings and analysis. Founded as a spin-off from the Karlsruhe Institute of Technology, Aquarray's technology is based on a unique surface structure that enables a dense grid of nano-volume reaction vessels. Together, they aim to take miniaturization to a new level and provide a solution that enables the development of novel, more effective workflows and screenings in areas where the availability of reagents, materials or cells is limited, paving the way for new applications.

3.1.2 GSK

GSK plc is a healthcare company that focuses on developing, manufacturing, and commercializing general medicines, specialty medicines and vaccines. It offers drugs for the treatment of diseases such as HIV, respiratory, cancer, immuno-inflammation, anti-viral, central nervous system (CNS), metabolic, cardiovascular, urogenital, anti-bacterials, dermatology and rare diseases. The company also offers over-the-counter (OTC) products for pain relief, oral health, nutrition, skin health and gastrointestinal diseases. GSK's vaccine portfolio covers various diseases including hepatitis, diphtheria, tetanus, whooping cough, rotavirus and HPV infections, measles, and bacterial meningitis. The company sells its products through wholesalers, pharmacies, hospitals, physicians and other groups worldwide.

3.1.3 PROMEGA

Promega Corporation is a leader in providing innovative solutions and technical support to the life sciences industry. The company's portfolio of over 4,000 products supports a range of life science work across areas such as cell biology, DNA, RNA and protein analysis; drug development; human identification and molecular diagnostics. For over 40 years these tools and technologies have grown in their application and are used today by scientists and technicians in labs for academic and government research, forensics, pharmaceuticals, clinical diagnostics and agricultural and environmental testing.

3.1.4 REVVITY (former PerkinElmer)

Revvity, Inc. provides health science solutions, technologies, expertise, and services that deliver complete workflows from discovery to development, and diagnosis to cure. It focuses on translational multi-omics technologies, biomarker identification, imaging, prediction, screening, detection and diagnosis, and informatics. With a global network and localized agility, the company serves a diverse range of organizations from pharmaceutical and biotech to clinical labs, academia, and governments.

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3.1.5 innoME

Established in 2015, innoME is a realisation partner for measuring technology and sensors in the medical industry. It develops smart products by integrating innovative and cost-effective sensors. These are applied in healthcare and biotechnology facilities for analytics, diagnostics and hygienic monitoring purposes. The company manages production processes for clients as well as in-house research and development. innoME is headquartered in Espelkamp, Germany, and has an additional location in Munich.

3.2 Results of co-development projects

3.2.1 AQUARRAY/REVVITY with IBCH-PAS: HTS optimization of microarray cell-painting

The aim of the project was to adapt and optimize the imaging possibilities of Aquarray – DMA-one slides containing 672 drops (14 columns and 48 rows, code: square 102)[5] using cell-painting techniques. Printed slides with microdroplets increase the miniaturization of research and the transition to a larger scale of imaging, reducing the costs of reagents, increasing the possibilities of high-throughput research in relation to cell research, their imaging and the use of cell painting techniques. As a partner site of EU-OPENSCREEN ERIC, IBCH-PAS has access to chemical libraries to test drugs at the scale of 384-well plates. Adaptation of the cell painting technique and process to the slide format could have a positive impact on the development of imaging techniques and opportunity to test chemical libraries directly in DMA-one slides.

In the beginning, the project faced technical challenges. It was observed that the distances between the drops on the slide were asymmetrical, which caused problems when printing these slides. Consequently, the initial cooperation with Aquarray started to deliver a print that was made more precise until we received appropriate slides for testing. In cooperation with Revvity, a new layout of the slide imaging plate was developed, and new reading parameters were set and fine-tuned. This optimization allowed the direct capture of photos of individual microdroplets on the slide using the Opera Phenix confocal microscope. HeLa cells were imaged and protocols were prepared for imaging various cell organelles based on the used cell painting technique. The following imaging dyes were used: PhenoVue Fluor 555-WGA (Ex:555/Em:570), Pheno Vue Fluor 488 – Concanavalin A (Ex:495/Em:520), PhenoVue Fluor 568 - Phalloidin (Ex:578/Em:603), PhenoVue Hoechst (Ex:357/Em:540), and PhenoVue 512 Nucleic Acid Stain (Ex:525/Em:590) (Figure 2).

[5] https://www.aquarray.com/dma-slide

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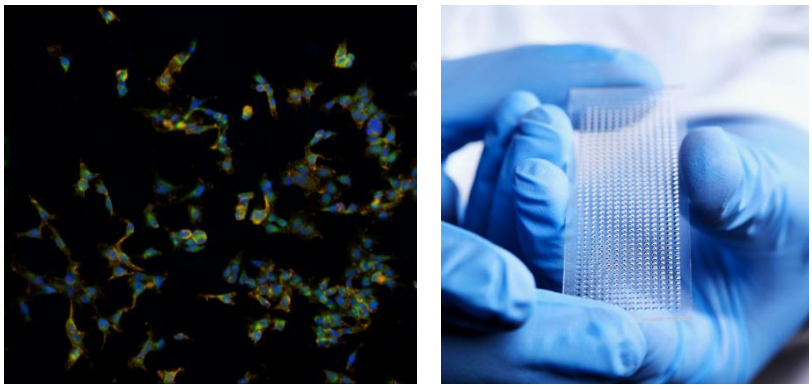

Figure 2: Left: HeLa Cell Line, Channels: Alexa 488, Alexa 568, Hoechst, 20x Air Objective, non-confocal. Right: depicting the microarray ´square 102´ containing 672 drops used in this study.

The HEK cell line was delivered to Aquarray for printing them in a microdroplet array on measurement slides, and the prepared DMA-one slides were screened with the ECBL Pilot Library (approx. 5,000 compounds) using the full cell painting technique with controls based on specific molecular actions, inducing specific mechanisms of action in the cells. The results will be validated with dose-response curves, and the generated data will be compared to literature to verify the compatibility of cell-painting and the microdroplet assay. After project finalisation, it is foreseen that the results will be published, and the publication linked to the Aquarray product. The validation of the miniaturised cell painting microdroplet assay will expand the possibilities of the DMA-one slides and enhance the visibility and applicability of this Aquarray product.

3.2.2 GSK with UiO: Phospho-flow cytometry to map signaling networks in disease conditions

EU-OPENSCREEN partner site, UiO has a broad expertise in phenotypic analysis of immune cells and cell lineages in human PBMCs (**P**eripheral **B**lood **M**ononuclear **C**ell) and mapping of signaling networks under various conditions e.g., different stimulations, compound treatment or similar, using flow cytometry with phosphorylation-specific antibodies, called phospho-flow. The aim of the co-development with GSK was to establish a tailored high throughput flow cytometry platform for immune cell phenotyping in combination with signaling network analysis to investigate the involvement of specific pathways in patient samples and whether these signaling pathways could be modulated by novel inhibitors from GSK's drug development pipeline. The study included patient samples from asthma and COPD (**C**hronic **O**bstructive **P**ulmonary **D**isease) patients collected at the Oslo University Hospital (OUS) sites *Rikshospitalet* (COPD) and *Ullevål Sykehus* (asthma), and healthy blood donor samples. For this purpose, a collaboration between UiO, two research groups at OUS, and GSK was established to facilitate the sample collection/processing, a patient information and consent form was created, and a study protocol was developed and approved by the Regional Ethics Committee (REK).

On the experimental side, a comprehensive flow cytometry antibody staining panel was developed using a combination of cell surface markers and transcription factors to distinguish T cell lineages including different populations of helper T cells, cytotoxic T cells

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and Regulatory T cells, respectively (Figure 3). To analyze signaling networks, cells were stimulated through TCR (T cell receptor) / CD28 for different time points, and downstream phosphorylation events were monitored with phospho-specific antibodies against proximal TCR signaling molecules and the MAP kinase and mTOR cascades including signaling molecules providing direct readouts for potential effects of GSK inhibitors. Furthermore, fluorescent cell barcoding was introduced to uniquely stain cells that underwent different treatments (stimulation / compounds) which enables combination of these samples into one prior to antibody staining and analysis which is crucial to compare results derived from the different conditions.

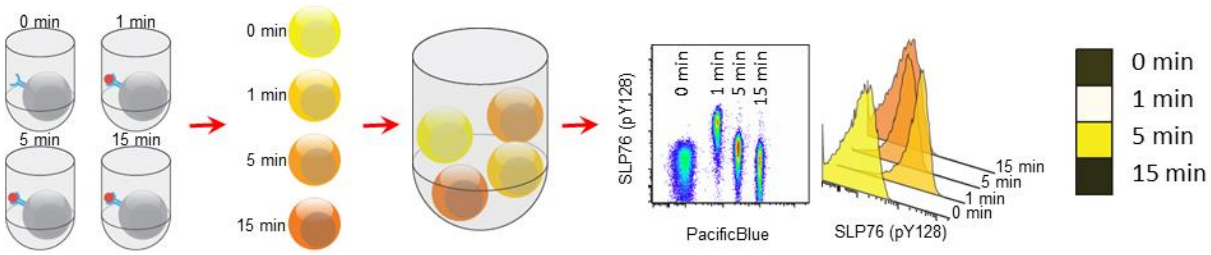

Figure 3: Workflow of a phospho-flow analysis: Stimulation, fluorescent cell barcoding (here one-dimensional with PacificBlue), combination of samples, deconvolution of signals based on PacificBlue barcoding and signal analysis. Additional barcoding dimensions (e.g., using PacificOrange) can be added to encode treatment with compounds.

After assay development, the collection of patient samples started and during this phase the development of the specific inhibitors was discontinued at GSK. Already collected samples were returned to the respective research groups at the Oslo University Hospitals for asthma and COPD.

3.2.3 Co-development projects in collaboration with Promega

In the case of Promega, multiple EU-OS partners sites were interested in the collaboration. Therefore, an open a call was offered in 2020 to the sites in which they could express their technology of interest and in-kind contribution to the co-development project. In total 9 proposals were received from 5 EU-OS partner sites (USC, MEDINA, CSIC, IBCH-PAS, and UH-FIMM). After an internal evaluation executed by Promega two projects were implemented with CSIC and MEDINA. The two collaborations are described in 3.2.3.1 and 3.2.3.2, respectively. After the implementation of the projects, Promega representatives said:

«We are very pleased with the EU-OPENSCREEN ERIC collaboration. The two co-development studies undertaken in Spain revealed a wealth of information about applications of our NanoBRET Intracellular Kinase Target Engagement system on new screening platforms. The insights we gained will help us to further validate and expand our assay capabilities.»

3.2.3.1 Promega with CSIC: Discovery of novel PIKfyve inhibitors as potential antiviral agents

PIKfyve is a kinase involved in endosomal maturation. It is responsible for the synthesis of phosphatidylinositol-3,5-biphosphate from phosphatidylinositol-3-phosphate, and is implicated in various trafficking events associated with the endocytic pathway, which are essential for endosomal maturation. Most of viruses require the endocytic pathway to infect

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the cell, therefore, PIKfyve inhibition could be an interesting target to avoid virus entry using this route in important viruses of clinical and economic relevance such as Ebola virus, SARS-CoV-2 or African Swine Fever virus.[6]

However, despite the potential of PIKfyve as a therapeutic target, the number of reported inhibitors as well as their chemical diversity is still lacking. Therefore, with the aim to search for new inhibitors, a structure-based virtual screening of our in-house chemical library, named MBC library[7] on the crystal structure of PIKfyve (PDB: 7K2V) was performed. To increase the chemical diversity, a two-step virtual screening, consisting of a shape screening based on the structure of known PIKfyve inhibitors, such as Apilimod or YM201636, followed by a structure-based virtual screening of the EU-OPENSCREEN chemical library, have been performed. (Figure 4).

Besides these virtual screenings, we initiated this co-development project with Promega, giving us access to their innovative NanoBRET™ Target Engagement (TE) assay with the aim to evaluate the intracellular kinase activity of the ECBL Pilot Library. The *in-house* implementation of the NanoBRET™ TE Assay developed specially for the PIKfyve kinase by Promega, combined with the results of both virtual screenings, culminated in the identification of a novel family of PIKfyve inhibitors with antiviral activity, illustrating the strength of the synergy of virtual and experimental screening campaigns. A publication is in preparation, and this new set of PIKfyve inhibitors can enter the drug development pipeline, hopefully leading to new treatments.

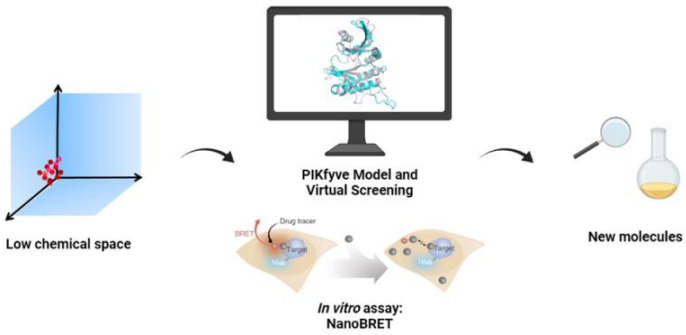

Figure 4: Schematic workflow of the identify new PIKfyve inhibitor through a combination of virtual screening and NanoBRET technology.

[6] García-Cáceres, J., Caballero, E., Gil, C., Martínez, A., Kinase Inhibitors as Underexplored Antiviral Agents, *J. Med. Chem*, **2022**, 65, 935-954

[7] Sebastián-Pérez, V., Roca, C., Awale, M., Reymond, J. L., Martínez, A., Gil, C., Campillo, N. E., Medicinal and Biological Chemistry (MBC) Library: An Efficient Source of New Hits, *J. Chem. Inf. Model*, **2017**, 57, 2143-2151

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3.2.3.2 *Promega with MEDINA: Targeting the NLRP3 inflammasome in inflammatory diseases*

The NLRP3 (NOD-like receptor family, pyrin domain-containing protein 3) inflammasome is a multiprotein complex that triggers the release of pro-inflammatory cytokines, and interleukin-1 beta. The aberrant modulation of the innate immune response by NLRP3 can lead to inflammatory and autoimmune diseases like asthma, joint inflammation, osteoarthritis, cardiovascular complications, autoimmune encephalomyelitis, Alzheimer´s, and melanoma.

Current NLRP3 agonists have limited micromolar potencies and show unwanted off-target effects that hamper their clinical application. Besides, the lack of efficient high throughput screening (HTS) assays hinders the identification of bioactive, potent, and specific NLRP3 agonists that could be developed into new drugs. To fill this gap, MEDINA, in collaboration with Promega, has developed the first HTS cellular setup based on the NLRP3 target engagement sensor recently reported by Promega (Figure 5). This screening platform has been utilized to screen a library of ~2500 chemically diverse bioactive small molecules from the ECBL. These compounds are active against 1,039 different targets, among them 654 approved drugs and 368 highly selective probes from the public domain. Each of these bioactive molecules were profiled in terms of inhibitory activity, clinical data, specificity as a chemical probe, and interference. Therefore, the library fulfils the requirements to quickly assess the robustness of the newly established HTS assay.

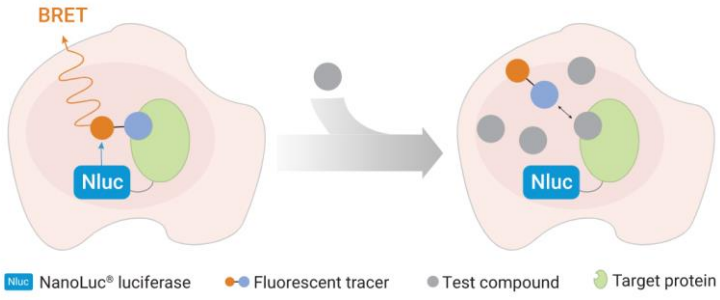

Figure 5: NanoBret technique using NanoLuc luciferase and a fluorescent tracer as developed by Promega.

First, a stable cell line was generated to constitutively express the NLRP3 NanoBRET™ target engagement sensor. Next, an HTS assay was developed using miniaturized 384-wells plates and automated/acoustic liquid handling devices. The HTS setup was successfully used to screen the bioactives with a Z´-factor > 0.7 and a confirmed hit rate of 1% (dose-response format). The top 10 best compounds were confirmed *via* target engagement interlaboratory studies performed between MEDINA and Promega. The corresponding nanomolar-to-low micromolar IC_{50} values of the compounds on NLRP3 strongly correlated with the functional inhibition of caspase-1 and IL-1β. Based on the literature and their mechanisms of action, among the compounds identified as NRLP3 inhibitors, there are deubiquitinators, indirect modulators (neutrophils, thioredoxin), and IL-1β inhibitors. Importantly, we also identified at least 6 novel NLRP3 inhibitors that could be developed into new drugs. The data demonstrates the robustness and efficiency of target-engagement technologies in drug discovery workflows.

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3.2.4 REVVITY with USC, Fraunhofer, KI: Development of an alpha CETSA assay for the validation of dCTPase inhibitors

The enzyme dCTPase pyrophosphatase 1 (dCTPase) regulates the intracellular nucleotide pool by degrading both canonical and noncanonical nucleotide triphosphates (dNTPs). dCTPase is highly expressed in various carcinomas and has links to cancer cell stemness. This insight opens up an exciting avenue for controlling nucleotide homeostasis in pathological conditions like cancer and inflammation.

Our recent work has revealed that inhibiting the enzyme MTH1, responsible for maintaining the dNTP pool, is an effective strategy for anticancer purposes. By inhibiting MTH1, we induce the increased incorporation of oxidized dNTPs in patient-derived xenografts, resulting in subsequent DNA damage and cell death. Subsequently, we have developed a novel class of potent and selective dCTPase inhibitors, which enhance the cytotoxic effects of cytidine drugs in leukemia cells. These inhibitors are derived from two distinct scaffolds and exhibit a range of inhibitory activities against dCTPase in biochemical assays, with IC_{50} values ranging from nM to uM.

To evaluate the intracellular inhibitory effect of 16 selected compounds on DCTPase we have established a medium-throughput workflow employing the alpha CETSA assay, which was developed by Pelago Bioscience and Revvity. The alpha CETSA assay is a Thermal Shift assay that uses a dual antibody proximity-based detection system conducted within the relevant cellular context. This assay maintains the protein in its native environment, with its natural partner proteins and physiological concentrations of cofactors and substrates. This approach ensures results that are relevant in a cellular setting thereby decreasing the risk of false positives, i.e. *in vitro* identified hits that are not active *in vivo*.

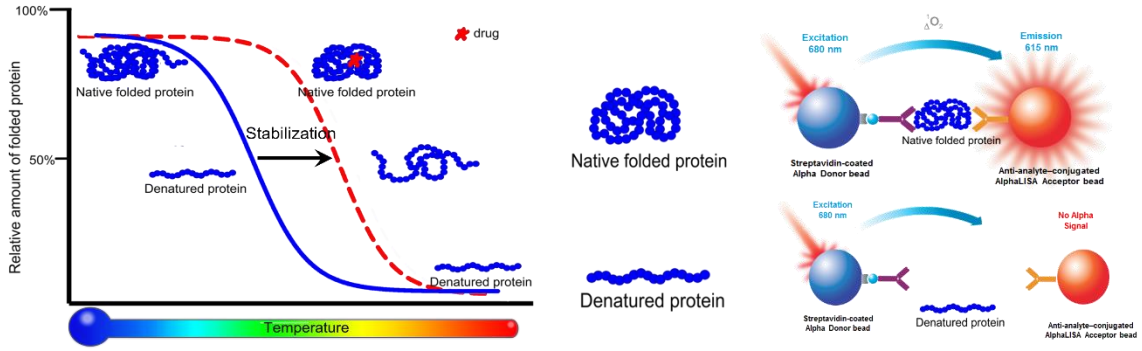

Figure 6: CETSA technique allows to study the interaction of ligands with their intended target biomolecules, where drug binding leads to an increase in melting temperature. The alpha CETSA assay uses endogenous protein levels in unmodified or primary cells in a no-wash, high-throughput format.

The assay´s development commenced by determining the optimal mouse/rabbit antibody combination and their respective concentrations, utilizing a HL-60 cell line. Subsequently, we measured a full denaturation curve in the presence and absence of a good dCTPase inhibitor, to identify the temperature at which the stabilization effect of compound binding was best

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measurable. With this foundation in place, we screened the 16 compounds synthesized by the Karolinska Institute (KI) in dose-response curves, ultimately obtaining IC_{50} values.

Notably, all compounds demonstrated a higher IC_{50} value with CETSA compared to the biochemical assays, a known effect attributed to the highly artificial environment of the latter. Furthermore, for some compounds, a greater shift in affinity was observed, transitioning from the low nM range to low uM values. This highlights the significant impact of intracellular conditions on compound uptake and ligand binding. In summary, the developed assay can serve as a valuable secondary screening tool, prioritizing compounds with optimal cellular uptake and target binding. Additionally, the adaptation of the alpha CETSA assay to overnight incubation enhances its flexibility, rendering it more suitable for high throughput screening. A publication about these findings is in preparation.

This project had a particular IP structure due to the licenced alpha-CETSA technique. While the kit was offered by Revvity as in-kind contribution, a licence fee had to be paid to Pelago BioSciences to perform the project. Furthermore, as the compounds were synthesized and provided by KI, they had an interest in the results to further develop the validated compounds. This shows that co-development projects with multiple different partners can be very successful, although requiring a longer than usual starting phase to define and agree on the project conditions.

3.2.5 innoME with CIPF: High-Throughput Mapping of Properties of Bioactives with the PermeaPad® Plate by the implementation of LC-MS/MS

This project was recently established between the biotech company innoME and CIPF as screening partner of EU-OPENSCREEN, and, due to its late inception, the project is still ongoing. The aim of the project is to implement LC-MS/MS as a suitable detection technique for the PermeaPad® Plate. The PermeaPad® technology was founded in 2015 by a professor at the University of Southern Denmark, who was looking to develop a transparent material that behaved similarly to gut tissue when exposed to researchers' formulations. This new technology was intended to reduce the use of laboratory animals for research while also meet rising demand for animal tissue in drug development. After the PermeaPad® Barrier was trademarked by the University of Southern Denmark, innoME prepared it for the market.

The parameter ´membrane permeability´ has become a key indicator to estimate and predict the *in vivo* performance of bioactive molecules such as environmental pollutants, and new drug-like chemical entities that are particularly interesting for the development of new medicines. In this project, we aimed to measure the apparent permeability coefficient (Papp) of 81 bioactive molecules utilizing PermeaPad® Plate in a high-throughput screening set-up. The initial detection method used for this purpose was UV-Vis spectroscopy, however, since more than 50% of the compounds could not be detected by UV-Vis, we developed a more sensitive LC-MS/MS method for the detection of these molecules.

A complete set of experiments was performed to find an optimal and high-throughput suitable LC-MS/MS method. Said method was optimized to be sensitive enough to detect the low concentrations of permeable compounds used in this screening, ranging from 0.001 µg/ml to

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0.01 µg/ml. Subsequently, the developed method was used for the analysis of both donor and acceptor vials to detect the total amount of compound permeating through the PermeaPad® membrane. In a next step, a comparison against widely used permeability assay will be made to gain more insight on the reliability and general performance of the assay. Mapping these data and correlating it with the respective physicochemical properties (c.q. molecular space) of the tested compounds will reveal the role of molecular space in drug absorption and could be used to develop mathematical models to predict bioavailability and membrane permeability for new drug-like chemical entities.

4. Conclusion

A total of 6 projects were executed, of which 4 were successful, and 1 is still ongoing with very promising results. These co-development projects gave our partner sites the opportunity to work with cutting-edge techniques, and we could provide the ILO members meaningful feedback on the practical execution of the assays they supplied. Furthermore, new bioactive compounds were identified, which could lead to new drugs potentially entering clinical trials in a few years, illustrating the lasting impact of these relatively small public-private partnerships. These promising results are also an encouragement to implement more projects with current partners and will motivate new private entities to join EU-OPENSCREEN ERIC. And, once published, the papers and the techniques will be interlinked to increase the visibility and relevance of EU-OPENSCREEN and the products provided by the private partners.

Challenges occurring during project implementation were used to improve the efficacy of the ILO. One project was halted because the industry partner GSK redirected its corporate focus, but the company remains a valuable partner in the ILO and is open to new co-developments. A major challenge was posed by the COVID-19 pandemic, moving all meetings online and grinding international transport to a sudden halt, resulting in a shortage of resources for several projects.

Overall, we obtained valuable feedback from these co-developments on practical and organizational issues which are used to improve the management of future co-development projects in the newly EU funded IMPULSE project, which will start in 2024. For instance, the project agreements of the successful collaborations will be used as a template for upcoming projects, to reduce the needed startup time. We also have split the co-development projects in two different structures, technological and scientific, to meet the industry needs for these diverse topics, and further information about these structures is available in a separate deliverable on the Innovation Management Plan (D7.3). The success of the co-developments in EU-OPENSCREEN-DRIVE is encouraging for future projects with pharmaceutical companies and biotech SMEs.

5. Abbreviations

CCMF: Central Compound Management Facility

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CETSA: Cellular Thermal Shift Assay

COVID-19: Coronavirus Disease of 2019

CIPF: Centro De Investigación Príncipe Felipe

CNS: Central Nervous System

COPD: Chronic Obstructive Pulmonary Disease

CSIC: Consejo Superior De Investigaciones Científicas

dCTPase: Eenzyme dCTPase pyrophosphatase 1

DNA: Deoxyribonucleic Acid

dNTPs: Deoxynucleoside Triphosphates

DMA: Droplet Microarray

EACL: European Academic Compound Library

EC: European Commission

ECBD: European Chemical Biology Database

ECBL: European Chemical Biology Library

ERIC: European Research Infrastructure Consortium

EU-OS: EU-OPENSCREEN ERIC: European Infrastructure of Open Screening Platforms for Chemical Biology European Research Infrastructure Consortium

EU-OS-DRIVE: EU-OPENSCREEN-DRIVE

Ex: Excitation

Em: Emission

HPV: Human Papillomaviruses

HTS: High-Throughput Screening

IBCH-PAS: Institute of Bioorganic Chemistry, Polish Academy of Sciences

ILO: Industry Liaison Office

IMG: Institute of Molecular Genetics of the Czech Academy of Sciences

IP: Intellectual Property

KI: Karolinska Institute

LC-MS/MS: Liquid Chromatography-Mass Spectrometry/Mass Spectrometry

MEDINA: Fundación MEDINA

NLRP3: NOD-like receptor family, pyrin domain-containing protein 3

OTC: Over-The-Counter products

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OUS: Oslo University Hospital

PBMCs: Peripheral Blood Mononuclear Cell

Papp: Apparent Permeability Coefficient

PPPs: Public-Private Partnerships

RNA: Ribonucleic Acid

SME: Small and Medium-sized Enterprises

USC: Universidad De Santiago De Compostela

UiO: University of Oslo

TCR: T-cell receptor

TE Assay: Target Engagement Assay

WP: Work Package

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