Translation research from lab to patients

Latest innovations by EPTRI

EUROPEAN PAEDIATRIC TRANSNATIONAL RESEARCH INFRASTRUCTURE

Donato Bonifazi – EPTRI Coordinator

Enpr-EMA Annual meeting
Amsterdam, 20th November 2025

INTRODUCTION TO EPTRI

Understanding who we are and why paediatric research matters

EPTRI brings together a broad spectrum of experts and institutions committed to advancing paediatric research and innovation.

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EPTRI - European Paediatric Transnational Research Infrastructure

What is it?

A pan-European initiative involving hundreds of research units gathered together to boost the paediatric research ecosystem and provide services for the development of health solutions for children.

A Research Infrastructure aiming to promote paediatric research and provide optimal support to facilitate the accruing of knowledge in the many research fields necessary to guarantee the access to high quality and safe paediatric medicine and medical devices.

To increase knowledge on children growth and ontogeny characteristics relevant for the identification of novel therapies dedicated to children and to provide services for their development

To implement competences, research strategies, access to key technologies, standardised models, and analytical tools and to offer to public and private stakeholders qualified basic, preclinical and translational research services covering paediatric medicines discovery and development

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Why is it important?

EPTRI's mission is to **overcome systemic barriers in paediatric research** by **supporting child-focused scientific innovation** and **contributing to the development of a new EU policy framework** aimed at advancing research leading to paediatric product development.

🧬 Scientific & Clinical

- Dynamic physiological changes
- Lack of paediatric-specific biomarkers
- Small and heterogeneous patient populations
- Limited child-friendly formulations and suitable excipients
- Off-label use and insufficient evidence-based repurposing
- Slow translation from non-clinical to clinical application

⚖️ Ethical & Methodological

- Ethical and methodological constraints in paediatric trials
- Restricted use of placebo and need to minimise risks/discomfort
- Long study timelines and high costs
- Limited patient and family engagement (e.g., YPAGs)

🏛️ Regulatory & Policy

- Incomplete or delayed Paediatric Investigation Plans (PIPs)
- Complex and lengthy regulatory pathways (Paediatric Regulation, MDR/IVDR)
- Low innovation incentives for paediatric-only conditions
- Insufficient regulatory support and coordination

🤝 Organisational & Collaborative

- Fragmented and uncoordinated research efforts
- Limited cross-disciplinary and cross-sector collaboration
- Lack of integrated infrastructures to support paediatric R&I

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Who we are?

As of October 2023, EPTRI has been established as a non-profit research organisation incorporated in the form of an *Association Internationale Sans But Lucrative* (AISBL) governed by Belgian law, based at Leuven University.

EPTRI consists of 26 members representing 14 different countries, bringing together a diverse range of expertise and institutions dedicated to paediatric research and innovation.

IRCCS Eugenio Medea
La Nostra Famiglia
The Cyprus Institute of Neurology & Genetics
KU Leuven
UZA
Milo Health
Fondazione per la Ricerca Farmacologica Gianni Benzi ONLUS
TEDDY Network – European Network of Excellence for Paediatric Clinical Research
Institute of Physiology CAS
Università degli Studi di Bari Aldo Moro
Universiteit Gent
Hôpital Universitaire des Enfants Reine Fabiola – Universitair Kinderziekenhuis Koningin Fabiola
ANDO – Associação Nacional Displasias Ósseas
Università degli Studi di Milano Bicocca
The Children's Memorial Health Institute
ATHENA Research & Innovation Information Technologies
Alma Mater Studiorum Università di Bologna
ALYN Hospital – Pediatric & Adolescent Rehabilitation Center
Penta
UCL
Sheffield Children's NHS Foundation Trust
Duchenne Data Foundation
Luxembourg Institute of Health
CVBF – Clinical Validation from Biopharmaceutical Findings
Dr. von Haunersches Kinderspital – Helfen Forschen Heilen. Seit 1846
pd
Med Uni Graz

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Who do we collaborate with?

INFRAFRONTIER — **European Research Infrastructure for Modelling Human Diseases**

INFRAFRONTIER-ERIC, through its Czech node (IMG-CCP), provides access to juvenile animal models and standardised non-clinical services.

instruct ERIC — **Leading research infrastructure in structural biology**

Instruct-ERIC contributes advanced structural biology and translational research capabilities. By offering high-throughput structural biology techniques—including Cryo-EM, NMR, and X-ray crystallography—alongside biophysical analyses, Instruct enables detailed mechanistic studies, biomarker discovery, and validation of molecular targets.

IIB INFRASTRUTTURA ITALIANA DI BIOINFORMATICA | elixir ITALY — **Italian Infrastructure for Bioinformatics (IIB)**

ELIXIR, via the University of Bologna (**UNIBO**), offers secure, interoperable, and FAIR-aligned bioinformatics platforms for multi-omics and real-world paediatric health data.

Expansion of Services Offering via Other Research Organisations

Key contributions include:

- **Real-world data and digital health:** Support for data integration, regulatory compliance, and the use of electronic health records in paediatric research.
- **Medical device innovation:** Provision of engineering, regulatory, and quality systems expertise to advance paediatric medical devices from concept to clinical application.
- **Clinical infrastructures and rare diseases:** Access to diverse patient populations, reference networks, and early-phase clinical trial capacity.
- **Patient engagement:** Ensuring that research priorities, study design, and outcomes reflect patient needs and perspectives.
- **Methodological and disease-specific expertise:** Guidance on trial design, small population methodologies, regulatory interactions, and targeted disease research.

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Which dissemination and exploitation activities are we engaged in?

EPTRI Toolkit

On Basic and Translational Paediatric Research for Patients and Families

EPTRI Special Issue

EPTRI has launched the research topic collection "Supporting the Pediatric Drug Development: From Basic Research to Clinical Studies and Technological Advancements"

EPTRI Special Issue

EPTRI has launched the research topic collection "Paediatric and Orphan Medical Devices: From Concept to Care—Transforming Innovation for Children's Health"

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EPTRI Policy Update: Ensuring Children's Needs in the New Pharmaceutical Legislation

EPTRI Position Paper

- Released in **October 2023**, subscribed by **24 institutions**
- Concerns for the repealing of the **Paediatric Regulation**

Key topics

- **Abolition of the Paediatric Regulation** was never intended by EU institutions
- The proposal **removes** clear obligations **PIPs**
- **PDCO** expertise would be dispersed across non-paediatric groups
- **Paediatric needs are omitted,** undermining children's health and access to appropriate medicines

EPTRI amendments for the EU Parliament

- Submitted in **November 2023**
- Proposed to MEPs

Aims

- Preserve **PDCO** expertise in a Working Group on Paediatric Medicinal Products
- Confirm the **mandatory** nature of **PIPs**
- Strengthen **paediatric repurposing** pathways
- Improve **identification of paediatric needs**
- Ensure **child-appropriate information** on medicines
- Enhance **paediatric pharmacovigilance** measures
- Secure **dedicated funding** for **paediatric research**

EPTRI letter during trilogue negotiations

- The **Council's June 2025 text** introduces **changes aligned with EPTRI's paediatric priorities**
- **Paediatric expertise** should be retained in a **permanent Dedicated Working Party** on paediatric medicinal products

Key proposals

- Preserve **paediatric expertise**
- **Strengthen paediatric focus in final texts**

THE TRANSLATIONAL RESEARCH JOURNEY – FROM LAB TO PATIENTS

Turning discoveries

into real treatments faster

Turning new discoveries into real treatments is a journey *from the lab to the clinic* to help children faster and better.

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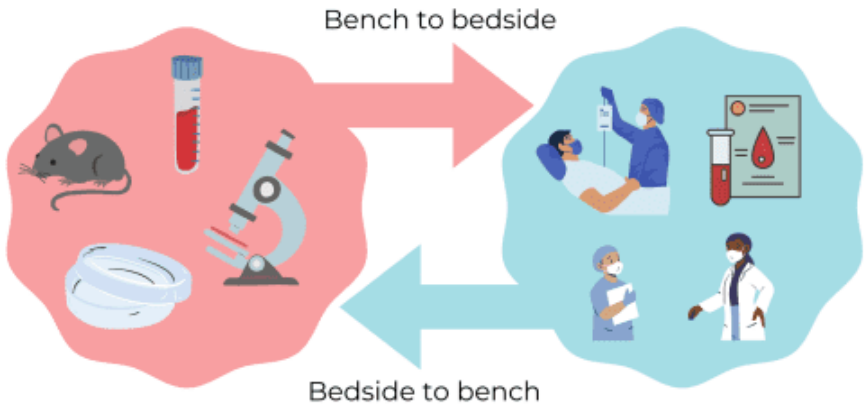


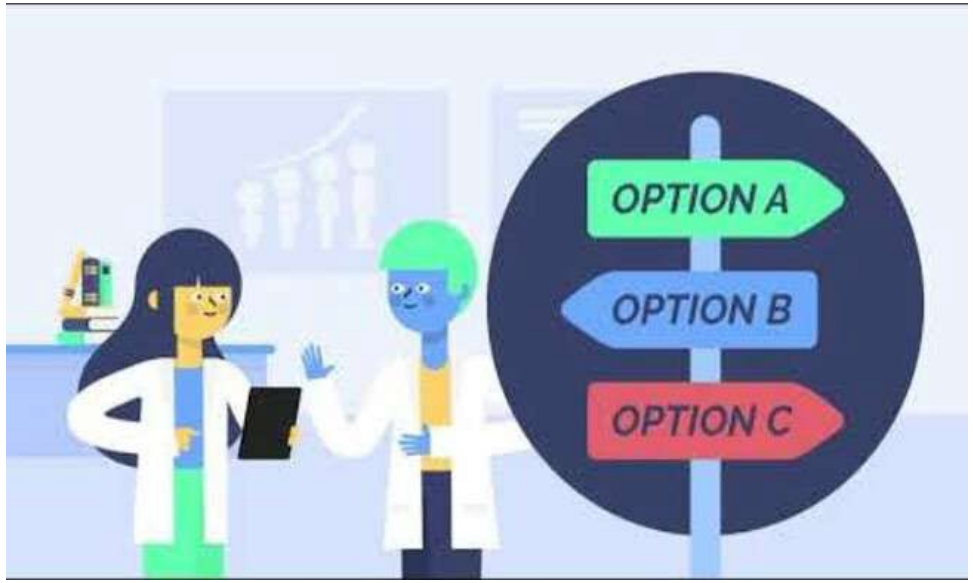
TRANSLATIONAL RESEARCH – FROM LAB TO PATIENTS

Translational research is the bridge that takes discoveries from lab and turns them into new medicines, better treatments, medical devices, or approaches that can directly help children and young people to stay healthy.

Translational research

LAB WORLD

EPTRI aims to enhance technology-driven paediatric research in drug discovery and early development, focusing on translating early research into clinical applications for paediatric medicines and medical devices.



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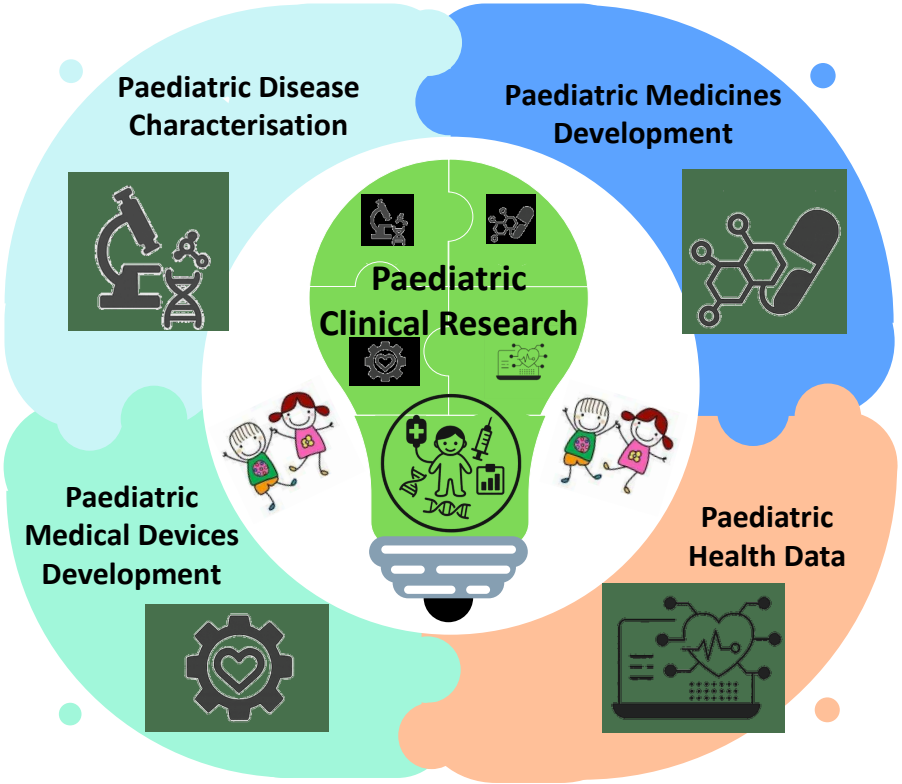
EPTRI INTEGRATED APPROACH TO PAEDIATRIC CLINICAL RESEARCH

Discovery → *In vitro & in vivo* preclinical → Biomarkers → Development → Early-phase Clinical → Late-phase Clinical → Access to patients

EPTRI integrates pre-clinical, developmental, and clinical research into a single paediatric-focused pathway, providing streamlined access to expertise and resources to advance child health innovations.

Disease characterisation combines pediatric profiling, translational research, and biomarker discovery using biophysics, omics, and computational tools to speed therapy development.

Medical Device Development facilitates design, prototyping, safety and usability testing of paediatric medical devices, guiding towards their commercialisation.



Medicines Development supports early drug development with non-clinical expertise, including *in vitro* systems, juvenile models, *in silico* predictions, paediatric formulations, and EMA procedures.

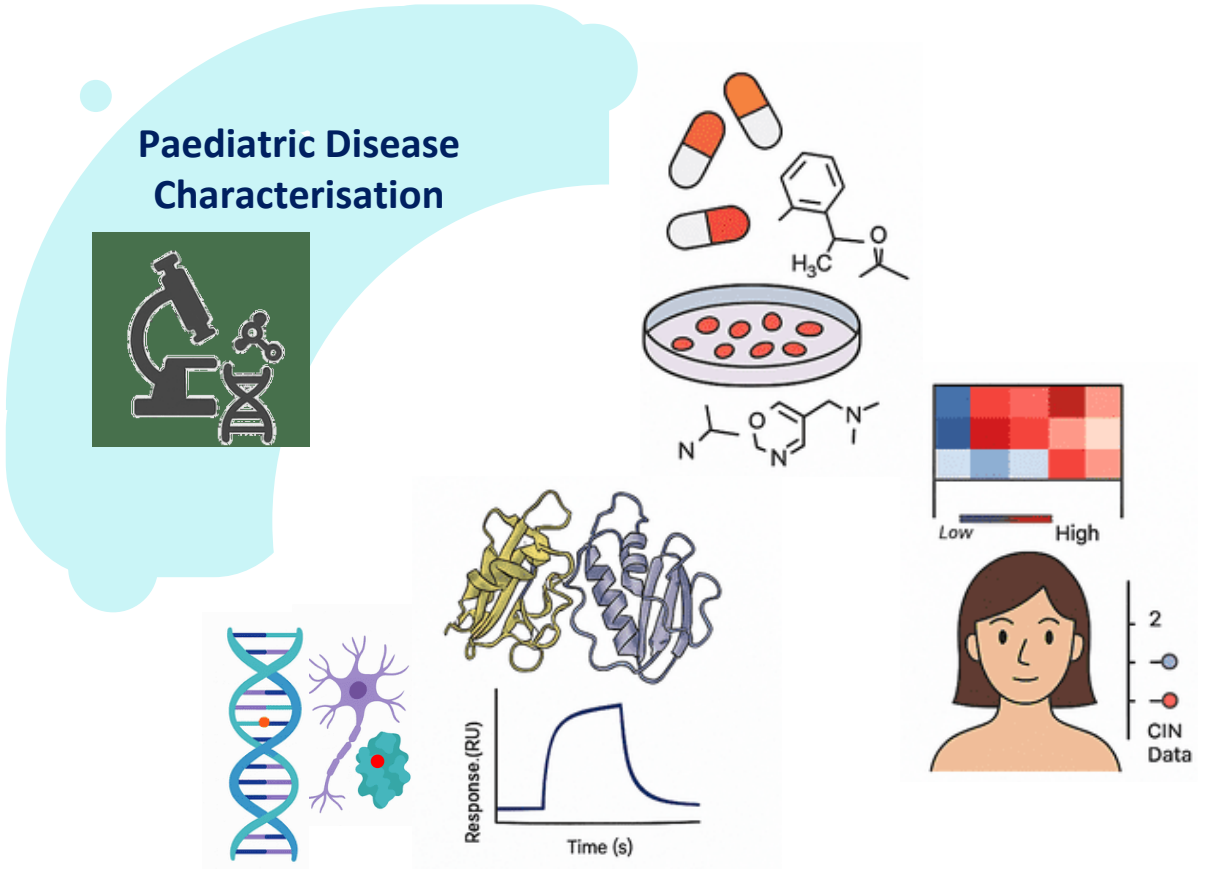
Health Data provides secure, GDPR-compliant access to real-world paediatric data, supporting FAIR sharing, anonymisation, eSource integration, secondary use, and child-specific privacy safeguards.

Clinical Research serves as the central hub, delivering comprehensive, patient-centred support, with disease characterisation, biomarkers, formulations, and R&D plans directly feeding into and enhancing its services.

PAEDIATRIC DISEASE CHARACTERISATION

Paediatric disease characterisation is crucial for understanding how maturation and ontogeny influence disease mechanisms and treatment responses. Mapping these age-specific pathways enables truly translational, child-focused drug discovery.

By integrating omics, structural and biophysical analyses, and modelling, we reveal how developmental biology shapes paediatric disease, uncovering druggable pathways, early hit-to-lead candidates, and biomarkers that bridge discovery to clinical translation.



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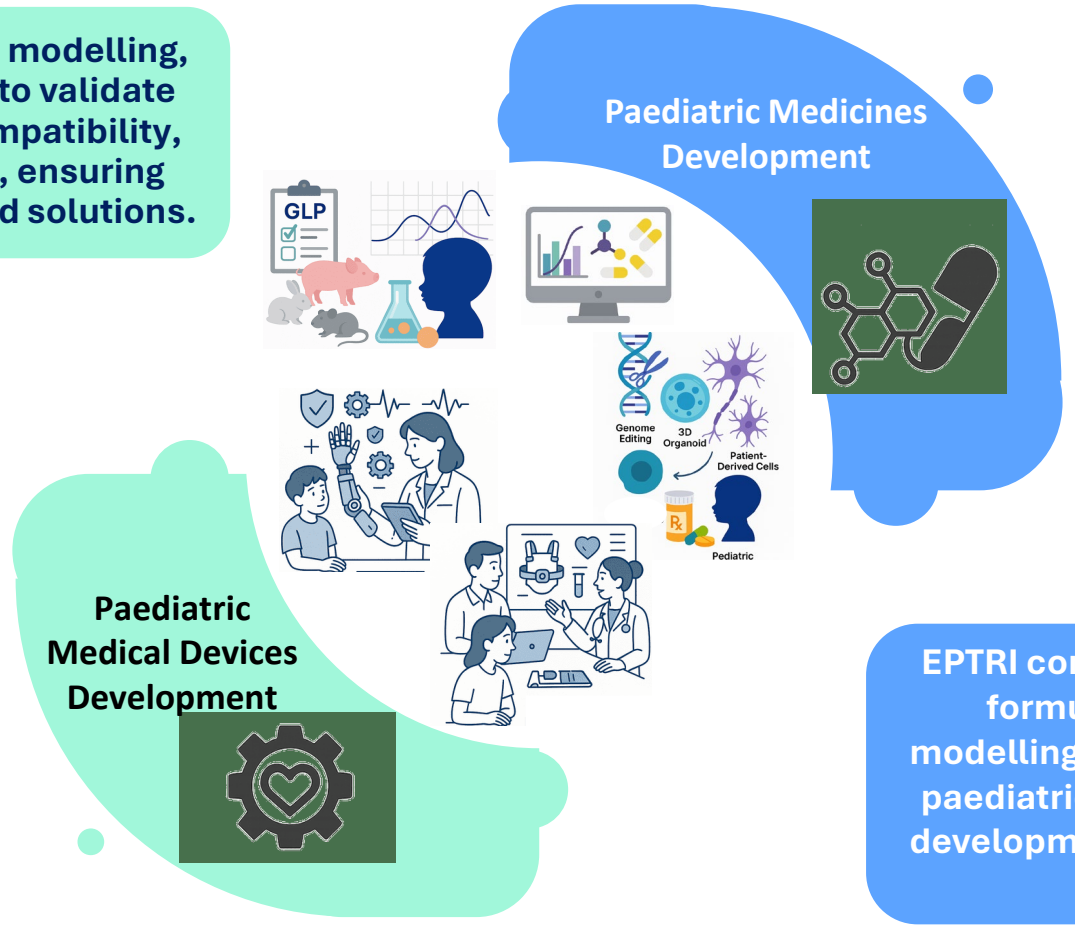
PAEDIATRIC MEDICINES AND MEDICAL DEVICES DEVELOPMENT

EPTRI accelerates the translation of paediatric disease characterisation into therapies and technologies, integrating discovery data, modelling, and validation to advance medicines and medical devices toward clinical readiness.

EPTRI leverages advanced design, modelling, usability testing, and YPAG input to validate paediatric devices through biocompatibility, safety, and MDR-aligned studies, ensuring safe, regulator-ready, child-tailored solutions.



EPTRI combines early ADME, juvenile models, formulation studies, pharmacokinetic modelling, and regulatory guidance to optimise paediatric candidates for safety, efficacy, and developmental stage, bridging pre-clinical data to clinical readiness.

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PAEDIATRIC HEALTH DATA

Paediatric Health Data forms EPTRI's digital backbone, ensuring pre-clinical, clinical, and regulatory data are standardised, interoperable, and reusable to maximise impact on paediatric research and policy.

It applies FAIR principles, harmonised data models, and metadata catalogues to link diverse paediatric datasets and enable seamless interoperability across EPTRI platforms.

It develops AI-driven tools for data integration and in silico modelling, enabling secure, compliant reuse within EPTRI and alignment with the European Health Data Space.

Paediatric Health Data

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PAEDIATRIC CLINICAL RESEARCH

Paediatric Clinical Research serves as EPTRI's translational and operational bridge, turning pre-clinical and regulatory knowledge into high-quality studies that advance safe, effective therapies for children.

It develops innovative, model-informed study designs that support dose extrapolation and feasibility assessments, integrating YPAG input to make paediatric trials more efficient and inclusive.

It provides trial operations support—from protocol development to site coordination, eCRF setup, monitoring, and data management—ensuring data integrity and quality across paediatric clinical studies.

It facilitates ethics and regulatory interactions, links clinical centres and trial networks, and promotes harmonised procedures across the paediatric research community.

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CASE STUDIES

Why translation research matters

Through its member institutions, EPTRI turns scientific progress into real benefits for children across the entire paediatric research pathway.

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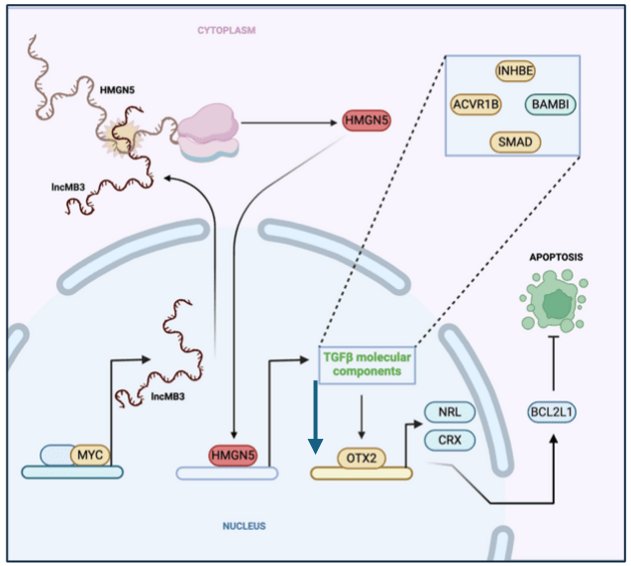
Case Study: Characterisation of the Disease Mechanisms Underlying Medulloblastoma

Medulloblastoma is a **paediatric cancer** representing the **most common malignant brain tumour in children**, accounting for approximately **30% of cases** (Northcott *et al.*, *Nat Rev Dis Prim*, 2019).

Disease Characterisation and Therapeutic Target Identification

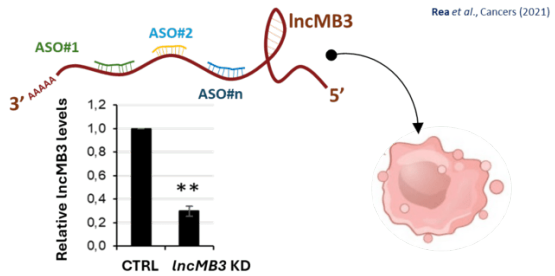
Comprehensive profiling of disease models to identify and validate potential molecular targets for intervention.



In medulloblastoma, **lncMB3 links the overactive *MYC* gene to pathways that prevent cancer cell death, promoting tumor growth and spread.**

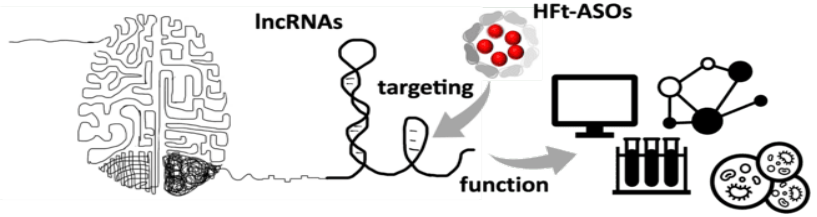
Therapeutic Strategy Development and *In Vitro* Validation

Design and optimisation of antisense oligonucleotide (ASO)–based therapeutic strategies, followed by *in vitro* functional validation.



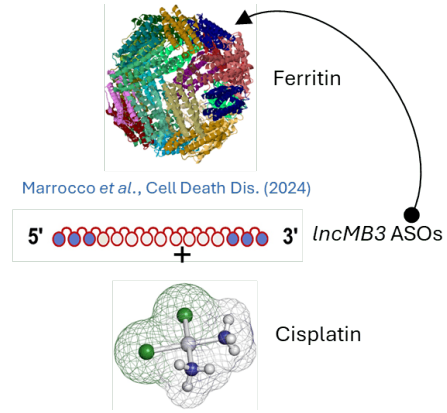
ASO treatment lowers the levels of lncMB3, reducing its activity in cancer cells.

From early discovery to therapeutic targets, this case study highlights that early understanding of the disease mechanisms is essential for developing effective and precise treatments.



Identification of an Efficient Delivery System

Evaluation and selection of optimal delivery systems for targeted and effective ASO administration.



Ferritin, a natural protein cage**, can be used to deliver lncMB3-targeting ASOs into medulloblastoma cells, boosting the effects of chemotherapy.**

Grandioso *et al.*, Cell Death Dis, 2025
Grandioso *et al.*, manuscript in preparation
Grandioso *et al.*, patent pending, #11116

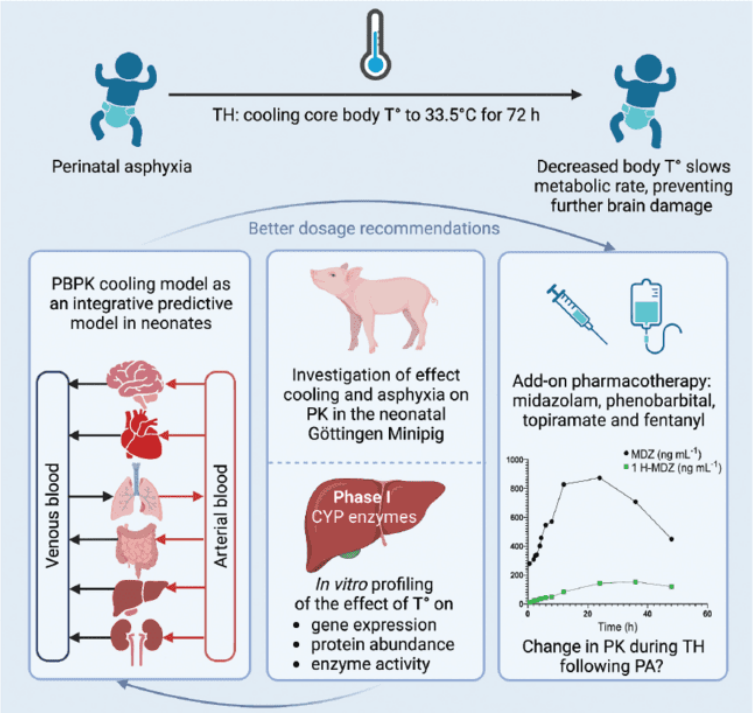
Case Study: iPREDICT

Innovative physiology-based pharmacokinetic model to predict drug exposure in neonates undergoing cooling therapy

BACKGROUND

Perinatal asphyxia (PA) causes oxygen deprivation at birth, potentially leading to **hypoxic-ischemic encephalopathy (HIE).** **Therapeutic hypothermia (TH)** - cooling infants to 33.5 °C for 72 hours followed by gradual rewarming - reduces mortality and neurodevelopmental impairment in moderate to severe cases.

The **iPREDICT project** combines **pre-clinical data** (*in vitro* enzyme studies, Göttingen minipig *in vivo* PK experiments) with **clinical and real-world human data** to *build a PBPK framework that predicts drug disposition under PA/TH conditions*.



Pre-clinical

***In vitro*/animal studies**
Measure drug clearance in hepatocytes and in neonatal Gottingen minipigs

Clinical

Clinical measurements
Collect drug levels in cooled neonates

In silico

Physiologically based parmacokinetic (PBPK) models
Predict drug exposure and optimise dosing in cooled neonates

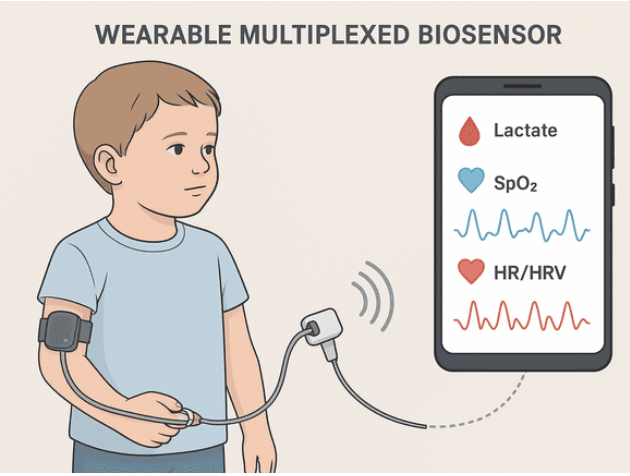
DOI: 10.1080/17425255.2023.2237412

Case Study: Wearable Multiplexed Biosensor For Cyanotic Congenital Heart Diseases

Develop a wearable, multiplexed biosensor aimed at preventing lactic acidosis in children with unrepaired congenital heart defects (CHD) and monitoring the physiological response to pulmonary valve replacement in children with repaired CHD.

BACKGROUND

- **Cyanotic congenital heart disease (CCHD)** affects about 25% of children with CHD and causes hypoxemia from abnormal blood flow, leading to cyanosis and digital clubbing.
- Unrepaired CCHD can trigger severe hypoxia and life-threatening lactic acidosis.
- Early evaluation of oxygenation and acid-base status is essential for timely intervention.



CONCEPT

A fully integrated invasive wearable device was envisioned, featuring:

- Enzyme-based electrochemical biosensors for lactate/pyruvate detection
- Micro-catheter for continuous blood sampling
- Wireless data transmission with software analytics

Goal: assess blood acid-base status and arterial oxygenation to enable early intervention.

Proof-of-of concept prototype

Combining commercially available sensors and finger-prick analysers

↓

Feasibility study

With healthy subjects to evaluate:
- Technical feasibility
- Data integration
- Usability in pediatric contexts

↓

Clinical

Fully non-invasive, continuous monitoring system

OrphaDev4Kids
Co-funded by the European Union

Case Study: EVENEW

Phase I/II Clinical Trial On Intratracheal Administration Of Allogeneic Umbilical Mesenchymal Cells-Derived Extracellular Vesicles In Preventing Bronchopulmonary Dysplasia (BPD) In Extremely Preterm Newborns

The trial aims to **evaluate the safety and efficacy of *EXOB-001*** consisting of extracellular vesicles derived from umbilical cord mesenchymal stromal cells **in the prevention of bronchopulmonary dysplasia (BPD)** in extremely premature neonates.

Preclinical Research → **Phase I** → **Phase II** → **Phase III**

Pre-clinical

- Consultancy for clinical development EVs in BPD, including development of the IMPD
- Orphan designation
- Scientific Advice (EMA, FAMHP, ISS)

Clinical

SINGLE ARM
DOSE ESCALATING
Bayesian Optimal Interval (BOIN) statistical approach

DOUBLE BLIND, RANDOMISED, PLACEBO-CONTROLLED, DOSE FINDING

- Study design
- Medical writing (IB, protocol)
- Management of clinical trial (regulatory process, clinical operations, monitoring, data management, statistics, pharmacovigilance)

Bayesian Optimal Interval (BOIN) statistical approach to find the new drug **Maximum Tolerated Dose.**

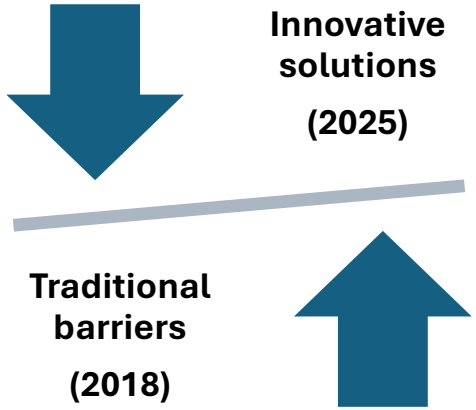
Case Study: GAPP

To increase the availability of paediatric medicines by developing a full clinical strategy on gabapentin tested in chronic pain and making results available for a PUMA application.

An **extrapolation model** was employed to **estimate the appropriate dosage** and to translate the **efficacy and safety data obtained from adult clinical trials to the paediatric population**.

TRADITIONAL APPROACH

Randomised, double-blind, double-dummy, active-controlled, multicentre phase III non-inferiority trial comparing gabapentin liquid to tramadol in children (3 months–<18 years) with moderate to severe chronic neuropathic or mixed pain.



NEW STUDY DESIGN

Multicenter, adaptive, prospective cohort study evaluating the pharmacokinetics, efficacy, and safety of gabapentin liquid in children (3 months–<18 years) with moderate to severe neuropathic, nociplastic, or mixed pain.

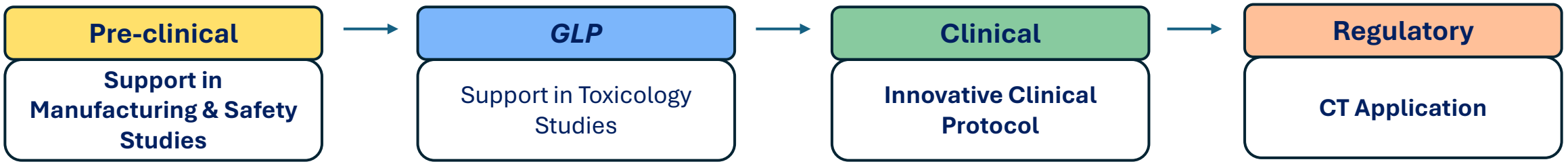
The main key barriers included:

- **Large patient population**
- **Large number of recruiting centres**
- **Wash-out period**
- **Opioid as active comparator**
- **Off-label access to patients**

Advantages:

- **Reduced sample size, through Bayesian model and adaptive design requiring fewer patients**
- **No wash-out, using prior or real-world data**
- **Avoids comparator (e.g., opioids), with a single arm study**

Case Study: Tumours with N-Myc amplification



- Manufacturing
  - Supplier chain validation
  - In Process Control
- GMP qualification and validation
- Formulation & Stability studies
- Release Test for Identitiy, Sterility and Potency

Safety
- PK/PD
- Safety Pharmacodynamis
- *In vivo*/*in vitro* acute toxicity

Clinical Protocol
Basket trial
paediatric patients aged 2-18 years old with refractory or relapsed selected tumours

Phase I increasing dose
Phase II - Accruing patients for efficacy with the maximum dose

Innovative approach
A Phase I/IIa single-arm trial with historical controls was designed to assess whether the new therapy shows sufficient promise against a specific tumour type. Safety and efficacy will be compared with a historical cohort, avoiding a randomised trial. Propensity score matching will adjust for baseline differences and minimise bias.

This study provides an example of a translational bridge dealing with the integration of preclinical data to perform a Clinical Trial Application for a Phase I/II Study.

EPTRI ONGOING ACTIVITIES: AMIGO PROPOSAL FOR IHI 12 CALL 2026

Concept proposal: Dr. von Hauner Children's Hospital – **LMU Munich**
Lead contacts: Prof. Christoph Klein, **Dr. Daniel Weiss**

EU-wide federated AI platform linking multi-omics and clinical data from paediatric hospitals to make children visible in drug R&D.
Data stay local (GDPR-compliant) and are accessible to industry, CROs and academia **to identify paediatric targets and repurpose existing drugs**.

- **Main goals:**
  - **Unlock paediatric-specific disease biology and enable precision care**.
  - **Shorten time-to-label** for paediatric indications (30–50 % reduction estimated).
  - **Build a pre-competitive ecosystem** connecting AI, hospitals and pharma.
  - **Generate new PUMA-eligible drug opportunities** and companion diagnostics.

- **Expected impact:**
  - Faster and safer **paediatric drug development**.
  - **New paediatric indications for known targets.**
  - **Sustainable AI data infrastructure** usable beyond the project.
  - Strengthened EU leadership in **digital and paediatric precision medicine.**

PROJECT STATUS

Consortium formation ongoing

CALL FOR PARTNERS

What are we seeking to co-create the first EU-wide federated AI platform focused on pediatric:

- **Pharma partners (target-to-drug expertise, use cases)**
- **Diagnostic/Medtech for CDx and monitoring**
- **Biotech & SMEs (repurposing, biomarkers)**
- **Regulatory/HTA & ethical governance experts**

Contact: coordinator@eptri.eu

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innovative health initiative

THANK YOU FOR THE ATTENTION