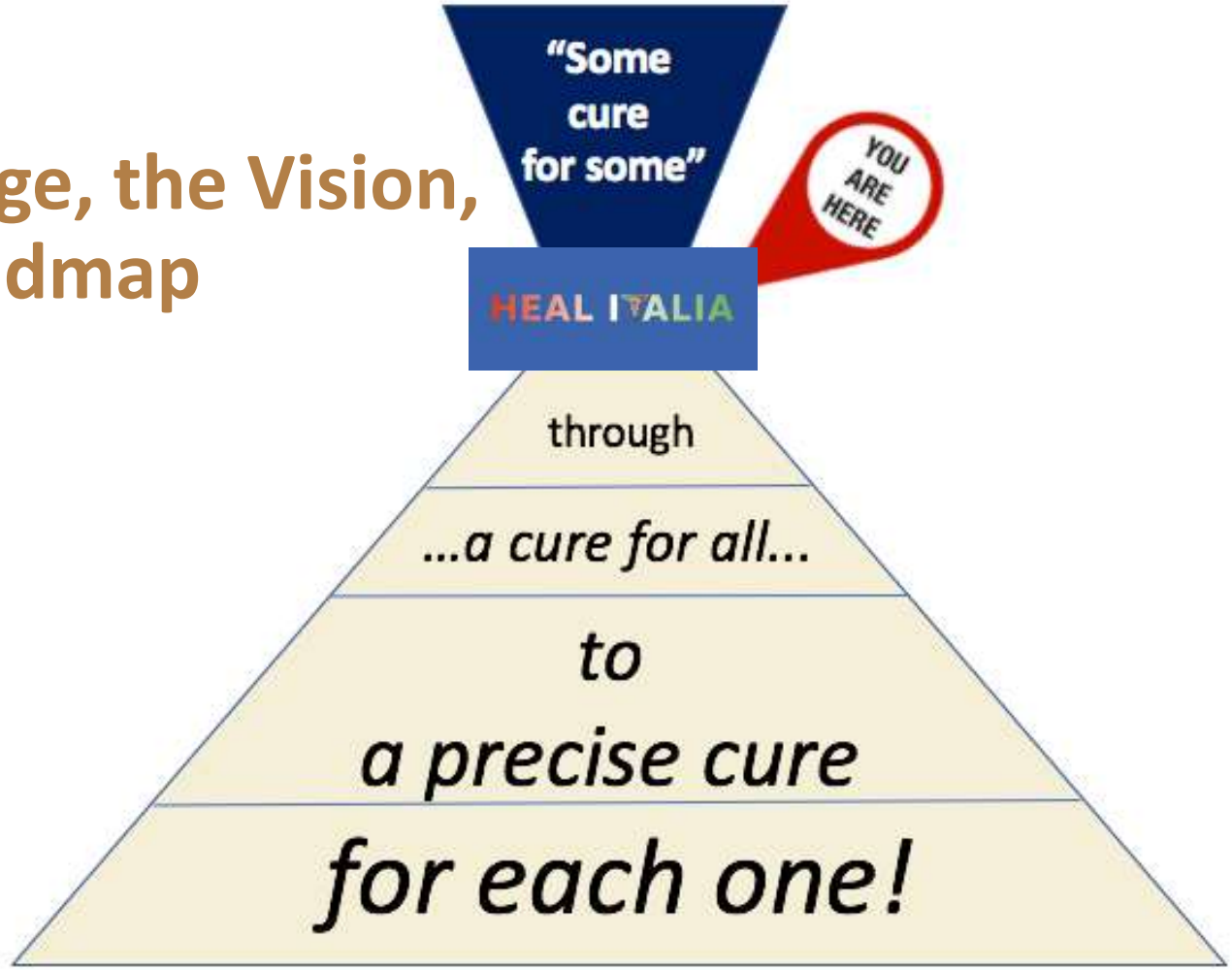
HEAL ITALIA

Health **E**xtended **AL**liance for **I**nnovative **T**herapies, **A**dvanced **L**ab-research, and **I**ntegrated **A**pproaches of Precision Medicine

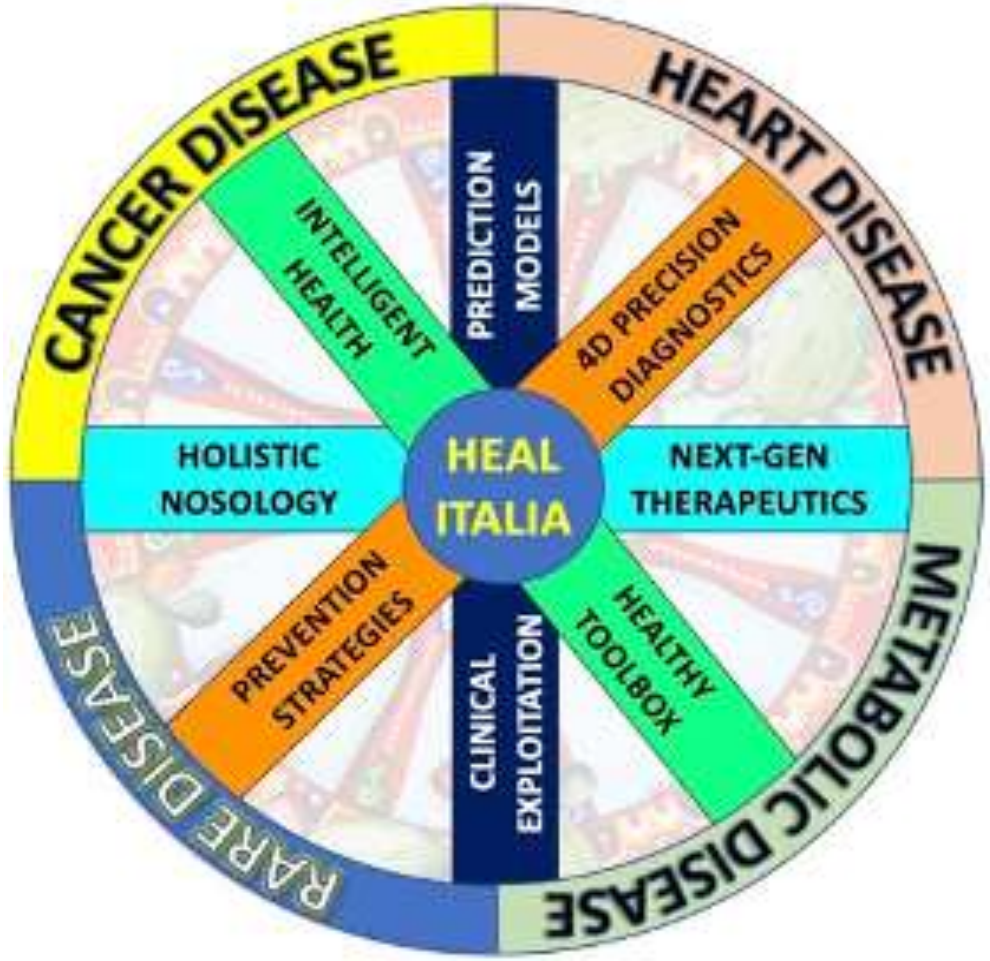
The project started on December 2020

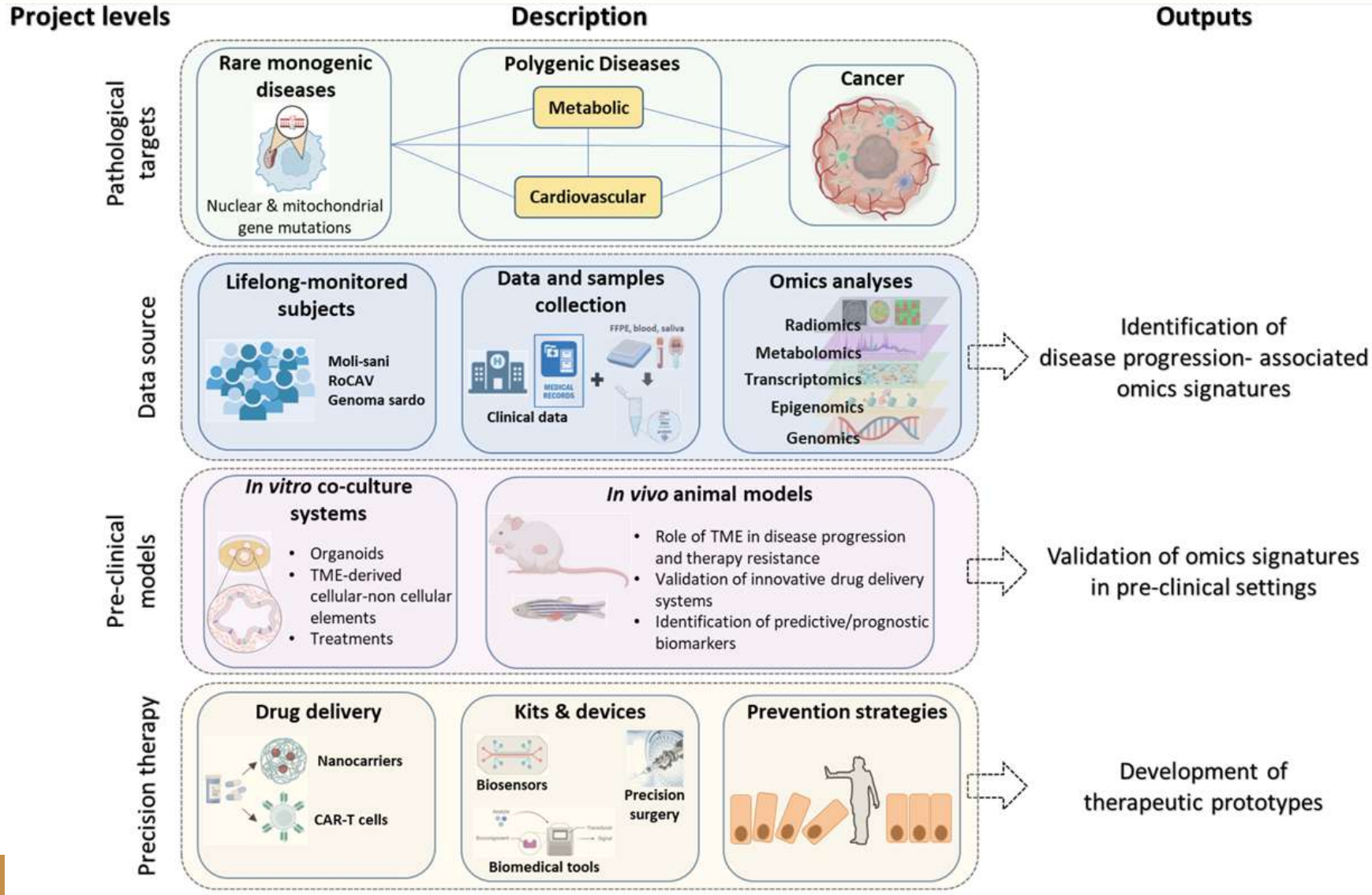
The Challenge, the Vision, and the Roadmap

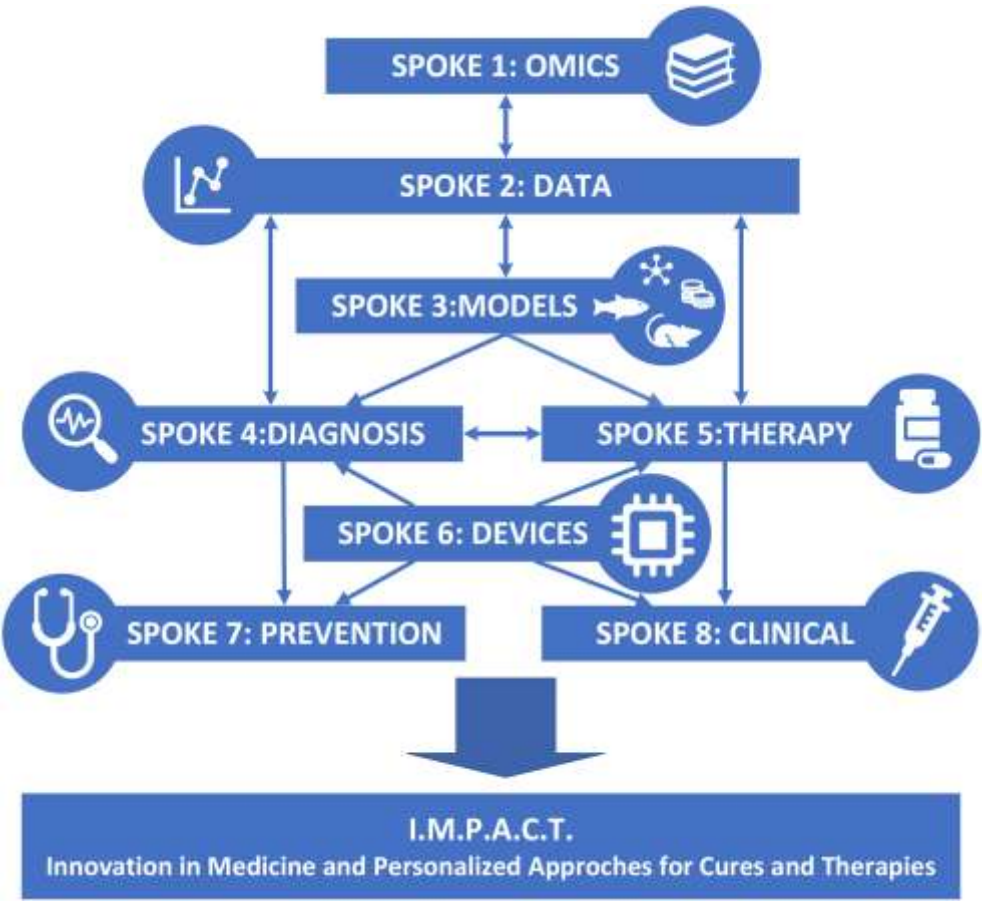


The Challenge, the Vision, and the Roadmap

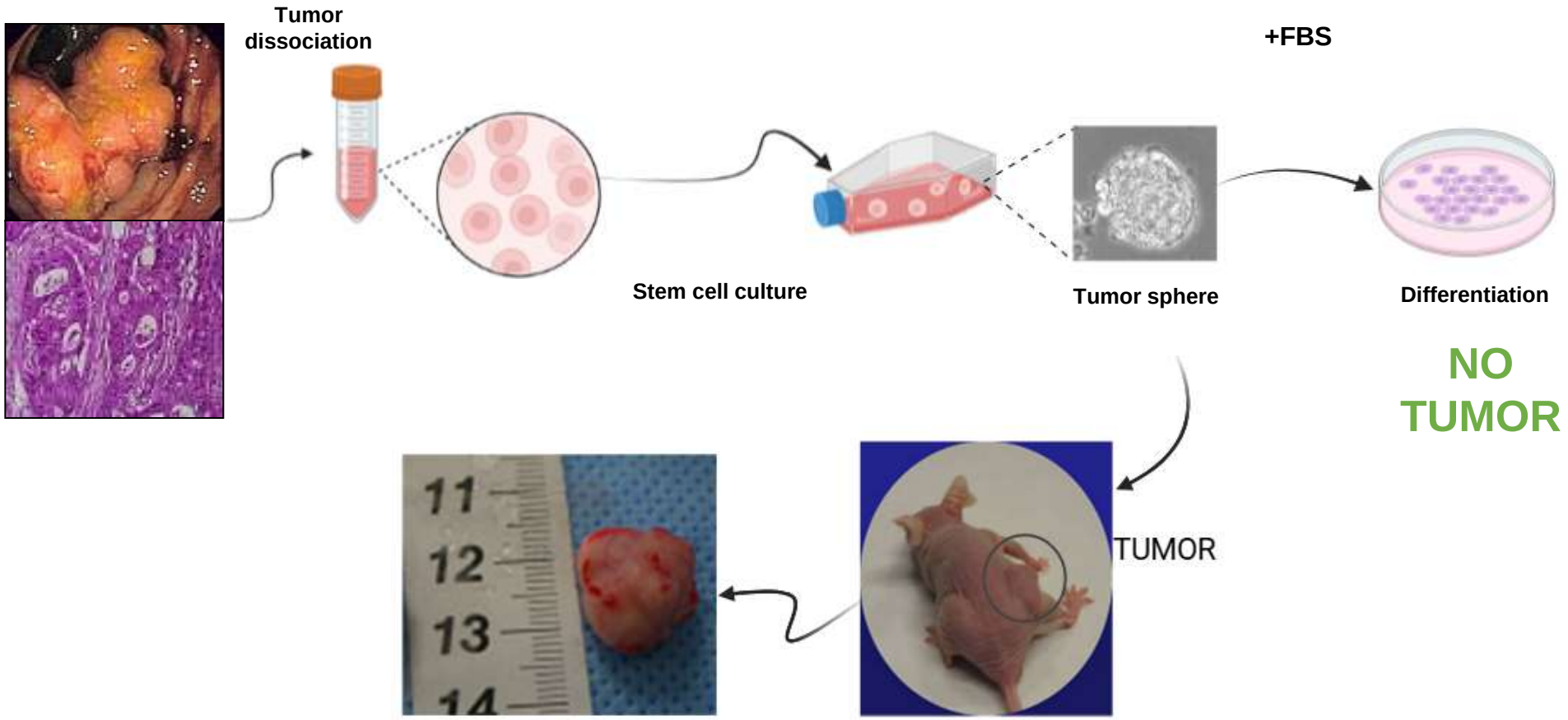
IT'S ALL CONNECTED

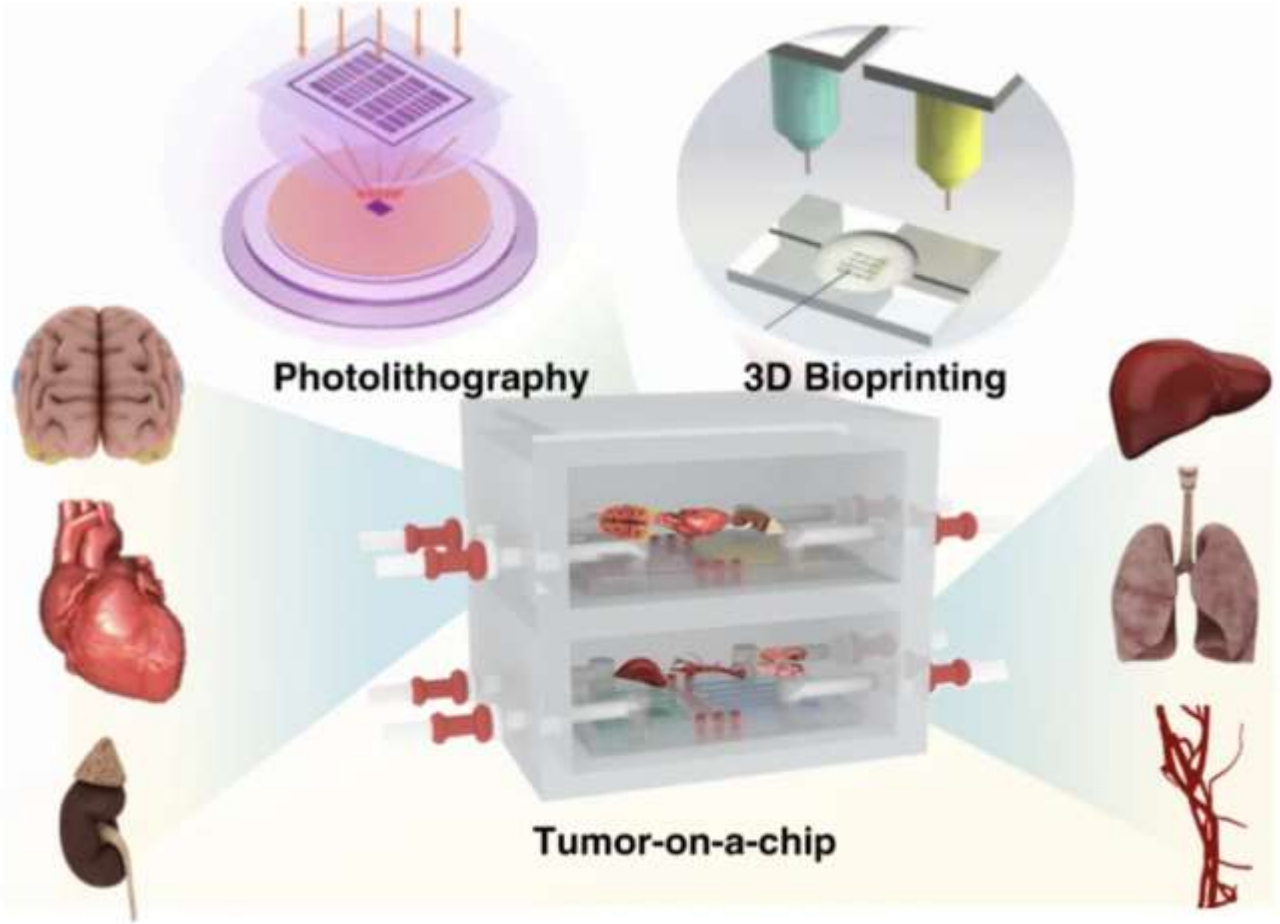



Project levels
Description
Outputs
Pathological targets
Rare monogenic diseases
Nuclear & mitochondrial gene mutations
Polygenic Diseases
Metabolic
Cardiovascular
Cancer
Data source
Lifelong-monitored subjects
Moli-sani
RoCAV
Genoma sardo
Data and samples collection
FFPE, blood, saliva
MEDICAL RECORDS
Clinical data
Omics analyses
Radiomics
Metabolomics
Transcriptomics
Epigenomics
Genomics
Identification of disease progression- associated omics signatures
Pre-clinical models
In vitro co-culture systems
Organoids
TME-derived cellular-non cellular elements
Treatments
In vivo animal models
Role of TME in disease progression and therapy resistance
Validation of innovative drug delivery systems
Identification of predictive/prognostic biomarkers
Validation of omics signatures in pre-clinical settings
Precision therapy
Drug delivery
Nanocarriers
CAR-T cells
Kits & devices
Biosensors
Precision surgery
Biomedical tools
Prevention strategies
Development of therapeutic prototypes

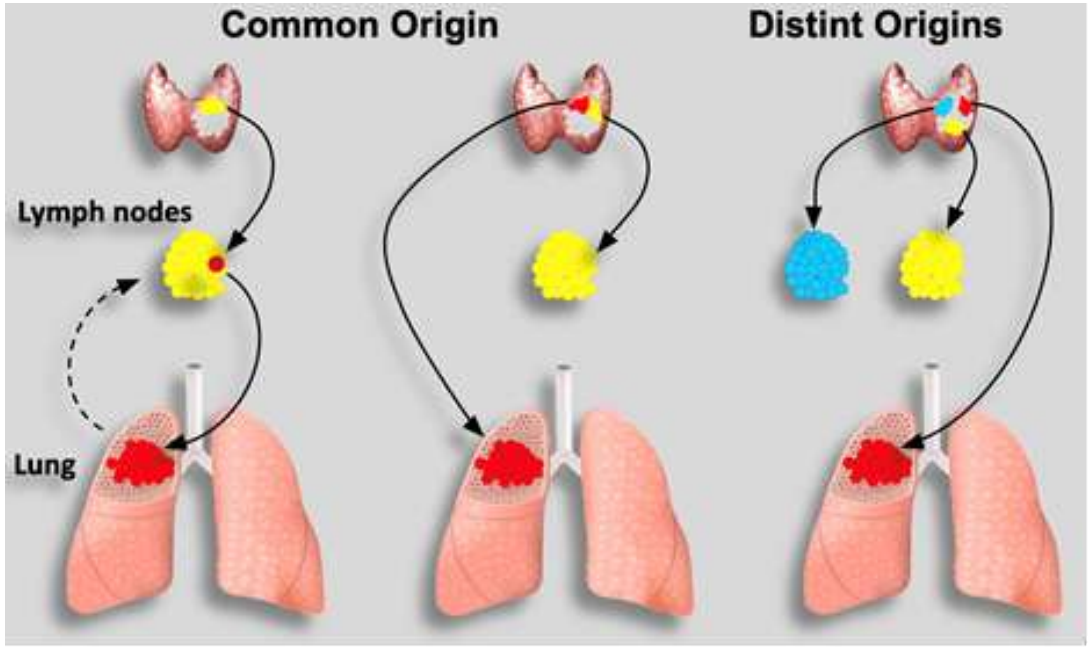


1. **Holistic Nosology.** *From patients to molecules and back;* mapping the omic landscape of clinical to molecular environment, to identify, classify, and refine the phenotypes of multifactorial diseases;
2. **Intelligent Health.** *Health Data Science:* Data management and development of advanced methods, algorithms, and machine learning approaches integrating health big data;
3. **Prediction models:** Advanced prediction models for prognosis and therapeutic response based on comprehensive data treatment;
4. **4D Precision Diagnostics.** Precision medicine integrating clinical and imaging biomarkers for a *"precise in space and time"* diagnosis;
5. **Next-Gen Therapeutics.** *From silico to bedside:* design and validation of innovative tailored and personalized therapeutic strategies;
6. **Healthy Toolbox:** Development of innovative devices for precision diagnosis and personalized therapy;
7. **Prevention Strategies:** Integrated and gender medicine approaches for prevention strategies based on environmental, lifestyle and clinical biometric data;
8. **Clinical Exploitation:** Clinical validation and implementation of innovative predictive, preventive, diagnostic and therapeutic precision medicine approaches, based on established or emerging molecular and clinical phenotyping and AI-driven decision-making protocols.


Tumor dissociation
+FBS
Stem cell culture
Tumor sphere
Differentiation
NO TUMOR
TUMOR
11
12
13
14


Photolithography
3D Bioprinting
Tumor-on-a-chip

Understanding the evolution and clonal dynamics of TC metastatic cells, identifying the molecular mechanism underlying TC progression



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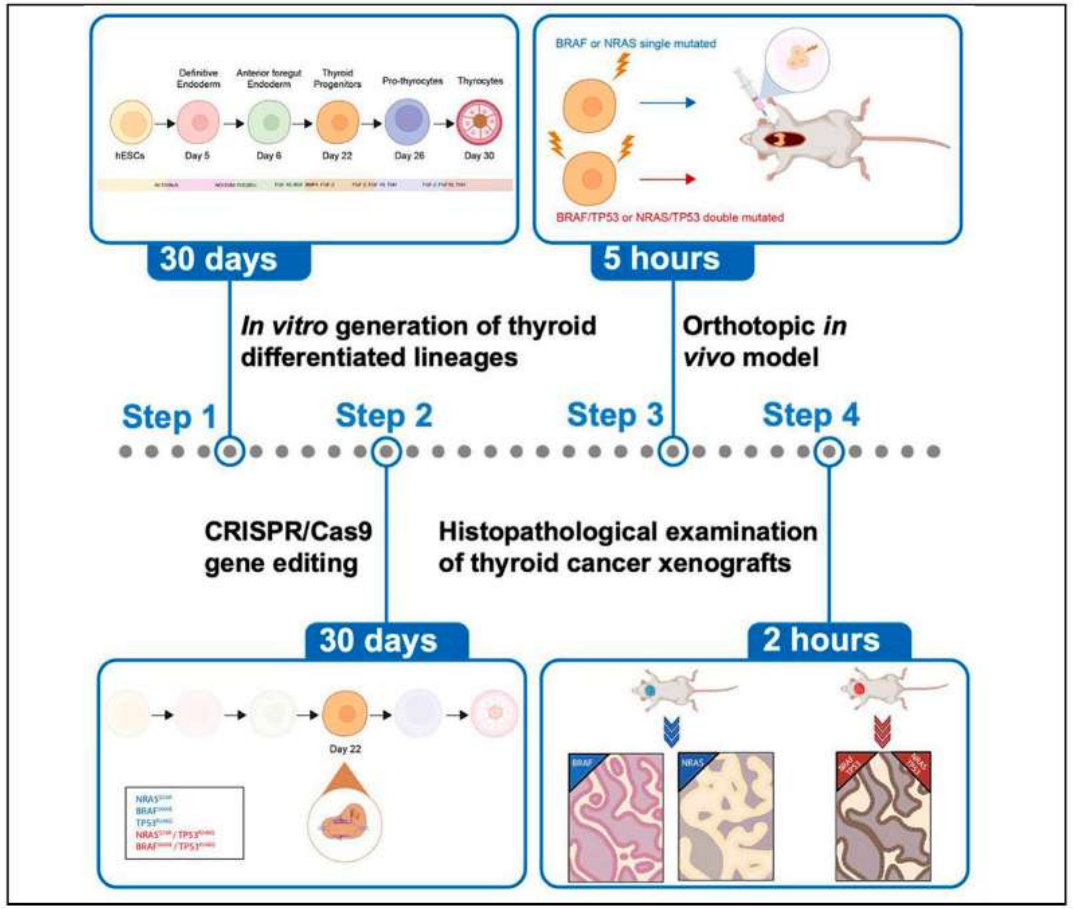
Generation of Thyroid Carcinoma Model



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Recapitulating thyroid cancer histotypes through engineering embryonic stem cells

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Veronica Veschi[1,9], Alice Turdo[2,9], Chiara Modica[1,9], Francesco Verona[2], Simone Di Franco[1], Miriam Gaggianesi[1], Elena Tirrò[1,3], Sebastiano Di Bella[2], Melania Lo Iacono[2], Vincenzo Davide Pantina[1], Gaetana Porcelli[2], Laura Rosa Mangiapane[2], Paola Bianca[2], Aroldo Rizzo[4], Elisabetta Sciacca[5], Irene Pillitteri[2], Veronica Vella[6], Antonino Belfiore[6], Maria Rita Bongiorno[2], Giuseppe Pistone[2], Lorenzo Memeo[7], Lorenzo Colarossi[7], Dario Giuffrida[7], Cristina Colarossi[7], Paolo Vigneri[3], Matilde Todaro[2,8] & Giorgio Stassi[1]

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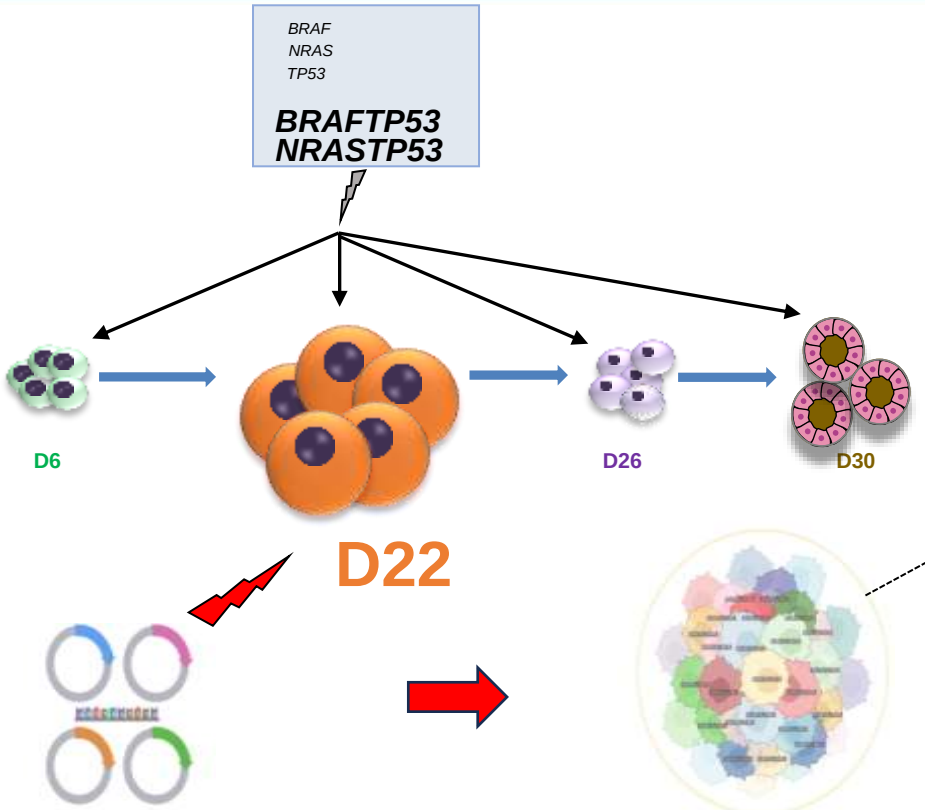
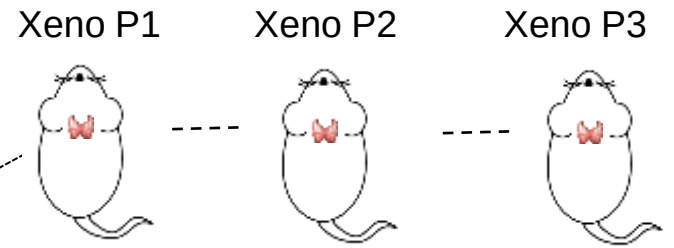
Generation of Thyroid Carcinoma Promotion and Progression model

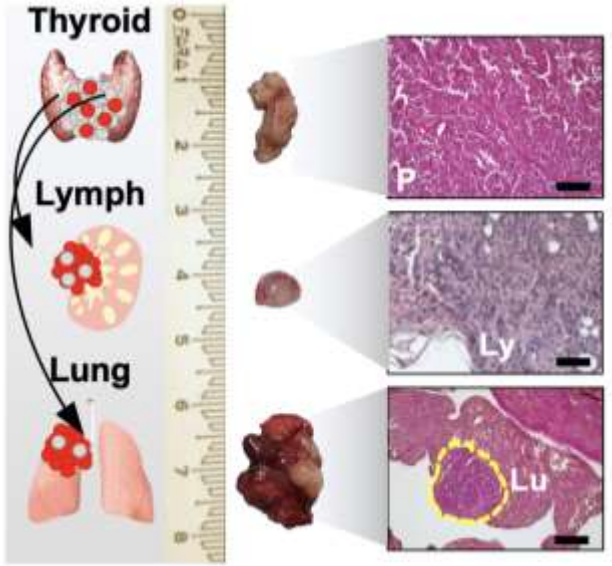
Analysis of Thyroid Carcinoma Clonal Evolution and Identification of Metastatic Thyroid Cancer Cells



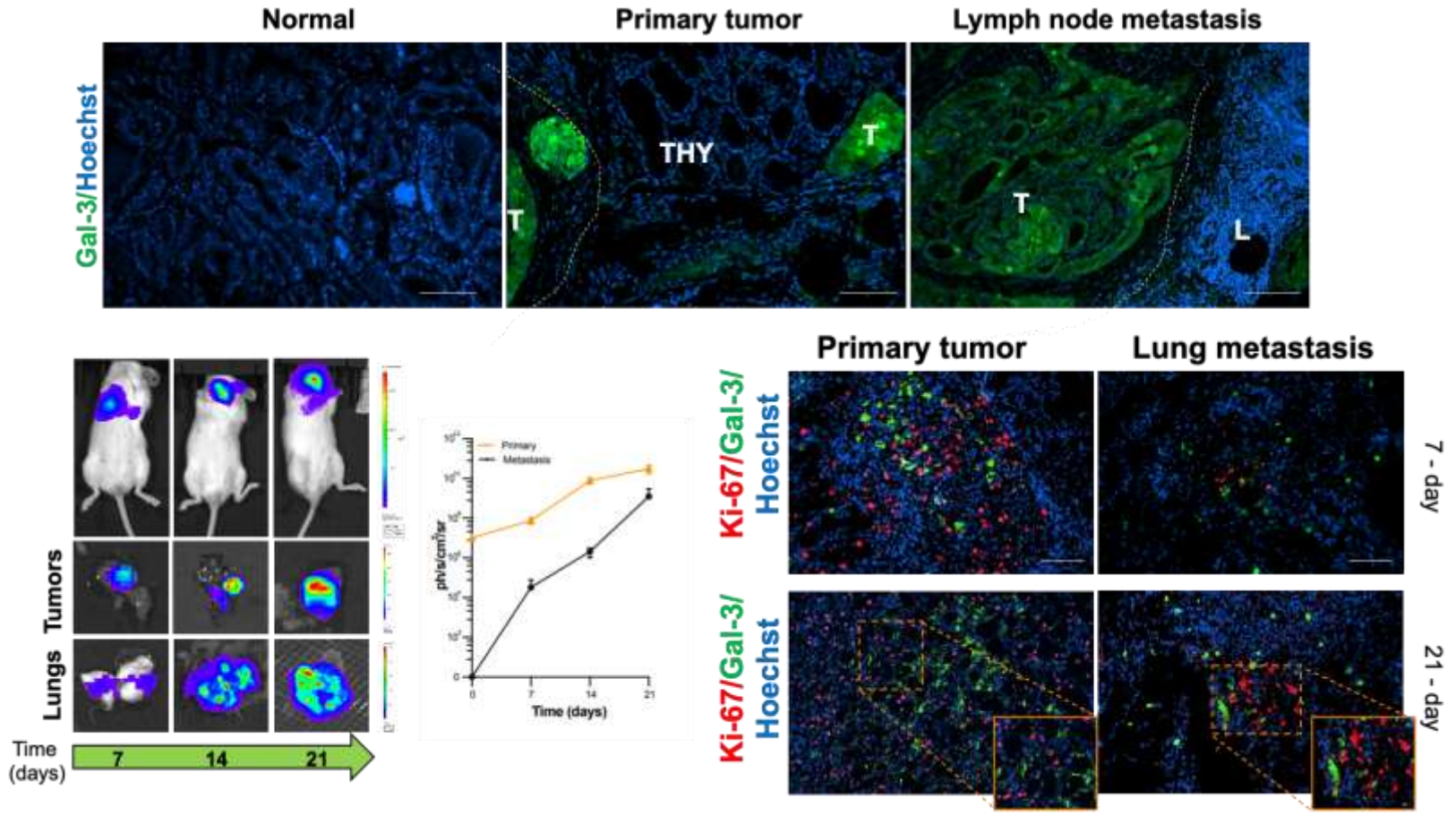
Library 50M of unique BARCODE sequences

BRAFTP53 or NRASTP53 Barcoded TPCs (starting population)





Gal-3 marks metastatic TC cells



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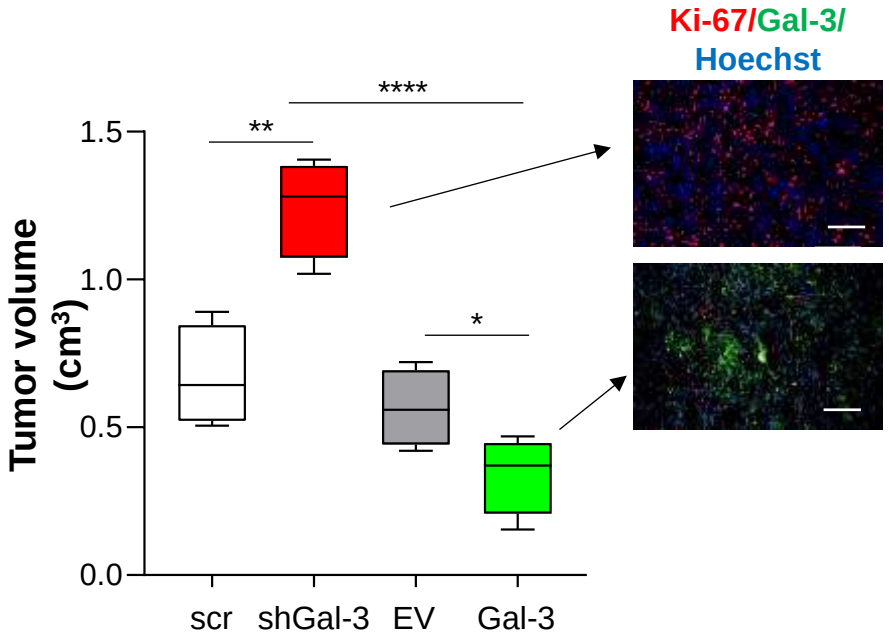
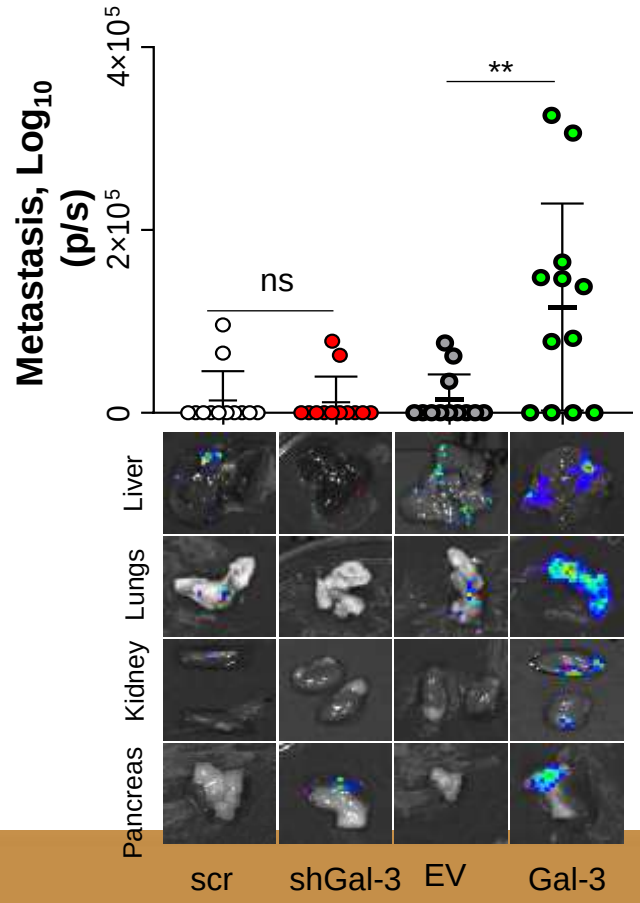
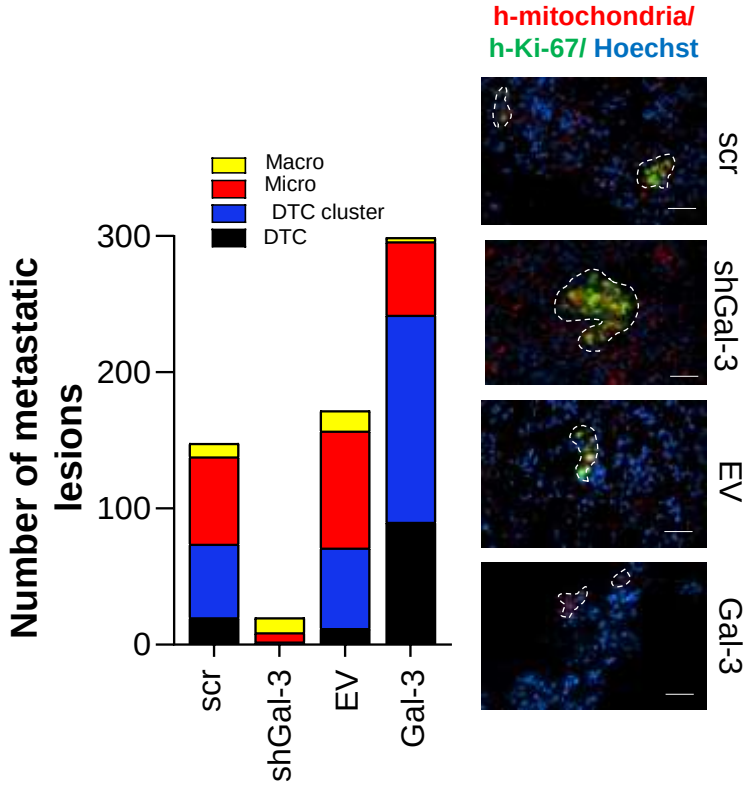
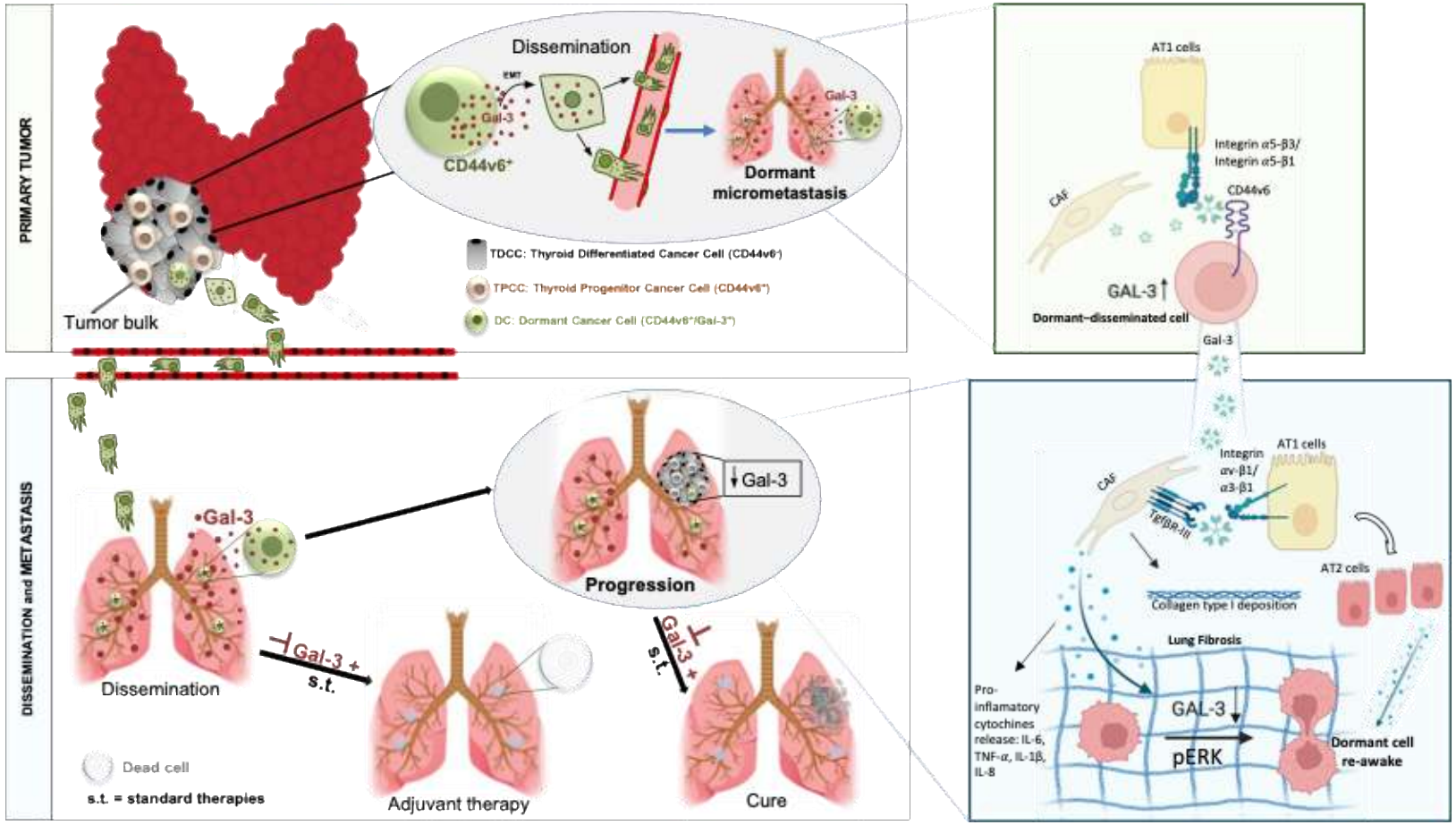
Dormant cancer cells expressing Gal-3 give rise to low-proliferating micrometastases

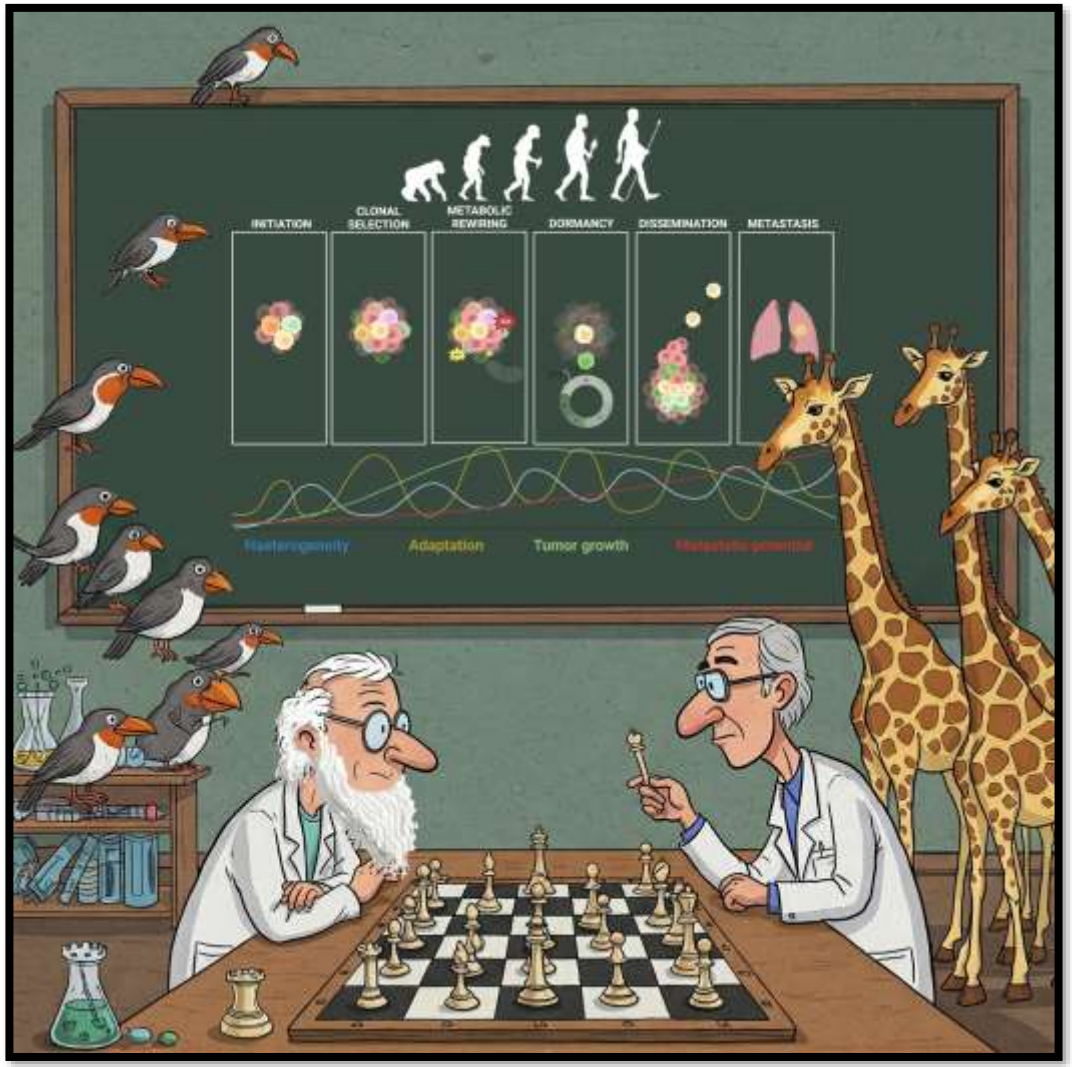




Dormant cancer cells expressing Gal-3 give rise to low-proliferating micrometastasis




PRIMARY TUMOR
Dissemination
EMT
Gal-3
CD44v6+
Gal-3
Dormant micrometastasis
Tumor bulk
TDCC: Thyroid Differentiated Cancer Cell (CD44v6-)
TPCC: Thyroid Progenitor Cancer Cell (CD44v6+)
DC: Dormant Cancer Cell (CD44v6+/Gal-3+)
DISSEMINATION and METASTASIS
•Gal-3
Dissemination
⊣Gal-3 +
s.t.
↓Gal-3
Progression
⊣Gal-3 +
s.t.
Dead cell
s.t. = standard therapies
Adjuvant therapy
Cure
AT1 cells
Integrin α5-β3/
Integrin α5-β1
CD44v6
CAF
GAL-3↑
Dormant–disseminated cell
Gal-3
AT1 cells
Integrin
αv-β1/
α3-β1
CAF
TGFβR-III
AT2 cells
Collagen type I deposition
Lung Fibrosis
Pro-
inflamatory
cytochines
release: IL-6,
TNF-α, IL-1β,
IL-8
GAL-3
pERK
Dormant cell
re-awake


INITIATION
CLONAL SELECTION
METABOLIC REWIRING
DORMANCY
DISSEMINATION
METASTASIS
Heterogeneity
Adaptation
Tumor growth

Route to Precise & Personalized Cure

New & More Precise Diagnostic Methods

Clinical & Environmental Data

New A.I.-based Data Treatment

Holistic Etiology & New correlations

New & Effective Prevention Strategies

New & Reliable Prediction Models

New Technologies, Kits & Devices

Personalized Precision Medicine

The HEAL Italia project exemplifies how the whole can indeed be greater than the sum of its parts, not only in terms of organizational structure but also in amplifying research impact.

New Networks and Collaborations: The cascading funding model has enabled partnerships with external entities, fostering innovation through Proof-of-Concept projects.

Implementation of Advanced Technologies: Sharing computational tools have standardized data analysis across SPOKEs, enabling large-scale genomic studies and enhancing translational research.