



EUROPEAN PAEDIATRIC TRANSLATIONAL RESEARCH INFRASTRUCTURE

# THEMATIC PLATFORM SUPPORTING PAEDIATRIC MEDICINES DISCOVERY

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ATHENA Research Center

EPTRI Stakeholders Roundtable  
Virtual Meeting July 9th, 2020



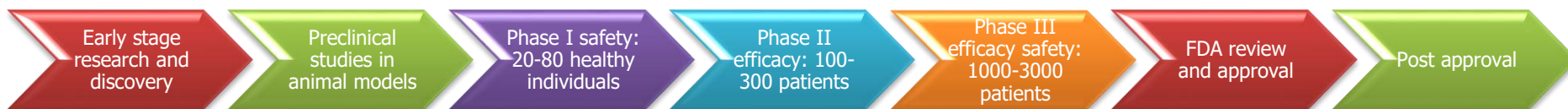
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# Paediatric Medicines Discovery Platform

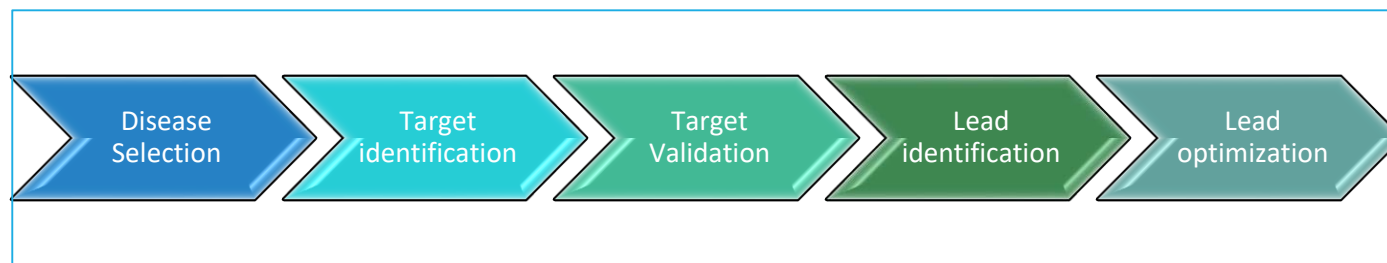
## Aim:

Offer access to academic drug discovery facilities specialized to paediatric diseases,  
Provide integrated services, coordinating efforts among European Centres of Excellence,  
Implement cutting edge technologies, to accelerate discovery and preclinical drug development in paediatrics

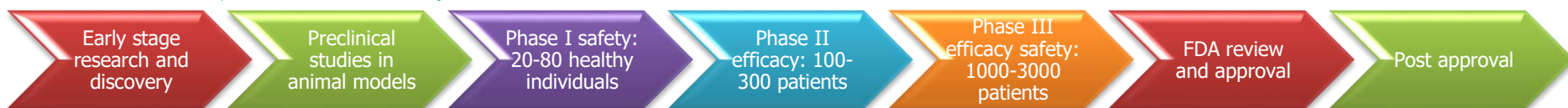
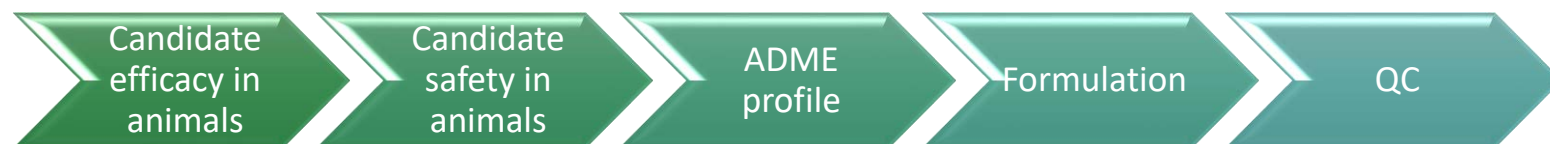
# Drug Discovery



# Drug Discovery

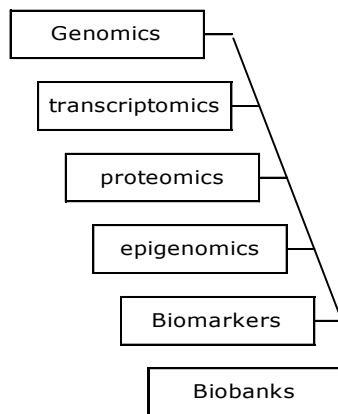


# Drug Discovery

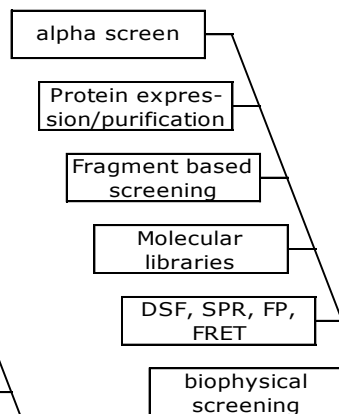


# Preclinical Drug Discovery

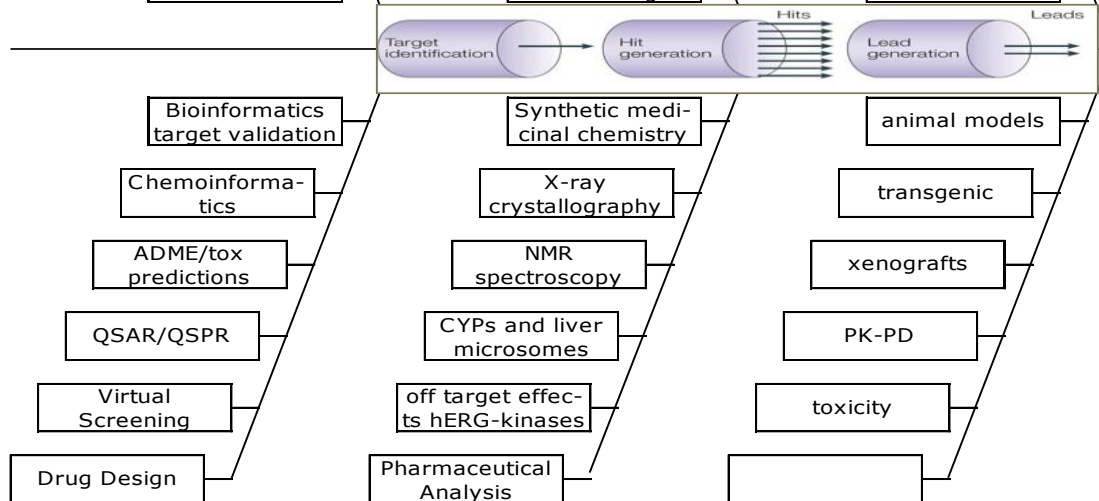
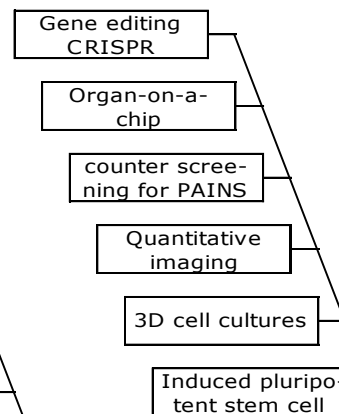
## Target Identification



## HTS development



## Cell based assays



## Preclinical Drug Discovery

From target to lead

# Preclinical Drug Discovery

## Target Identification

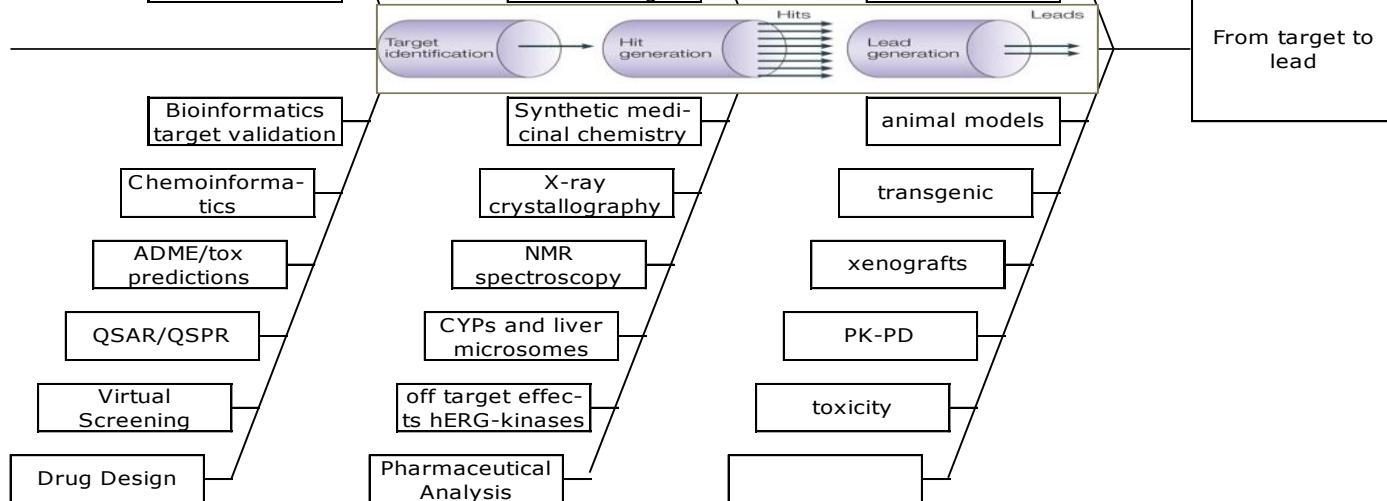
- Genomics
- transcriptomics
- proteomics
- epigenomics
- Biomarkers
- Biobanks

## HTS development

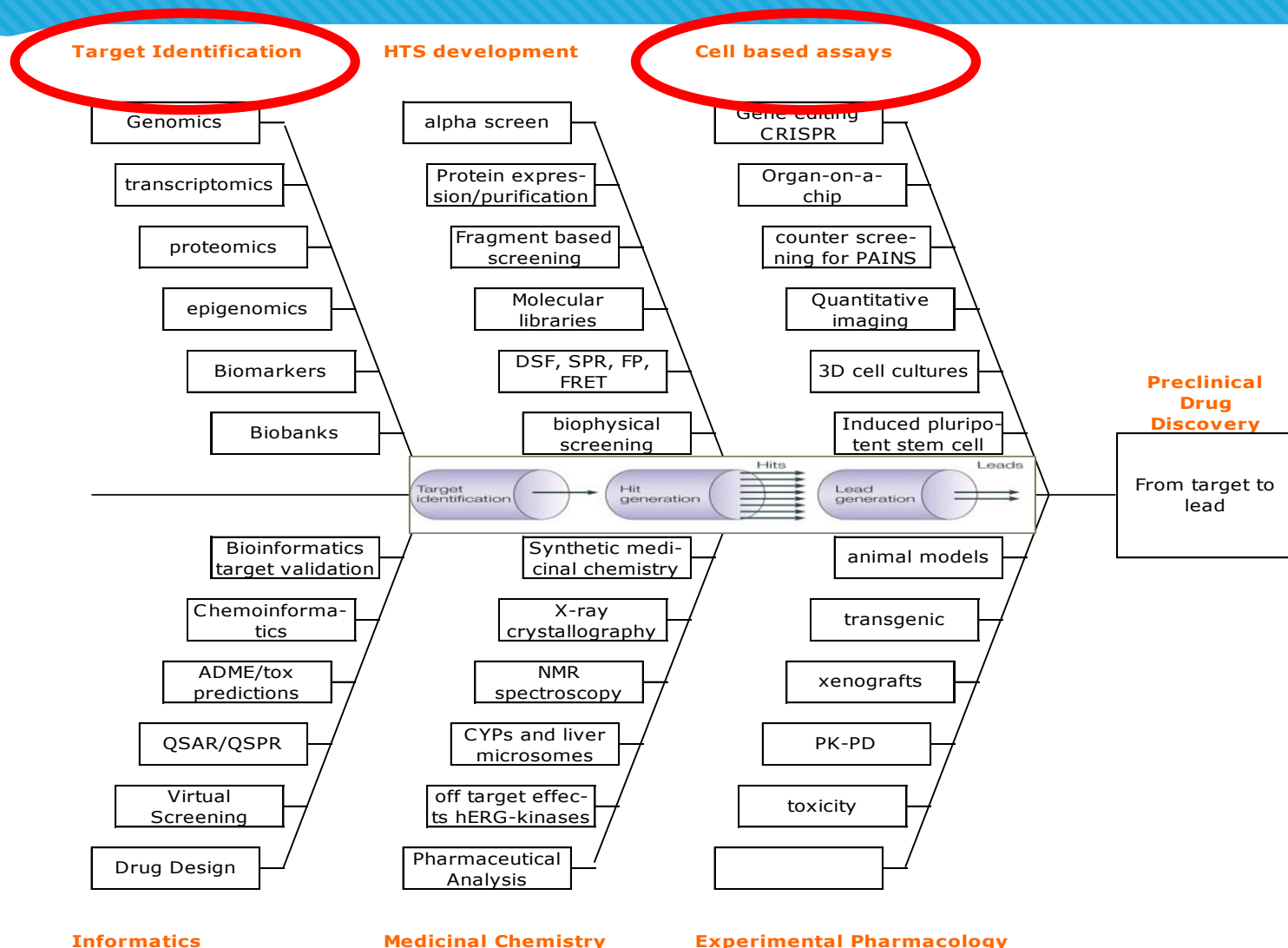
- alpha screen
- Protein expression/purification
- Fragment based screening
- Molecular libraries
- DSF, SPR, FP, FRET
- biophysical screening

## Cell based assays

- Gene editing CRISPR
- Organ-on-a-chip
- counter screening for PAINS
- Quantitative imaging
- 3D cell cultures
- Induced pluripotent stem cell

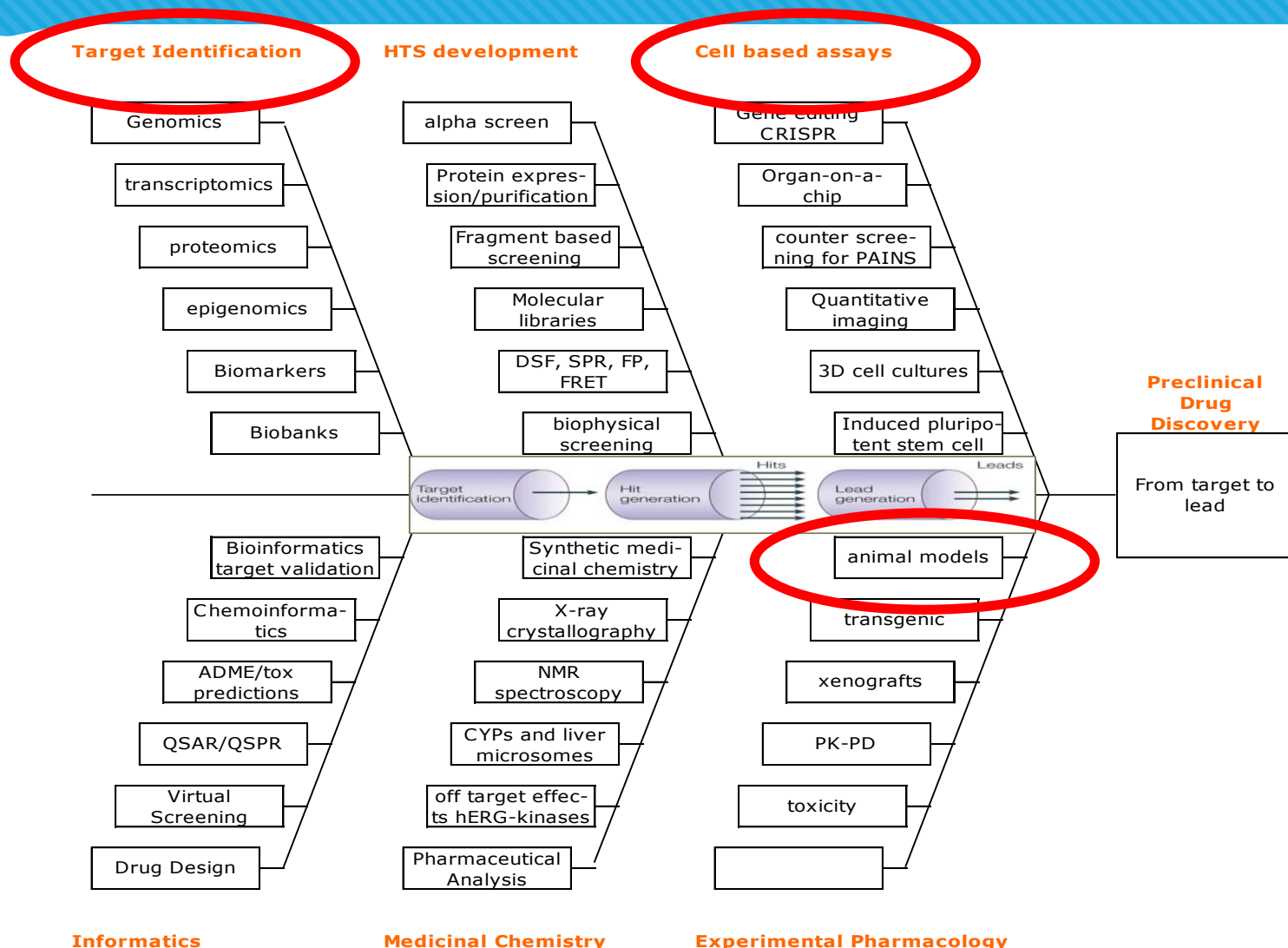


# Preclinical Drug Discovery





# Preclinical Drug Discovery



# EPTRI unique collection

## Cell models

*Disease specific cell models for*

- *muscular dystrophies,*
- *brain injury,*
- *apoptosis,*
- *cancer etc*

## Specialised cell models

- *3-dimensional cell cultures,*
- *microtissue products, nano-culture spheroid plates, micropattern plates,*
- *Patient derived disease models (oncology, ) on the basis of biobank samples.*
- *Stem cells*

# EPTRI unique collection

## Animal models

### Paediatric diseases animal models

*Mouse model of premature ageing (Hutchinson-Gilford Progeria)*

*Drosophila model for Congenital disorders of glycosylation (CDGs);*

*Mouse model for Duchenne Muscular Dystrophy (mdx)*

*Mouse, rat, hypoxia*

*Transgenic mice, xenografts*

*Drosophila model of motor neuron disease in particular hereditary spastic paraplegia genes*

*Periventricular leukomalacia, cerebral ischemia*

*Mouse models of primary immunodeficiency*

*Mice ADPKD model; juvenile rabbit BPD model; rabbit CDH model; PREPL mice model;*

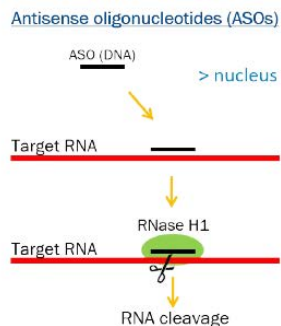
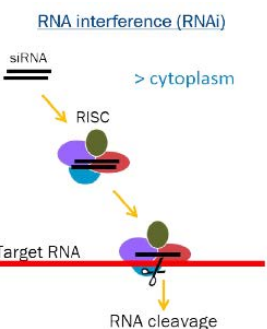
*Zebrafish Dravet model*

*Murine medulloblastoma model.*

*Mouse model of PCD with hydrocephalus and infertility*

# Areas of services provided

## Target validation



**CRISPR/Cas9 gene editing**

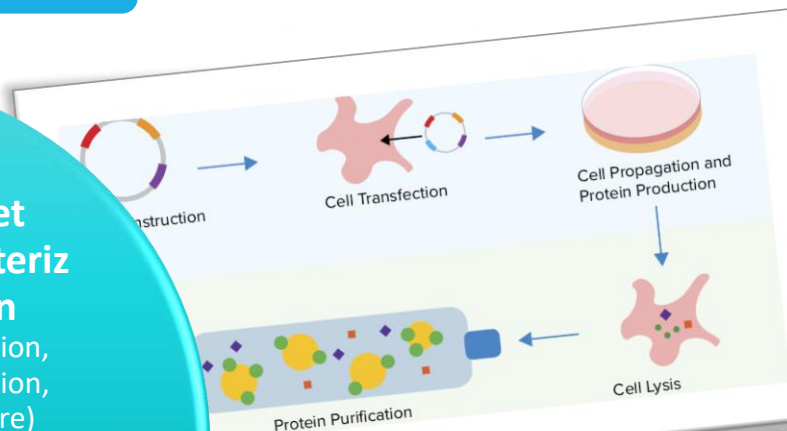
crRNA + tracrRNA

**Genetic Approaches**  
(knock-out, si-RNA, antisense)

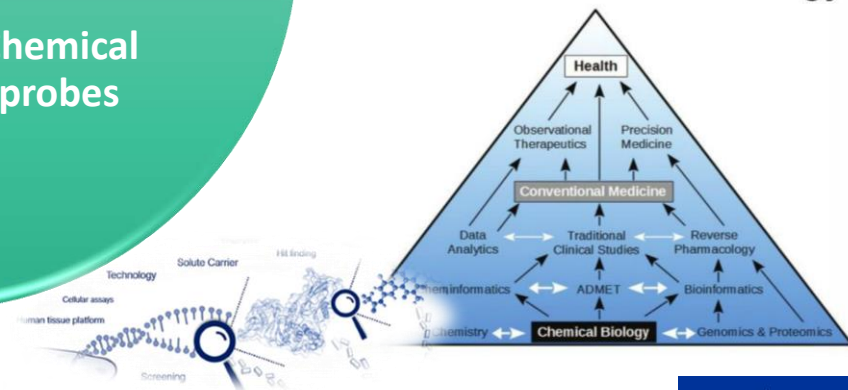
**Target Characterization**  
(expression, purification, structure)

**Bioinformatics**

**Chemical probes**



## Translational Chemical Biology



**ePTRI**

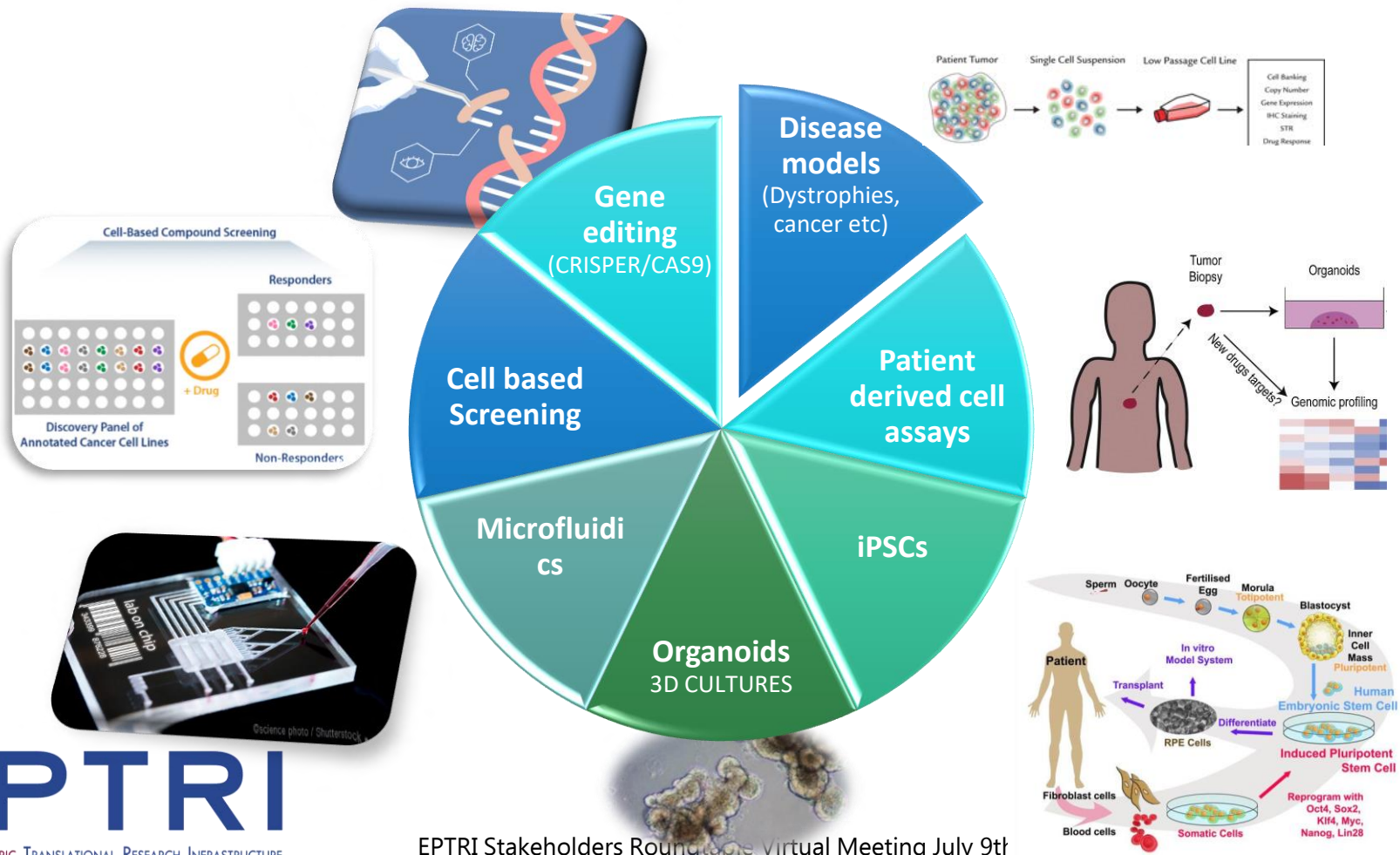
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# Areas of services provided

## Paediatric disease specific cell models



# Areas of services provided

## ANIMAL MODELS

### Zebrafish models

- Phenotypic characterization of novel genes identified in paediatric disease
- Generation of zebrafish mutant lines for modelling paediatric diseases
- Generation of zebrafish xenogeneic tumour models
- Chemical screening in Zebrafish models

### Rabbit Bronchopulmonary Dysplasia model

- Assessment of the neurotoxicity following perinatal exposure
- Assessment of the mechanisms and effects of therapeutic interventions in the juvenile bronchopulmonary dysplasia model.

### Göttingen Minipig model

- Safety assessment of paediatric drugs in development in healthy juvenile Göttingen Minipigs
- Study of the effect of cooling therapy on the PK of several drugs used in NICU in a neonatal Göttingen Minipig asphyxia model

### Rodent models of Rett syndrome and *MECP2* or *CDKL5* related disorders

- Preclinical studies, by testing the efficacy of therapeutic strategies, starting from the young age of P5

### Rodents model of hereditary paediatrics disease.

- Metabolic profile and Behavioural phenotyping
- Preclinical studies of new compounds

### Rodent models of paediatric neurodevelopmental disorders

- Analysis of the effects of acute or chronic drug administration on molecular, biochemical and morphological features
- Resuscitation and neuroprotection studies with different levels of oxygen and drugs

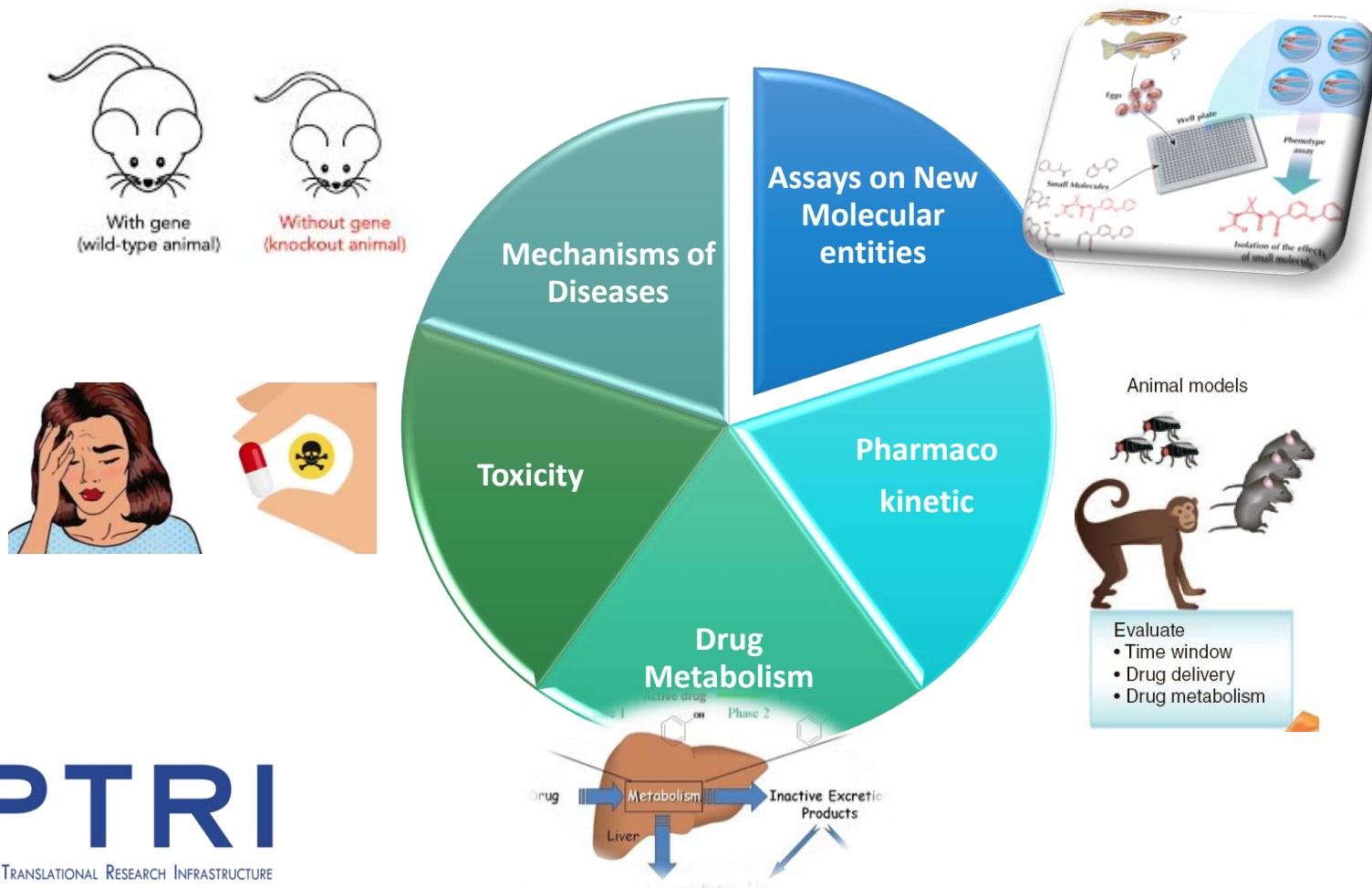
### Rodent models of paediatric neurodevelopmental disability related to schizophrenia, epilepsy and ASD

- Behavioural and physiological phenotyping analysis to test paediatric drugs' efficacy in vivo



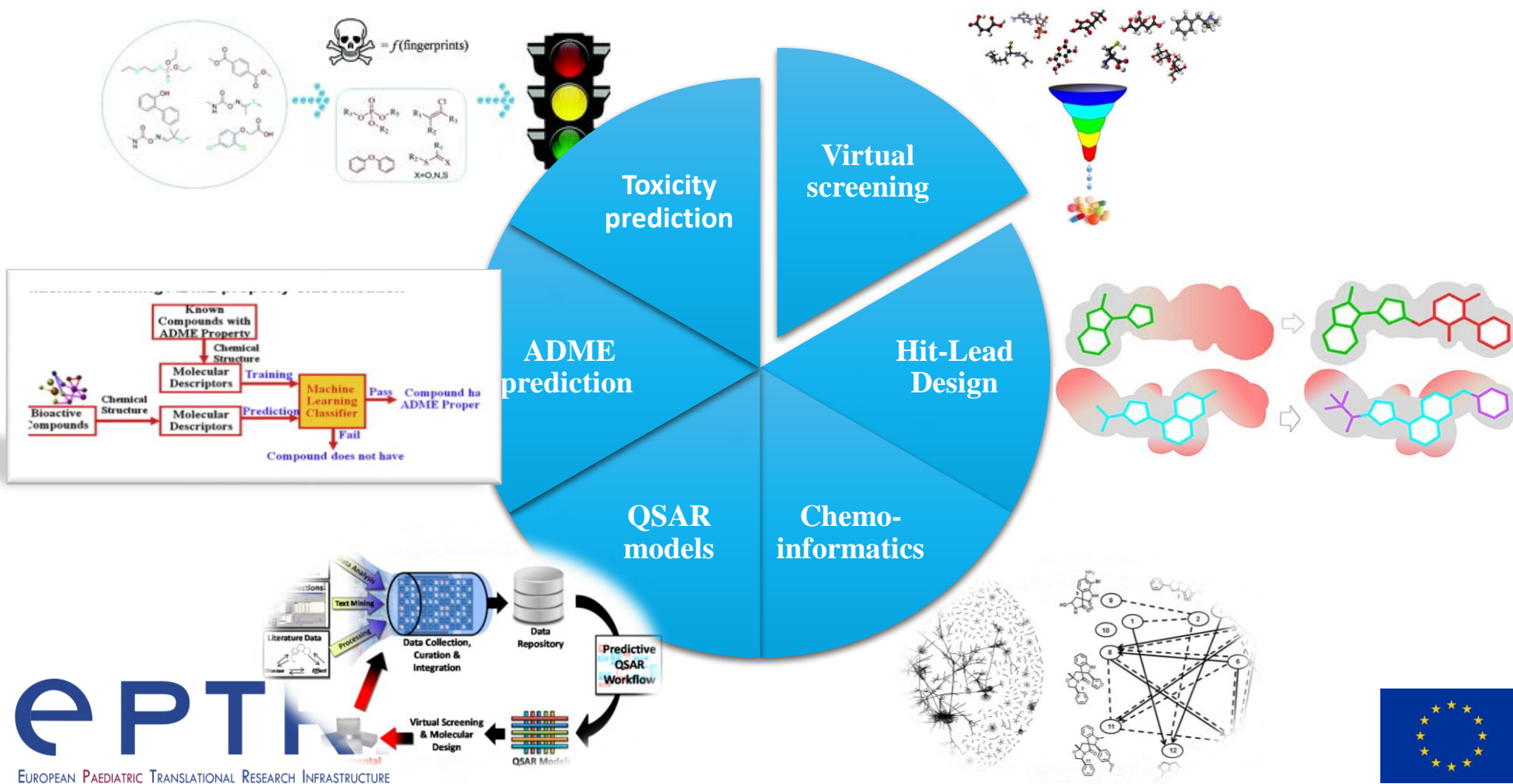
# Areas of services provided

## Paediatric disease specific animal models



# Areas of services provided

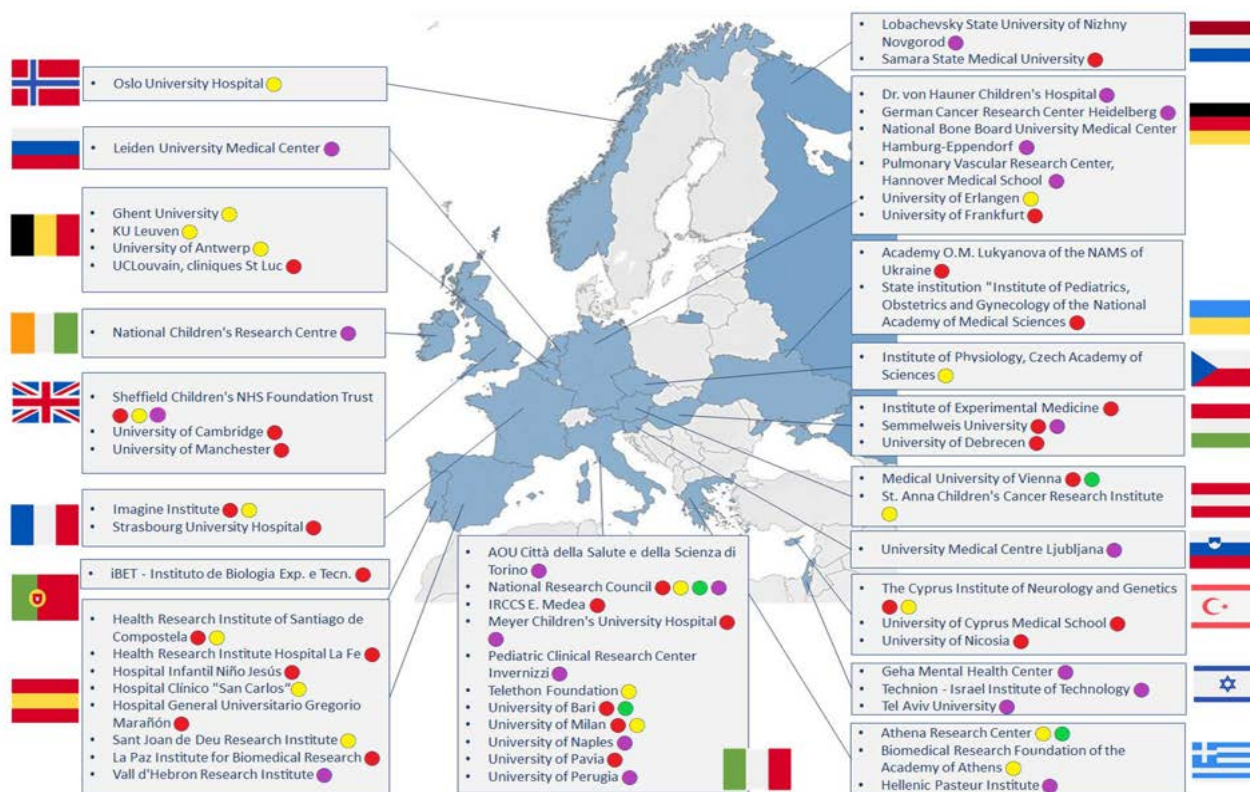
## In Silico models





# Resource description

## Paediatric Medicines Discovery TRP



Countries

N° 19

Institutions

N° 58

Research Units

N° 82

### Research Activities

New Target identification:

● cell and tissue studies

● animal studies

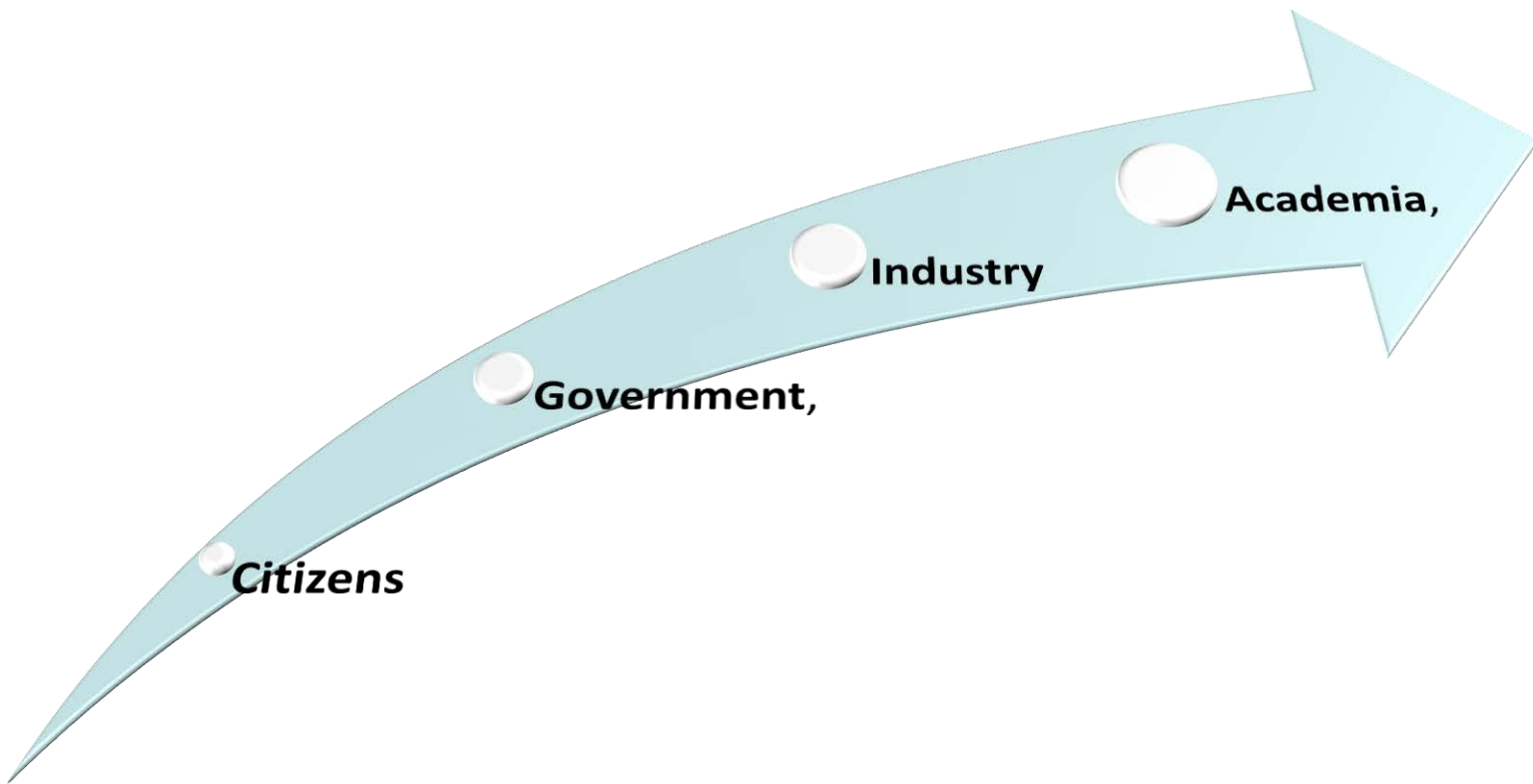
● other

● In silico drug screening and preclinical studies

# SWOT



# PAEDIATRIC MEDICINES DISCOVERY



**PRECISION  
THERAPIES  
FOR  
CHILDREN**

**ePTRI**

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