UKE HAMBURG

Institute of Tumor Biology

THE EUROPEAN LIQUID BIOPSY SOCIETY

ELBS General Assembly, Montpellier

PROLIPSY: Early detection of prostate cancer

Stefan Werner| October 28th 2022

Universitätsklinikum Hamburg-Eppendorf

ERA-NET: Aligning national/regional translational cancer research programmes and activities

TRANSCAN-2

Joint Transnational Call for Proposals 2016 (JTC 2016) on:
"Minimally and non-invasive methods for early detection and/or progression of cancer"

PROLIPSY

πρόληψη prólipsi prevention

Project Aims:

Early detection of prostate cancer by analyzing circulating blood-based biomarkers.

AIM 1: Assessing which Liquid biopsy marker will provide the best discrimination between the patients with histologically proven PCa and age-matched non-cancer controls.

AIM 2: Identifying high-risk PCa patients with aggressive tumors as defined by a Gleason score (“gold standard”)of 8 or higher, will be performed.

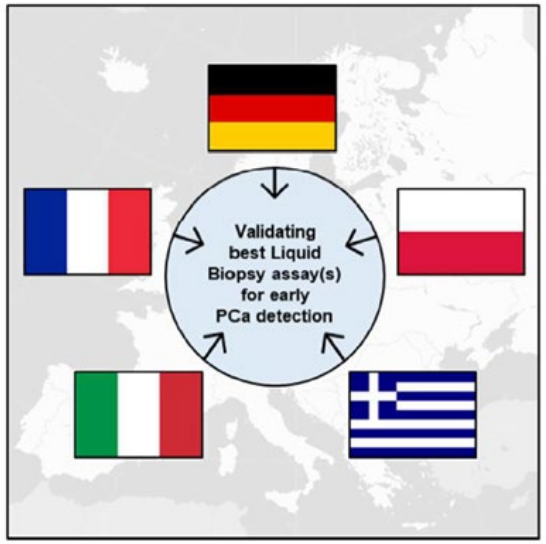
PROLIPSY Project Structure

Discovery Period (1st year)

PIs	Klaus Pantel	Desiree Bonci	Catherine Alix-Panabières	Evi Lianidou	Maciej Zabel
Assays	CTCapture	Exosomes RRPA miRNA	EPIDROP	cfDNA	Cyto-Track

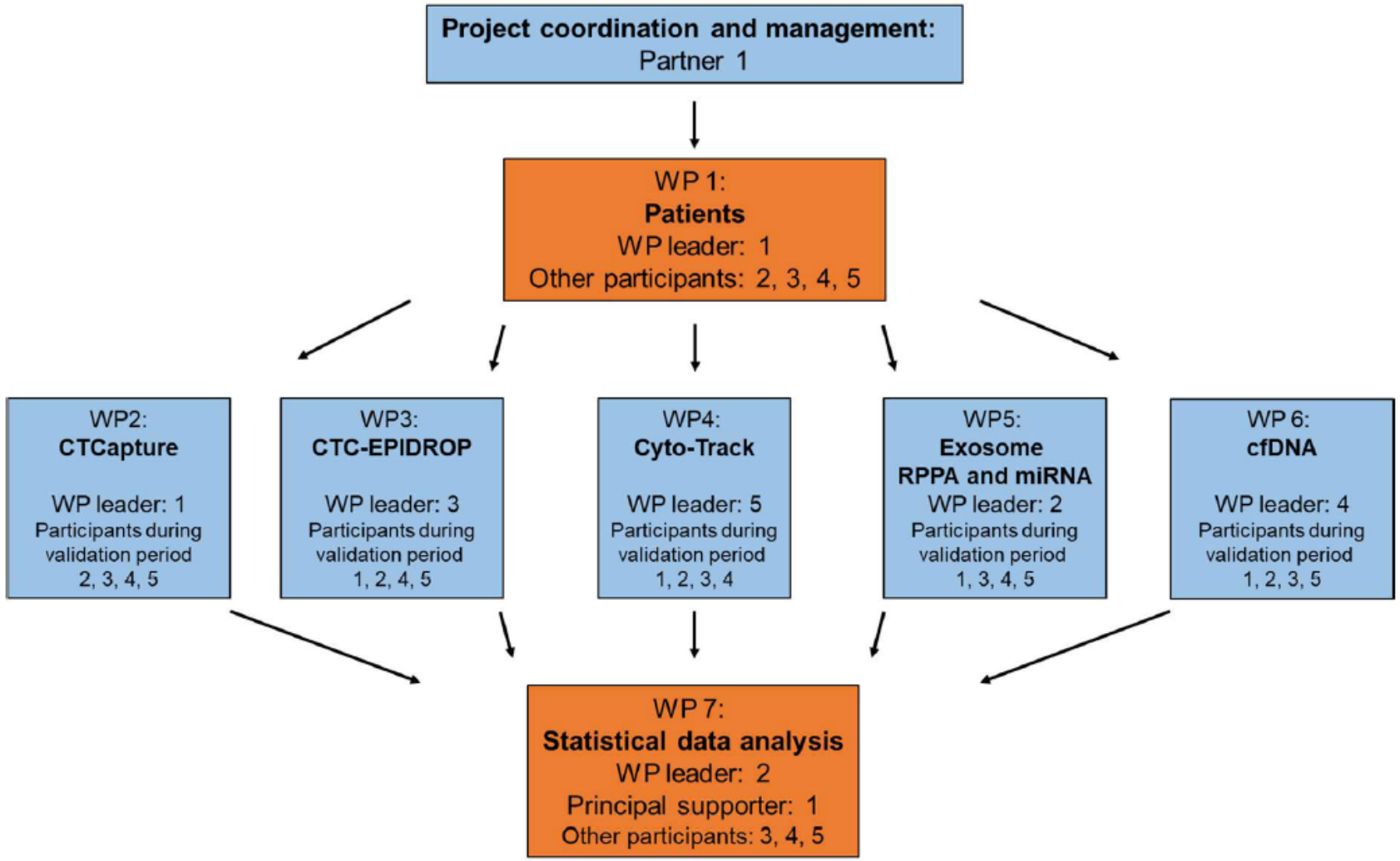
Selection of the best candidate assays for validation in entire patient cohort

Validation Period (2nd & 3rd yeas)

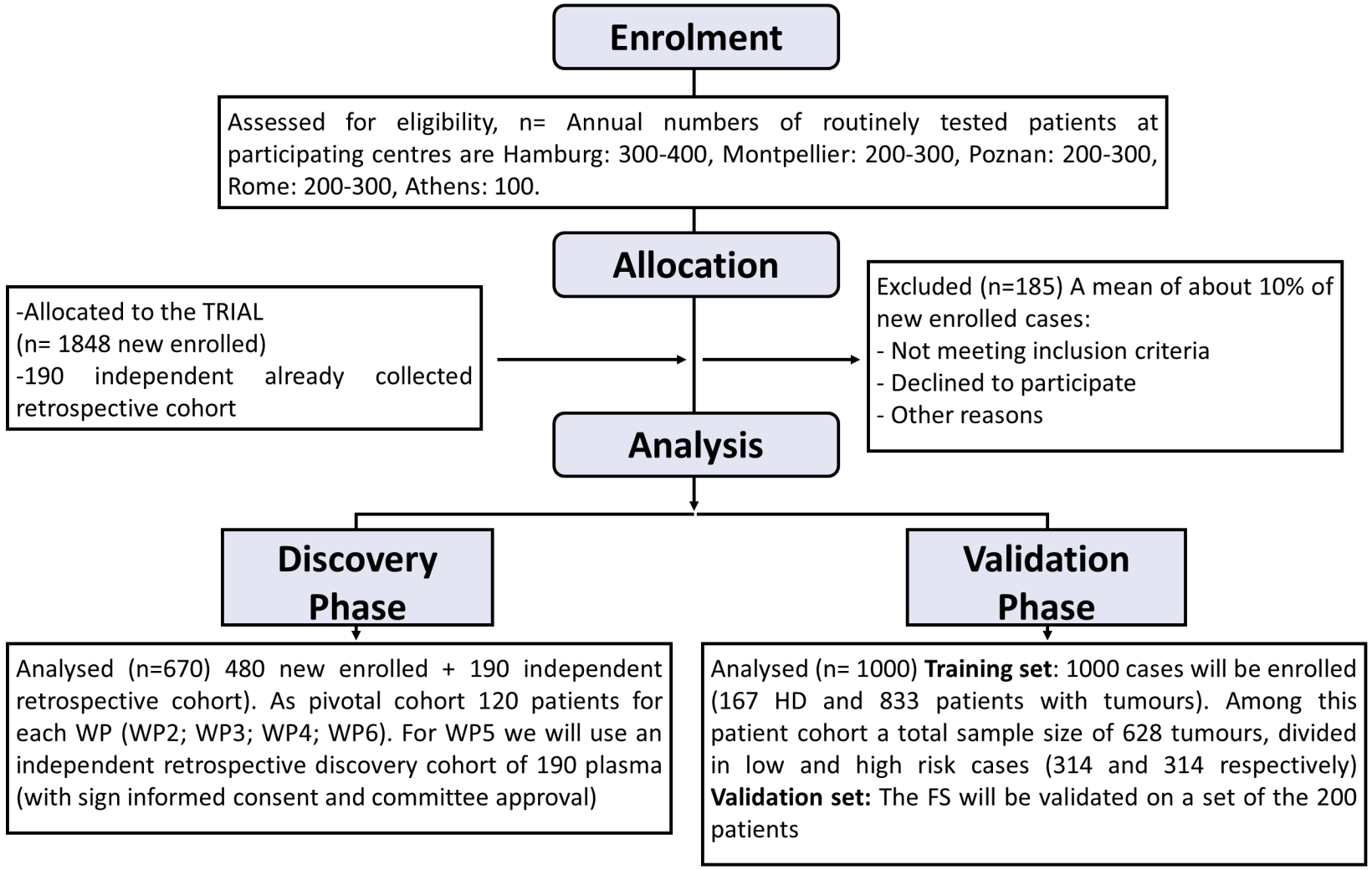


Validation of best assays within a multicentre ring trial

Interactions between work packages



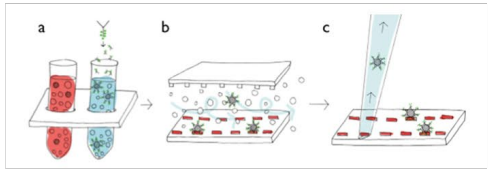
Clinical Trial Flow Chart

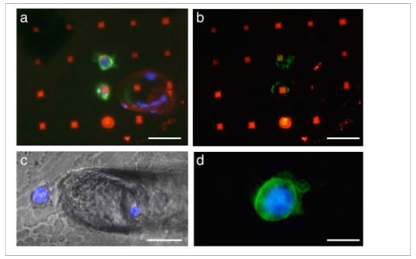


CTC detection assays using 20 ml blood taken directly before biopsy

CTCapture:

Major advances of the newly developed Capture-CTC chip are (i) flexibility of enrichment with biotinylated antibodies against different tumour-associated cell surface antigens, (ii) accessibility of isolated CTCs for follow up analysis.



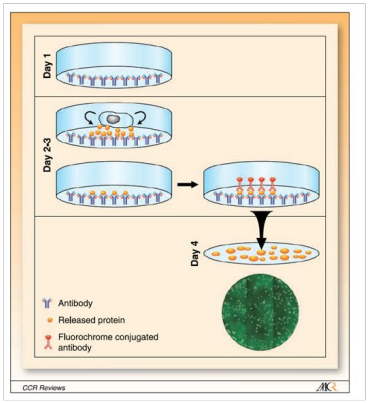


Brinkmann et al. Sci Rep 2015; PMID:26493176

EPIDROP:

This assay is based on the secretion, shedding or active release of specific marker proteins. The unique feature of this functional assay is the detection of viable CTCs at the single-cell level .

Alix-Panabières et al. Clin Cancer Res. 2008

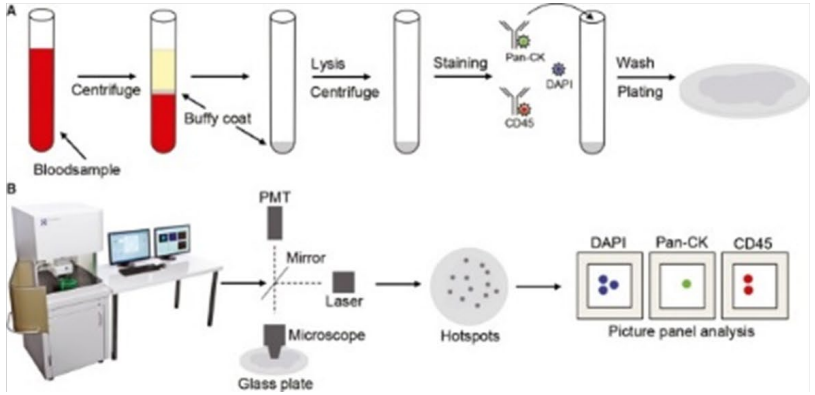


Kuske et al. Sci Rep 2016. PMID:28000772
Markou et al. Clin Chem. 2018. PMID:29122836

Cyto-Track:

This scanner-like technology uses glass disc, of surface much larger than conventional microscope glass slide, and enables spread of up to 100 million nucleated blood cells in a monolayer. A rotating disc is scanned by the laser and position of each stained CTC.

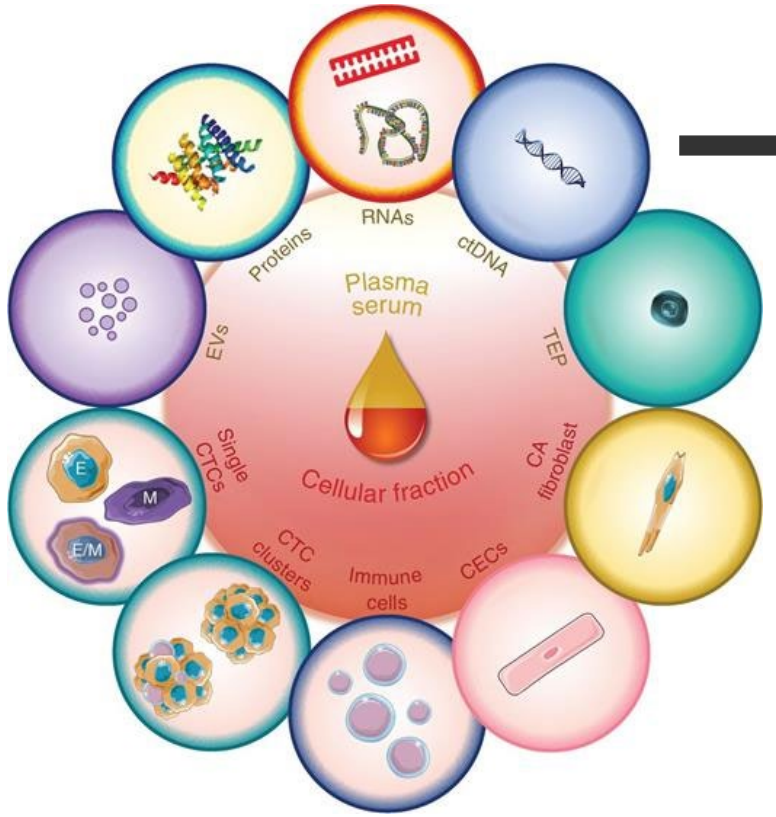
Hillig et al. APMIS. 2014. PMID:24164622
Hillig et al. Tumour Biol. 2015. PMID:25608842



Exosome RPPA and miRNA:

RPPA analysis revealed that in serum exosomes there are around 40 protein endpoints significantly different between healthy donors and PCa patients. Based on these data, we will analyse 177 antigens at the beginning of the study and in the pivotal set in an independent retrospective cohort of plasma exosomes.

Cannistraci et al. Oncogene 2017. PMID:28192399



Alix-Panabieres & Pantel. Caner Discovery 2019. PMID:33811121

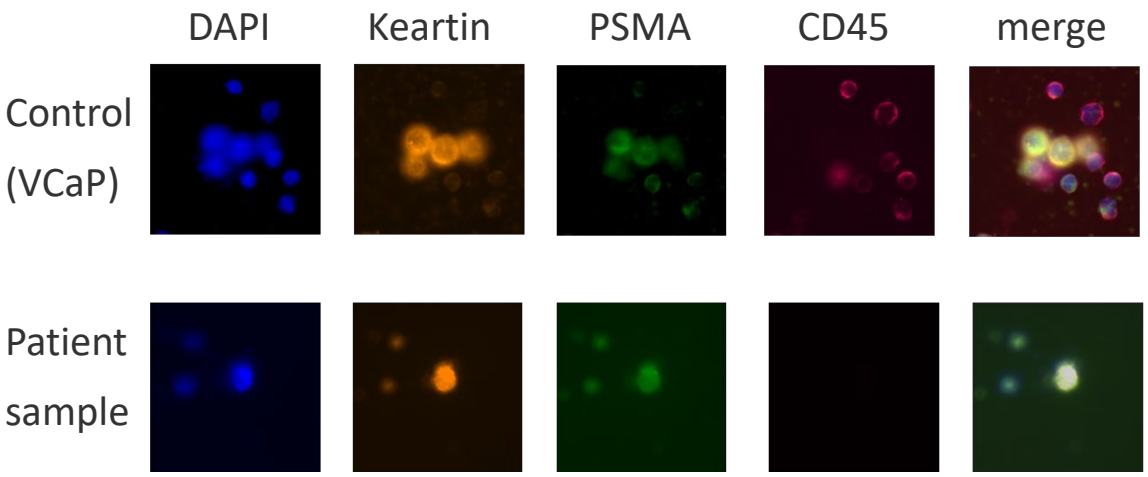
cfDNA:

Detection of the prostate cancer specific epigenetic biomarkers GSTP1, APC and RASSF1 genes and driver gene fusions (TMPRSS2:ERG) as well as driver focal deletions (PTEN, RYBP and SHQ1) and driver amplifications (AR and MYC) will be analysed in cell free DNA of enrolled patients.

Lianidou. Mol Oncol. 2021. PMID: 33942482
Londra et at. Cancer 2019. PMID:34572834
Chimonidou et al. Clin Chem 2011.PMID:21700955
Chimonidou et al. Clin Chem 2013.PMID:23136251

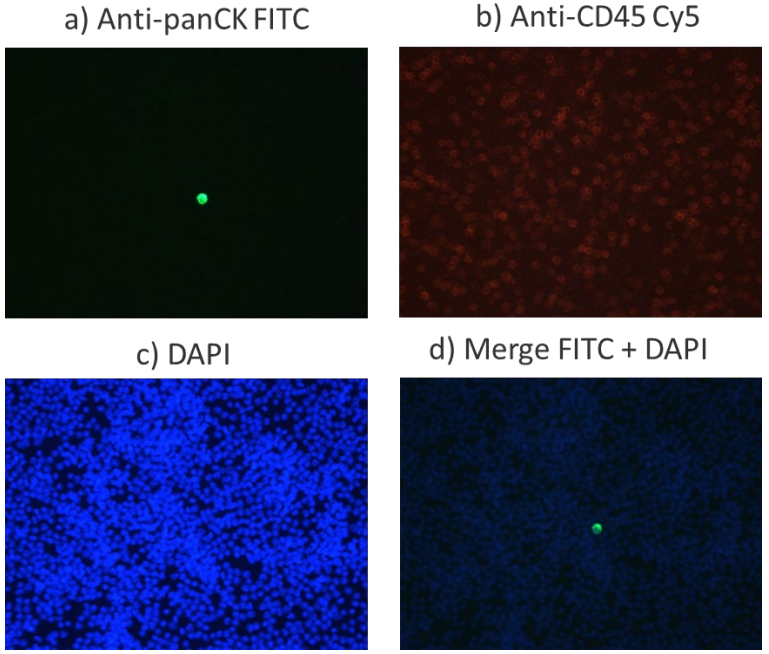
Results at the end of the discovery phase

CTCapture (Parsortix)



38 PCa samples analyzed, only 2 patients presented CTCs

Cyto-Trac



59 PCa samples analyzed

only 6 patients presented CTCs

No statistical difference between cancer patients vs. healthy donors

No statistical difference between high- and low-risk PCa patients

Both assays are not sensitive enough in non-metastitic PCa patients and were not tested on international level

Results at the end of the discovery phase

EPIDROP: The assay has constantly been improved, but has not been tested on clinical samples.

cfDNA: Assays for targeted analysis has been developed and tested on a pilot cohort. We found no statistical difference between cancer patients vs. healthy donors, but we were able to detect cancer-specific genomic alterations.

Exosome RPPA and miRNA: By analysing a retro-specific cohort 37 differentially and significantly expressed antigens and 4573 possible miRNAs has been identified a biomarker candidates.

→ We decided to focus on establishing cfDNA and exosome biomarkers during the discovery phase and to further optimize the EPIDROP assay during the validation phase.

Research activates during the validation phase

- **Withstand the COVID19 pandemic and continue to work experimentally and recruit patients despite restrictive measures.**
- **Establish additional DNA methylation markers with an genome-wide approach.**
- **Establish additional biomarkers from exosomes and validate the previously identified.**
- **Optimize the EPIDROP assay.**
- **Support each with samples, knowledge, material and working hands.**

WP5: Plasma circulating miRNAs (ACTC lab, ATHENS)

372 plasma samples:
Athens: 48, Germany: 104,
France: 120, Poland: 100, Healthy donors: 30

Group of candidate - miRNAs based on:
- RNA sequencing
- Literature

→ Selection of 20 miRNAS

Validation of the selected panel for early detection

n=310 plasma samples (early stage prostate cancer, and benign diseases)

RT-qPCR analysis of selected miRNAs by single plex RT-qPCR

Explorative phase (training group) :

Development and analytical validation of four different multiplex cDNA synthesis assays (5 miRNAs in each assay).

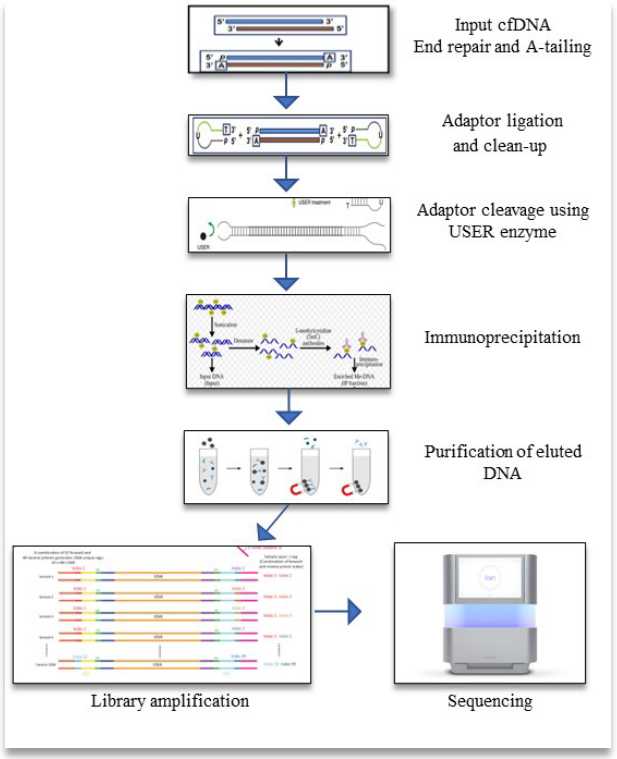
Addition of cel-miR-39 in each plasma sample (600µL) as an exogenous control to estimate recovery rates

Single-plex RT-qPCR analysis for all 20 selected circulating miRNAs:
- Healthy donors, N=30
- PSA<10 ng/µL, N=30
- PSA>20 ng/µL, N=30

Final selection of circulating miRNAs that are upregulated in early prostate cancer

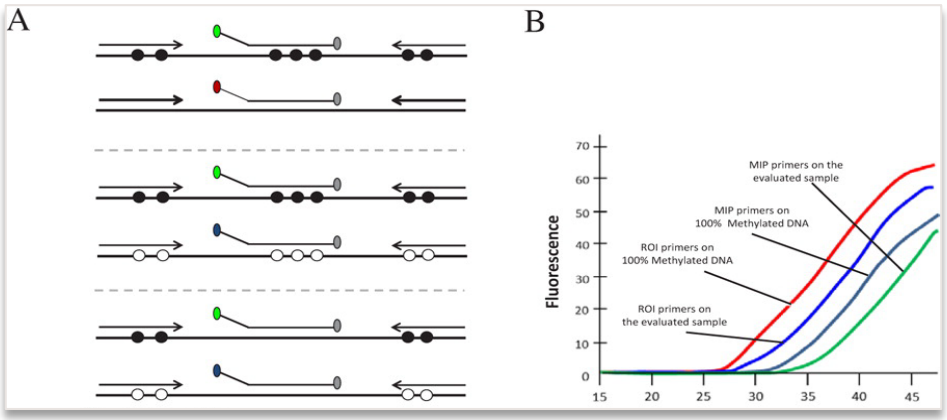
WP6: DNA methylation markers (epigenetics), ACTC lab, ATHENS

PHASE 1: cell free Methylated DNA immunoprecipitation Sequencing, cfMeDIP-seq, ILLUMINA platform



- ILLUMINA next Seq 2000
- 60 plasma samples
- healthy donors, N=7
- prostate hyperplasia, N=5
- PSA<10 ng/µL, N=24
- PSA>20 ng/µL, N=24

- We annotated 3.449 statistically significant regions, that include 70 CpG islands
- **12 genes were selected to be validated by real time Methylation Specific PCR (MSP)**



PHASE 2: Discovery of cell-free DNA Methylation markers for early detection of prostate cancer

PILOT PHASE

Development and analytical validation of real time MSP assays for the selected 12 genes

Analysis of 60 plasma samples (previously sequenced)

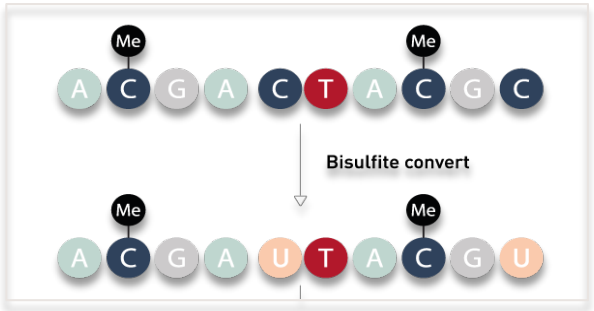
Selection of DNA methylation markers differentially detected in non-cancerous and early prostate cancer

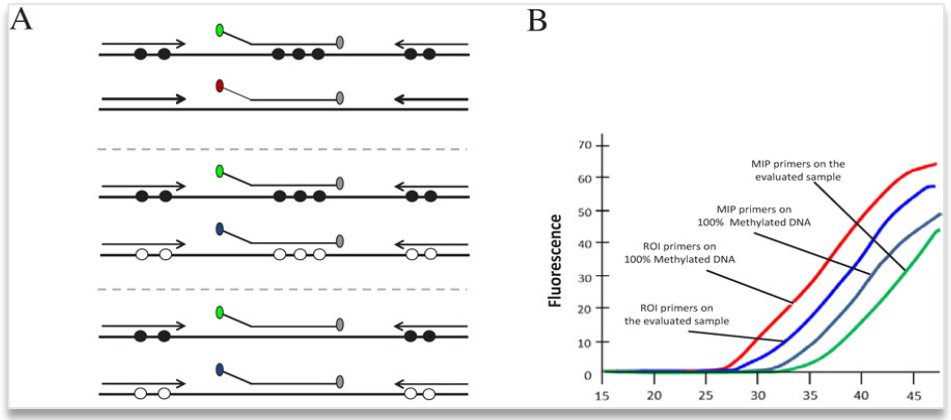
Validation phase

n= 400 plasma samples (early stage prostate cancer, and benign diseases)

Real time MSP analysis of selected DNA methylation markers

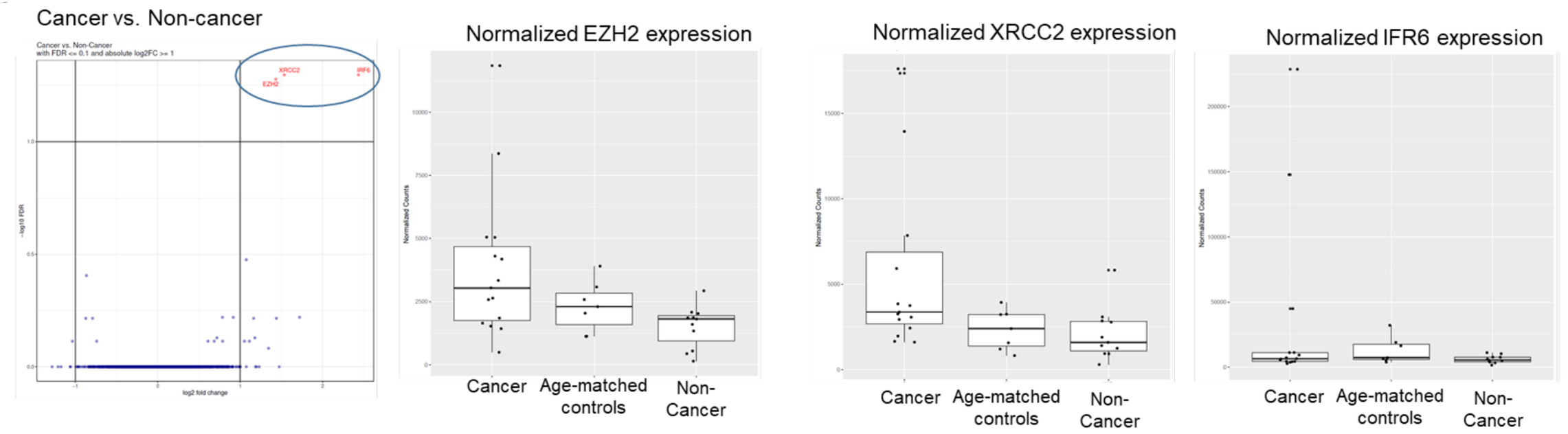
Validation of the selected panel for early detection of prostate cancer





Identifying differential expressed mRNA in SoRTEV-isolated exosomes plasma using the HTG EdgeSeq Oncology Biomarker Panel

- 92 SoRTEV-isolated exosome samples has been analyzed.
- 42 samples processed passed HTG EdgeSeq post-sequencing metrics.



- EZH2 and XRCC2 transcripts in exosomes are candidate biomarker for early prostate cancer detection.

Current state of the art validating blood-based biomarkers for early prostate cancer detection

- Total 1023 patients have been recruited by the end of the PROLIPSY study.
- Assays for assessing 20 miRNAs in exosomes have been established and are ready for validation in larger patients cohort.
- 12 MSP assays for the selected 12 genes have been developed and are ready for validation in larger patient cohort.
- The EPIDROP assay is now ready for testing on clinical samples (NCT04581109).
- EZH2 and XRCC2 transcripts have been identified as candidate biomarker for early prostate cancer detection.

Future Perspectives

- The PROLIPSY study will be finalized within the ELSBS network.
- ELBS approved protocols can help to set-up future studies more efficiently.
- ELBS could help to establish virtual biobanking and standards for collection of minimal sample and clinical data.

PANcreatic CAncer Initial Detection via liquid biopsy (PANCAID)

Prof. Dr. Klaus Pantel (Coordinator)
Universitaetsklinikum Hamburg-Eppendorf (UKE)

Prof. Matthias Löhr (Co-Coordinator)
Karolinska Institutet (KI)

Meeting with European Commission (Zoom), 14 September 2022

CONSORTIUM

Participant No.	Participant organisation name	Country
01 UKE (COO)	UNIVERSITAETSKLINIKUM HAMBURG-EPPENDORF	DE
02 KI	KAROLINSKA INSTITUTET, Stockholm	SE
03 CNIO	FUNDACION SECTOR PUBLICO ESTATAL CENTRO NACIONAL INVESTIGACIONES ONCOLOGICAS CARLOS III	ES
04 MUG	MEDIZINISCHE UNIVERSITAT GRAZ	AT
05 UMEA	UMEA UNIVERSITET	SE
06 PCE	Pancreatic Cancer Europe ASBL	BE
07 IMM	IMMUNOVIA AB (SME)	SE
08 concentris	CONCENTRIS RESEARCH MANAGEMENT (SME)	DE
09a UKSH	UNIVERSITATSKLINIKUM SCHLESWIG-HOLSTEIN	DE
09b CAU	CHRISTIAN-ALBRECHTS-UNIVERSITAET ZU KIEL (affiliated entity)	DE
10 CHU	CENTRE HOSPITALIER UNIVERSITAIRE MONTPELLIER	FR
11 UKHD	UNIVERSITATSKLINIKUM HEIDELBERG	DE
12 UU	UPPSALA UNIVERSITET	SE
13 UCAM	THE CHANCELLOR MASTERS AND SCHOLARS OF THE UNIVERSITY OF CAMBRIDGE	UK
14 HUJI	THE HEBREW UNIVERSITY OF JERUSALEM	IL
15 CMR	COLLECTIVE MINDS RADIOLOGY AB (SME)	SE
16 MACCABI	MACCABI SHEIRUTEI BRIUT FOUNDATION	IL
17 FIBIRYCIS	FUNDACION PARA LA INVESTIGACION BIOMEDICA DEL HOSPITAL UNIVERSITARIO RAMON Y CJAL	ES
18 ZAVA	ZAVA Deutschland GmbH (SME)	DE

- ✓ 18 Partners from 8 countries
- ✓ 4 SME/industriy partners
- ✓ 1 Patient organisation
- ✓ 1 affiliated entity

CONSORTIUM

A team including world-class experts in translational research on PDAC, Liquid biopsy, Data handling/Computational data analysis, Health economy and ethical aspects of cancer screening

Expertise	Partners
Liquid biopsy (CTC, EV, ctDNA)	UKE, MUG, HUJI, CNIO, UCAM, KI, UU, CHU
Pancreatic cancer patient care	KI, Umeå, CNIO, UKHD, MACCABI, UKSH, FIBIRCIS
Risk group maintenance (IAR, IPMN)	KI, Umeå, CNIO, UKHD
Genetic aspects	MUG, KI, CNIO
Data collection and analysis	CMR, CNIO, HUJI, IMM
Health economy	UKE, KI, IMM, CMR
Ethics	KI, PCE, MACCABI
Dissemination, communication, open science practices	IMM, concentris, PCE
Digital software products	ZAVA
Exploitation, innovation management and intellectual property	IMM, concentris,
Project management and coordination	concentris, UKE, KI

AIM & OBJECTIVES

MAIN OBJECTIVE: To provide a minimally invasive blood test using a comprehensive panel of liquid biopsy diagnostics (LBx) for early detection of pancreatic cancer (PDAC) and the malignant conversion of premalignant to invasive lesions.

SPECIFIC AIMS:

1. Accumulate the **critical size of data sets and biobanks of blood samples** from IARs, IPMN and early PDAC patients managed at EU-wide clinical centers of excellence as prerequisite for the subsequent analytical steps (WP1).

2. Perform a **comprehensive LBx approach** including the most relevant analytes currently available such as ctDNA, exosomes, circulating tumour cells (CTCs) and host cells as well as circulating proteins and metabolites (WP2).

3. Combine the results from all of these individual analytes into a **multi-marker panel by computational combinatorial analysis including AI approaches**, and finally validate the multi-marker panel on independent cohorts of patients and individuals at risk (IARs) (WP3).

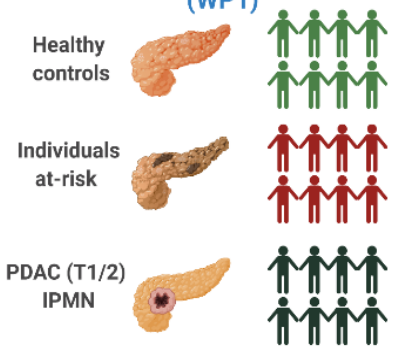
4. Support the implementation of the blood test into medical practice (including re-imbursement) by **defining the target population** for such a blood test from a **socio-economic** (WP4) and **ethical** (WP5) perspective.

5. Design the **protocol of a prospective multi-center study** in Europe aimed to demonstrate **clinical utility** of LBx diagnostics in the management of individuals at high risk to develop PDAC.

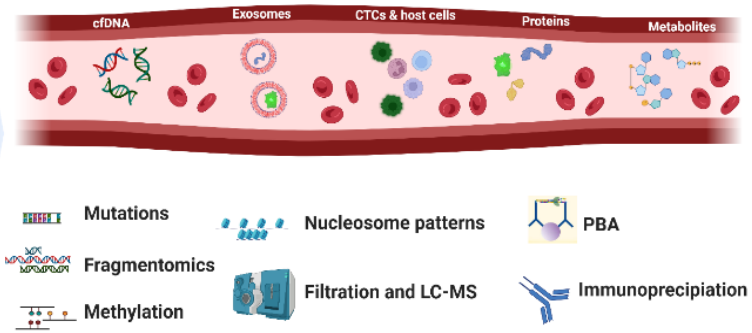
AIM & OBJECTIVES

PANcreatic CAncer Initial Detection via liquid biopsy

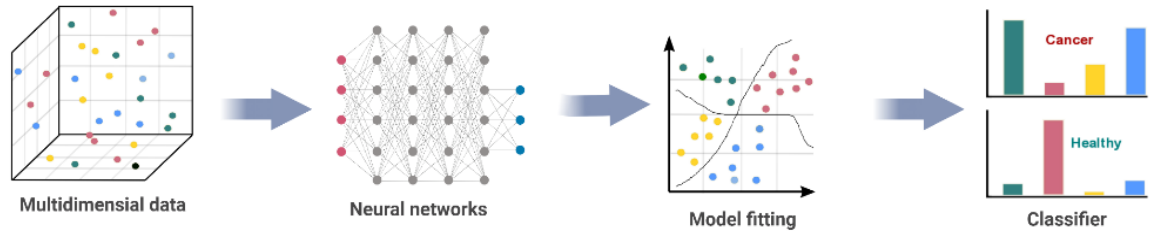
Establish a unique resource of blood samples for technical and clincal validation (WP1)



Establish a breakthrough blood test for early diagnosis of PDAC (WP2)



Identify the best composite biomarker panel by integrating multimodal features (WP3)



Health economics (WP4)

Consider the socio-economic impact of early PDAC diagnosis

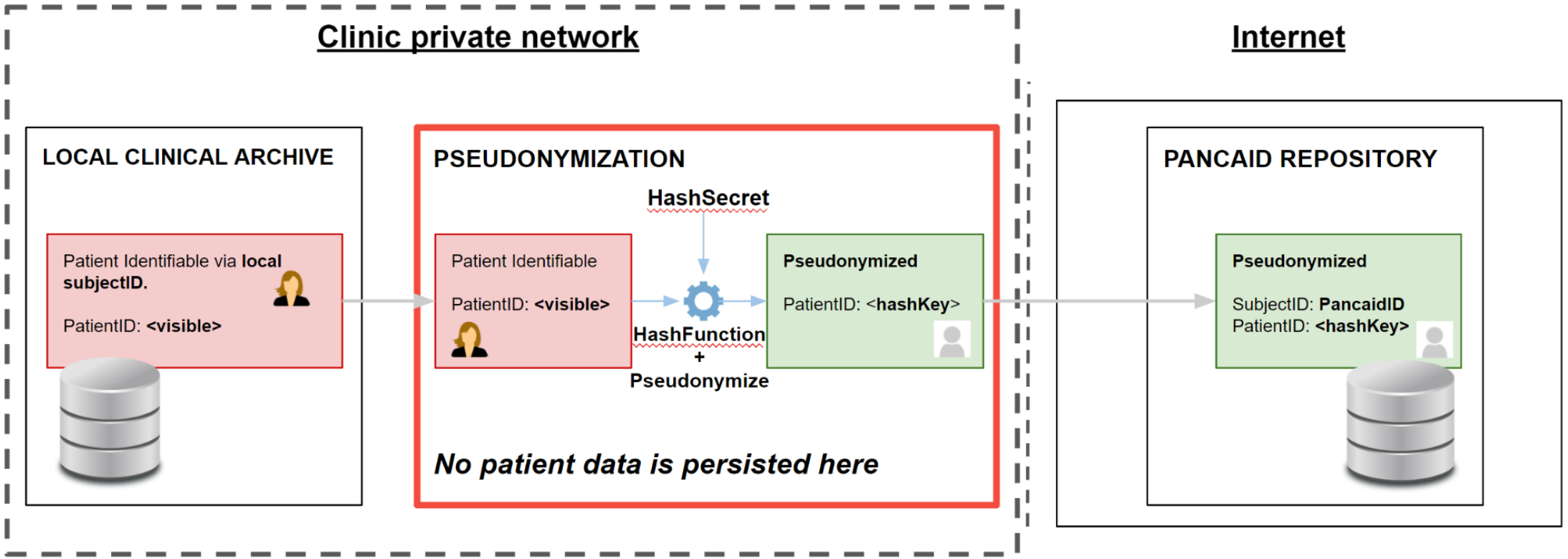
Ethics (WP5)

Define the ethics parameters relevant to early PDAC detection

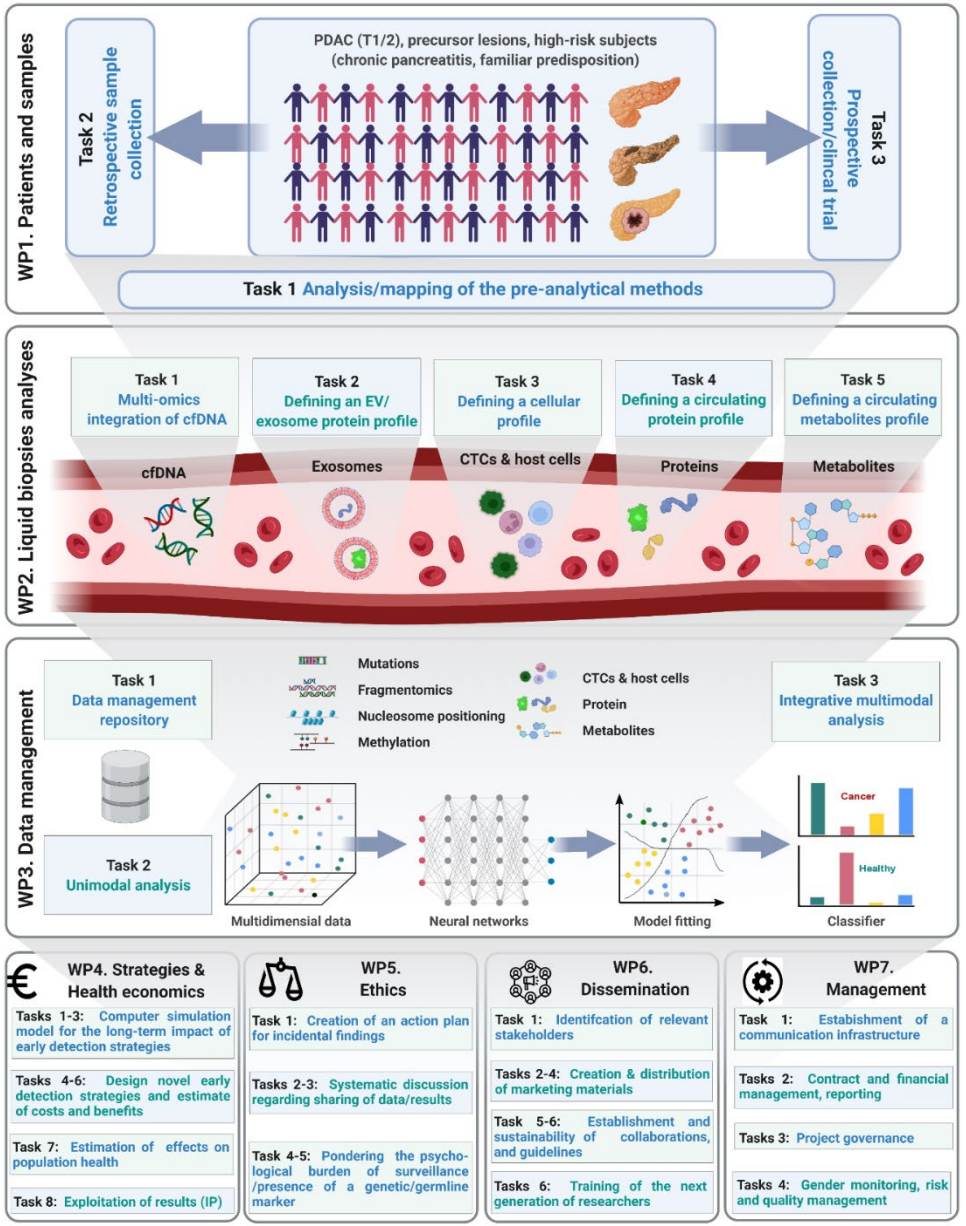
Overarching Result

Design the protocol of a prospective multi-center study aimed to demonstrate clinical utility of liquid biopsy diagnostics in the management of individuals at high risk to develop PDAC.

DATA SAFETY


Clinic private network
Internet
LOCAL CLINICAL ARCHIVE
Patient Identifiable via local subjectID.
PatientID: <visible>
PSEUDONYMIZATION
HashSecret
Patient Identifiable
PatientID: <visible>
HashFunction
+
Pseudonymize
Pseudonymized
PatientID: <hashKey>
No patient data is persisted here
PANCAID REPOSITORY
Pseudonymized
SubjectID: PancaidID
PatientID: <hashKey>

WORK PLAN


WP1. Patients and samples
Task 2
Retrospective sample collection
PDAC (T1/2), precursor lesions, high-risk subjects
(chronic pancreatitis, familiar predisposition)
Task 3
Prospective collection/clincal trial
Task 1 Analysis/mapping of the pre-analytical methods
WP2. Liquid biopsies analyses
Task 1
Multi-omics integration of cfDNA
Task 2
Defining an EV/ exosome protein profile
Task 3
Defining a cellular profile
Task 4
Defining a circulating protein profile
Task 5
Defining a circulating metabolites profile
cfDNA
Exosomes
CTCs & host cells
Proteins
Metabolites
WP3. Data management
Task 1
Data management repository
Mutations
Fragmentomics
Nucleosome positioning
Methylation
CTCs & host cells
Protein
Metabolites
Task 3
Integrative multimodal analysis
Task 2
Unimodal analysis
Multidimensial data
Neural networks
Model fitting
Cancer
Healthy
Classifier
WP4. Strategies & Health economics
Tasks 1-3: Computer simulation model for the long-term impact of early detection strategies
Tasks 4-6: Design novel early detection strategies and estimate of costs and benefits
Task 7: Estimation of effects on population health
Task 8: Exploitation of results (IP)
WP5. Ethics
Task 1: Creation of an action plan for incidental findings
Tasks 2-3: Systematic discussion regarding sharing of data/results
Task 4-5: Pondering the psycho-logical burden of surveillance /presence of a genetic/germline marker
WP6. Dissemination
Task 1: Identifcation of relevant stakeholders
Tasks 2-4: Creation & distribution of marketing materials
Task 5-6: Establishment and sustainability of collaborations, and guidelines
Tasks 6: Training of the next generation of researchers
WP7. Management
Task 1: Estabishment of a communication infrastructure
Tasks 2: Contract and financial management, reporting
Tasks 3: Project governance
Tasks 4: Gender monitoring, risk and quality management

Clinical Studies

- PANCAID-00-METH
  - Methodological pre-study comparing different LiBx methods on the same samples to identify the best method(s) suitable for stored samples
- PANCAID-01-LIMIT
  - Retrospective analysis of samples (LiBx, tissue) with limited disease = early PDAC
- PANCAID-02MDIPMN
  - Retrospective analysis of samples (LiBx, tissue) from main duct IPMN
- PANCAID-03-BDIPMN
  - Retrospective analysis of samples (LiBx [tissue]) from branched duct IPMN
- PANCAID-04-IAR
  - Retrospective analysis of samples (LiBx [tissue]) from individuals at risk for IPMN
- PANCAID-05-HRG
  - Retrospective analysis of samples (LiBx [tissue]) from patients with chronic pancreatitis, aged 55-65, heavy smokers, and newly onset diabetes mellitus
- PANCAID-06-LONGSEQ
  - Retrospective analysis of sequential samples collected in individuals in which some (n = 378) developed PDAC
- PANCAID-07-PROSAM
  - Prospective pilot study in high risk individuals during the course of PANCAID
- PANCAID-08-RANDOM
  - Prospective randomized clinical study investigating the optimal LiBx method(s), endpoint resection rate

PRE-EXISTING ARCHIVAL BIOBANKED SAMPLES

Cohort (Country)	*Owner*	*(D) Description and (R) Rationale*	*Status*	*n*	*Vts.*	*Ctrls.*	*Data*	*Samples*
MolDiaPaCa (EU)	**Karolinska SPP**	**D:** Population-based PDAC **R:** Biomarker discovery	Data and samples	1400	1	500*	CLIN, NGS	
	Owner: KI **KI ExPACT**	**D:** PDAC chemotherapy patients **R:** EV-based biomarker discovery	Data and samples	100	3			
PANCAIM (EU)	**CamChaTCa**	**D:** patients with PDAC for omics AI analysis **R:** Biomarker discovery	Data and samples	300	1		CLIN, RAD, PATH, NGS	
	Owner: KI							
Karolinska IAR		**D:** Individuals at risk for PDAC **R:** Biomarker discovery	Data and samples	100	1		CLIN, PATH	
Karolinska IPMN		**D:** premalignant lesions (IPMN) **R:** Biomarker discovery	Data and samples	145	1		CLIN, PATH	
Umeå prospective populat.		**D:** Development of PDAC **R:** Biomarker discovery	Data and samples	374	5	10000	CLIN, PATH	
BMB-CCC (Kiel, UKSH) Owner: UKSH		**D:** Patients with CP, IPMN **R:** Biomarker discovery	Data and samples	104	1		CLIN, PATH	
		D: Patients with PDAC (T1/T2) **R:** Biomarker discovery	Data and samples	62	1		CLIN, PATH	
UKHD Owner: UKHD		**D:** Patients with PDAC (T1/T2) **R:** Biomarker discovery	Data and samples	1500	1		CLIN, PATH	
MACCABI HMO populat.		**D:** Patients with PDAC (T1/T2) **R:** Biomarker discovery	Data and samples	190	5	10000	CLIN, PATH	
PanGenEU (CNIO)		**D:** Patients with PDAC **R:** Biomarker discovery	Data and samples	639		559	CLIN, MED, EPIDEM, NGS, MICROB	
Total EXISTING samples		**D:** PDAC, IPMN, IAR, risk group **R:** Biomarker discovery	Data and samples	**4814**		12059		
PANCAID-08-RANDOM		**D:** prospective collection of sequential liquid biopsies (PDAC, IPMN, IAR, controls*) **R:** Biomarker verification	Planned study following PANCAID	4620	3	5000		

Vts. – visits (if > 1: average over all samples, range can be 1-20), Ctrls – controls, - CLIN - Clinical and biochemical data, BC – buffy coat, C – cytokines, EPIDEM – epidemiology, MED – medi chemotherapy), METAB – metabolomics, METHYL – methylation, MICROB – microbiome, NGS- DNA genomics, PATH – pathology (H&E), RAD – radiology/imaging, Sal. 16S – saliva 16S MG – saliva metagenomics

*: Controls include healthy subjects, benign pancreatic diseases (acute, chronic, autoimmune pancreatitis), benign non-pancreatic diseases (as per PanGen definition)

= blood; =BC; =tissue; .=stool; =saliva; .=urine

NEEDS, RESULTS & MEASURES

SPECIFIC NEEDS

What are the specific needs that triggered this project?

- ✓ **PDAC is one of the most lethal cancers in Europe.**
- ✓ **Early detection of PDAC is rare.**
- ✓ **LBx opens new diagnostic avenues to reduce PDAC mortality.**

EXPECTED RESULTS

What do you expect to generate by the end of the project?

- ✓ **Successful interlaboratory validation of LBx test for PDAC.**
- ✓ **Novel composite biomarker blood test.**
- ✓ **Definition of the target population (end-user) based on the socio-economic and ethical assessments.**
- ✓ **Database and biobank will be made available to other scientific projects.**

D & E & C MEASURES

What dissemination, exploitation and communication measures will you apply to the results?

- ✓ **Exploitation through patenting the novel blood test.**
- ✓ **Dissemination towards the scientific community and industry.**
- ✓ **Communication towards citizens and patients (involving patient advocacy groups & patient organisation PCE).**
- ✓ **Communication towards policy makers.**

TARGET GOUPS, OUTCOME & IMPACTS

TARGET GROUPS

Who will use or further up-take the results of the project? Who will benefit from the results of the project?

- ✓ **Citizens**
- ✓ **Patients and their families**
- ✓ **Clinicians**.
- ✓ **Health care systems in EU**
- ✓ **Pharmaceutical companies**
- ✓ **Scientific community**

OUTCOMES

What change do you expect to see after successful dissemination and exploit-tation of project results to the target group(s)?

Reduced mortality of PDAC.

- ✓ **Better screening modalities for IARs.**
- ✓ **Better upfront discrimination better localized and disseminated PDAC (better planning of the clinical management)**
- ✓ **High use of the scientific discovery published**
- ✓ **A major company exploits/uses the new product for their digital technology (e.g., Apps).**

IMPACTS

What are the expected wider scientific, economic and societal effects of the project contributing to the expected impacts outlined in the respective destination in the work programme?

According to the **EU Cancer Mission:**

- ✓ **Scientific:** New breakthrough scientific discovery on biology of PDAC development
- ✓ **Economic/Technological: N**ew cancer screening blood test for PDAC opening a new market of LBx.
- ✓ **Medical:** High-impact consortium tackling the challenge of early detection and improved treatment of PDAC
- ✓ **Societal:** Reduced mortality and higher life quality for PDAC patients

AUSTRIAN INSTITUTE OF TECHNOLOGY
TOMORROW TODAY

CALL FOR COLLABORATION WITHIN HORIZON EUROPE AND IHI: YOUR PATIENTS AND CLINICAL NEEDS, OUR MULTI-OMICS LIQUID BIOPSY EXPERTISE

MOLECULAR DIAGNOSTICS

AIT Austrian Institute of Technology

CHRISTA NÖHAMMER, PHD

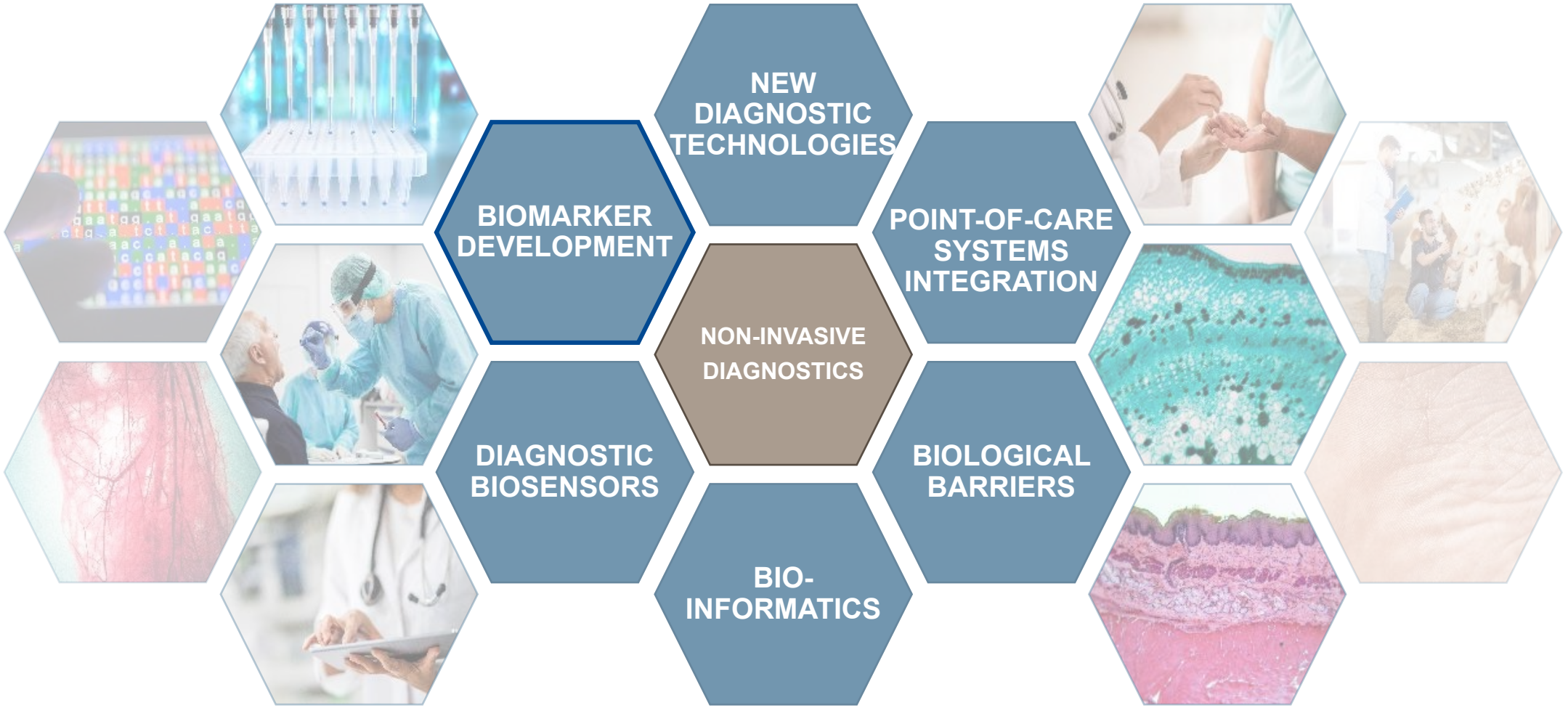
christa.noehammer@ait.ac.ac

WE ARE NOT NEWCOMERS WITH RESPECT TO EU PROJECTS …

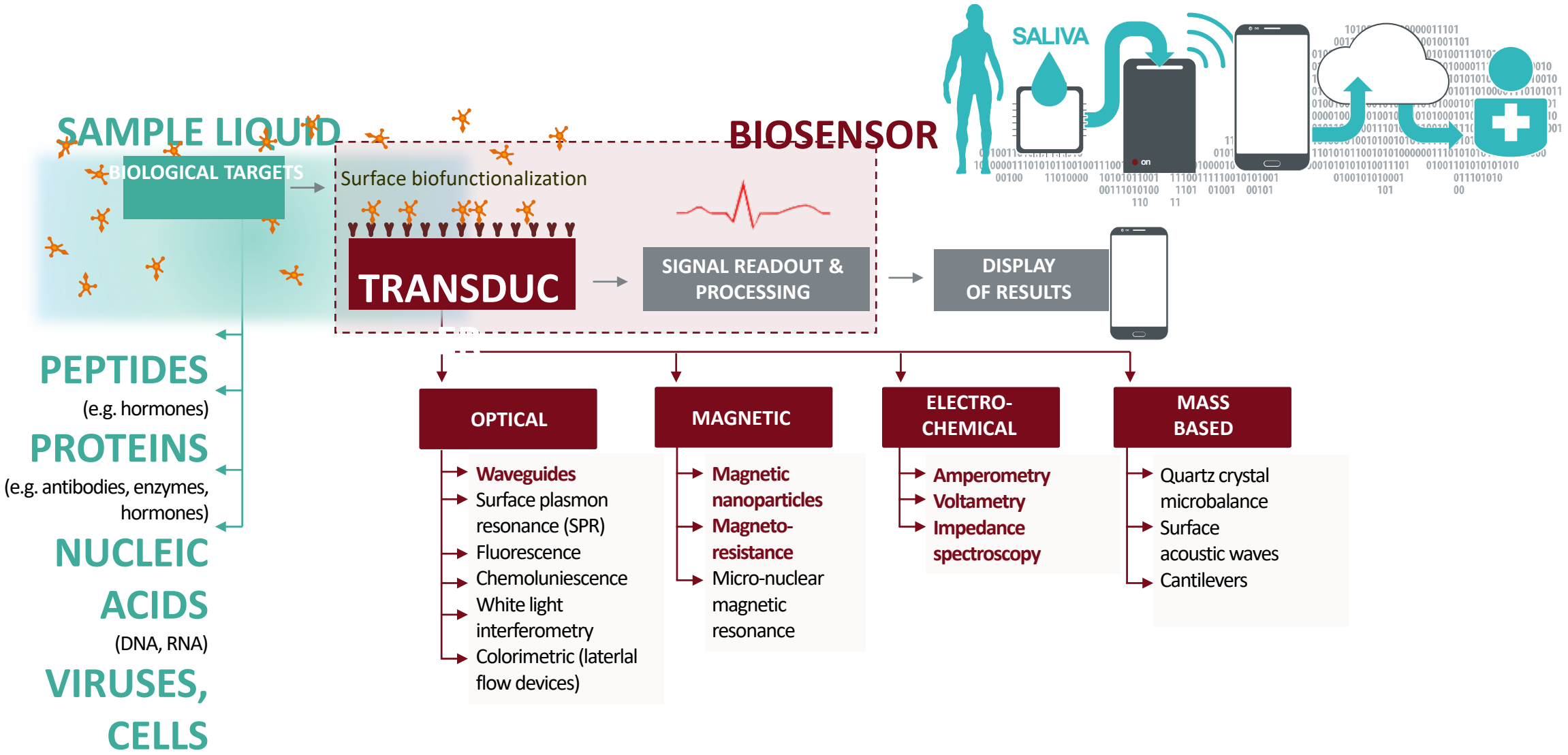
ACRONYM & Project Website	GA-ID & CORDIS-Link	CALL	START	END
FAPIC	634137	H2020-PHC-2014-two-stage	01.05.2015	31.10.2020
ULTRAPLACAD	633937	H2020-PHC-2014-two-stage	01.05.2015	31.10.2018
DIAGORAS	633780	H2020-PHC-2014-two-stage	01.06.2015	31.05.2019
MARA	686647	H2020-FETOPEN-2014-2015-RIA	01.12.2015	31.08.2020
OCTCHIP	688173	H2020-ICT-2015	01.01.2016	31.03.2021
PLASMOfab	688166	H2020-ICT-2015	01.01.2016	31.12.2018
ChipScope	737089	H2020-FETOPEN-1-2016-2017	01.01.2017	31.12.2020
GREENSENSE	761000	H2020-NMBP-PILOTS-2017	01.01.2018	31.03.2022
IMPETUS	761167	H2020-NMBP-PILOTS-2017	01.01.2018	31.10.2022
ELSAH	825549	H2020-ICT-2018-2	01.01.2019	30.06.2023
HEcoPerMed	824997	H2020-SC1-2018-Single-Stage-RTD	01.01.2019	30.06.2022
IM2PACT	807015	H2020-JTI-IMI2-2017-12-two-stage	01.01.2019	31.12.2023
BIOMAP	821511	H2020-JTI-IMI2-2017-13-two-stage	01.04.2019	31.03.2024
proEVLifeCycle	860303	H2020-MSCA-ITN-2019	01.10.2019	30.09.2023
HandheldOCT	871312	H2020-ICT-2019-2	01.01.2020	31.12.2024
ImmUniverse	853995	H2020-JTI-IMI2-2018-15-two-stage	01.01.2020	31.12.2024
DECISION	101005111	H2020-JTI-IMI2-2020-21-single-stage	01.07.2020	30.06.2024
MARILIA	952110	H2020-EIC-FETPROACT-2019	01.09.2020	28.03.2023
SWIMMOT	899612	H2020-FETOPEN-2018-2019-2020-01	01.10.2020	30.09.2024
REAP	101016964	H2020-ICT-2020-2	01.01.2021	31.12.2024
PARC	101057014	HORIZON-HLTH-2021-ENVHLTH-03	01.05.2022	30.04.2029
InChildHealth	101056883	HORIZON-HLTH-2021-ENVHLTH-02	01.09.2022	31.08.2026
MOBILISE	101073982	HORIZON-CL3-2021-DRS-01	01.10.2022	30.09.2025

REFERENCE EU PROJECTS (H2020, IMI2, HE)

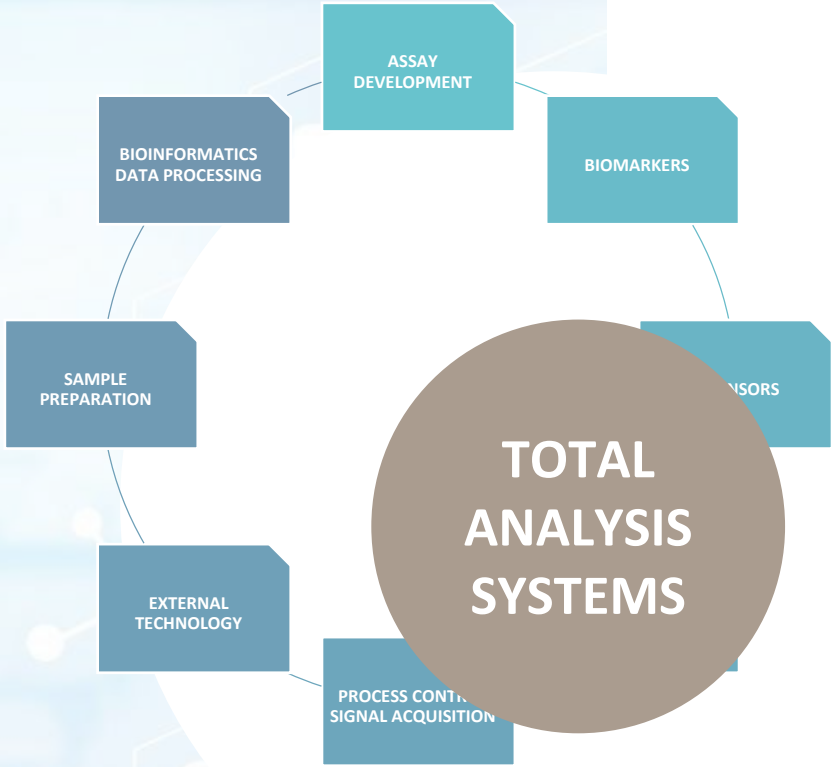
OUR TECHNICAL CORE COMPETENCIES



BIOSENSOR DEVELOPMENT OVERVIEW



POINT OF CARE DEVICES OVERVIEW



MAJOR REQUIREMENTS

- Rapid analysis <30min
- Compact systems
- Automation
- Cost-effective analysis

BIOLOGICAL BARRIERS
Expertise & OVERVIEW

RESEARCH AND SERVICE APPLICATIONS

Identification and assessment of relevance and causality of novel biomarkers

Disease models (inflammation, cerebral ischemia, CNS diseases, etc.)

Assessment of therapeutic strategies with barriers as targets

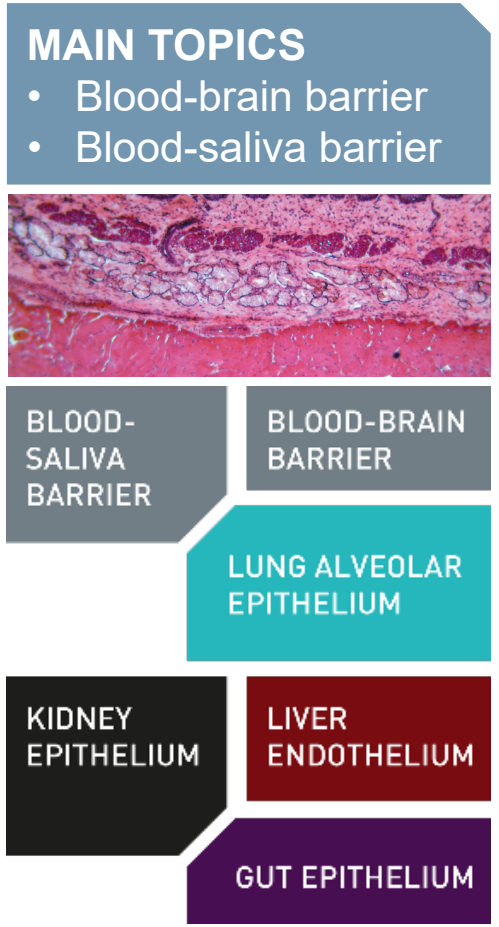
Development of novel (human) disease models (also hiPSC based)

Permeability & toxicity studies (drugs, nanoparticles, chemicals, biomarkers, etc.)

Effects on barrier properties (physical, transport, metabolic barrier)

Cell-cell communication studies, elucidation of species differences

Variety of advanced *in vitro* model set-ups (BBB spheroids, hollow-fibre models, etc.)



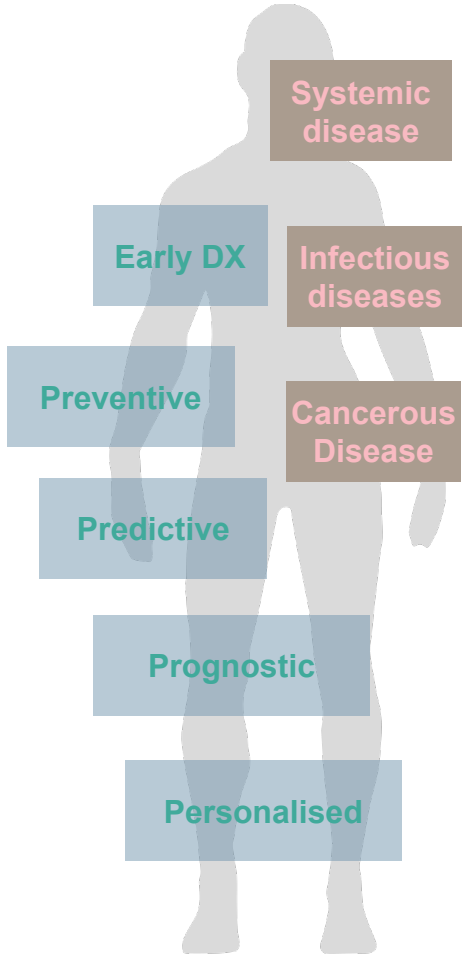
Biomarker Development

BIOMOLECULES

DNA
- Genotyping
- **DNA Methylation**
- Genetic Abberations

RNA
- Gene Expression - mRNA
- **miRNA**
- ncRNA

PROTEIN
- **Auto Antibody Profiling**
- Targeted proteomics
  (>3000 plex & 92plex panels)



TECHNOLOGIES

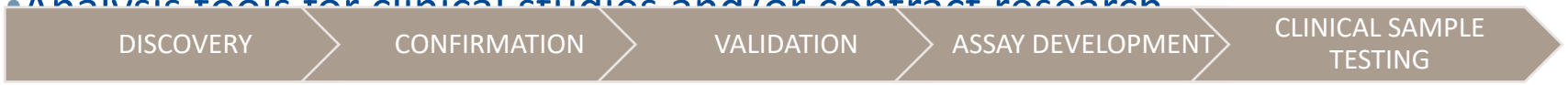
- **Pre-analytics** of various sample types
- **DNA microarrays** - various formats
- **Next generation sequencing**
- **PCR:** 96x, 384x qPCR
  HT-qPCR formats (24.192, 48.48, 96.96)
- **Immunomics** on Protein & Peptide – micro- & bead-arrays
- **Targeted proteomics** via **PEA** – proximity extension assays & 96.96 HTqPCR & NGS
- **Bioinformatics** support
  - assay design & analysis pipelines
  - data integration
  - multi-modal analysis
  - pathway analysis & biological interpretation
  - secure in house computing infrastructure

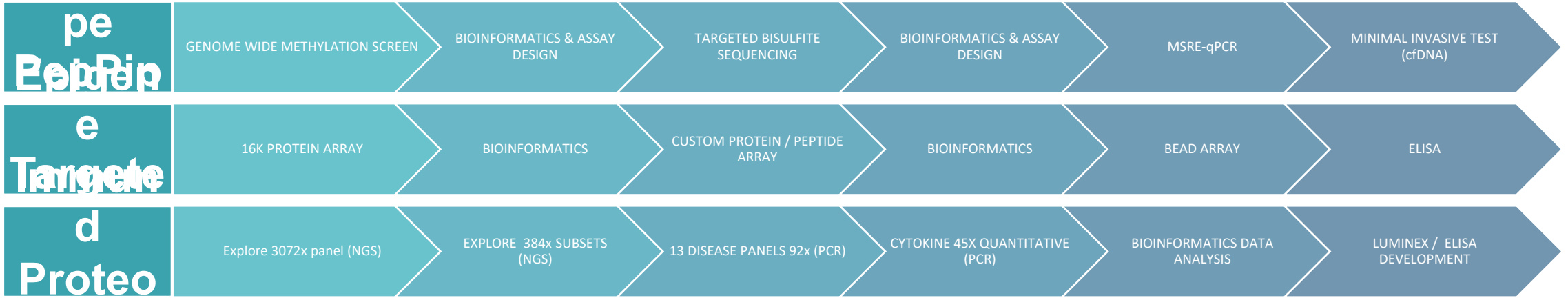
AIM: IMPROVING MINIMAL INVASIVE DIAGNOSTICS

sample preanalytics → omics discovery → multiplexed confirmation → validation on large sample sets → minimal invasive assays

MULTI-OMICS & ANALYsES Pipelines

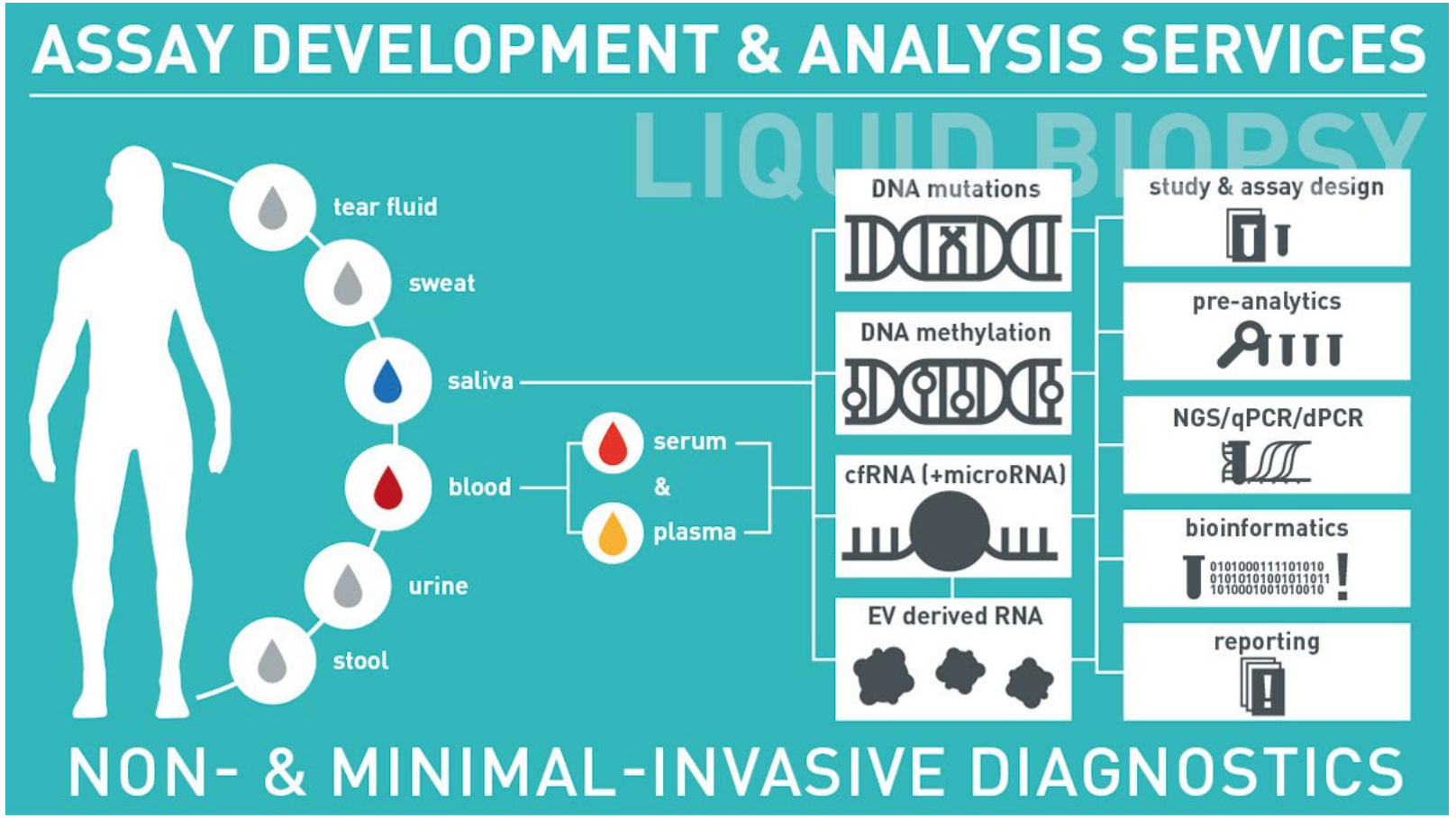
- Analyses of DNA, RNA and proteins in clinical samples (tissue, blood, saliva, EVs)
- Open for any disease and clinical needs
- Analysis tools for clinical studies and/or contract research



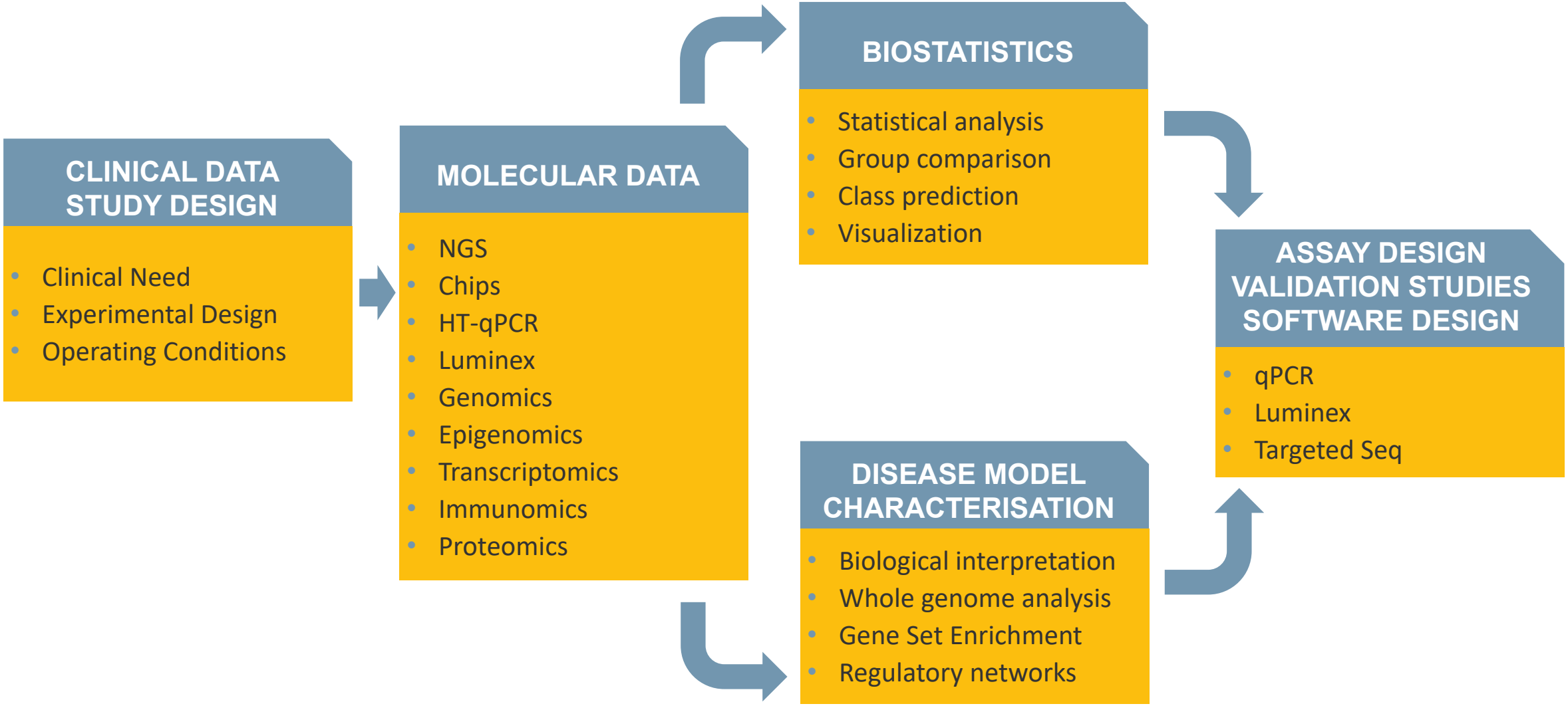


LIQUID BIOPSY

expertise



Bioinformatics
Expertise & Overview



OUR PATENT PORTFOLIO

// DNA-methylation biomarker panels

Cancer: Lung, Breast, Colon, Thyroid

// Autoantibody biomarker panels

Cancer: Breast, Colon, Lung, Prostate

Ulcerative colitis

// Thyroid cancer m-RNA expression biomarker

// New molecular diagnostic technologies

Autonomous sensing molecules

Nanostructures with catalytic activity

Molecular robot

// Fast and highly specific DNA-based multiplex detection

// Methods of pathogen detection

Upcoming Calls fitting our Multi-OMIcs Expertise (deadline Apr12/13 2023)

HORIZON-HLTH-2024-STAYHLTH-01-05-two-stage: **Personalised prevention of non-communicable diseases** - addressing areas of unmet needs using multiple data sources, RIA 8-12 Mio €

Enable the understanding of areas of unmet need in NCDs prevention, possibly also addressing disease mechanism, management of disease progression and relapse. Providing new approaches for prevention, focussing on the digitally supported personalised dimension, that can be adopted and scaled up.

HORIZON-HLTH-2023-DISEASE-03-07: **Relationship between infections and non-communicable diseases ,** RIA 6-7 Mio €

The proposals are expected to elucidate and provide a better understanding of causative links between infections and non-communicable diseases onsets, and/or the impact of infections on the exacerbation of existing NCDs or vice versa, in children and/or adults.

Research on cancer is excluded as it will be covered by the Mission on Cancer.

HORIZON-HLTH-2023-ENVHLTH-02-03: **Health impacts of endocrine-disrupting chemicals:** bridging science-policy gaps by addressing persistent scientific uncertainties, RIA 6-7 Mio €

Provide forward-looking mechanistic information on potential hazards and health risks of exposures to EDCs, through

Upcoming Calls fitting our Multi-OMIcs Expertise (deadline Apr12/13 2023)

HORIZON-MISS-2023-CANCER-01-01: **Addressing poorly-understood tumour-host interactions to enhance immune system-centred treatment and care interventions** in childhood, adolescent, adult and elderly cancer patients.
RIA 7-12 Mio €

Obtain a systematic understanding of processes underpinning tumour-host interactions in poorly-understood* cancer subtypes, at any stage of the disease in any age group and part of society, with a 5-year overall survival less than 50% from time of diagnosis.

* Includes refractory cancers and their and their subtypes in childhood, adolescent, adult and elderly cancer patients.

HORIZON-MISS-2023-CANCER-01-03: **Pragmatic clinical trials on minimally invasive diagnostics.**
RIA 6-8 Mio €

Design and conduct randomised or cluster-randomised academic investigator-initiated pragmatic clinical trials to deliver effective and evidence-based diagnostic interventions for choosing between care options.

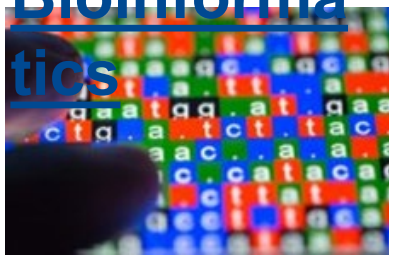
Pragmatic clinical trials focus on evaluate effectiveness, implementation by healthcare systems, the effect of diagnostics in routine (real-world) clinical practice, taking into account stratification, such

IHI Call 3 Topic 1: **Screening platform and biomarkers for prediction and prevention of diseases of unmet public health need**

Services:

Assay development

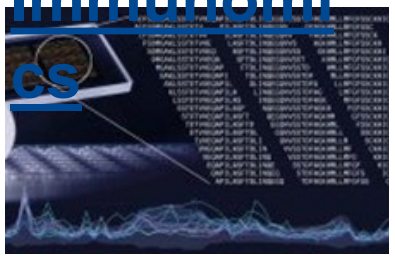
Bioinformatics



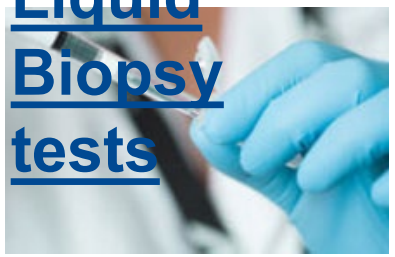
Biological barriers

Biomarker development

Immunomics



Liquid Biopsy tests



Olink - service provider

Saliva diagnostics

Sensor technologies

Systems integration

https://molecular-diagnostics.ait.ac.at/

AUSTRIAN INSTITUTE OF TECHNOLOGY
TOMORROW TODAY

Thank you!

Dr. Christa Nöhammer, Senior Scientist

christa.noehammer@ait.ac.at / molecular-diagnostics.ait.ac.at

OUR LABORATORIES INFRASTRUCTURE

// Molecular Biology Laboratories

Modern Molecular Biology Laboratories

S2 Laboratory

PCR Laboratory

Cell Culture Laboratory

Microarray Printing

High Throughput Systems (e.g. NGS)

// Chemistry Laboratory

// Physics Laboratory

// Clean Room and CTFT (Center of Thin Film Technology)

Magnetron Sputtering

Materials Inkjet Printer

Optical Lithography

Atomic Force Microscopy

Quality: ISO:9001, GMP & GLP like standards

HORIZON-HLTH-2023-ENVHLTH-02-03: Health impacts of endocrine-disrupting chemicals: bridging science-policy gaps by addressing persistent scientific uncertainties, RIA 6-7 Mio Euro

Research actions should provide forward-looking **mechanistic information on potential hazards and health risks of exposures to EDCs**, through **innovative molecular epidemiological, multifactorial models** and **systems biology approaches**, exploiting the use of new approach of **non-animal methodologies when relevant**, and should include several of the following activities:

- **Studying the impact of EDCs on target organs and in multi-organ models, and physiological barriers,** such as the placenta, the blood-brain barrier, the blood-saliva barrier, intestinal, pulmonary and immune cells as well as their interaction with microbiota;
- **Elucidating the health burden of EDCs, for which sufficient data exist, in disturbances in the development of the nervous and cardiovascular systems, the immune system, bone development and disease, obesity, diabetes, hormone-dependent cancers and fertility** (e.g. minipuberty, prepuberty and puberty);
- Providing **better biological and imaging biomarkers to predict EDC-mediated health outcomes**;
- Gaining **better insights into the developmental origins of health and disease,** especially for those where less data are available. Assessing the **occurrence and relevance of multiband transgenerationally inherited effects, including molecular and epigenetic mechanisms** that drive multigenerational effects;
- Gaining better insights into the most sensitive windows of susceptibility, during which exposure are of particular importance for health effects;
- **Better understanding of the effects of chemicals and chemical mixtures on the underlying mechanistic crosstalk between** endocrine axes, endocrine pathways and other **key biological systems, including immune, neurological and metabolic functions**;
- Improving the understanding of chemical mixture effects, including with other toxins and at low doses. The role of the microbiome in the activation or detoxification of these chemicals should be explored where relevant.
- Investigating biological effects of realistic mixtures to get a more detailed understanding of the endocrine effectome, taking advantage of computational toxicology and development of up-to-date models (including state of the art new approach non-animal models such as human organoids and organ-on-a-chip technology);
- **Exploiting systems biology approaches** in order to understand how exposure to an EDC results in an altered phenotype

Scope: Increasing evidence suggests that several **infections might influence the development of many non-communicable diseases (e.g. multiple sclerosis, Alzheimer, post-covid-19ncondition[133]),** or that NCD may be influenced by concurrent presence in the same individual of one (or more) infections. On the other hand, NCDs might represent risk factors for IDs.
The proposals are expected to **elucidate and provide a better understanding of causative links between infections and non-communicable diseases onsets**, and/or the impact of infections on the exacerbation of existing NCDs or vice versa, in children and/or adults.
The **analysis of genetics, immune status, immune or inflammatory responses, microbiome, lifestyle and/or other relevant factors** (e.g. differences in age, sex/gender, vaccination status, ethnicity) should be integrated to get information for prevention, early diagnosis, risk factors, and to better understand causative links as well as the progression of those non-communicable diseases.
In determining the connection between one or multiple concomitant infection(s) and the development of non-communicable disease(s), the proposals might address any infection including those with pandemic potential (viral, bacterial, or fungal) with non-communicable diseases of major importance. **Research on cancer is excluded** as it will be covered by the Mission on Cancer.
Special attention should be given to vulnerable individuals, such as those with known existing preconditions.
Preclinical research, observational studies and/or clinical studies can be considered for this topic. Proposals could include patient follow-up to identify conditions that may appear only after a patient has recovered from the infectious disease. Those proposals including clinical evaluation should give a sound feasibility assessment, provide details of the methodology, **including an appropriate patient selection and realistic recruitment plans, justified by available publications and/or preliminary results.**
The applicants are encouraged to incorporate artificial intelligence (AI) tools that enable advanced quality data analysis and for assessing and predicting the risk of developing a disease and/or the risk of disease progression/severity where relevant.
Projects funded under this topic that focus on COVID-19 and post COVID-19 condition (also known as long-COVID) are strongly encouraged to collaborate and build links with (one of) the relevant **EU-funded projects, such as ORCHESTRA[134]**. They should also pay special attention and link to the newly established European COVID-19 data sharing platform[135].

HORIZON-HLTH-2024-STAYHLTH-01-05-two-stage: Personalised prevention of non-communicable diseases - addressing areas of unmet needs using multiple data sources

RIA, expected EU contribution per project between 8 and 12 million Euro

Proposed research is expected to deliver on all of the following points:

 Enable the understanding of areas of unmet need in NCDs prevention, possibly also addressing disease mechanism, management of disease progression and relapse. Providing new approaches for prevention, focussing on the digitally supported personalised dimension, that can be adopted and scaled up.

 Devise new or improved ambitious policy and intervention options, with expected high population-wide impact on the target groups in question. To be proposed and made available for effective health promotion and disease prevention including targeted communication strategies to successfully reach out to the risk groups.

 Design an **integrated, holistic approach** that includes several of the following aspects: **genetic predisposition to NCDs, meta-genomics, epigenomics, the microbiome, metabolomics, sleep disorders, large cohorts, molecular profiling in longitudinal health screening, impact of lack of physical activity, novel predictive biomarker candidates,** diets and nutrition, eating habits for designing customised dietary patterns (geographical variation), and the influence of choice environment on personal choices.

 Study the ethical, legal and social aspects as well as health economics of the personalised prevention tools and programmes being developed. Consider optimal health counselling and communication to the patients/citizens. Address legal aspects of balancing the right not to know and the obligation of helping people in danger. Furthermore, the proposed research is expected to deliver on several of the following points:

 Develop and validate effective strategies to prevent NCDs and optimise health and wellbeing of citizens (including the most vulnerable). Propose the strategies to policy makers along with mechanisms to monitor their progress. The strategies need to be aligned with relevant national and European health laws and policies.
 Provide scientific **evidence on interactions between the genetic predisposition to multifactorial diseases and environmental factors or environmental triggers.** Propose scientifically supported personalised prevention strategies that ensure how to modify the environmental drivers of behavioural risk factors.
 Develop new computational tools combining and analysing comprehensive data with different dimensions to identify risk factors and modifiers. Creating procedures and algorithms to combine information from different sources (with standardised common data models) to generate risk scores for several diseases and provide health promotion recommendations for the individual as advised by healthcare professionals. Furthermore, develop advanced computational modelling techniques for predicting disease risk and predisposition (addressed together in an integrative approach) and identifying the optimal solution/intervention for different target groups and individuals.
 Develop tools and techniques to increase the efficiency and cost- effectiveness of on the one hand interventions, adjusting their scope, characteristics and resources, and on the other hand healthcare infrastructure and how it promotes and delivers health promotion, disease prevention, and care effectively to the different population groups.
 Design tools to collect various data to advance health promotion and disease prevention and strategies for providing omics essays for the general patient with a focus on costeffectiveness and flexibility.
 Determine how to optimise the benefits of physical activity, smart monitoring of physical activity and sedentary behaviour with measurable data, addressing barriers to uptake and implementation of healthy lifestyles in daily life, understanding what promotion methods work and why, behavioural science to understand healthier choice environments. Balancing the ecosystem associated with the economic, social, and health consequences of NCDs.
 Conduct data mining of real world data and develop quantifiable and distinguishable indicators from wearables data, taking into account ‘light-weight’ AI means to ensure patient privacy and short reaction times.
 Demonstrate with a practical prototype on a given health challenge: from multimodal data collection to identification of an effective prevention strategy to be tested and validated for one or several NCDs.