

EPTRI General Assembly and Scientific Meeting **Warsaw, 28-29 July, 2026**

Creating Preclinical Models for Rare Diseases: RD-Factory as a Platform, Netherton Syndrome as a Case Study

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EPTRI Scientific Meeting | 28-29 July 2026 | Warsaw, Poland

EPTRI General Assembly and Scientific Meeting

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- Content:**
- The Czech Centre for Phenogenomics (CCP) – introduction
 - INFRAFRONTIER – introduction
 - IMPC (catalogue of mammalian gene functions)
 - Towards rare and pediatric diseases
 - RD-Factory programm
 - Netherton syndrome – an example



empowering
research and scientific
excellence

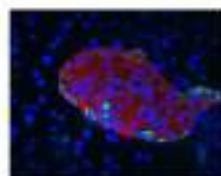
10^{years}

What can we help you with



Model Generation

Genetically modified rodent models have become a key tool in basic and biomedical research. The ability to engineer the mouse genome has greatly transformed biomedical research in the last decade. [Find out more](#)



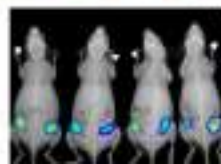
Phenotyping

The genomes of humans, mice and other species have been completely sequenced, yet the knowledge of genome sequences as such does not shed light on questions concerning the functions of these sequences. [Find out more](#)



Animal Facility

The Animal Facility Module of the Czech Center for Phenogenomics is based on the latest advances in housing, breeding and care of laboratory mice and rats. [Find out more](#)



Preclinical Testing

The Czech Centre for Phenogenomics can offer a very broad portfolio of highly standardized assays useful for preclinical studies on rodents including established disease models. [Find out more](#)

From our Bluesky



Czech Centre for
Phenogenomics (CCP)

ccp.phenogenomics.biology.cz



CCP celebrates 10 years of biomedical research excellence. Proud to be part of this success story, CCP has grown into one of Europe's leading phenogenomics centres, advancing rare disease research, gene therapies, and infectious disease studies. [#empoweringlife](#)



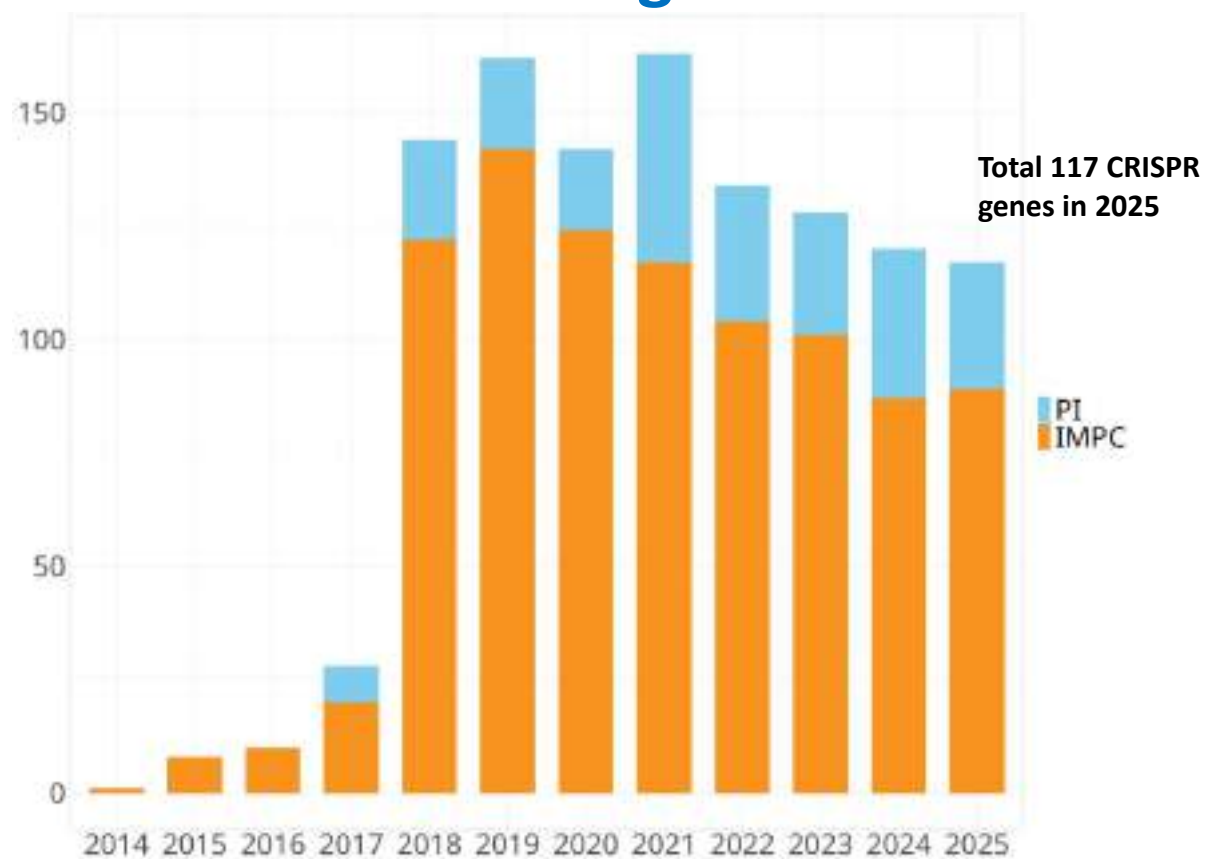
On June 4, 2026, we welcomed U.S. Ambassador to the Czech Republic Nicholas Marick and Tubo Fahr (Program Director at NIDDK) to our center. We were pleased to showcase our unique research infrastructure, take a rare behind-the-scenes look beyond the phenobarrier. [#Science](#) [#ResearchInfrastructure](#)



- 140 staff members
- 9,000 sqm
- Basic research
- Preclinical development
- 100-150 new mouse models per year
- CCP full operation since 2016

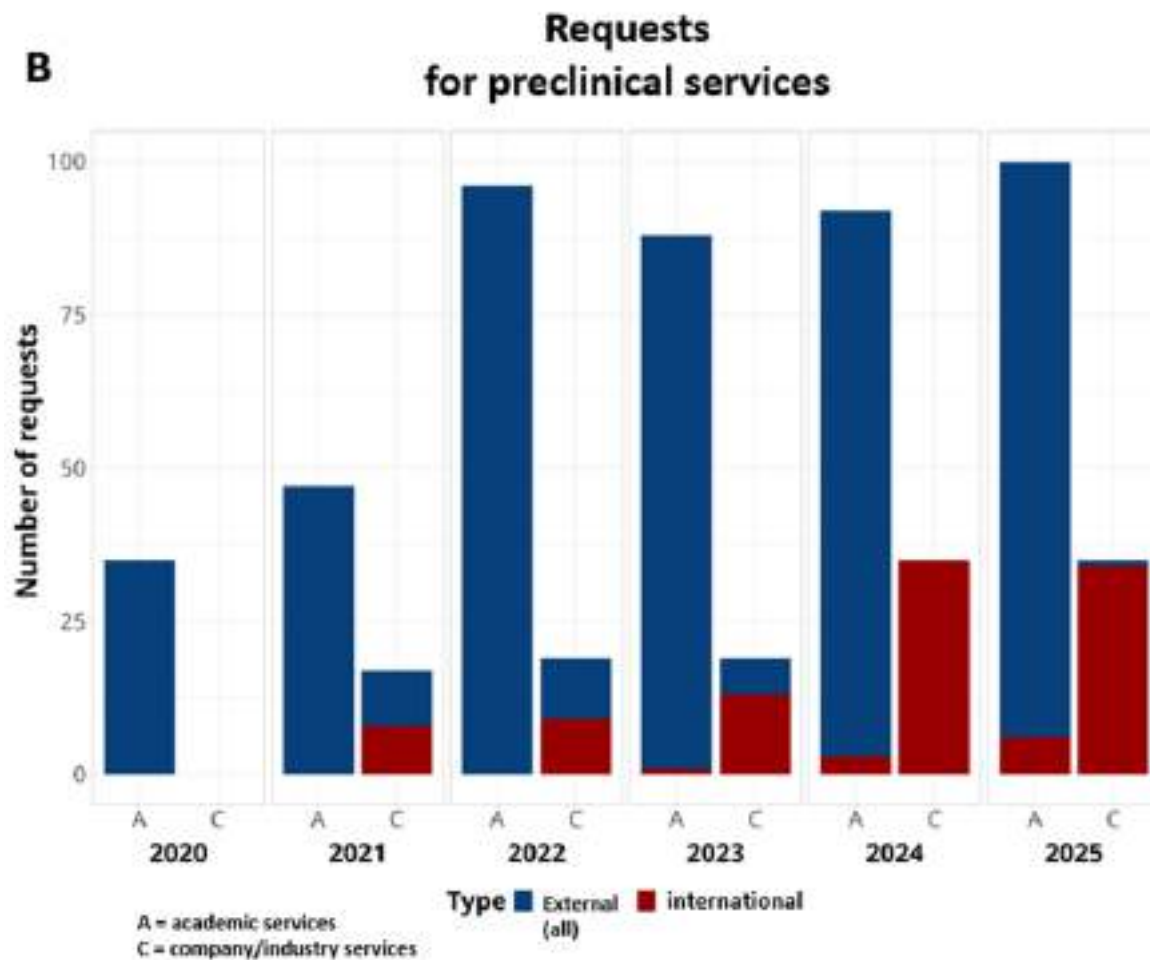
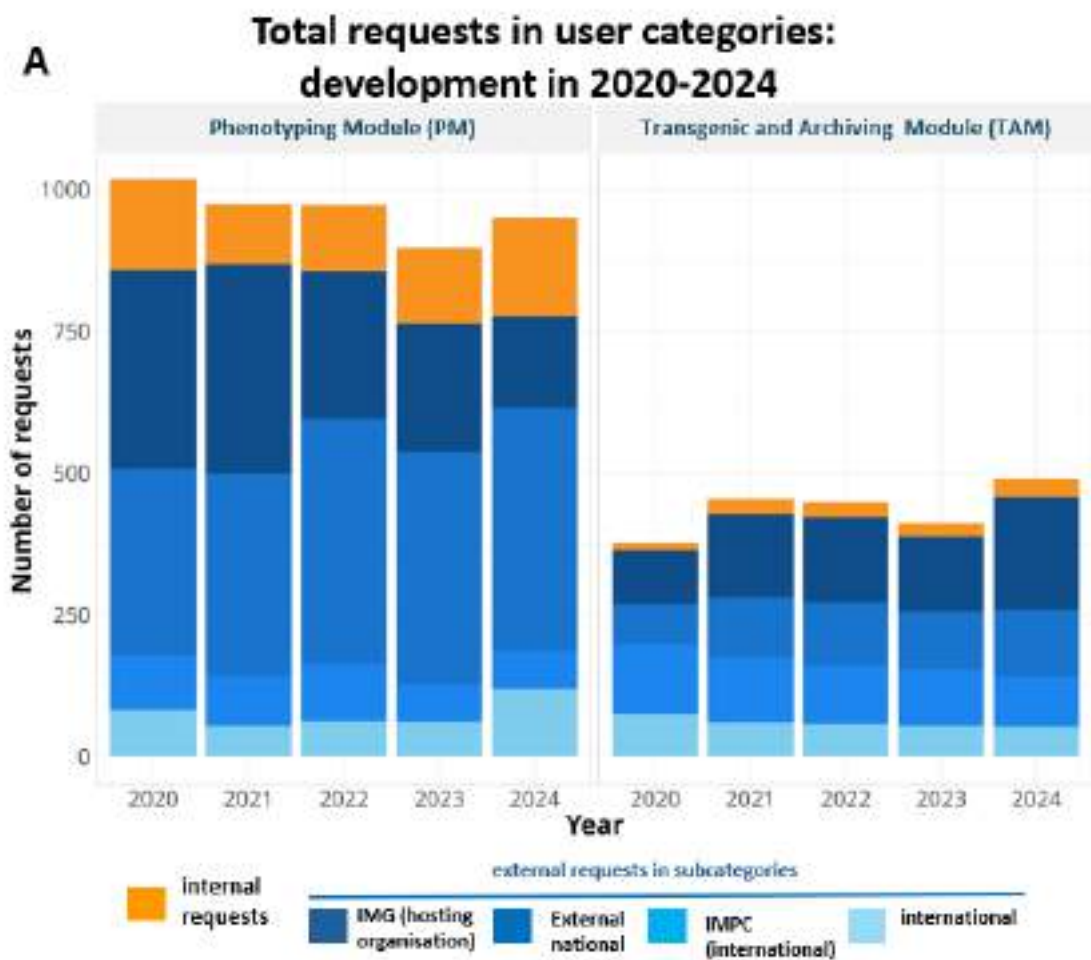
CCP: Service to the scientific community & building resources

>1000 CRISPR genes !



CCP- requests for services :

high stable demand with increasing number for large preclinical services



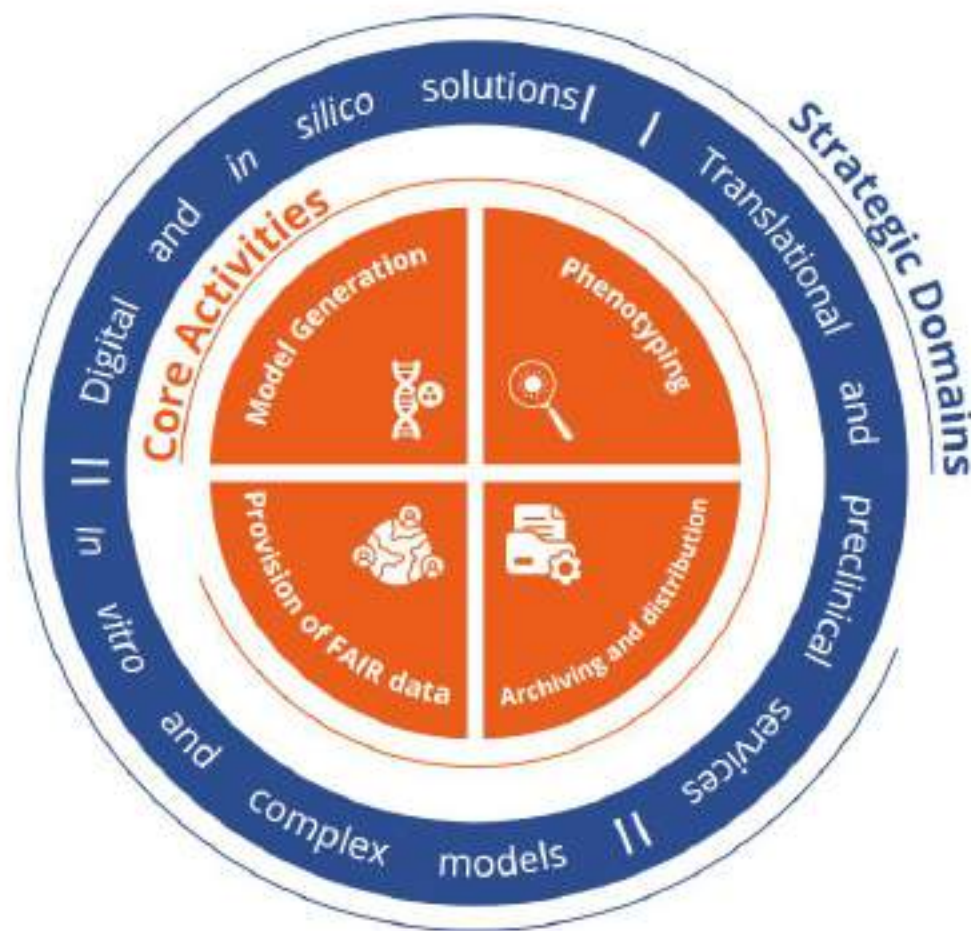


INFRAFRONTIER



**“From *models* to
causal mechanisms,
from *mechanisms*
to *medicine* ...**

... advanced rodent model generation, systemic as well as specialized phenotyping and archiving and distribution of models that mimic health and disease are the core services of INFRAFRONTIER ...



Data release 24 is now here with over 138 million data points! Total of 9,605 knockout genes are phenotyped. Read more [here](#).

GENES

PHENOTYPES

HELP, NEWS, BLOG

Search All 9605 Knockout Data...



① What you need to know about IMPC data



What you need to know about IMPC data

- » We generate our own data, it is **not aggregated** from publications
- » We are targeting genes that are yet to be studied
- » We have **standardised** production methods to knock out genes
- » Mutants and wildtype mice tested under the **same phenotyping protocols**

[Learn more about IMPC data](#)

9605 total knockout genes phenotyped

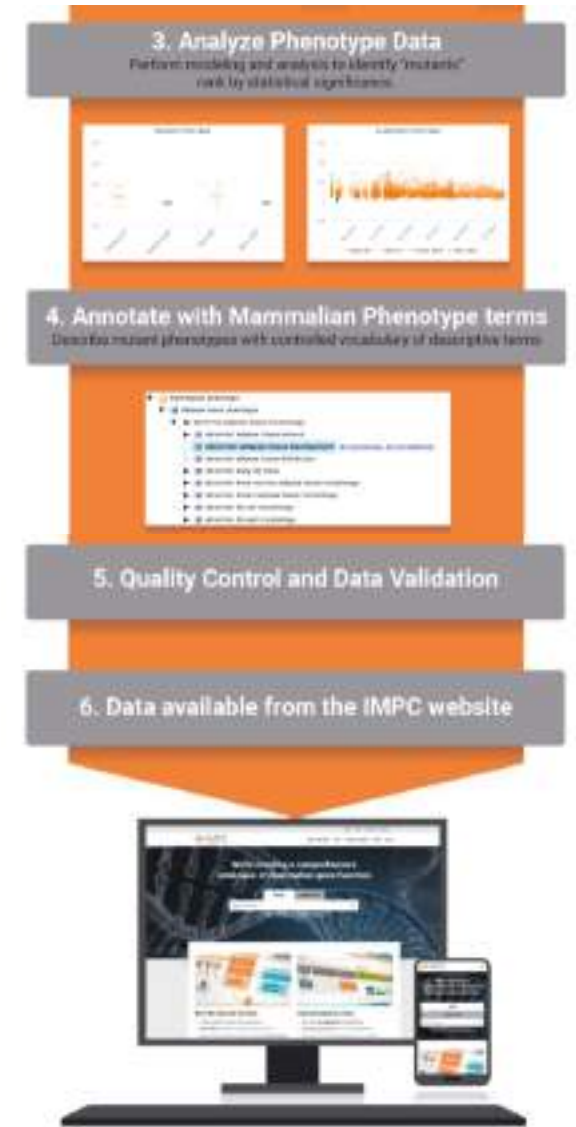
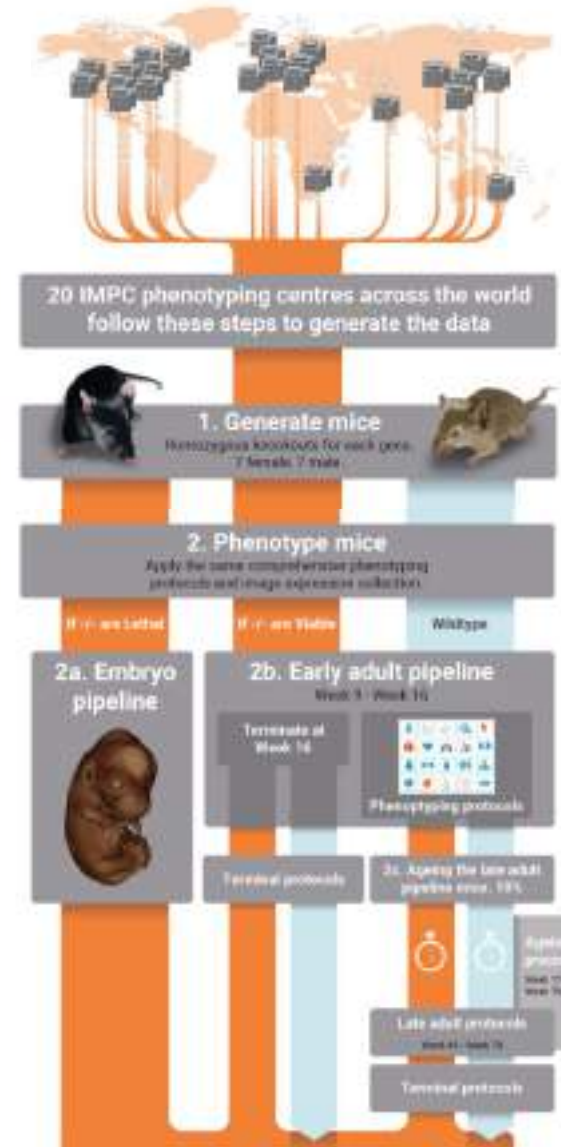
- » Number of phenotyped lines: **10341**
- » Statistically Significant Calls: **111664**
- » Data Release Version: **24**
- » Published: **16 March 2026**

[View Release Full Report](#)

IMPC: mission and goals

.....to generate a comprehensive catalogue of mammalian gene function and provide the foundations for the functional analysis of human genetic variation

- insight into the function of **every gene** by the creation and analysis of null mutations
- relationship between genome and phenome by the generation of putative human pathogenic variants in both **coding and non-coding** sequences



Phenotype traits: Open access

GENES
PHENOTYPES

Search All 7022 Knockout Data... 🔍

Gene: Uchl1

?
Log In to follow

Name: ubiquitin carboxy-terminal hydrolase L1

MGI ID: MGI:103149

Synonyms: PGP9.5 PGP 9.5

Viability: Homozygous viable

Embryo viewer: N/A

Other links: MGI [↗](#) Ensembl [↗](#)

Significant
Not Significant
Not tested

View body weight measurements

Significant phenotypes (7)

Measurements chart (235)

All data table (538)

Expression & Images (97)

Disease models (1446)

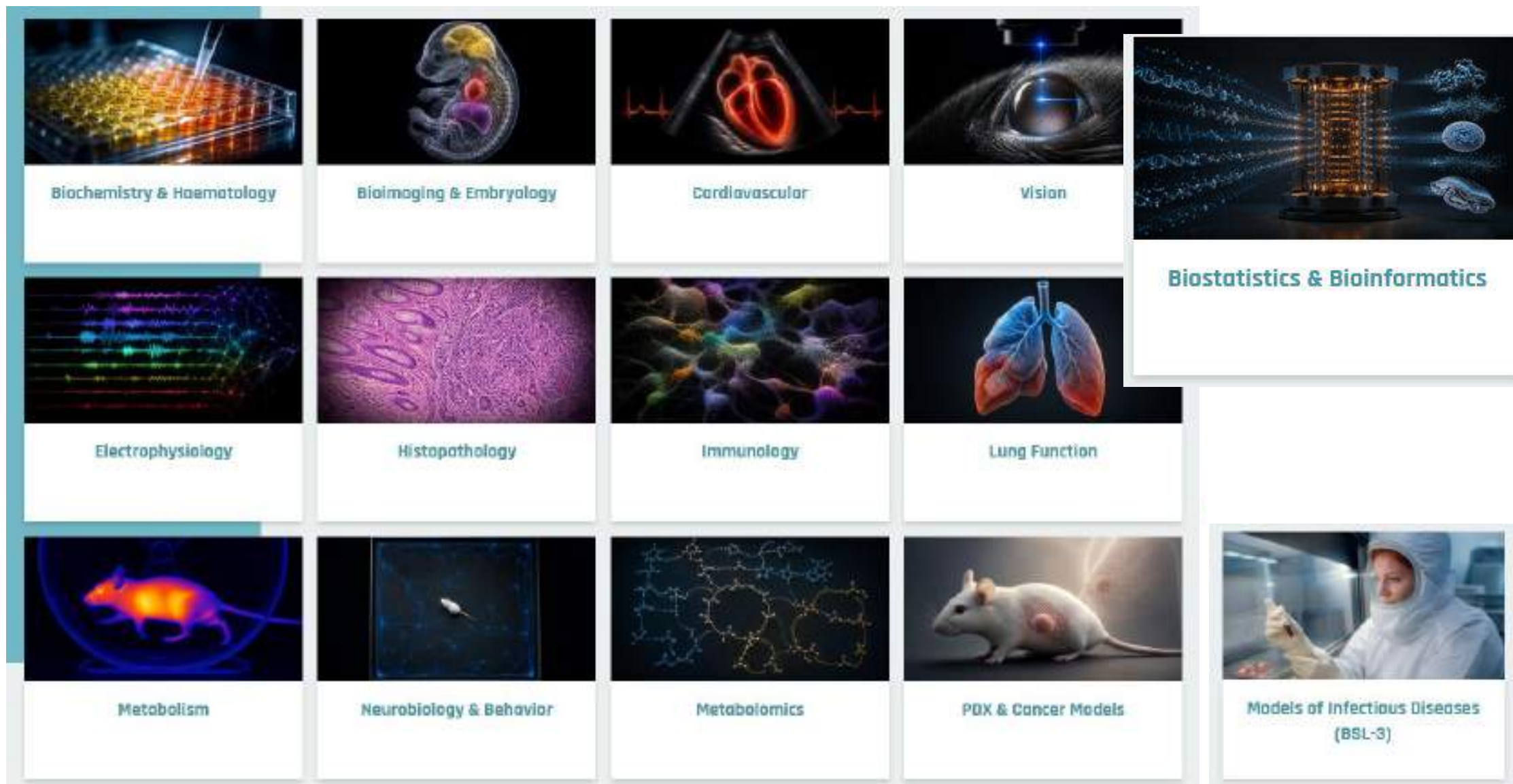
Order (2)

📁 Significant phenotypes (7/7)
📊 Measurements chart (235/235)
📋 All data table (538/538)

X

Phenotype	System	Allele	Zyg	Sex	Life Stage	P Value
abnormal circulating serum albumin level		Uchl1 ^{DKO(BLCCOMM)tmng}	HET	♀ ♂	Early adult	1.32×10 ⁻⁰⁸
abnormal spine curvature		Uchl1 ^{tm1n2UCOMM} /tmng	HET	♀ ♂	Early adult	1.63×10 ⁻¹¹

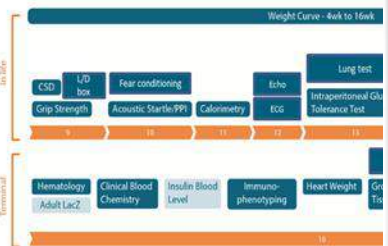
Phenotyping platform



..... towards rare/pediatric diseases

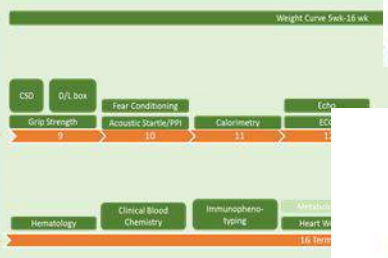
Systematic phenotyping pipeline towards specialized phenotyping

IMPC/CCP standard phenotyping

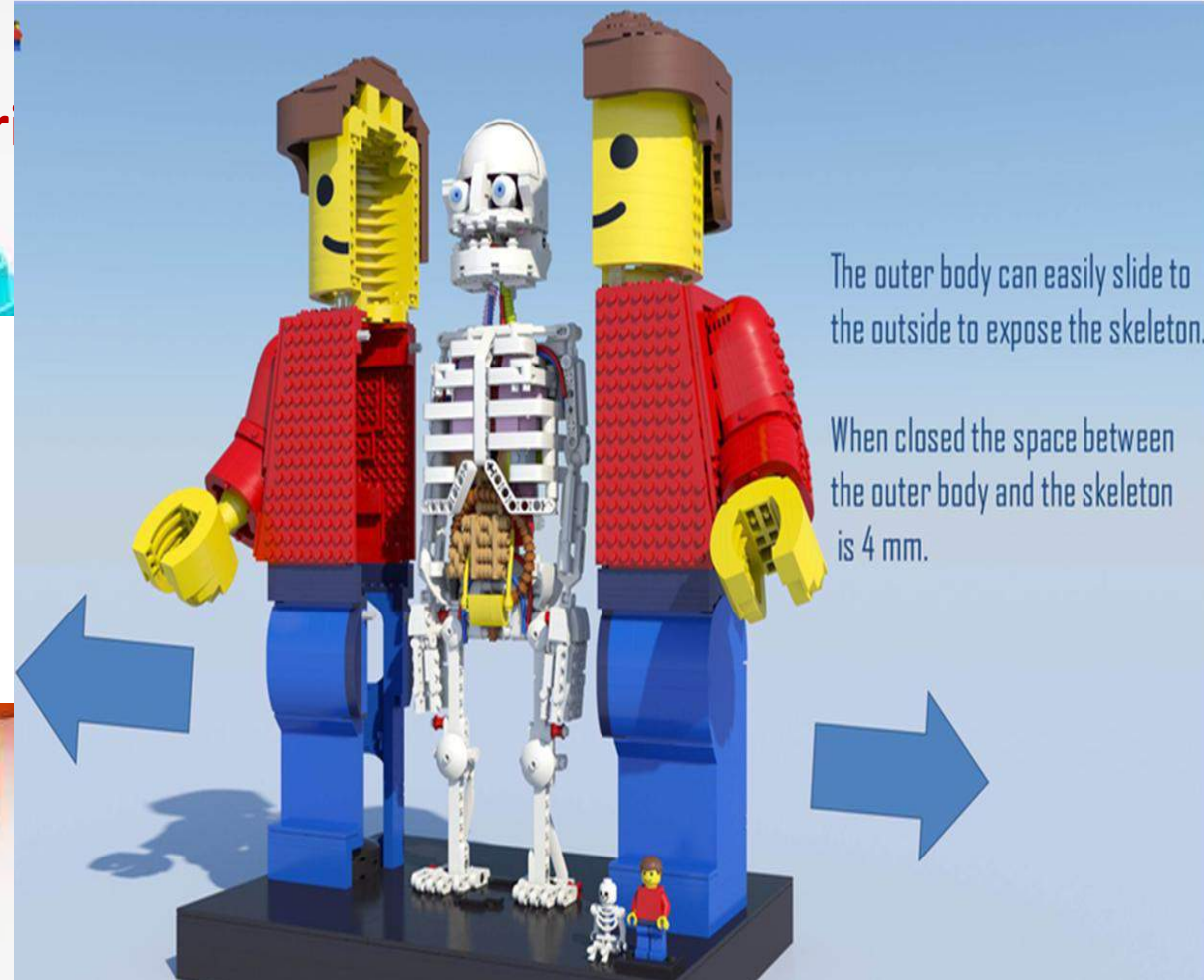


800-1000 parameters

Rat phenotyping pipeline



phenotyping ,lego' bricks

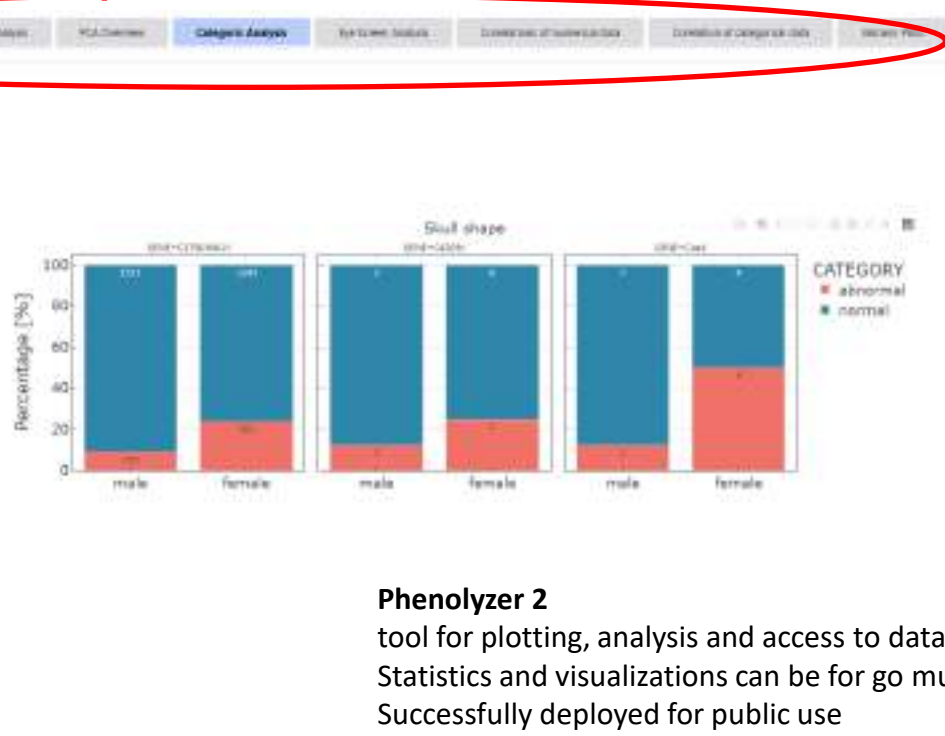


Pheno-pipeline: specific analysis ,Phenolyzer 2‘

<https://tesla.img.cas.cz/apps/ccp/phenolyze-2/>

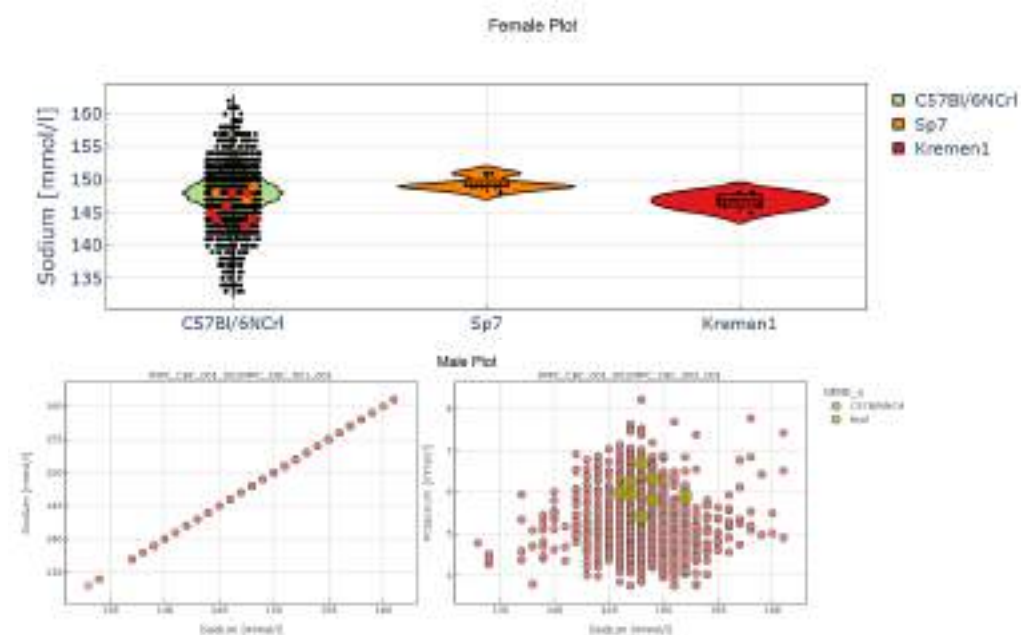


Selection type of analysis



Selection of time span for WT

Selection procedure, parameter and Gen



Phenolyzer 2

tool for plotting, analysis and access to data in our database

Statistics and visualizations can be for go multiple genes.

Successfully deployed for public use

<https://ccp-tools.img.cas.cz/apps/phenolyze-2/>

Added volcano plots. Phenolyzer integrates advanced methods such as principal component

analysis (PCA), correlation, and regression analyses

Subgroup analysis based on allelic configuration

Vastly improved performance of the applications

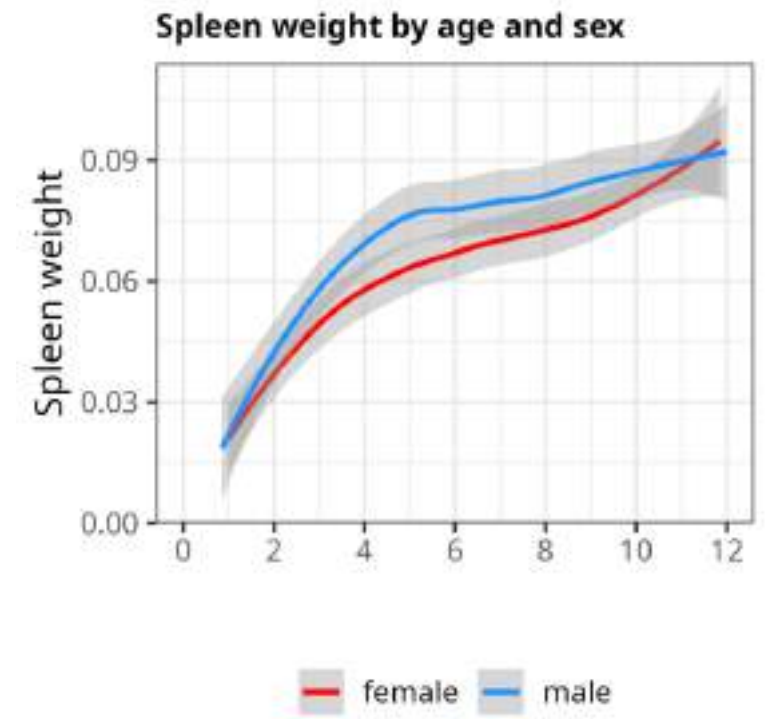
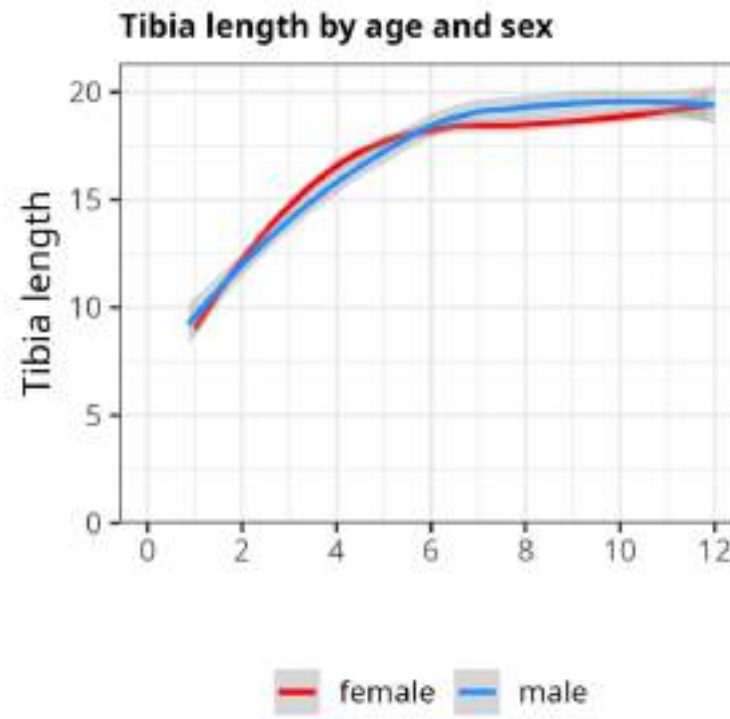
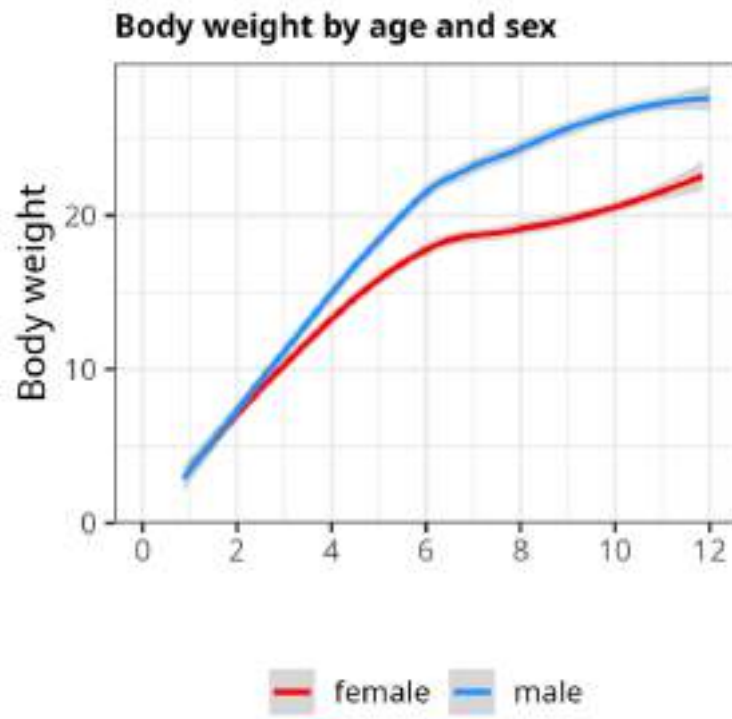
CCP's Juvenalis study:

phenotyping juvenile mice to understand pediatric diseases

- **Many rare diseases manifest in childhood**, when organ systems are still developing; therefore, adult-only phenotyping can miss early, disease-relevant phenotypes.
- **Juvenile phenotyping in mice** (from early postnatal stages up to adulthood) allows us to capture dynamic changes in immune, skeletal, and cardiac development that mirror pediatric disease trajectories.
- The **Juvenalis study establishes age-matched baseline data in wild-type animals and applies tailored pipelines to subviable mutant strains** that cannot complete the full IMPC screen.
- Using these **baselines**, we can interpret early phenotypes in subviable strains and connect them more directly **to pediatric presentations of rare human diseases**.

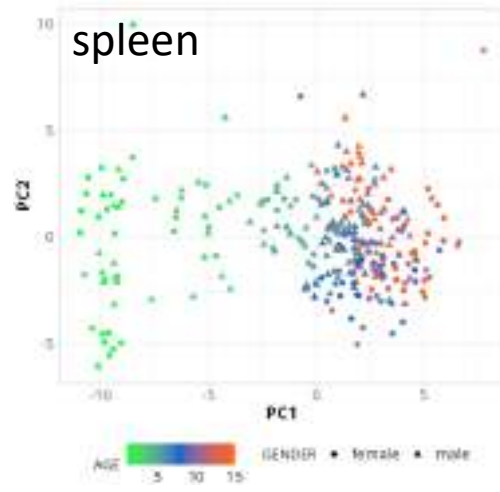
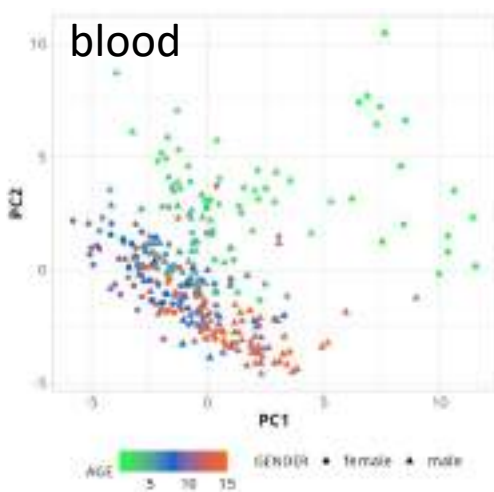
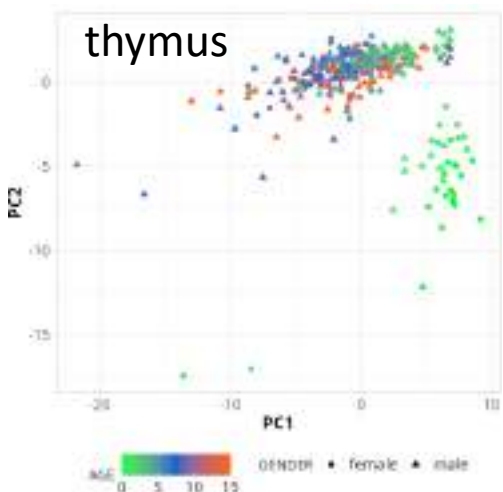
CCP's Juvenalis study:

Example control data baselines (10 females, 10 males)



CCP's Juvenalis study:

Immunology pipeline: the dynamics of immune system development



Thymus- one panel

thymus Panel	
viability	Hoechst33258
CD19	PB
CD8	BV605
GITR	BV711
Annexin V	FITC
CD5	PerCPy5.5
TCRbeta	PE
CD25	PE-Cy7
CD4	APC
CD44	APC-eF780

populations

- DN1-DN4 thymocytes
- DP thymocytes
- CD4+ thymocytes
- CD8+ thymocytes
- T regulatory cells
- pre-postselection T cells

Fc Block

Blood- one panel

blood Panel	
viability	Hoechst33258
CD5	BV421
CD44	BV510
CD8a	BV605
GITR	BV711
Ly6G	BV785
CD45	FITC
CD11b	PerCPy5.5
CD161	PE
CD19	PE-CF594
CD25	PC7
CD4	APC
Ly6C	AF700
CD62L	APC-Cy7

populations

- T helper cells (eff/ resting)
- T regulatory cells (eff/ resting)
- T cytotoxic cells (eff/ resting/ naive)
- NK cells
- NKT cells
- B cells
- monocytes
- neutrophils
- eosinophils

Fc Block

Spleen- two panels

spleen Panel A	
viability	ghost dye UV450
CD5	BV421
CD49d	BV510
γδTCR	BV605
GITR	BV711
CD4	FITC
Klrg1	PerCPy5.5
CD44	PE
CD25	PC7
CD8a	PE-CF594
CD161	APC
CD62L	APC-Cy7

Fc Block

populations

- γδT cells
- T helper cells (eff/ resting)
- T regulatory cells (eff/ resting)
- T cytotoxic cells (eff/ resting/ naive)
- NK cells
- NKT cells

spleen Panel B	
viability	ghost dye UV450
CD5	BV421
Ly6G	BV421
CD19	BV510
Bst2	BV605
CD21	BV711
Ly6C	FITC
CD11b	PerCPy5.5
CD21/35	PE
F4/80	PE-Dazzle594
CD11c	PC7
CD161	APC
MHCII	APC-Cy7

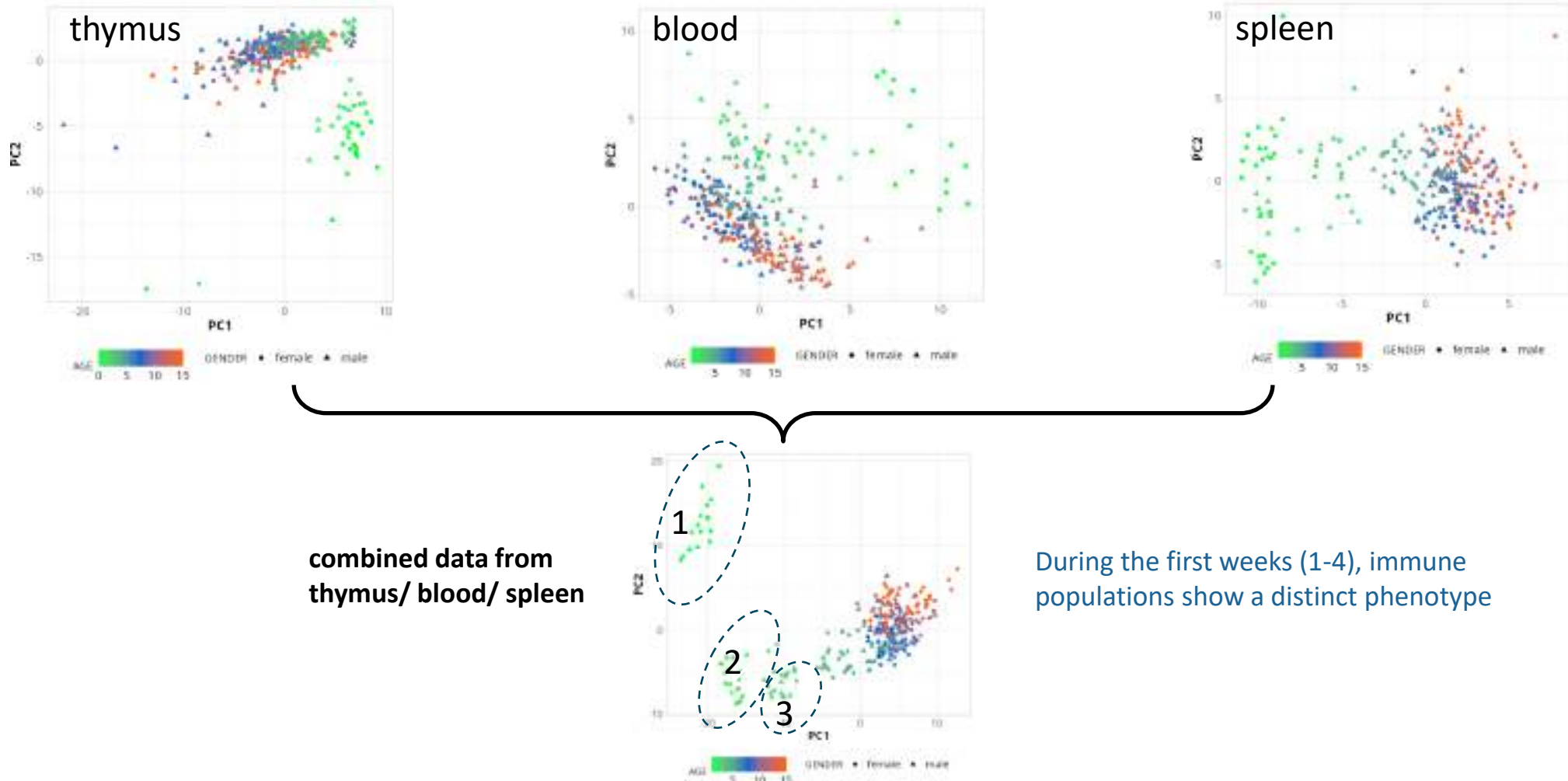
Fc Block

populations

- B cells
- macrophages
- monocytes
- neutrophils
- eosinophils
- cDC
- pDC
- T cells
- NK cells
- NKT cells

CCP's Juvenalis study:

Immunology pipeline: the dynamics of immune system development



CCP's Juvenalis study:

All tested strains show increased blood neutrophils, suggesting an imbalance in the immune system

mouse-model examples:

▪ Fgf23 mutant:

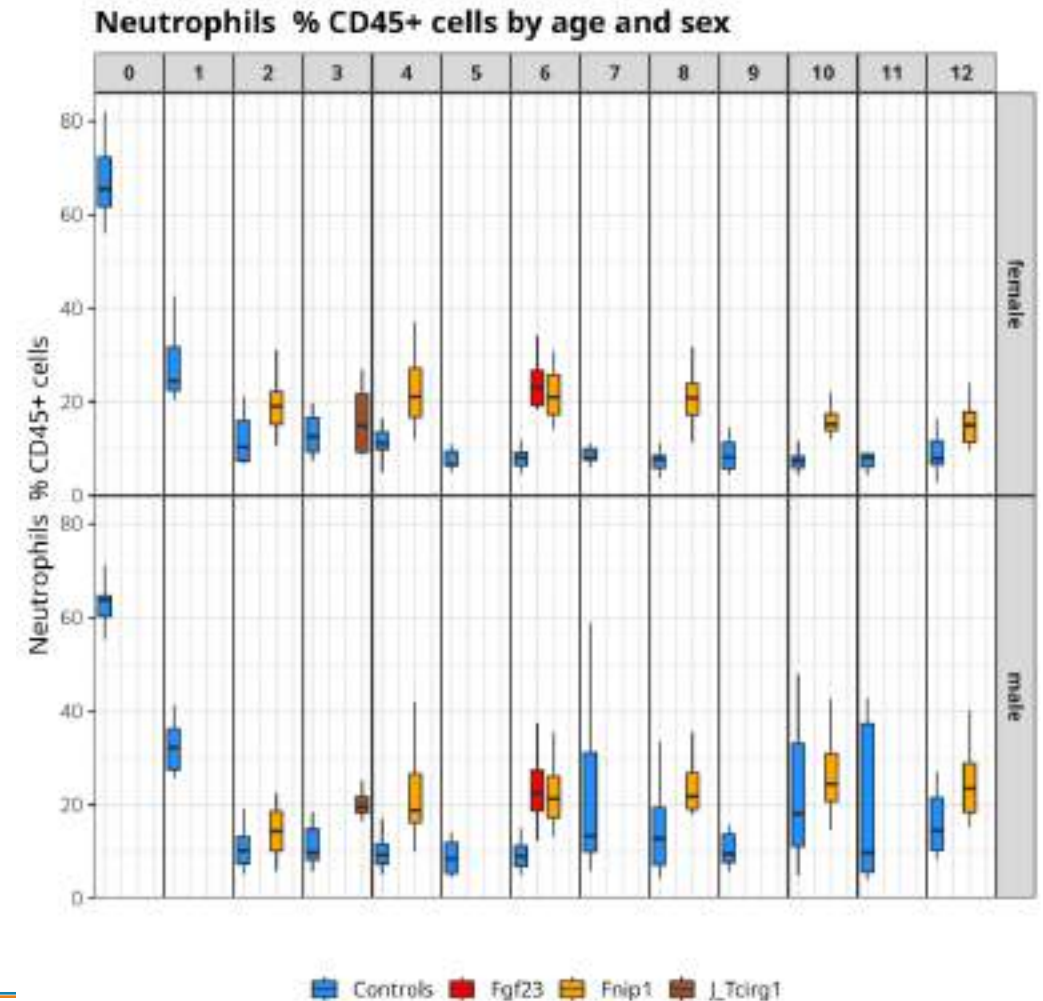
Early skeletal phenotypes measured up to 6 weeks, modelling disturbed bone and mineral metabolism relevant to pediatric skeletal disorders.

▪ Tcirg1 mutant:

Strong juvenile immune and cardio phenotypes measured up to 3 weeks, reflecting early-life immune imbalance and altered cardiac maturation.

▪ Fnip1 mutant:

Immunology and cardiac phenotyping up to 12 weeks, capturing prolonged developmental effects on immune system and heart relevant to childhood-onset rare disease.



New Strategic Goal

Rare Diseases - Pathogenic Gene Variants



**Current patient needs
&
technological
development**

Towards Rare Diseases - pathogenic gene variants

for the period: 2027-2035

A statement and details of the IMPC's goals for the next ten years:

Goal 1

Complete the generation of a null mouse mutant resource for the coding genome that delivers a comprehensive catalogue of mutant strains available to study mammalian gene function.

Goal 2

Design and produce a genome-wide mouse strain resource of human disease-associated coding variants associated with rare disease that can be used for validation of putative functional variants and insight into disease mechanism(s).

Goal 3

Design and generate mouse strains that model genetic variation in the non-coding genome for the IMPC and the global research community to use in a collective effort to assess functionality and mechanism(s) in health and disease.

Goal 4

Phenotype mouse strains with null mutations, human-disease coding variants, and variants in the non-coding genome to provide a comprehensive catalogue of baseline information on mammalian gene function, validate putative functional variants, examine the effects of mutations in the non-coding genome, and provide data-driven insight into disease mechanism(s) and other phenotypic outcomes.

Goal 5

Explore genetic context to realise the wider potential for mouse functional studies to provide models and mechanistic insights for therapeutic development, both conventional therapeutics and for precision medicine.

Goal 6

Develop data integration, analysis, and visualisation approaches to translate mouse functional genomics studies to the human gene and disease knowledge base and vice versa, underpinning synergies in the fundamental understanding of genetic and disease systems – enabled and strengthened by dynamic interactions and networks with human genome centres, clinical genetics consortia, and data-curated biobanks that we serve.

the Czech Centre for Phenogenomics



together with

the Institute of Molecular and Translational Medicine,



and other partners announces

RD (rare disease)-Factory programm:

the research programm to tackle rare diseases and their therapies

RD - factory program:

OPEN CALL FOR RD/GENE NOMINATIONS

We are pleased to announce the ***RD-factory PROGRAM*** call for proposals for preclinical studies on pathogenic gene variants causing rare human genetic diseases. The objective is to:

- create a suitable mouse model (disease-associated coding variants associated with rare disease) for the description of disease development and for therapy testing.
- design and test new therapeutic and curative gene and small molecule and biological and/or cellular therapies.
- test new appearing drugs and therapeutic approaches.
- provide services for development of novel diagnostic approaches for rare diseases, including the diagnostic, prognostic, predictive and monitoring biomarkers.

Online Application started *October 1, 2024*

There is no deadline for submissions, and nominations can be made any time.

RD - factory program – continuous call :

Nomination and Evaluation Process

- The nomination call is open now till **December 2026**, with potential for extension.
- Proposals are submitted through the **CCP online form** and evaluated in average within four weeks of registration.
- **Nominations not selected initially** will be reconsidered at **re-evaluation workshops** scheduled for July and December **2026**.

Selection

The selection from nominated rare diseases had **several aspects**:

- selected **diseases** are currently **not sufficiently researched** and are **not being intensively worked on elsewhere in the world**.
- We also evaluated whether our expertise could advance knowledge about these diseases and whether the proposal is feasible regarding **capacity and funding**.

Selection process



1
Nomination analyzed,
information completed



2
Check for existing
research program
or therapy



3
Assess our
technical
capacity,
feasibility



4
Larger community
can benefit

Possibilities to interact with
research communities,
maximal usage of the
models



n-lorem
FOUNDATION

- MANBA
- MAPK8IP3
- MAST4
- MECP2
- MED13L
- MEF2C
- MFN2
- MFSD8
- MNI
- MORC2
- MTAP
- MTOR
- MT-ND1
- MYH7
- MYT1L



**The Jackson
Laboratory**

RD - Factory program:

1 st round	2 nd round	3 rd round
CTNNB1 Syndrome	LCHAD deficiency	GRIN2B-related Neurodevelopmental Disorder
MADD Deficiency	DEAF1 Syndrome – DEAF1	Refsum disease (PHYH mutation)
Pitt Hopkins Syndrome	Ataxia Telangiectasia – ATM	Drug resistant epilepsy (RRAGB mutation)
Harlequin Ichthyosis	Familiar Mediterranean Fever (FMF) – MEFV	Neurodevelopmental Disorder with severe Motor Impairment and Absent Language syndrome (DHX30 mutation)
Canavan Disease	DEE PACS2 syndrome – PACS2	Tetralogy of Fallot
Bloom Syndrome	AGO1-related syndrome	Myofibrillar Myopathy Type 13 with Rimmed Vacuoles syndrome
ADSL Deficiency	CFC Syndrome Type 4 – MAP2K2	SPATA5
KCNH1-Related Developmental and Epileptic Encephalopathy	SATB2-associated syndrome (SAS)	TBA
Liang-Wang Syndrome (LIWAS)	ARSACS (Autosomal Recessive Spastic Ataxia) – SACS	TBA
YWHAG Developmental and Epileptic Encephalopathy	NBIA – C19orf12 (c.204_214del) MPAN	TBA
Lessel-Kreienkamp Syndrome (Ago2)	CORD (Cone-Rod Dystrophy) – ABCA4	TBA
Developmental Epileptic Encephalopathy (DEE65)	KAT6A Syndrome (Arboleda-Tham)	TBA

**31 selected RDs
from 130+ nominated**

RD-Factory programm - example:

Netherton syndrom

Netherton Syndrome (NS)

- Autosomal recessive
- Prevalence 1 : 200 000
- Caused by mutations in the gene **SPINK5**
- Gene **SPINK5** encodes for **LEKTI**
- **LEKTI** - inhibitor of serine proteases - important for the proteolytic homeostasis of the skin/epidermis



Saleem et al. 2018

Symptoms

- skin barrier failure, Ichthyosis Linearis Circumflexa
- generalized red, scaly skin (erythroderma)
- fragile "bamboo hair" that breaks easily,
- severe immune system problems like allergies and high IgE; frequent infections



Netherton Syndrome (NS)

Current treatment

emollients for treatment of the skin disorder
topical steroids and topical immunomodulators
IL-17 antagonist secukinumab.

Experimental

Small molecule protease inhibitors
ShRNA inhibition of proteolytic pathway
Gene substitution/repair

SC
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Institute of Molecular Genetics
at the Czech Academy
of Sciences

 IMG

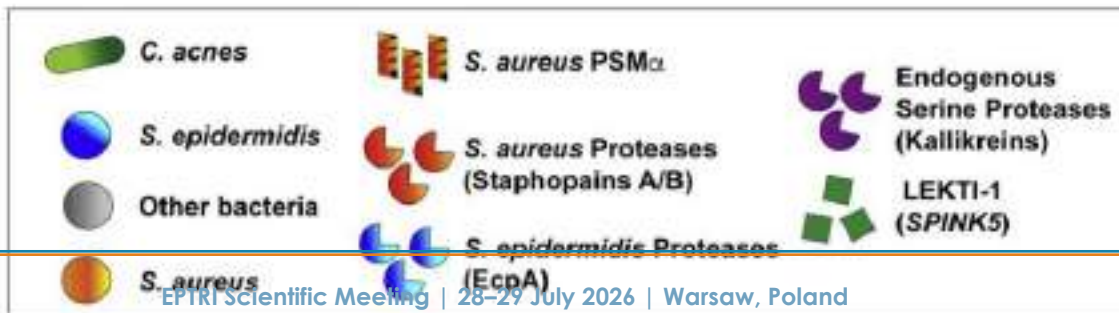
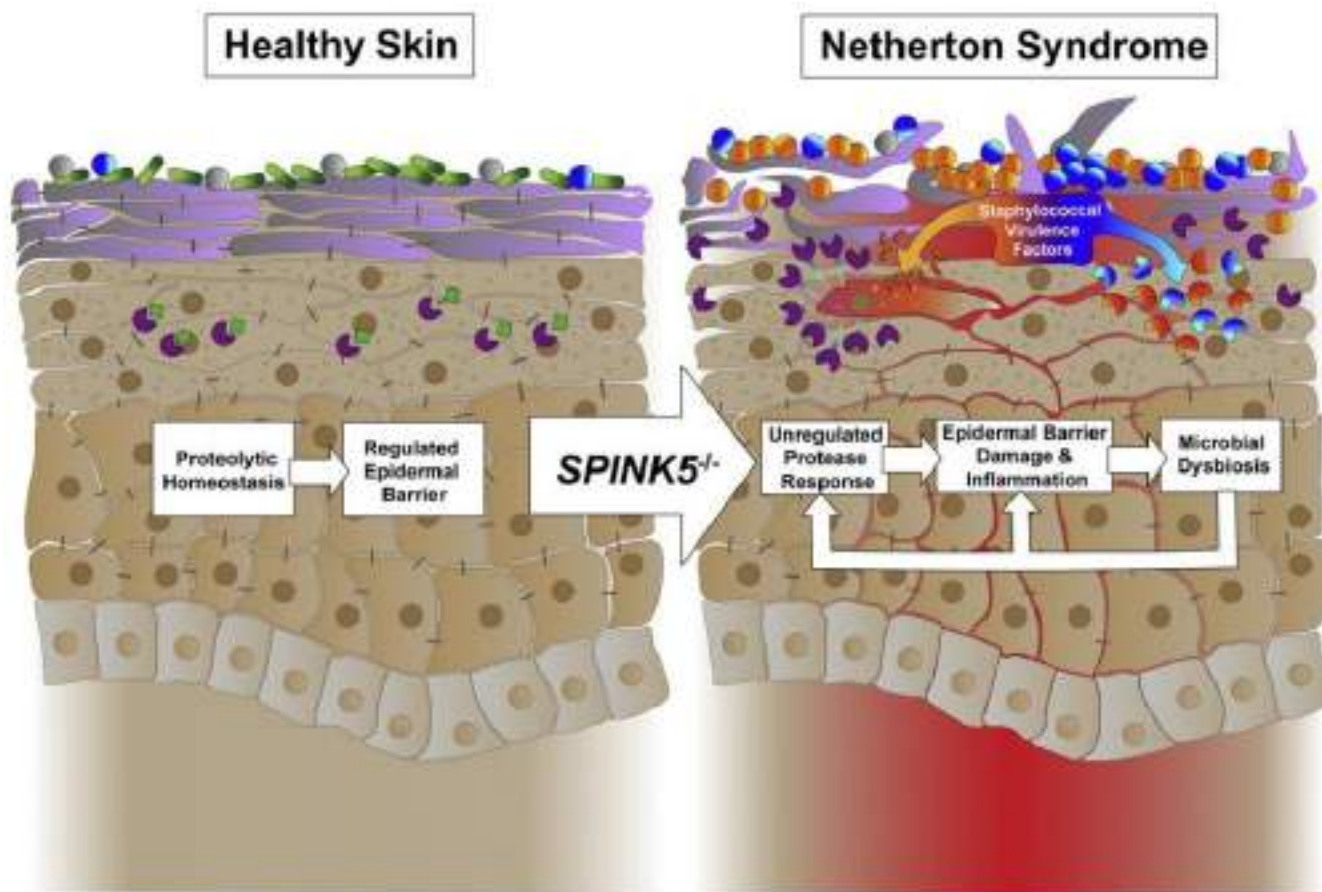


↑ Proteolytic activity of kallikreins
(KLK5, KLK14, KLK7)

Netherton Syndrome

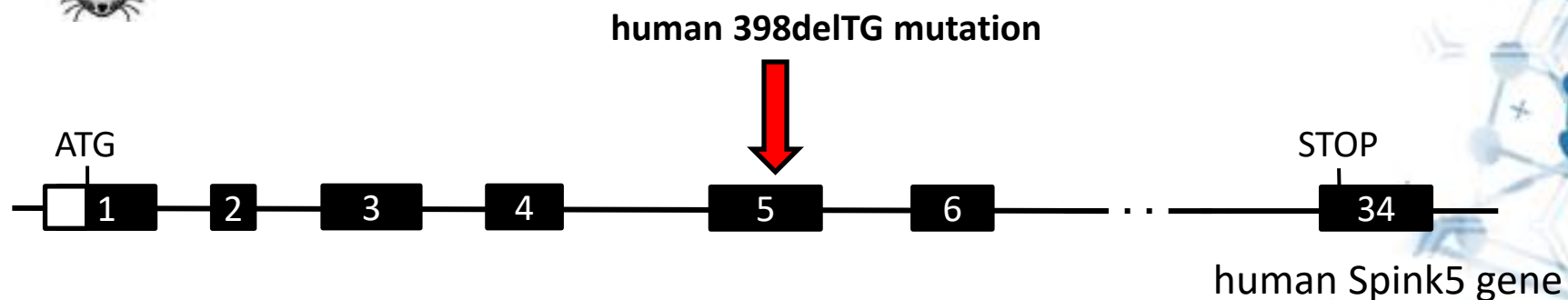
↓ LEKTI
↑ Proteolytic activity of
kallikreins (KLK5, KLK14, KLK7)

Epidermal barrier damage



Generation of a first mouse model for Netherton syndrome

Spink5 -/-



human wt: 5' CTG TGT GCT GAG AAT GCG 3'
human 398delTG: 5' CTG TGC TGA . . . 3'

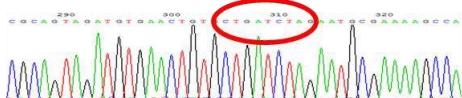
murine wt: 5' CTG TGT GCT GAG AAT GCG 3'
murine 402delTG: 5' CTG TGC TGA . . . 3'

Netherton syndrome:

KLK5 and KLK7 Ablation Fully Rescues Lethality of Netherton Syndrome-Like Phenotype

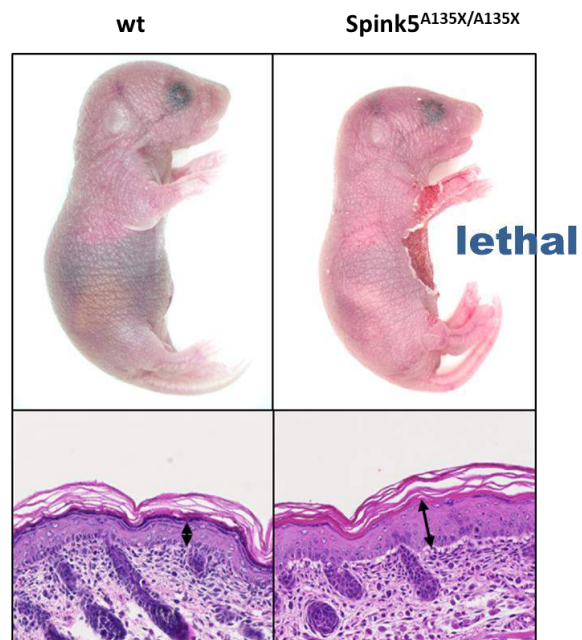
Generation of a mouse models for Netherton syndrome

Spink5^{-/-} cDNA sequencing:

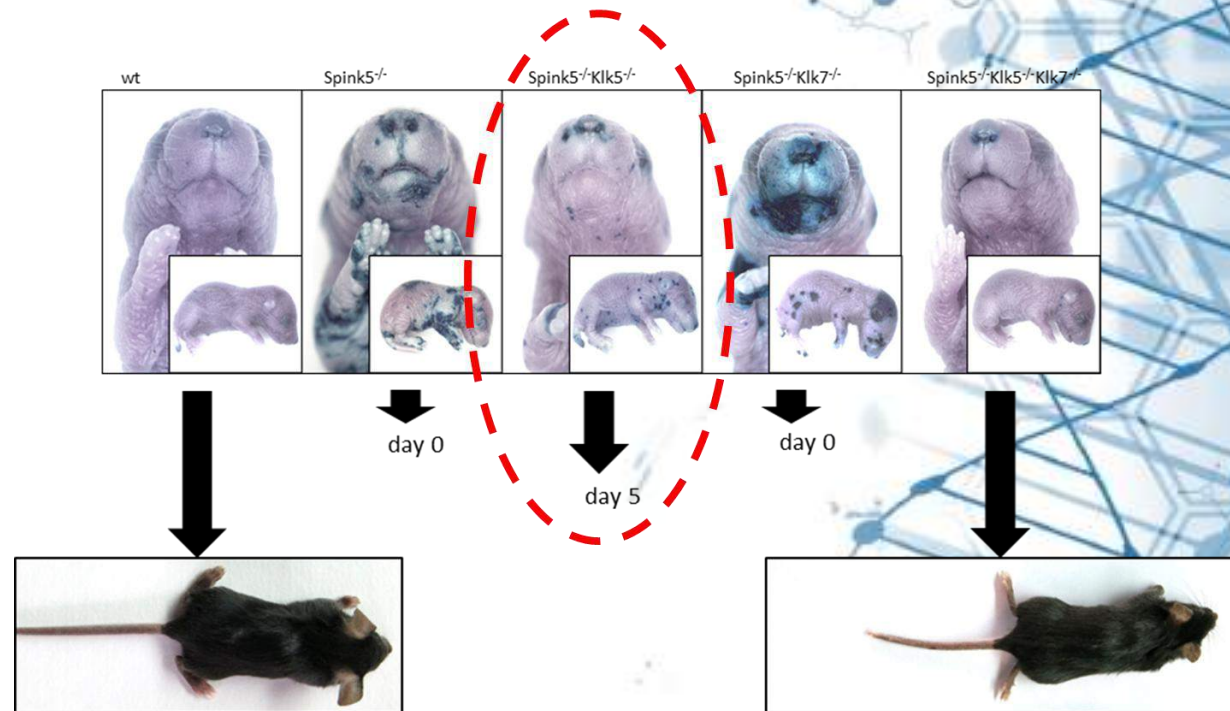


Abnormal differentiation of epidermis:

Acanthosis
Parakeratosis



Epidermal barrier disruption in NS mouse model is rescued by inactivation of KLKs 5 and 7



Kasperek et al., PLOS Genetics, 2017

CCP vision: validated humanized avatars for translational testing

- Humanized 'avatar' models represent highly precise, human-relevant disease models designed to mimic key molecular and phenotypic features of patient disease.
- standardized platforms for rare disease research and preclinical development.
- enabling testing of gene therapy concepts, vector/delivery solutions, and other targeted therapeutic interventions.
- Our long-term aim is to validate these models to a level where they can be recognized by EMA as reliable tools for therapy development and preclinical testing.

[Home](#) [Programme](#) [Registration & Abstracts](#) [Sponsors](#) [Venue](#) [General Information](#) [Contacts](#)

Main topics

Rare/genetic diseases
→
Experimental models
→
Therapies for genetic diseases

Keynote & Featured lectures

Stanley J. Crooke
n-Loxam Foundation, USA

Tim Bertram
NSF Regenerative Medicine
Engine, USA

Kiran Musunuru
Perelman School of Medicine
at the University of
Pennsylvania, USA

Invited speakers

José A. Sánchez-Alcaraz, ISF

Hans-Toni Börsdorf, ISL

Mariana Bracco, PIR

Marcela Buchková, CZE

Ayda Canedo, ITA

Helen-Yung Gee, KOR

Reetta Hietala, FIN

Marcel J. Jansen, NLD

Miroslava Kolářová, CZE

Michèle Krásovská, CZE

Marah Liles, GBR

Roberto Nakashima, USA

Jen Procházka, CZE

Carla Rivolta, CHE

Markus A. Rüegg, CHE

Francisco J. Sánchez-Rivera, USA

Radosław Sudaśki, CZE

Jessie-Hui Tang, KOR

David Sander, CZE

Bertram Voss, DEU

PATIENT & RESEARCH SESSION

Katrina Goldstoneová, CZE

Radosław Sudaśki, CZE

Jen Zisk, CZE

News

REGISTRATION IS OPEN

Please register [here](#).

ABSTRACT SUBMISSION IS OPEN

Submit your abstract [here](#).

Previous meetings

[7th CCP Phenogenomics
Conference 2025](#)

[6th CCP Phenogenomics
Conference 2024](#)

[5th CCP Phenogenomics
Conference 2023](#)

[4th CCP Phenogenomics
Conference 2022](#)

[3rd CCP Phenogenomics
Conference 2021](#)

[2nd CCP Phenogenomics
Conference 2020](#)

[1st CCP Phenogenomics
Conference 2019](#)

Bluesky

Czech Centre
for
Phenogenomics



Invitation:
You are
welcome!

EPTRI General Assembly and Scientific Meeting Warsaw, 28-29 July, 2026

Thank you for your attention !