Biomarkers and diagnostics in paediatric research

Bridging Translational Science and Clinical Development

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Responsabile Clinical Trials Quality Team
Centro Studi Clinici Sviluppo Farmaci Pediatrici
Rete Incipit



TEDDY General Assembly and Scientific Meeting
18 – 20 September 2026, Bari, Italy

19 Settembre 2026

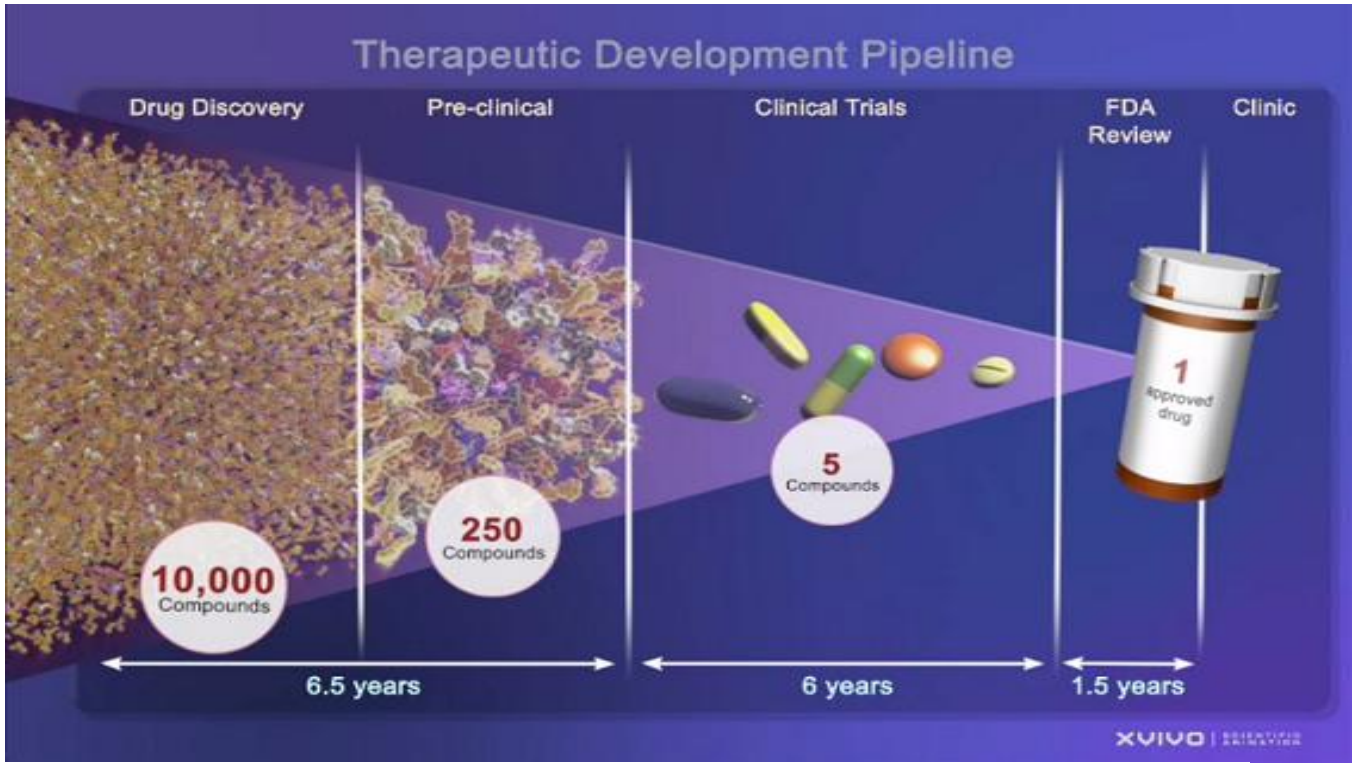
Clinical Research at OPBG

- The main Pediatric Hospital in Italy
- One of the main European Research Hospital in Europe
- A Large Research Area with laboratories for traslational research
- Clinical Trial Centre, more than 400 studies and 1000 patients followed (2010)
- Phase I Site (MD Alessandra Simonetti)
- Centre for Clinical Studies and Pediatric Drug Development
- Clinical Trial Quality Team for no profit studies (2022)

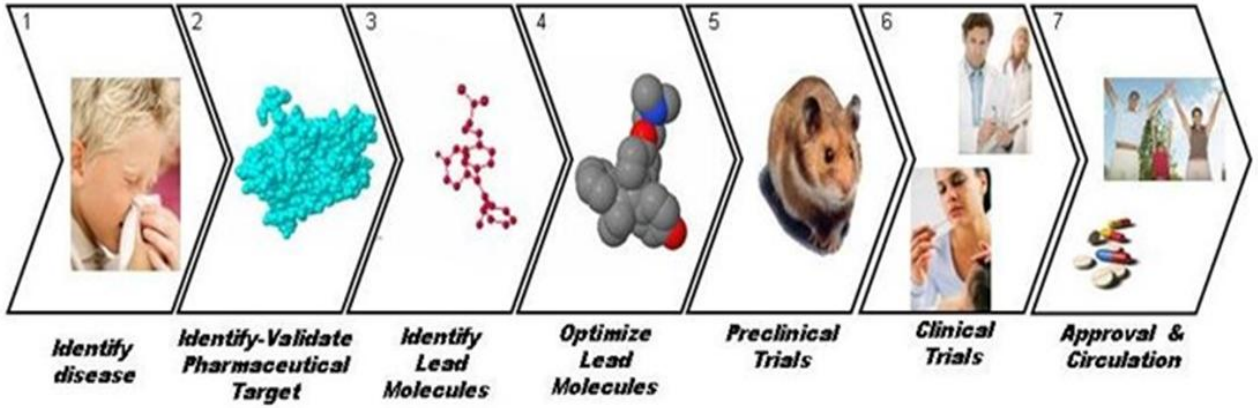







Therapeutic Development Pipeline
Drug Discovery
Pre-clinical
Clinical Trials
FDA Review
Clinic
10,000 Compounds
250 Compounds
5 Compounds
1 approved drug
6.5 years
6 years
1.5 years
XVIVO

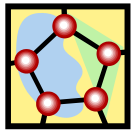



1
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7
Identify disease
Identify-Validate Pharmaceutical Target
Identify Lead Molecules
Optimize Lead Molecules
Preclinical Trials
Clinical Trials
Approval & Circulation

Drug development

PRE-CLINICAL STUDIES
5-6 Years

Compound selection
(bioinformatics, biochemistry)
n.10.000





250
Cell colture (*in vitro*)
Animal studies (*in vivo*)

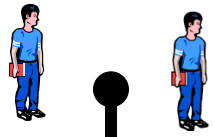
Request of clinical trial authorization



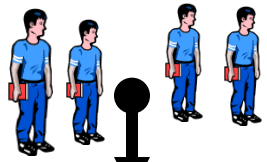
5

CLINICAL STUDIES
5-7 years

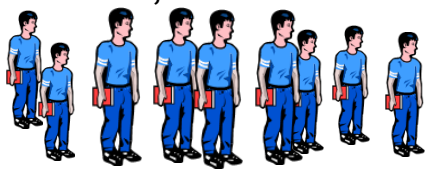
Phase I
Safety and PK
(healthy and patients, ~20-80)
n.5



Phase II
Safety, Efficacy,
Hypothesis generation
(patients, ~100-200)



Phase III Controlled,
Confirmative
(patients, ~1000-3000)

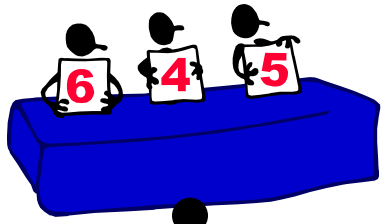


Registration
1-2 years

Marketing Authorization Request



Regulatory evaluation
(FDA, EMA)

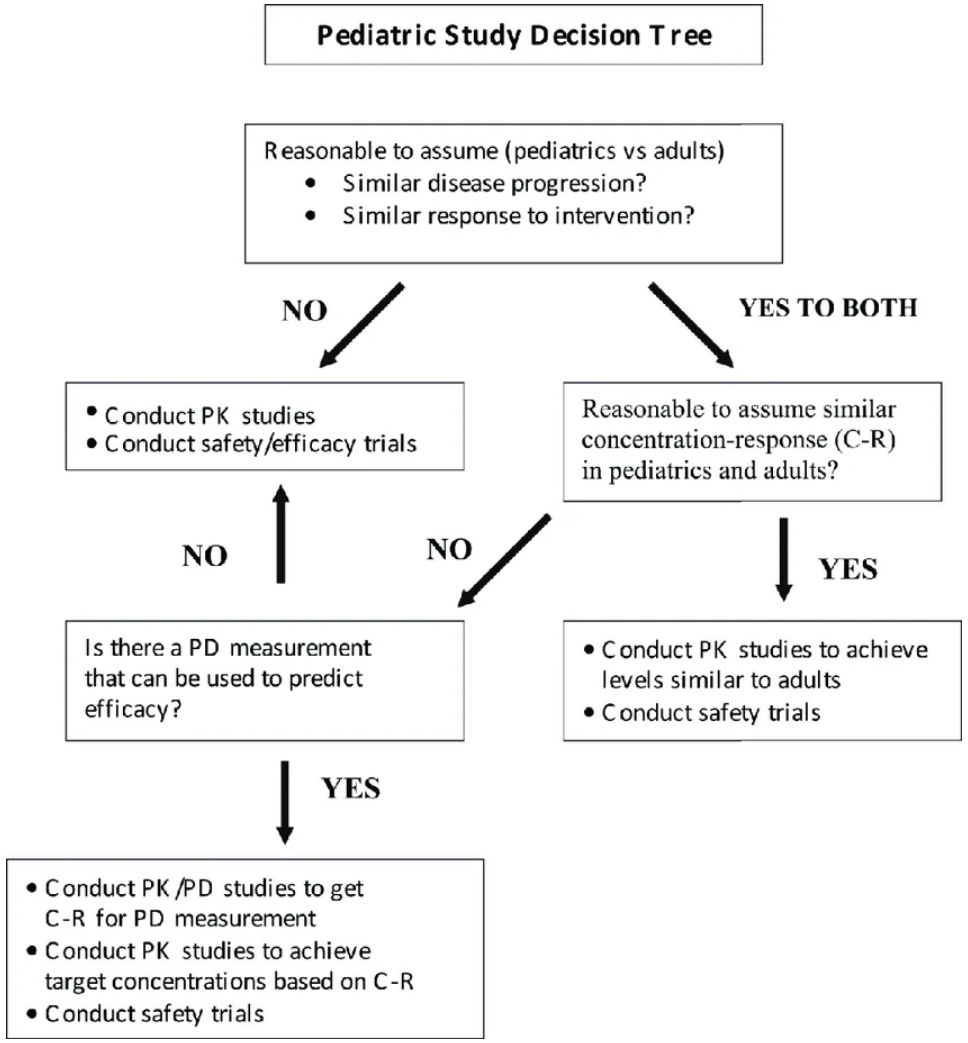




n.1

Market
Rembursement

Pediatric Studies Decision Tree



Definition of Biomarker

A characteristic that is objectively measured and evaluated as an indicator of normal biologic or pathogenic processes, clinical outcome or pharmacological responses to a therapeutic intervention

Diagnostic

Used for diagnosis, monitoring, or stratified sampling in trials

Prognostic

Allows the selection of patients regardless of the treatment received

Predictive

Identify patients most likely to benefit from a specific treatment

Companion diagnostic: test associated with the safe and effective use of a specific medicinal product, with a separate but coordinated regulatory assessment

Surrogate Endpoint

A biomarker intended to substitute for a clinical endpoint.

A surrogate endpoint is expected to predict clinical benefit (or harm, or lack of benefit or harm) based on epidemiological, therapeutical, pathophysiological or other scientific evidence.

Examples:

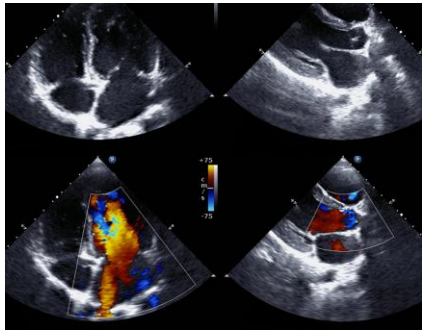
- Blood Pressure (Cardiovascular events, response to anti-hypertensives)
- HIV-RNA (Viral replication, response to antiretrovirals)

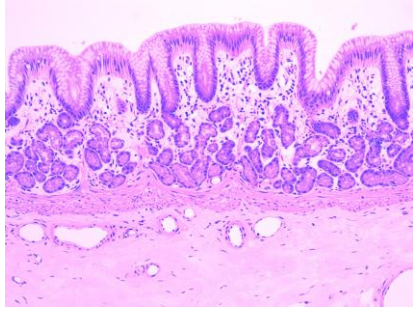
Classification

- Genetic
- Biochemical
    - PK, CD4+, Creatinine, eCRF, ALT, AST
- Anatomical /Radiological
  - Tumor Size, Myocardial volume
- Histological
  - Biopsy
- Symptoms/Signs
  - BP, Exercise HR, Hospitalisation, ,

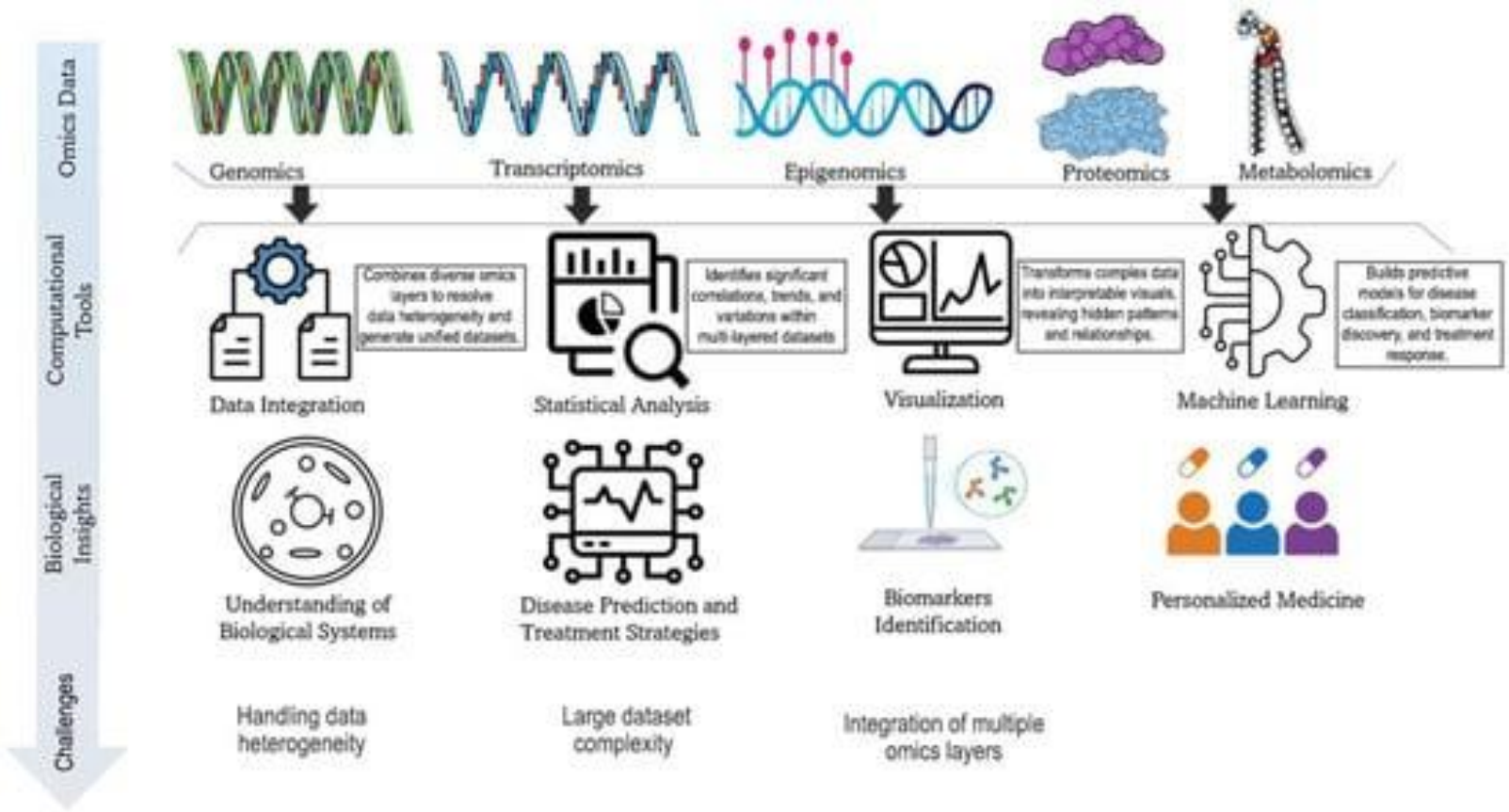
  Questionnaires (es PHQ-9, PedsQoL)











By integrating data from genomics, transcriptomics, proteomics, metabolomics, and other omics layers,
these platforms allow for a more systemic view of biological processes, thereby facilitating the identification of biomarkers, drug targets, and pathways that would otherwise remain hidden in single-omics analysis. Papadaki et al, 2025

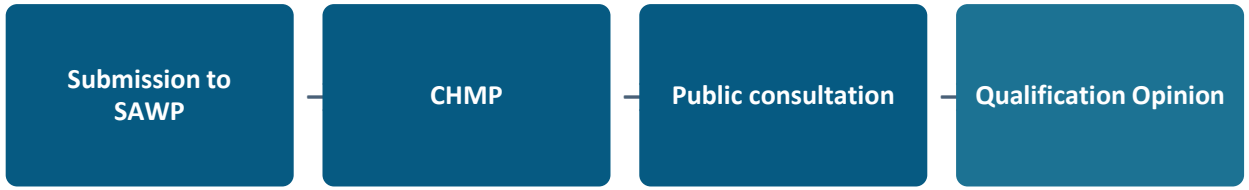
The Validation and Qualification Gap

1. Analytical Validation
Does the assay measure the biomarker accurately and reliably?

2. Clinical Validation
Is the biomarker associated with disease biology or clinical outcomes?

3. Clinical Utility
Does the biomarker improve clinical or development decisions?

Many promising biomarkers fail to progress from scientific discovery to demonstrated clinical utility.




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Innovative research methodologies in the EU regulatory framework: an analysis of EMA qualification procedures from a pediatric perspective

Viviana Giannuzzi[1]*, Arianna Bertolani[2,3], Silvia Torretta[3], Giorgio Reggiardo[2], Eleonora Toich[2], Donato Bonifazi[2,3] and Adriana Ceci[1,3] on behalf of the European Paediatric Translational Research Infrastructure (EPTRI)

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Why Biomarkers Matter in Pediatric Research

Scientific Challenges

- Dynamic physiology across developmental stages
- Age-dependent biological variation
- Limited pediatric reference ranges



Methodological Challenges

- Rare and ultra rare diseases
- Small sample sizes
- Recruitment difficulties
- Need for international multicenter studies

Operational Challenges

- Limited access to biospecimens
- Sample volume limitations
- Standardization and quality control



Regulatory Challenges

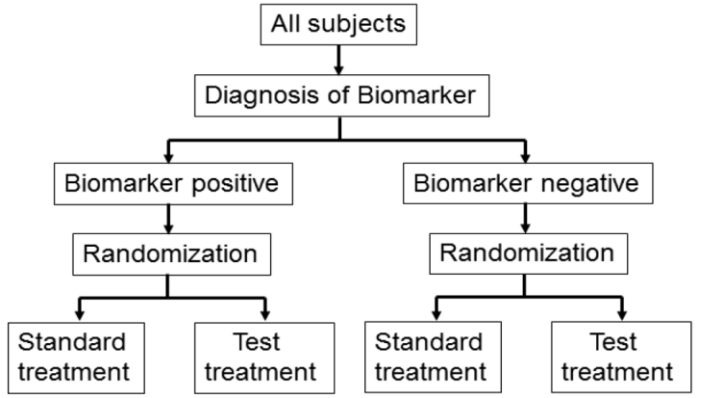
- Limited qualification of pediatric biomarkers
- Need for sensitive and early endpoints
- Lack of pediatric-specific evidence

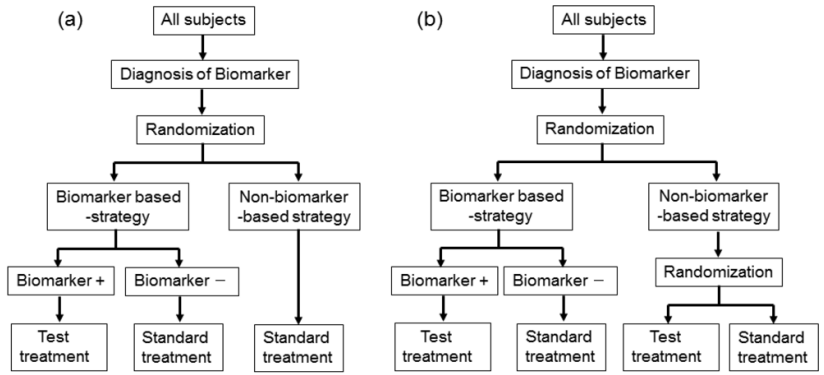
Pediatric biomarkers cannot always be extrapolated from adult populations.

The Value of Biomarkers Across Drug Development

Where Biomarkers Add Value

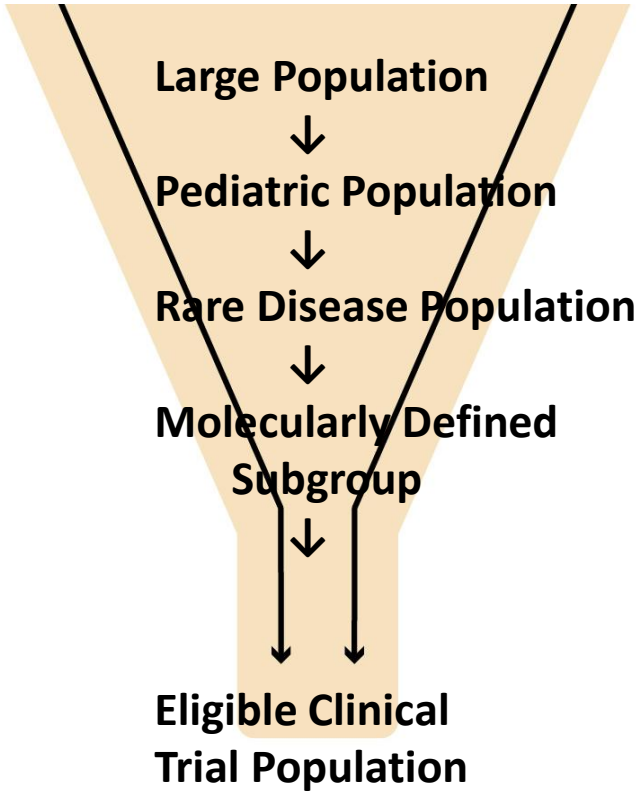
Disease Understanding
↓
Target Identification
↓
Biomarker Discovery
↓
Patient Stratification
↓
Clinical Trial Design
↓
Regulatory Decision-Making
↓
Clinical Implementation





Biomarkers reduce uncertainty, improve efficiency, and increase the probability of clinical success.

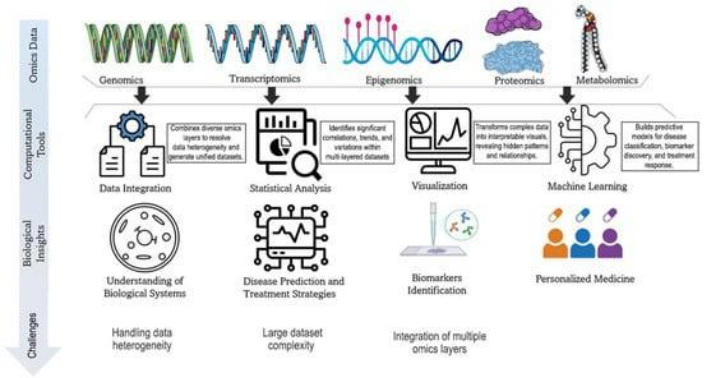
The Rare Disease Funnel Challenge



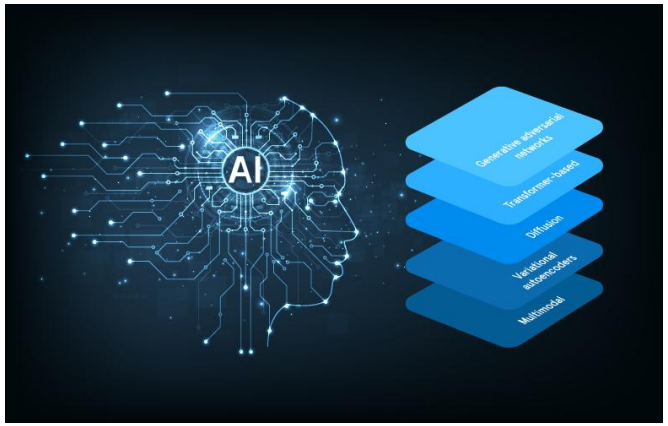
Technological Advances

- Next-generation sequencing (NGS)
- Multi-omics approaches
- Advanced molecular diagnostics
- Digital biomarkers
- Imaging biomarkers
- Real-world data integration
- AI-assisted data interpretation

- Patient engagement









The convergence of advanced diagnostics, data science, and translational research can transform pediatric drug development.

Building the Infrastructure for Biomarker and Clinical Pediatric Research

Key Enablers

- Biobanks
- Genomic platforms
- Integrated clinical-data ecosystems
- National and international collaborative networks
- Accredited laboratory facilities

European Reference Networks

TEDDY

ePTRI
European Paediatric Translational Research Infrastructure

BBMRI.it
Biobanking and BioMolecular Resources Research Infrastructure of Italy

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

INCiPiT
Italian Network for Paediatric Clinical Trials

Successful biomarker development requires an ecosystem, not a single technology.

AiC Associazione Italiana Celiachia

Circulating miRNAs as potential early predictors of T1D onset in celiac disease patients

OPEN

ANDREA MASOTTI, BAMBINO GESÙ CHILDREN'S HOSPITAL-IRCCS, ROME, ITALY

Fellowship Calls

2019

This project aims to discover circulating microRNAs (miRNAs) in diabetic patients with celiac disease, to identify early predictors of diabetes in celiac patients. Celiac disease and diabetes share common autoimmune mechanisms and genetic predispositions, which suggests a potential overlap in their pathogenesis. Circulating miRNAs are small, stable, and easily detectable in blood, making them ideal candidates for non-invasive biomarkers. By profiling miRNAs in this specific cohort, we will identify unique miRNA signatures that correlate with the early stages of diabetes, allowing a timely intervention, reducing the risk of fatal events of ketoacidosis and/or permanent ilnesses, thus improving patient outcomes.

Case Study: Spinal Muscular Atrophy (SMA)

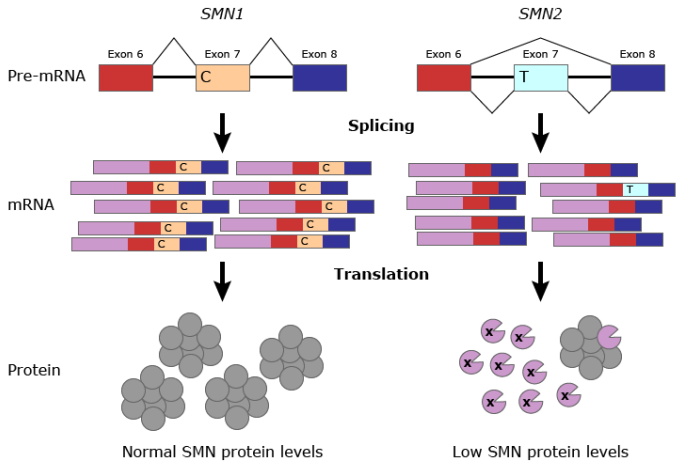
SMA represents one of the most successful examples of how biomarkers and diagnostics can drive therapeutic innovation.

The Journey

Genetic Discovery (SMN1 mutation)
↓
Molecular Diagnostic Testing
↓
Biomarker Development
↓
Newborn Screening Programs
↓
Earlier Patient Identification
↓
Targeted Therapies
↓
Improved Long-Term Outcomes

Impact

- Earlier diagnosis
- Pre-symptomatic treatment
- Improved motor outcomes
- Better survival and quality of life



SMN2 copies (genotypes)	Phenotype
1	SMA 0/1
2	SMA 1
3	SMA 2/3
4+	SMA 3/4,

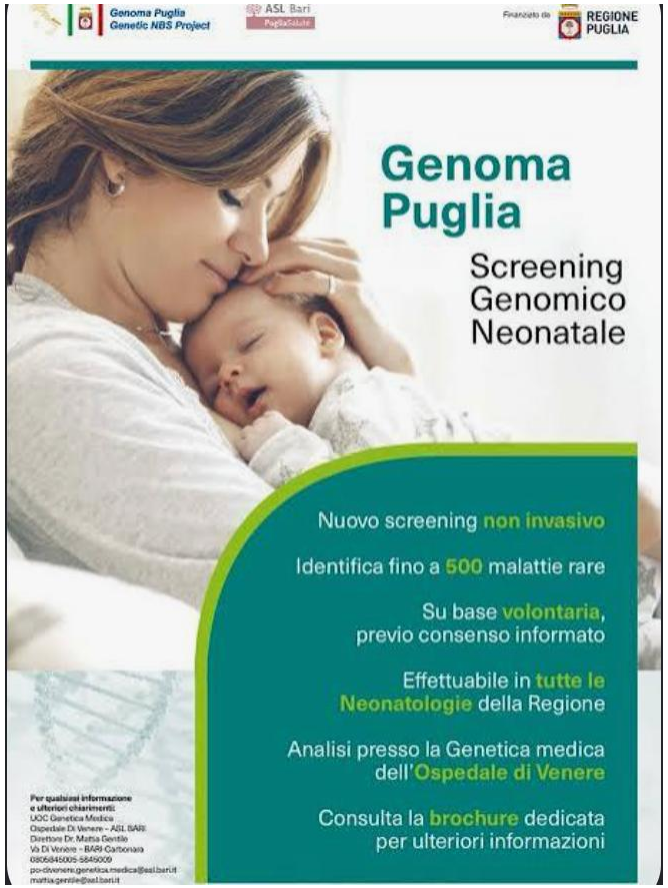
Drug	Via	SMA
Nusinersen	Intratecal	5q
Onasemnogene abeparvovec	EV	1 clinic; 2 (≤13,5 kg); presymptomatic 2-3 copies SMN2
Risdiplam	Oral	1, 2, 3; 1-4 copies SMN2

Diagnostics and biomarkers have fundamentally changed the natural history of SMA.

Case Study: Spinal Muscular Atrophy (SMA)

Initial Barrier	Solution
Delayed diagnosis	Genetic testing and screening
Small patient populations	International collaboration
Clinical heterogeneity	Molecular stratification
Late clinical endpoints	Early biological markers
Difficult trial recruitment	Biomarker-guided patient identification

Biomarkers can transform obstacles into opportunities for innovation.



ANNALS of Clinical and Translational Neurology
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RESEARCH ARTICLE

Early spinal muscular atrophy treatment following newborn screening: A 20-month review of the first Italian regional experience

Delia Gagliardi[1], Eleonora Canzio[2], Paola Orsini[3], Pasquale Conti[2], Vita Sinisi[2], Cosimo Maggiore[2], Maria Carla Santarsia[2], Giuseppina Lagioia[4], Giovanna Lupis[2], Isabella Roppa[2], Gaetano Scianatico[2], Daniela Mancini[2], Stefania Corti[1,5], Giacomo Pietro Comi[1,6], Mattia Gentile[3,#] & Delio Gagliardi[2,#]

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and

Abstract

Objectives: Mandatory newborn screening (NBS) for spinal muscular atrophy (SMA) was implemented for the first time in Italy at the end of 2021, allowing the identification and treatment of patients at an asymptomatic stage. **Methods**: DNA samples extracted from dried blood spot (DBS) from newborns in Apulia region were analysed for SMA screening by using a real-time PCR-based assay.

Conclusion

Biomarkers are a critical bridge between translational research and clinical development.

Pediatric biomarker development faces unique scientific, operational, and regulatory challenges.

Advanced diagnostics and emerging technologies are enabling more precise patient stratification.

In rare diseases, biomarkers can dramatically improve trial design, patient selection, and therapeutic success.

The ultimate goal is not the biomarker itself, but better outcomes for children through more personalized and effective therapies.

In pediatric research, biomarkers are not simply tools for measurement.

They are instruments for reducing uncertainty,

accelerating innovation,

and ensuring that the right therapy reaches the right child at the right time.