Working in partnership in Chemical Biology and early Drug Discovery across Europe

European Infrastructure of Open Screening Platforms for Chemical Biology

European RI for Chemical Biology and early Drug Discovery

EU-OPENSCREEN provides access to

- Technologies (e.g. screening platforms)
- Resources (e.g. compound collections)
- Expertise (e.g. in medicinal chemistry)
- Data (e.g. bioactivity data)

Users from academia and industry

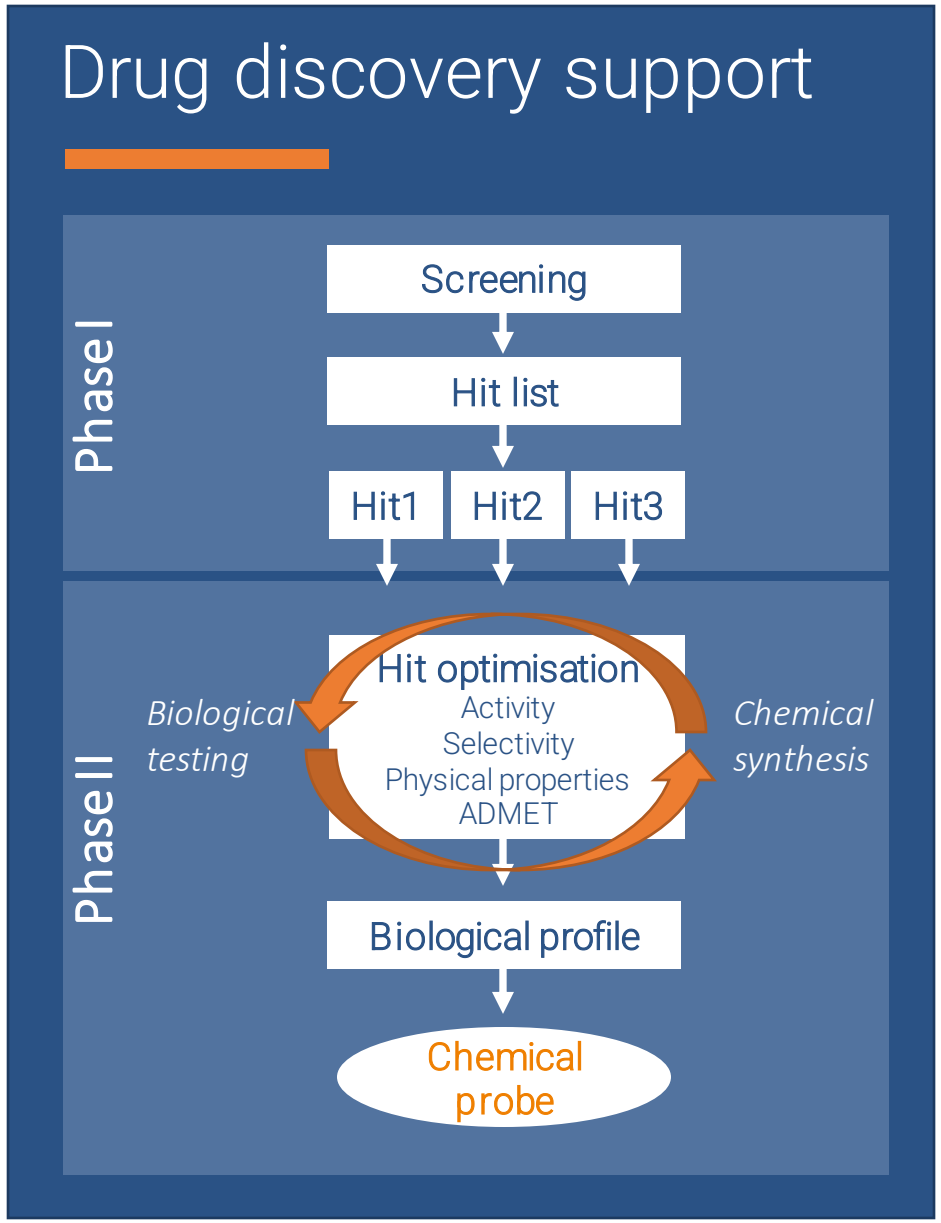
EU-OPENSCREEN Partner sites

- EU-OPENSCREEN is a distributed RI with 24 partner sites across Europe
- Host country: Germany
- 3 partner site categories:
  - Screening platforms (17)
  - Chemistry groups (6)
  - Database host (1)
- Partner site accreditation is a 3-step procedure:
  - Nomination of site by ministry
  - Evaluation by external reviewers
  - Approval of individual sites by all ERIC member countries, based on evaluation reports

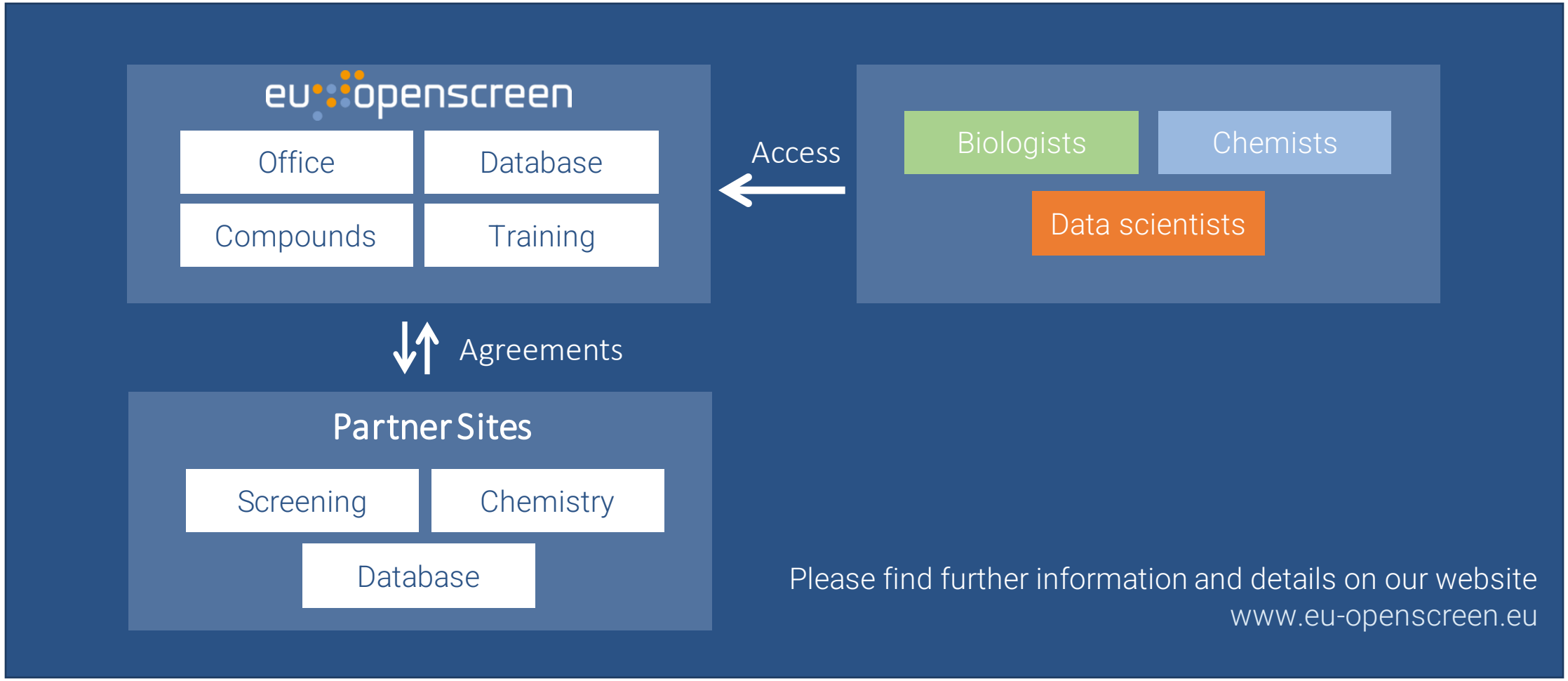
Mission

To support researchers in developing novel tool compounds for basic and applied research.

- Integrated network of state-of-the-art screening platforms and medicinal chemistry groups
- Co-develop novel screening technologies with industry partners
- Establish screening standards for academia
- Provide stakeholder forum for chemical probes
- Offer training opportunities



Operational model



Support for researchers

Biologists

provide biological assays suitable for screening
(i.e., robust signal read-out, suitable for miniaturization and automation)

» Identification of active 'tool'-compound for the target-of-interest

Chemists

make their compounds available to other researchers in a regulated, transparent framework

» Identification of novel bioactivities of compounds

Data scientists

access primary screening data which is available in open-access database without restrictions on use

» Modelling of structure-activity relationships

Support for biologists

High-throughput screening-amenable assay optimisation, miniaturisation and transfer onto one of our HTS platforms.

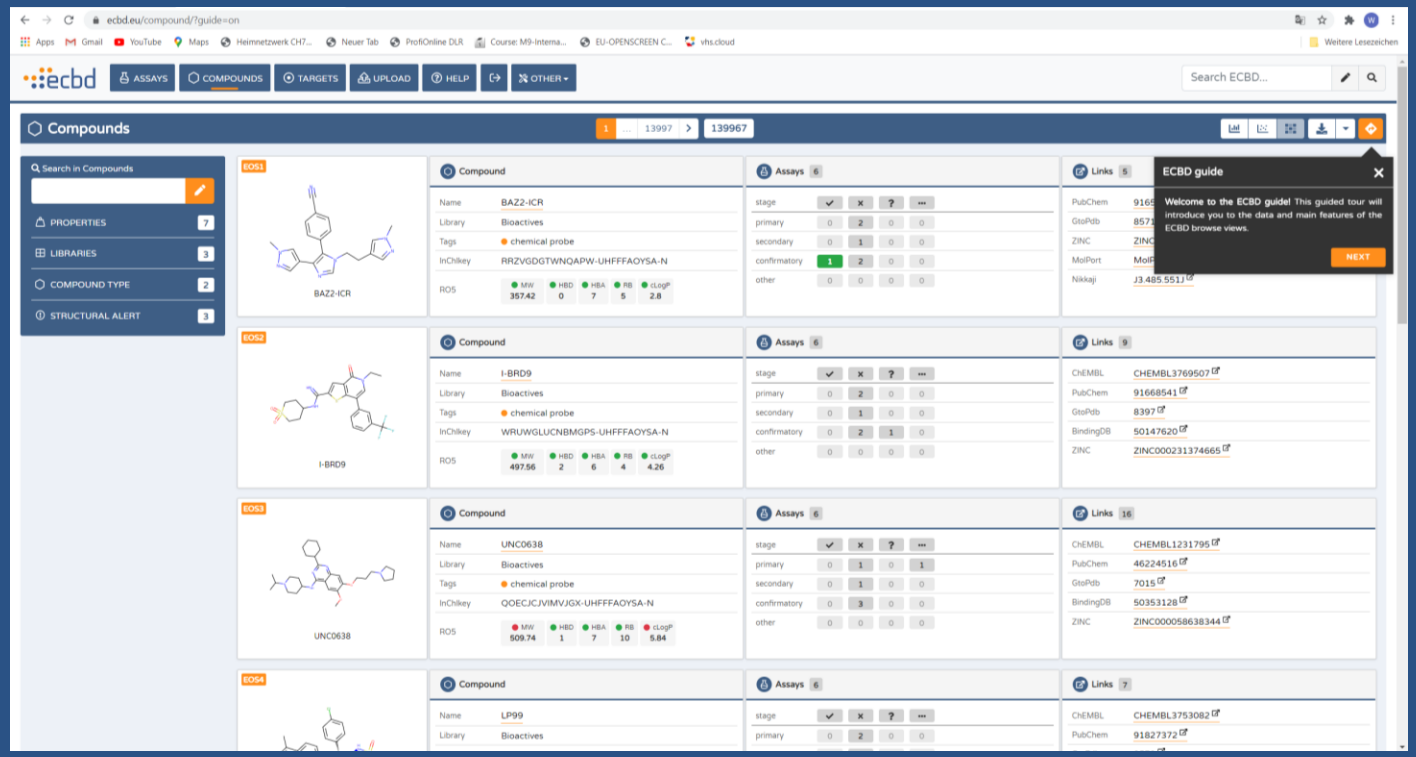
High-content screening (HCS) and High-throughput screening (HTS) of our small molecule libraries, using a variety of read-out technologies that are commonly applicable to the majority of assays.

Biological safety level (BSL) 1-3 laboratories

Various compound libraries available, incl. known bioactives/drug repurposing collections (e.g Drug Repurposing Hub), natural products collections, fragment library and small-molecule diversity libraries.

Chemical hit-to-lead optimisation

Support for data scientists



European Chemical Biology Database (ECBD)

Open-access database:

- Maximise re-use of FAIR data
- Data available without restrictions on use
- Optional embargo period up to 3 years
- Data links to other databases (e.g. ChEMBL)

EU-OPENSCREEN Libraries

European Chemical Biology Library (ECBL)

Diversity library

- 96.096 structurally highly diverse compounds
- Average MW = 350 g/mol
- 0.0005 % of PAINS

Horvath D. *et al.*, ChemMedChem **2014**, *9*, 2309


CHEMMEDCHEM FULL PAPERS

ChemPubSoc Europe

DOI: 10.1002/cmdc.201402126

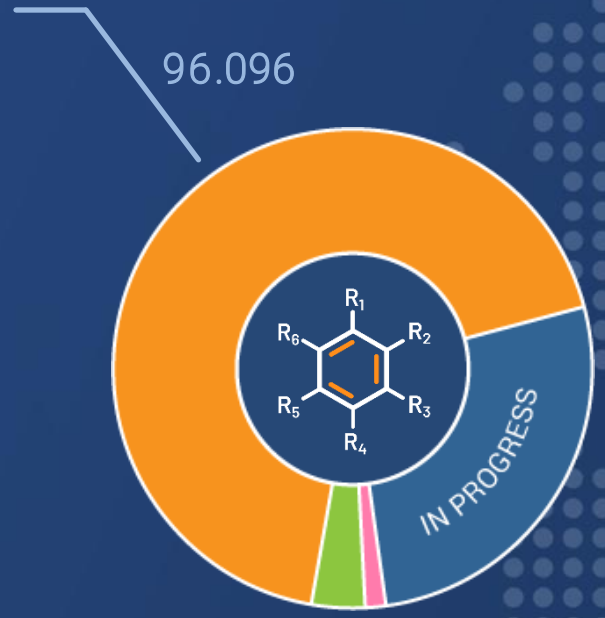
Design of a General-Purpose European Compound Screening Library for EU-OPENSCREEN

Dragos Horvath,*[a] Michael Lisurek,[b] Bernd Rupp,[b] Ronald Kühne,[b] Edgar Specker,[b] Jens von Kries,[b] Didier Rognan,[c] C. David Andersson,[d] Fredrik Almqvist,[d] Mikael Elofsson,[d] Per-Anders Enqvist,[d] Anna-Lena Gustavsson,[e] Nikita Remez,[f] Jordi Mestres,[f] Gilles Marcou,[a] Alexander Varnek,[a] Marcel Hibert,[g] Jordi Quintana,[h] and Ronald Frank[b]

European Chemical Biology Library (ECBL)

Pilot library

- 2.464 bioactives: active against 1039 different targets, contain 654 approved drugs and 368 highly selective probes
- 2.464 representative compounds of the diversity library
- 88 assay interference compounds in 4 dilutions



European Chemical Biology Database
https://ecbd.eu/

The European Academic Compound Library (EACL)

Novel compounds sourced from chemists worldwide

- Target is 40.000 compounds
- Regulated and confidential access (e.g. MTA)
- IP stays with the chemist
- Embargo period up to 3 years
- User friendly online submission: http://www.eu-openscreen-cmpds-donation.eu/login.php

Fragment Library (since 2020)

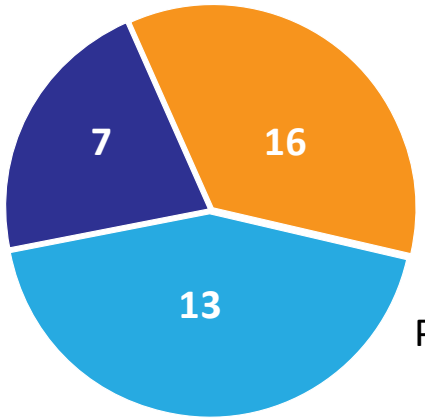
Set of low MW and ultra-low MW fragments

- 968 fragments with HAC > 8 in DMSO-d_6
- 88 so called "minifrags" with HAC < 8 in DMSO-d_6 (O'Reilly M. *et al.*, Drug Discov. Today **2019**, *24*, 1081)
- Derived from the fragment space of the ECBL
- Collaboration with INSTRUCT/ iNEXT-Discovery sites

Current portfolio of screening projects

SERVICES:

Pre-applications (incl. grant support)

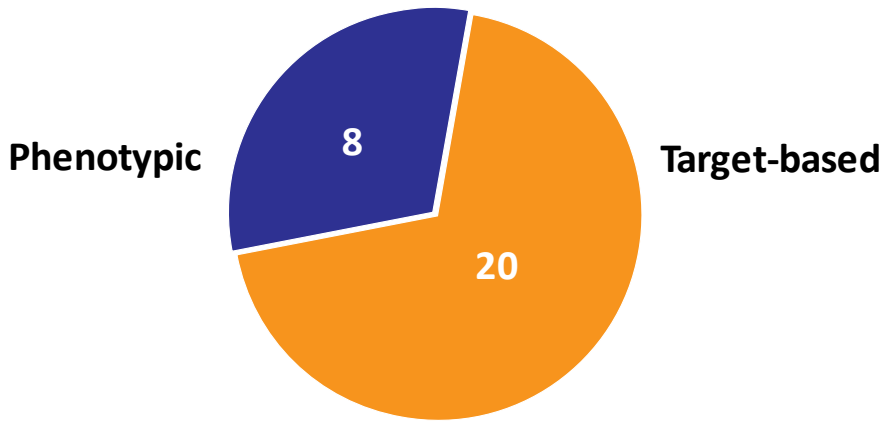


ECBL (100k) screening (including 13 EU-OPENSCREEN-DRIVE projects):

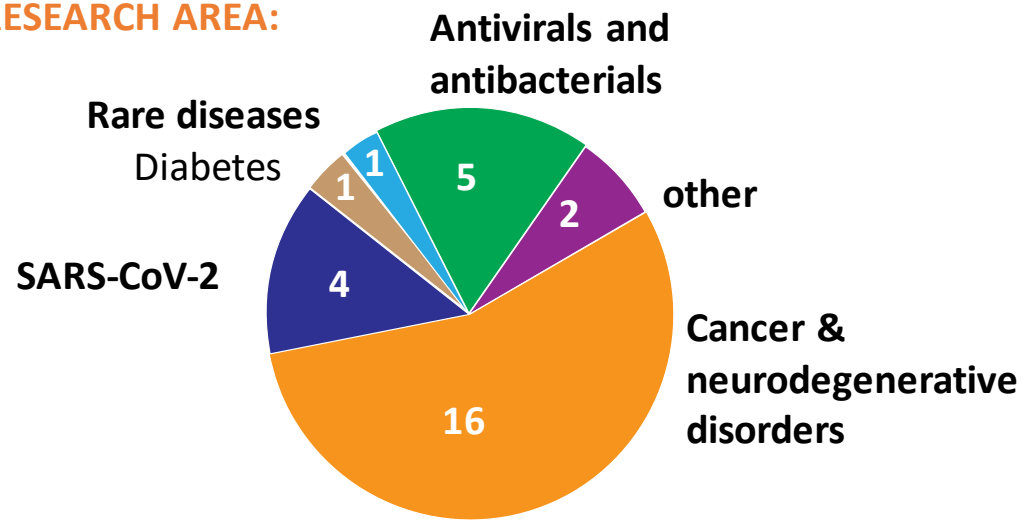
- 2 progressed in H2L

Pilot (5k) screening

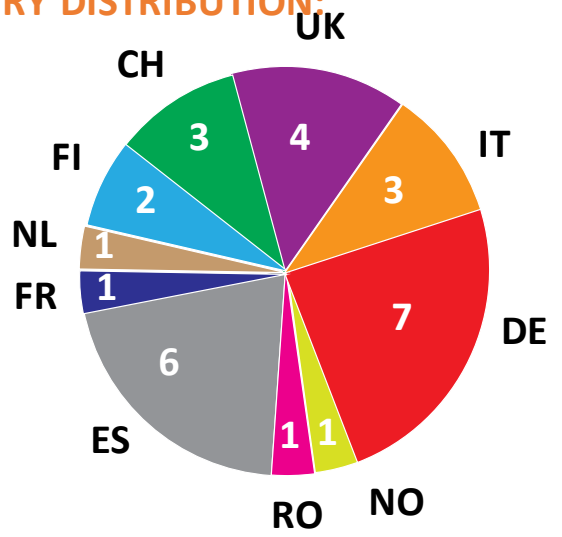
SCREENING:



RESEARCH AREA:



USER COUNTRY DISTRIBUTION:



Personalized Medicine

PREVENTION

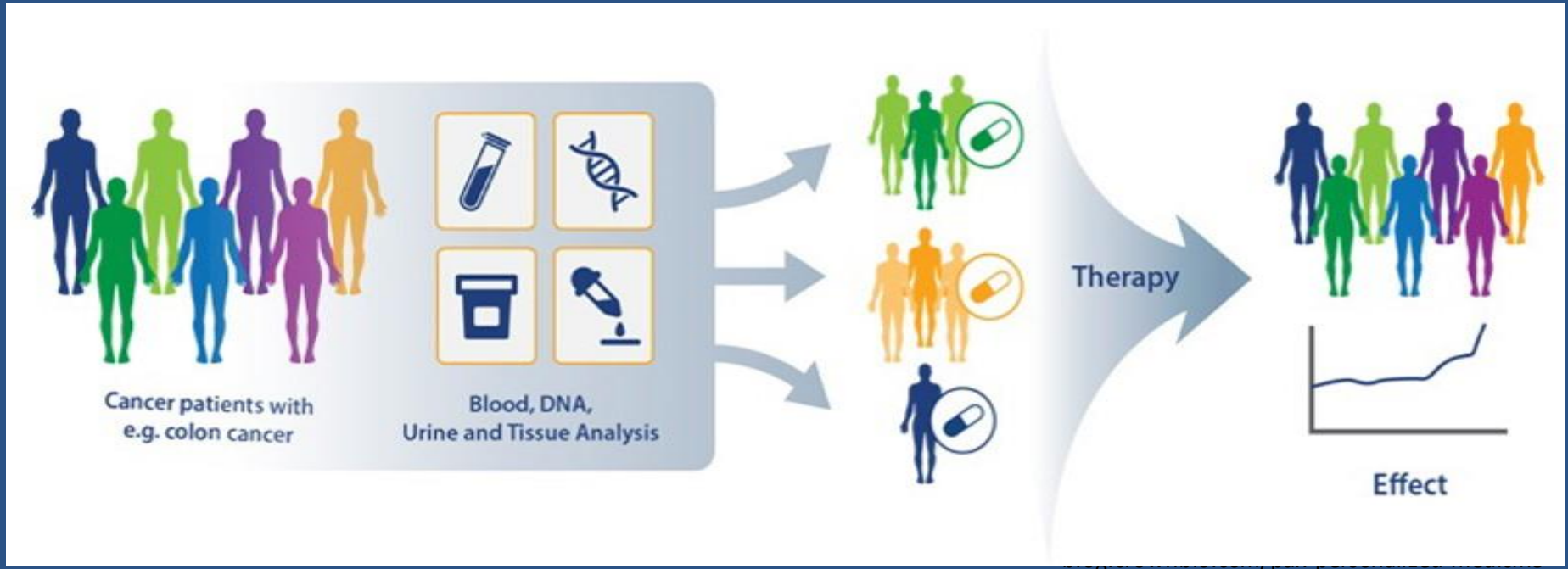
Early detection of patients at risk, improve preventive measures

DIAGNOSIS

Accurate disease diagnosis enablig individualized treatment strategy

TREATMENT

Improved outcomes through targeted treatmens and reduced side effects

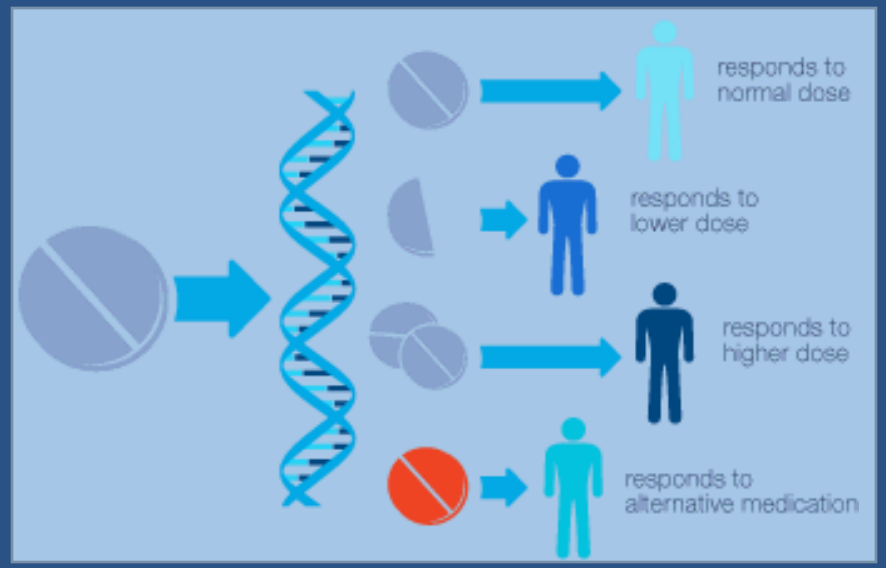


EU-OS strategies for personalized medicine in Drug Discovery

Target identification | Hit finding | Hit to Lead | Lead optimization | Preclinical development | Phase I | Phase II (PoC+lib) | Phase III | Submission to launch

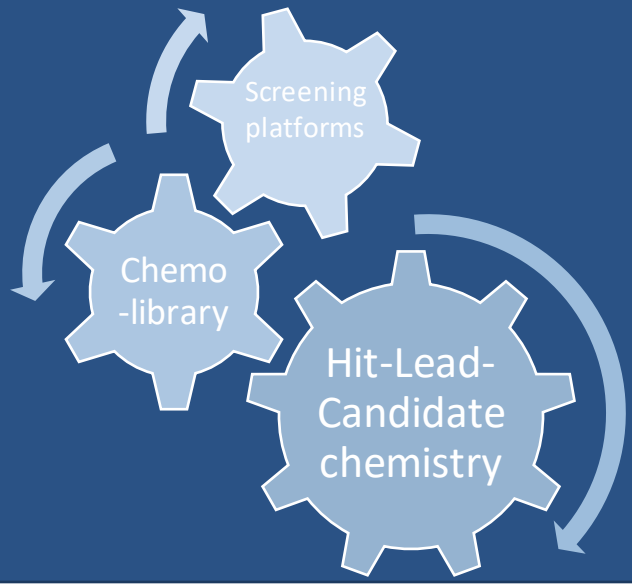
TARGET IDENTIFICATION AND VALIDATION

Chemical biology for **hits identification** for personalised Drug Discovery, improving the treatment of patients



PHARMACOLOGICAL TOOLS

Developing tools for different technologies combining chemical libraries, screening platforms and lead optimization



EU-OPENSCREEN Spanish Partner sites

Pharmacogenomics Platform for High Throughput Screening and ES-OPENSCREEN node

Advanced Therapies Area
Centro Investigación Príncipe Felipe

http://www.VicentResearchLab.com
https://www.cipf.es/

EU-OS Specialised Screening Site in Complex Cellular assays.

Hit to Lead by means of Nanomedicine design.

Collaborative research programs with academia and industry. Experience in **international research consortia** (H2020, ERC, ITN, …)

Other Relevant Networks: Red Traslacional para la aplicación clínica de Vesículas Extracelulares (TENTACLES) . EuroBioimaging. TransBionet/Elixir

Team: Dr María J Vicent (Coord.)
Dr Mar Orzáez
Esther Masià

- **Phenotypic assays in complex cellular systems** including primary cultures and **patient derived models** (2D and 3D, co-cultures, exosome-based assays). **Personalized medicine.**
- **Image storage and analysis capabilities** (CIPF-FISABIO Biomedical Imaging- Dr M de la Iglesia) and **Bioinformatic expertise** (Bioinformatics and Biostatistics Unit- Dr F García) to perform the clustering and annotation of the Chemical library**.** Use of a **radiomics analysis** and application of **artificial intelligence tools** to speed up data interpretation for HCS (Cell Painting in 2D and 3D models).
- Achievements: vast expertise in phenotypic assays from primary and patient-derived samples, Personalized Assay development. >200 papers in Oncology, Regenerative medicine (Stem cells), Neurodegeneration, Inflammation, rare diseases and nanomedicine. 4 licenced patents, 2 in exploitation.

Pharmacogenomics Platform for High Throughput Screening and ES-OPENSCREEN node

Translational Medicinal and Biological Chemistry

http://cib.csic.es/research/structural-and-chemical-biology/translational-medicinal-and-biological-chemistry

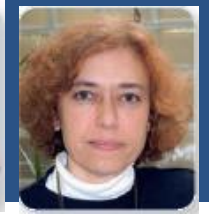
Med-Chem academic laboratory (Madrid, Spain) with wide experience in structure based drug design (SBDD) and chemical genetics mainly for small heterocyclic compounds.

Collaborative research programs based on national and international projects and agreements with academia and industrial companies.

Other Networks: Biomedical research network for neurodegenerative diseases (ISCiii-CIBERNED)

- Medicinal Chemistry and Chemoinformatics for drug discovery and hit to lead optimization beyond biological activity: looking for increase drug-like properties
- Disease-modifying agents for unmet severe pathologies such as neurodegenerative and infectious diseases. Synthetic chemistry design to scale up the final pathways.
- *Achievements:* vast expertise in early drug discovery, proprietary MBC chemical library of diverse small molecules, more than 250 publications (2016-2021), >10 licensed patents, 4 own molecules in clinical trials sponsored by different companies.

Team: Prof Ana Martinez
Dr Nuria Campillo Dr Carmen Gil



Pharmacogenomics Platform for High Throughput Screening and ES-OPENSCREEN node

FUNDACIÓN CENTRO DE EXCELENCIA EN INVESTIGACIÓN DE MEDICAMENTOS INNOVADORES EN ANDALUCÍA

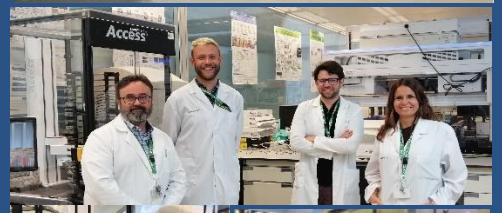
Fundación MEDINA
Natural Products Drug Discovery

http://www.medinadiscovery.com

Non-profit research organization (Granada), High throughput screening platform for drug discovery and reference center in natural products research

Collaborative research programs based on national and international grants (H2020, HE, IMI) and partnerships with academia, international research organisations and biopharma companies.

Other Screening Networks: Former ISCIII-RICET (Research in Tropical Diseases); Red Española de Metabolómica RED2018-102457-T



Coord.
Dr Olga Genilloud

Dr Fernando Reyes

- **Unique HTS Screening Platforms** to support **phenotypic and target-based assays development**, and hit discovery to early preclinical development; early safety/ ADME and toxicology studies
- **Largest natural products libraries** (200K samples) and **microbial collection** (190K strains) for drug discovery
- **Analytical platform for metabolomic biomarker discovery**
- **Internal discovery programs for new drugs and biomarkers** in infectious and tropical diseases, oncology and neurodegeneration.
- **Achievements**: early pipeline of 42 new families of novel natural products, more than 275 publications (2013-2022), 9 ongoing EU and international projects, more than 20 collaborations wiih large biopharma and biotech companies, **85 large scale and medium scale screening projects, 75 licenses and 5 international patents**

Pharmacogenomics Platform for High Throughput Screening and ES-OPENSCREEN node

Innopharma Pharmacogenomics Screening Platform

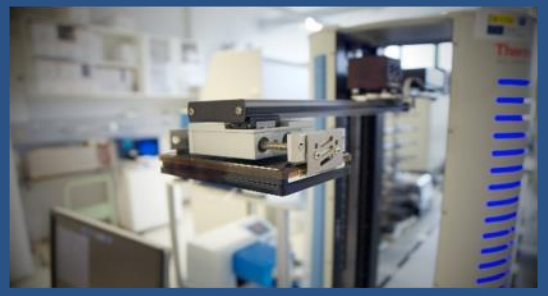
-HTS platform from CIMUS Research Center, for translational medicine and **IDIS** (ISCIII).

-Connecting disruptive academic research to drug discovery in worldwide programs, collaborations, services and academic training networks (>100 collaborations, 3 Marie Curie-ITN). Experience in **international research networks and consortia** (H2020, IMI, Fast-Track to Innovation…)

-Connecting early drug discovery to clinical proof-of-concept in consortia with **Kaertor Foundation** (>70 academic groups, 40 biotechs and pharma companies)

-Precision medicine oriented leadership connected to PTEMI and **leading the Spanish Genomic Medicine IMPACT project** (Ángel Carracedo) and **Complementary Actions of Biotechnology for health** (Mbel Loza)

BioFarma Innopharma



Head: Prof. Mabel Loza
Prof, Angel Carracedo

USC UNIVERSIDADE DE SANTIAGO DE COMPOSTELA

-Low-molecular weight chemical Spanish public library (60.000 compounds) and EU-OPENSCREEN library (140.000 compounds), linked to large libraries from global pharmaceutical companies through **strategic partnerships**.

-In vitro state of the art in pharmacogenomics: More than 300 phenotypic and target-based assays available based on translational models. Target ID, biomarkers, companion patient stratification.

-80 scientific publications and **28 funded projects** in the last three years.

-Pipeline with 35 projects from disruptive science from academy and spin-off companies to apply to drug discovery.

-Achievement Efficiency: A unique public pharmacogenomics platform very efficient in translation to clinical PoC (**16 new drugs to clinical trials in PPP** collaborations, last one an oral antiviral for etiological treatment of COVID-19).

EU INFRA-SERV project: canSERV

Cutting-edge services for the identification of multi-variate biomarker for personalized cancer treatment:

- MEDINA
  - Metabolomic profiling of cancer stem cell-derived exosomes
  - Untargeted LC-HRMS metabolomics for cancer biomarkers
- USC
  - Development of immunophenotyping assays from patient samples
- SINTEF
  - Sequencing of patient samples and bioinformatic pipelines for processing of (meta)genomic and transcriptomic data
  - Microfluidic systems for biomarker detection
  - Cytokine and protein quantification by antibody-based detection
- CIPF
  - Exoscreen from biofluids (using Alphascreen Technology)
  - NMR metabolomics in clinical tissue and biofluid samples

Submitted grant proposals on rare diseases

HLTH-2021-DISEASE-06-04: Development of new effective therapies for rare diseases (1st step out of 2)

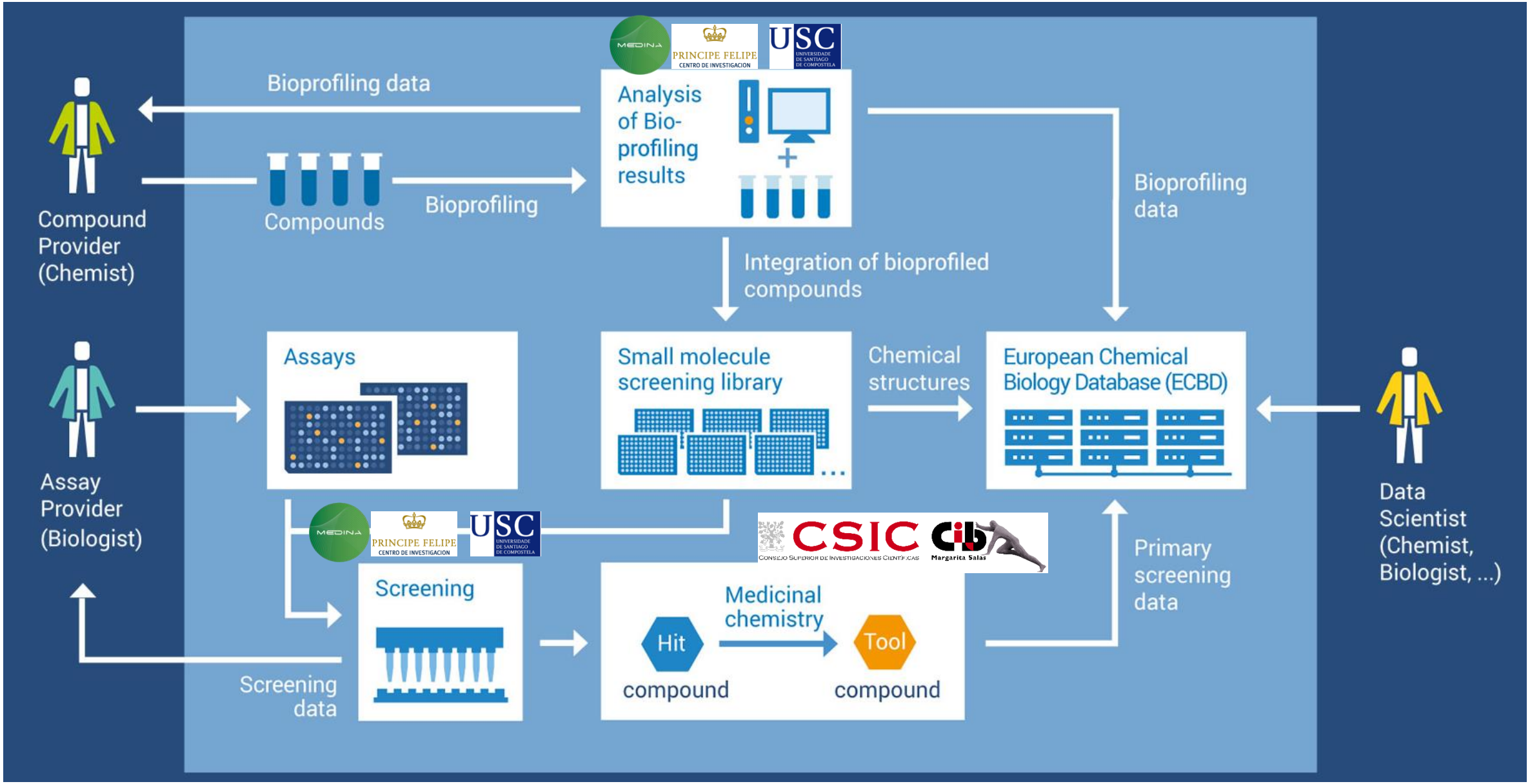
- RED-OPENCURE (repeat expansion DNA diseases), EU-OPENSCREEN as coordinator
  - 23 partners, from EU-OPENSCREEN: CSIC, DTU, LIOS, MU, SINTEF, ICHB PAN, IBB PAN, ITMP
  - Budget: 8m€
- MITOTREAT (mitochondrial DNA replication diseases)
  - 15 partners, from EU-OPENSCREEN partners: assay dev and screening sites
  - Budget: 8m€
- Experimental plans for both grants will include use of rare disease patient-derived cells for assay development, screening of the EU-OPENSCREEN 100.000 compound libraries, and for profiling lead compounds for potency, selectivity and safety

Grant proposal involves work with patient-derived cells

INFRA-2022-TECH-01-01: R&D for the next generation of scientific instrumentation, tools and methods (all 10m€ requested budget):

- **AMALFI-DD: MS cellular HTS assays,** EU-OPENSCREEN as coordinator
  - 8 partners, from EU-OPENSCREEN (1m€): SINTEF (0.6m€), IMTM (1.3m€)
  - Consortium of 4 infrastructures (EU-OPENSCREEN, ELF, EATRIS, ELIXIR) will develop 45 cellular high throughput screening assays based on label-free mass spectroscopy technology, establishing the required experimental hardware and IT/database infrastructure
  - Up to 17 assays will screen the entire EU-OPENSCREEN compound library of 100.000 compounds
  - Of these, at least 9 assays will be validated at IMTM **with patient-derived cells (tumor spheroids, primary human tissue) to improve translatability of in vitro models** to clinical efficacy and safety

How To Interact?



EU-OPENSCREEN will work in close collaboration with you to ensure effective communication and efficient project development with our partners with the final goal of strengthening drug discovery in Europe and beyond.

Contact:
scientific-projects@eu-openscreen.eu

Thank you!

eu:openscreen
https://eu-openscreen.eu

eu:openscreen drive
https://drive.eu-openscreen.eu

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