

Network analysis in oncology: How will integration of omics data with imaging biomarkers affect outcomes?



15th Biennial Symposium
of the International
Society for Strategic
Studies in Radiology

IS3R
2023

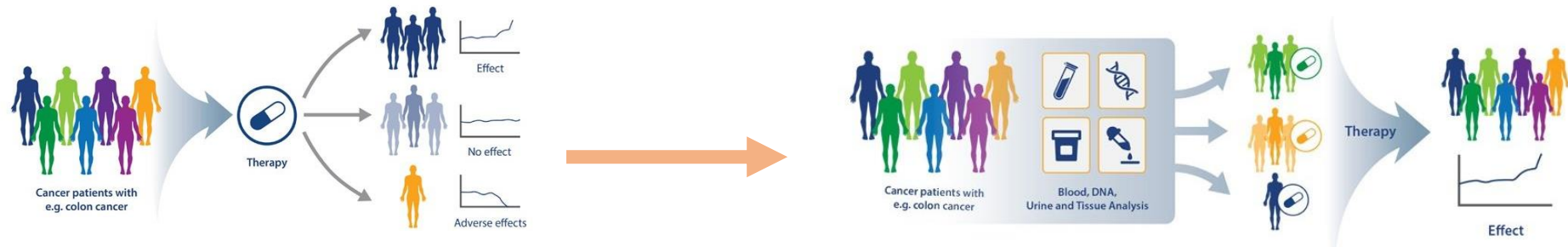
Berlin/Germany
August 24–26, 2023

Carlo Catalano

Background

➤ *Objectives in Oncology and Precision Medicine*

- **Early diagnosis**
- Tumors **molecular profiling**
- Development and implementation of **targeted therapies and prediction of treatment-response**
- **Implementation of patients' compliance and reduction of side effects** related to treatments
- **Primary and secondary prevention (screening programs)**



➤ Imaging repositories

- The **AI4HI** initiative: **5 research projects**, developing digital storage systems for **oncological imaging data**, with specific attention to Artificial Intelligence
- These projects lie on the **Horizon 2020**



EUCAN
IMAGE



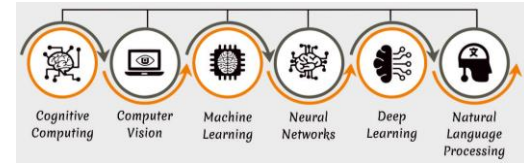
PRIMAGE
Medical imaging
Artificial intelligence
Childhood cancer research

ProCancer-I
EUCAIM

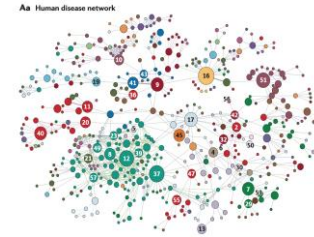


A
INCISIVE

➤ Computational Medicine



- **AI** for analysis and standardization of data acquisition, elaboration/aggregation and interpretation



- **Network analysis** for data integration, recognition of the causes and definition of aggregation clusters with the same characteristics

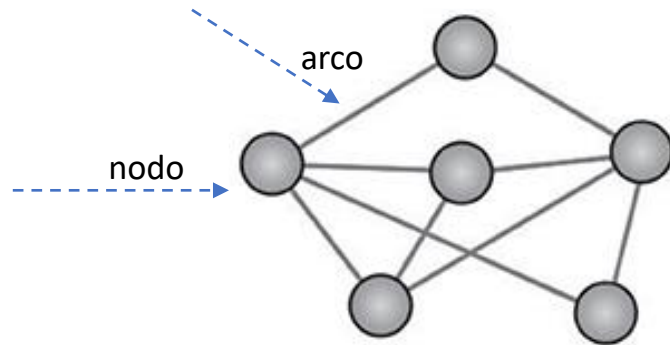
➤ Network Medicine



A new discipline, profoundly different from artificial intelligence, which uses **network sciences** to try to identify the **causes** of diseases by integrating different types of data, from molecular to clinical data and images



A **network** is a set of **nodes** (or vertices) and of **connections** (links, arcs)



➤ Network Medicine

identify **biomarkers** for **complex pathologies** such as in oncology

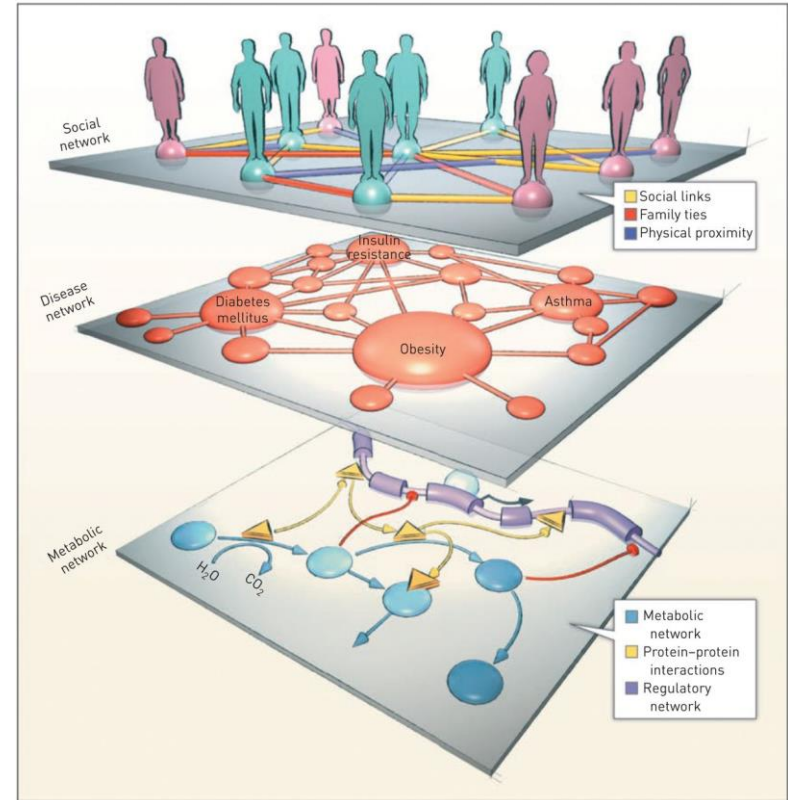
identify new **disease genes**

discover the biological significance of **mutations**

screening

early diagnosis

identify **pharmacological targets**



➤ How does it work?

Leading Edge
Review

Interactome Networks and Human Disease

Marc Vidal,^{1,2,*} Michael E. Cusick,^{1,2} and Albert-László Barabási^{1,3,4,*}

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- Cells can be thought of as complex networks of macromolecular interactions, the totality of which constitutes the **"interactome"**
- Network Analysis addresses complexity by **"simplifying" complex systems**, summarizing them as **components (nodes) and interactions (edges)** between them

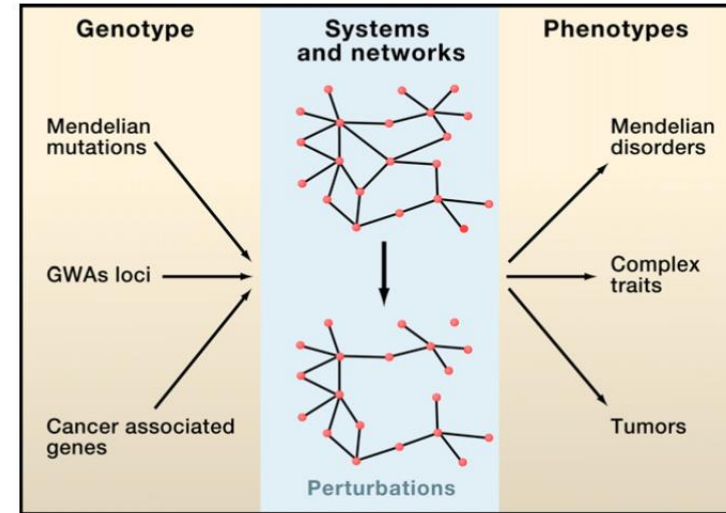
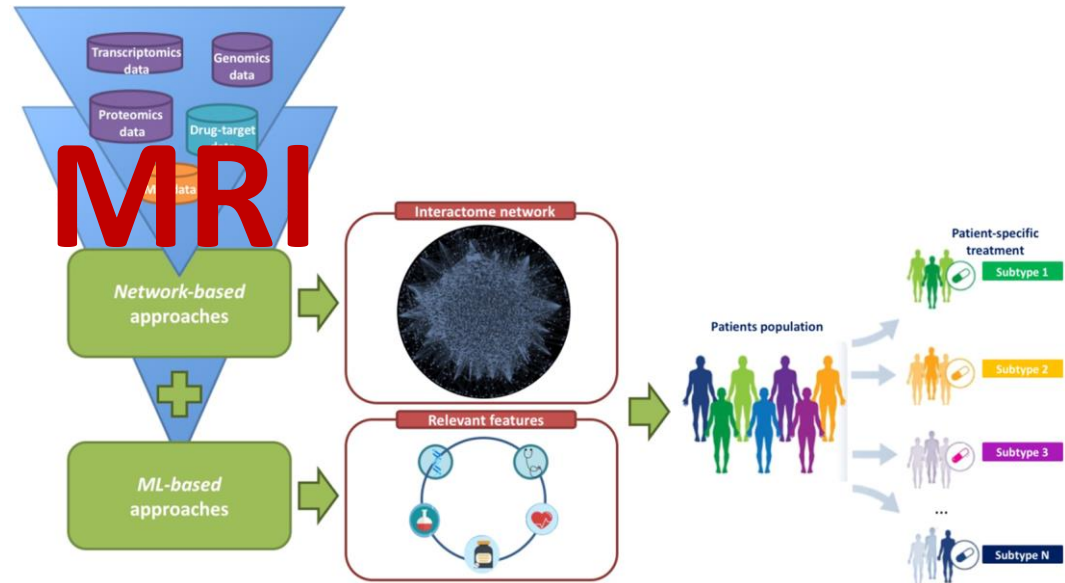


Figure 1. Perturbations in Biological Systems and Cellular Networks May Underlie Genotype-Phenotype Relationships

By interacting with each other, genes and their products form complex cellular networks. The link between perturbations in network and systems properties and phenotypes, such as Mendelian disorders, complex traits, and cancer, might be as important as that between genotypes and phenotypes.

➤ Network Medicine

- genetics
- epigenetics
- transcriptomics
- metabolomics
- proteomics
- **imaging**



Network Analysis



Network Medicine Global Alliance

Representing 31 leading universities
improving global health and advancing

npj | Systems Biology
and Applications

www.nature.com/npsba

COMMENT OPEN

A global network for network medicine

Bradley A. Maron¹, Lucia Altucci², Jean-Luc Balligand³, Jan Baumbach⁴, Peter Ferdinandy⁵, Sebastiano Filetti⁶, Paolo Parini⁷, Enrico Petrillo⁸, Edwin K. Silverman^{1,9}, Albert-László Barabási^{9,10,11}, Joseph Loscalzo^{1,9,12} and International Network Medicine Consortium*

Check for updates

Network Medicine is now an established scientific discipline, having generated key insights on integrated mechanisms underlying complex human diseases. The next discovery phase will emphasize innovating analytics that optimize networks for advancing precision medicine. Accomplishing this goal will require organizing a scientifically diverse team studying big datasets shared globally.

npj Systems Biology and Applications (2020)6:29; <https://doi.org/10.1038/s41540-020-00143-9>



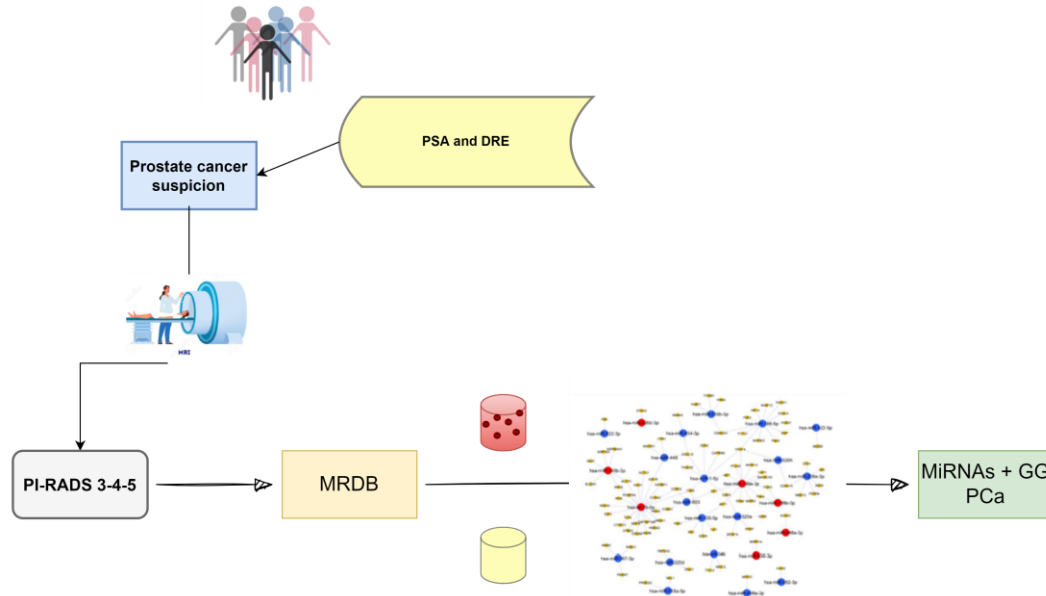
➤ Network Medicine

- ✓ Lung diseases: pulmonary arterial hypertension, asthma e BPCO
- ✓ **Oncology: Breast, Glioblastoma, Lung, Ovary and Prostate**
- ✓ Cardiac diseases: coronary artery disease and hypertrophic cardiomyopathy
- ✓ Neurodegenerative diseases
- ✓ Infectious diseases: COVID-19
- ✓ Diseasome
- ✓ Drugs repositioning
- ✓ Network approaches to rehabilitation

➤ Prostate cancer early detection

Article

Network Analysis Integrating microRNA Expression Profiling with MRI Biomarkers and Clinical Data for Prostate Cancer Early Detection: A Proof of Concept Study



➤ **OBJECTIVE:** To integrate PCa molecular data with imaging biomarkers using Network Analysis

- **M&M:** All patients underwent **MRI** and **MR-directed biopsy**. Expression profiling of **microRNAs** was performed on **total plasma (TP)**, **extracellular vesicles (EV)** and **tissue**

Network Analysis and Clinical Outcomes

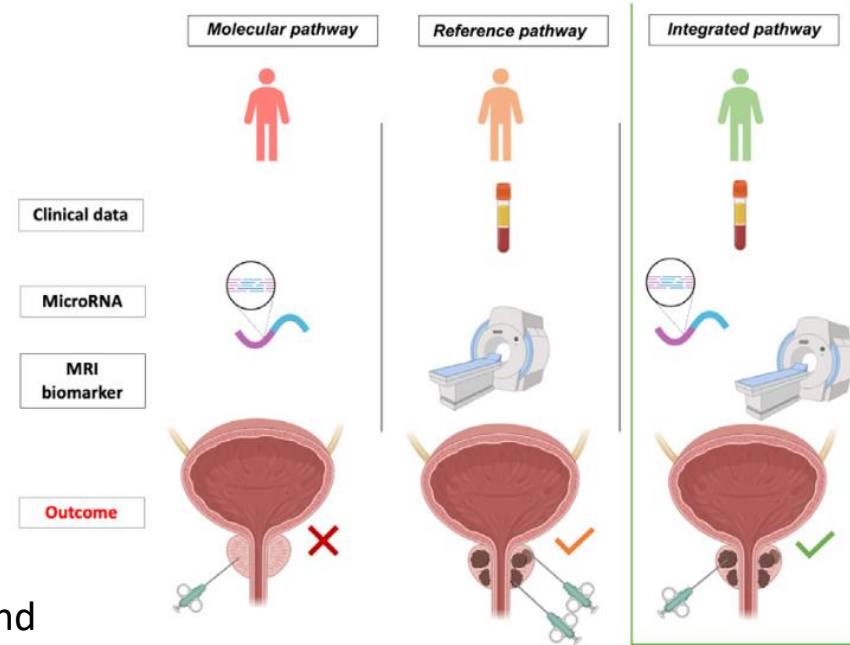
available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com



Prospective Validation Study of a Novel Integrated Pathway Based on Clinical Features, Magnetic Resonance Imaging Biomarkers, and MicroRNAs for Early Detection of Prostate Cancer

Martina Pecoraro^{a,y}, Giuseppina Catanzaro^{b,y}, Federica Conte^c, Zein Mersini Besharat^b, Emanuele Messina^a, Ludovica Laschena^a, Sofia Trocchianesi^d, Elena Splendiani^d, Alessandro Sciarra^e, Carlo Catalano^a, Paola Paci^f, Elisabetta Ferretti^{b,a}, Valeria Panebianco^{a,*}

- Prospective single-center cohort study
- **261 patients:** MRI, MRI-directed fusion biopsy, and circulating microRNAs
- **Network-based analysis:** to identify **MRI biomarkers** and **microRNA drivers** of clinically significant PCa
- **CONCLUSION:** The proposed **integrated pathway** (clinical data, MRI biomarkers, and microRNAs): **best net benefit** with a biopsy avoidance rate of about 20% at a low disease probability



Network Analysis and Clinical Outcomes: Challenges

- **Main challenges to the adoption of computational tools:**
- Cost related issues
- **Design of clinical trials and adequate data**
- Legal and ethical regulations (explainability)
- **Definition of significant benefits on clinical impact**
- Equity

Enterprise maturity



Fear of unknown



Finding a starting point



Vendor strategy



Computational Profile: Digital Twin

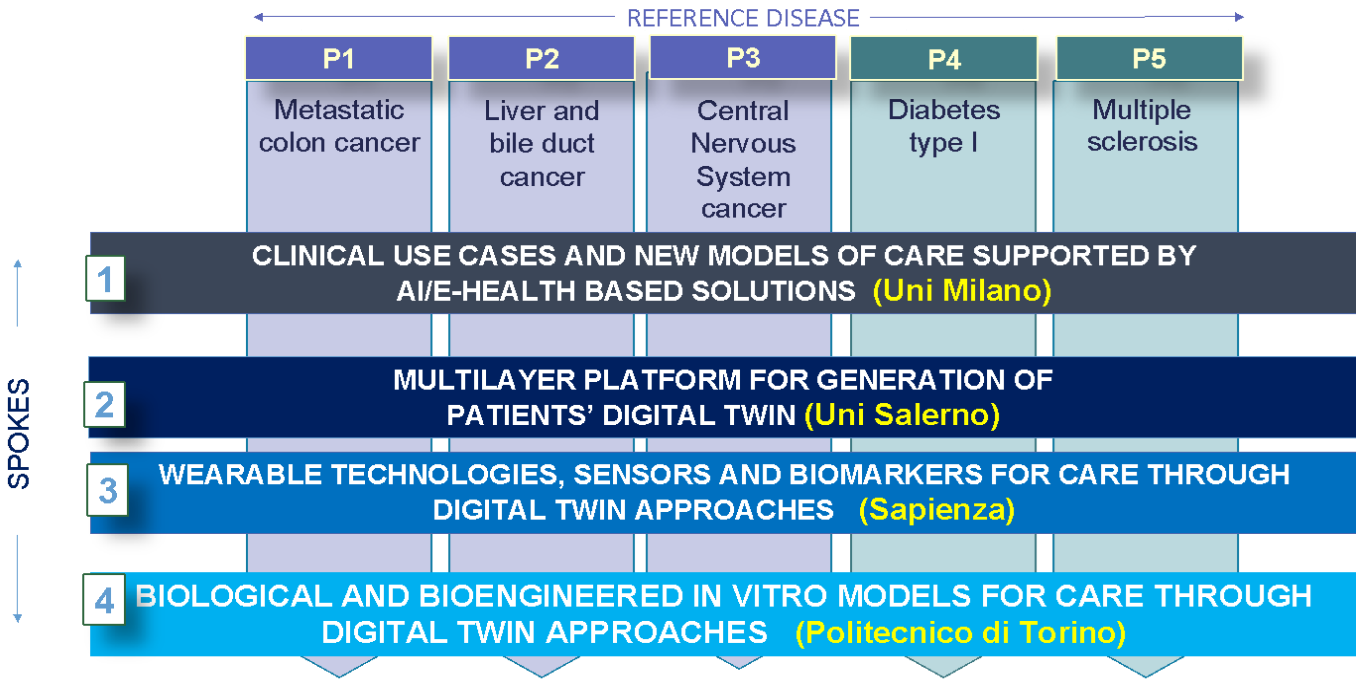
- **Clinical data, laboratory testing, diagnostic imaging, digital pathology, genetics, molecular phenotyping, and omics data can be used and integrated for a better characterization of the population**
- **Mathematical and statistical methods can be employed for the analysis and interpretation of collected biomarkers and for the development of Digital Twins**
- **Digital Twin technologies:**
 - to predict treatment-related complications;
 - to multiscale a personalized pathological model of tumors to test and prescribe optimal therapies;
 - to track the evolution of diseases;
 - to optimize workflows, reduce operational tasks and support decision making



Digital Twin: Outcomes

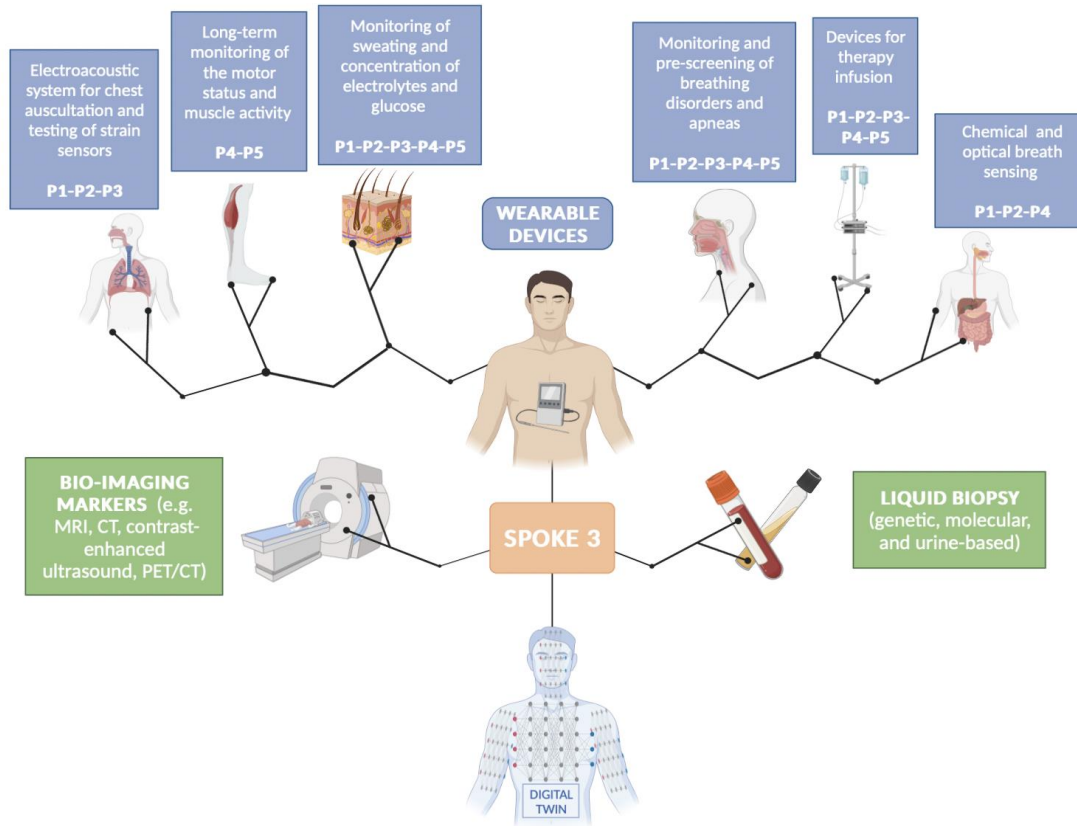
➤ **D³ 4 Health: Digital Driven Diagnostics, prognostics and therapeutics for sustainable Health care (136.5 M€, 28 centers)**

- **HUB – Sapienza**
- **4 SPOKES**
- **5 diseases**



Digital Twin: Techniques

➤ D³ 4 Health: Digital Driven Diagnostics, prognostics and therapeutics for sustainable Health care



- Results of **prospective observational studies** from both **development** and **simulation** tests on the **wearable technologies** and sensing solutions: **new biomarkers**, used to construct and define the **Digital Twin** for each reference pathology

- **New disease-specific biomarkers**
- **> Oncological offer** (from early diagnosis to prevention with screening programmes)
- **Computational profiles** to implement new **diagnosis** and **prevention models**

Digital Twin

