Institut Clinique de la Souris

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The French Contribution to the IMPC

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Institut Clinique de la Souris
Centre européen de recherche en biologie et en médecine
CERBMgie

phenomin

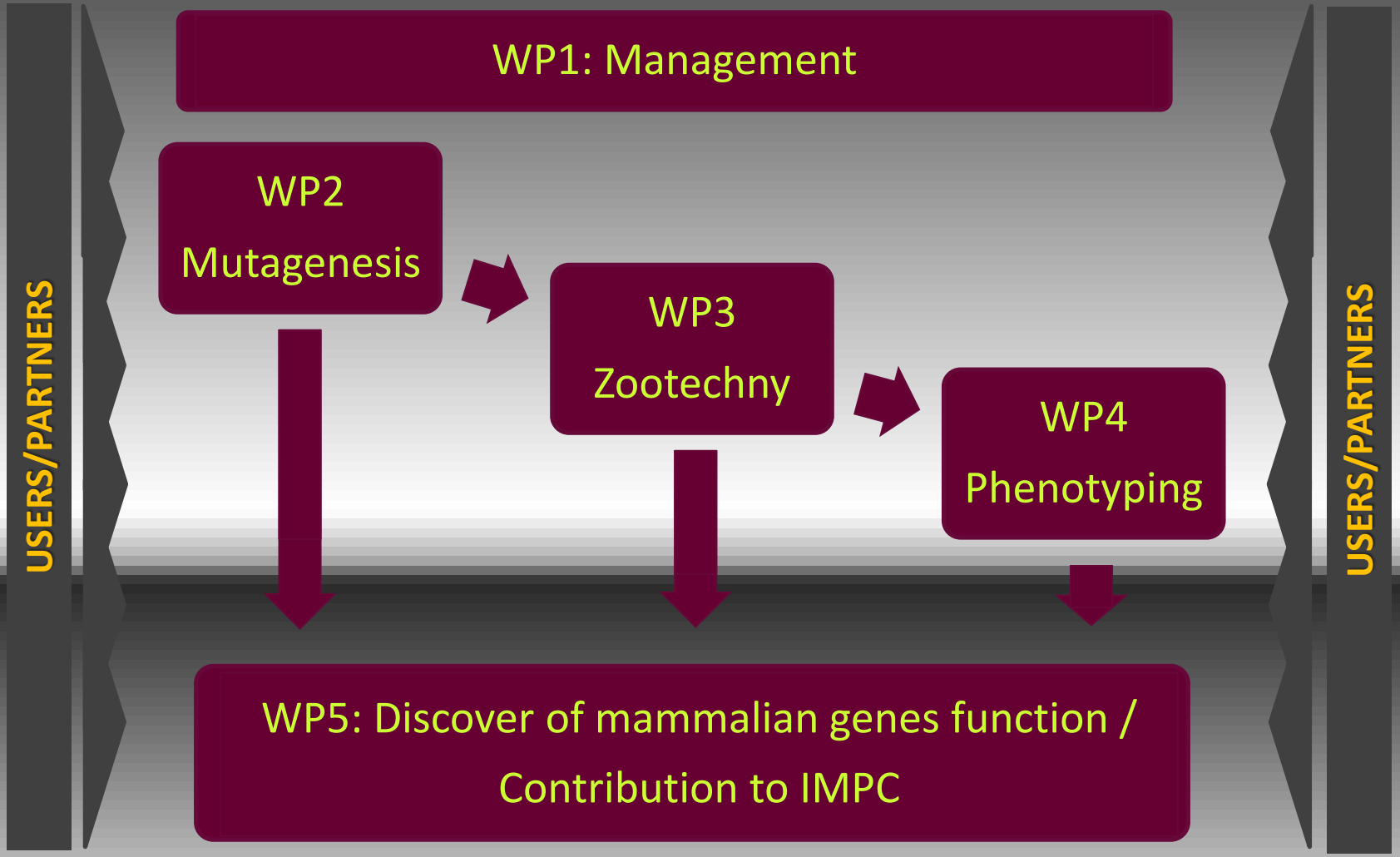
The French National Infrastructure for Mouse PHENOGENOMICS

M. Selloum, M.-C. Birling
G. Pavlovic, A. Ayadi,
T. Sorg, Y. Herault

C. Olivier, S. Lerondel
P. Lopes, C. Fremond,

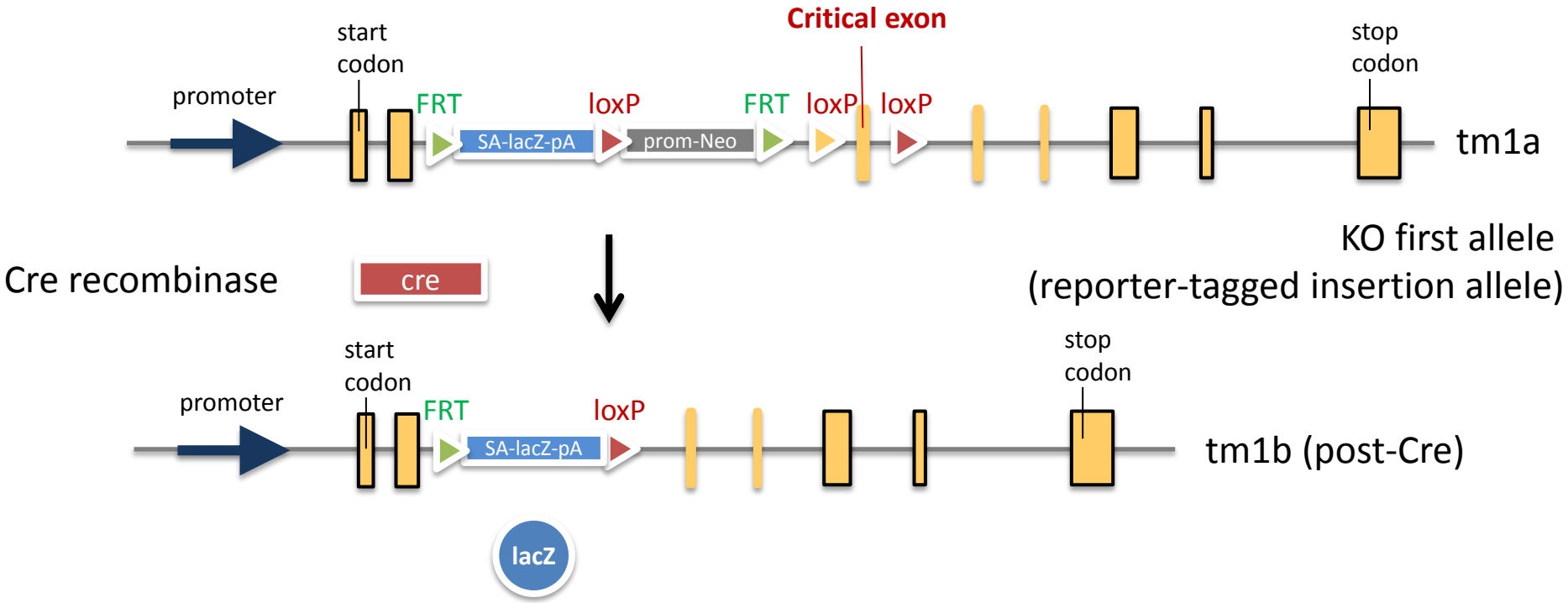
F. Fiore, B. Malissen,

phenomin


WP1: Management
WP2
Mutagenesis
WP3
Zootechny
WP4
Phenotyping
WP5: Discover of mammalian genes function /
Contribution to IMPC
USERS/PARTNERS
USERS/PARTNERS

phenomin

1. ES Cells to Mouse	180	40	30
2. Mouse to Cohort	180	40	30
3. Cohort to Phenotype	250		250
4. Archive and Distribute	180	40	30
5. Tech and Tools Dev	1,2,3	4	1,3


Critical exon
start codon
stop codon
promoter
FRT
loxP
FRT
loxP
loxP
SA-lacZ-pA
prom-Neo
tm1a
KO first allele
(reporter-tagged insertion allele)
Cre recombinase
cre
start codon
stop codon
promoter
FRT
loxP
SA-lacZ-pA
tm1b (post-Cre)
lacZ

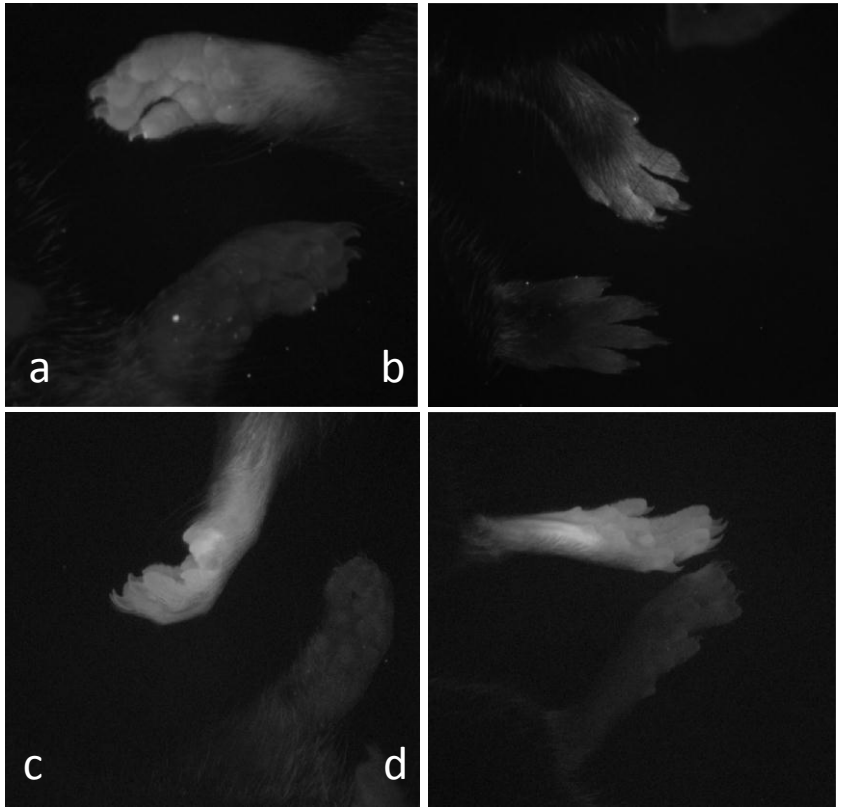
QC and procedures from ES to cohorts

- southern blot analysis for recombination confirmation as well as confirmation of the presence of the 3' loxP site,
- karyotyping of 2 validated clones
- micro-injection in 50 BALB/cN blastocytes
- establishment of chimeras
- breeding of the 4 best chimeras (chimerism >45%)
- GLT assessment (tm1a alleles for cryo)
- Generation of tm1b KO allele (post-Cre)
- IVF quick expansion→ Het (4 males and 8 females)
- Het x Het cross→ Hom (4 males and 4 females)
- Hom X Het crosses: production of cohort, fertility and viability tests (n=4)Males and females)
- 1 Cohort of control per week

Genetic Tools Dev.: Speeding up the Cre-Step with Fluo marker

Rosa26$^{Cre\text{-}GFP/0}$

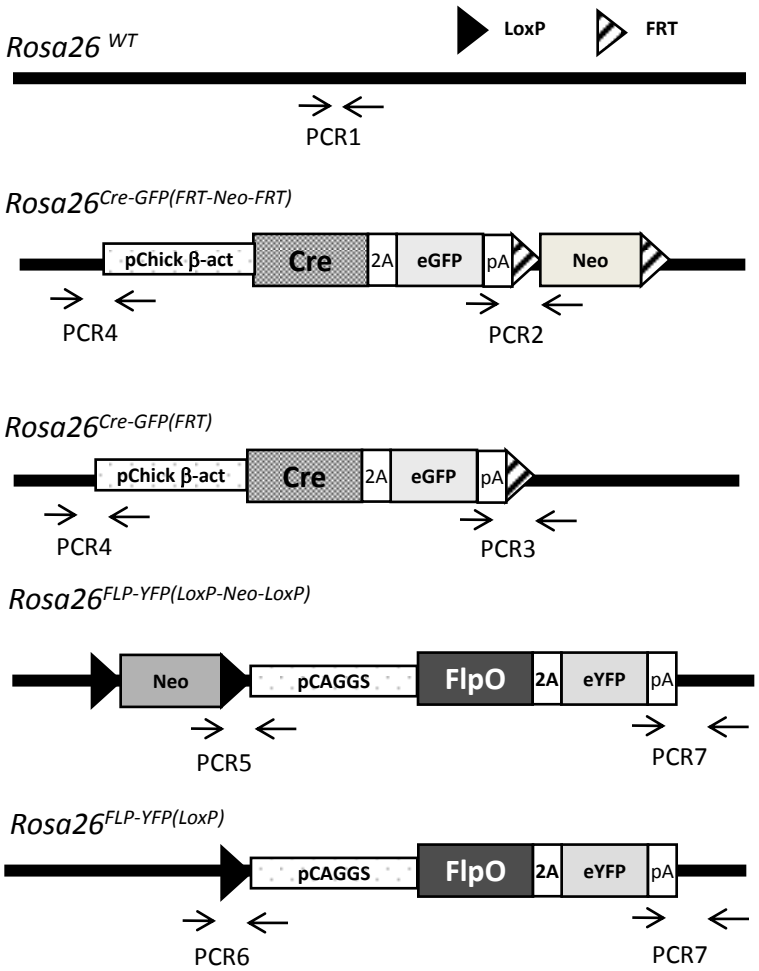
Rosa26$^{Flp\text{-}YPF/0}$

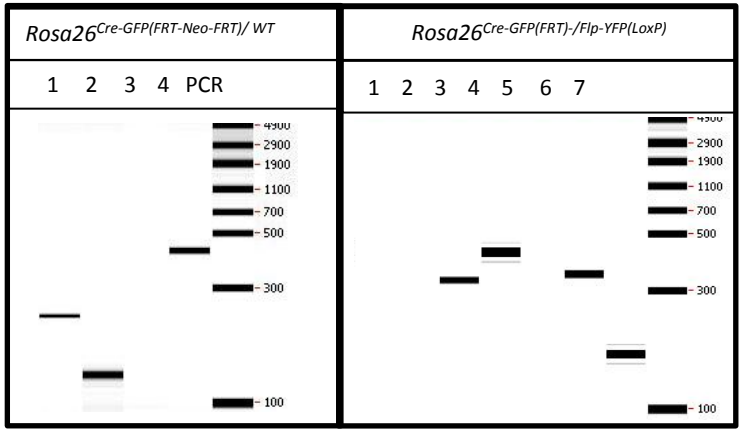


B6N

M-C. Birling, G. Pavlovic

Genetic Tools Dev.: and Maternal Cre effect

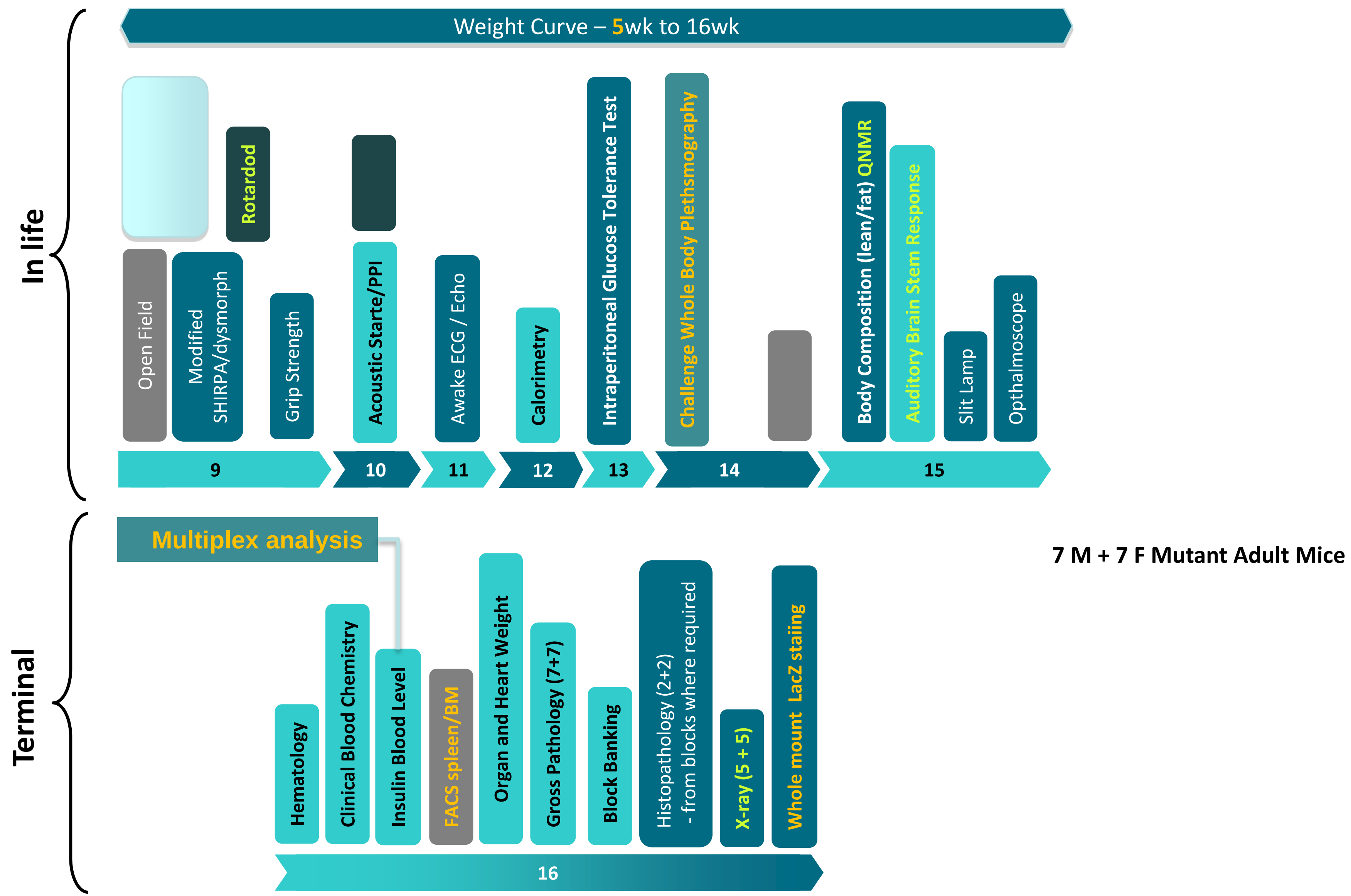




Paternal Rosa26 alleles	Maternal Rosa26 allele: WT	Maternal Rosa26 allele: Flp-YFP(loxP-Neo-loxP)
WT	WT/WT 14	WT/Flp-YFP(LoxP-Neo-loxP) 13
Cre-GFP (FRT-Neo-FRT)	**Maternal contribution** ***Cre-GFP (FRT)/ WT*** **10**	Cre-GFP (FRT) /Flp-YFP(loxP) 7

Paternal Rosa26 alleles	Maternal Rosa26 allele: WT	Maternal Rosa26 allele: Cre-GFP (FRT-Neo-FRT)
WT	WT/WT 29	WT/Cre-GFP(FRT-Neo-FRT) 28
Flp-YFP (LoxP-Neo-loxP)	**Maternal contribution** ***Flp-YFP (loxP)/WT*** **28**	Flp-YFP(loxP)/Cre-GFP (FRT) 13

M-C. Birling, G. Pavlovic


Weight Curve – 5wk to 16wk
In life
Open Field
Modified SHIRPA/dysmorph
Rotardod
Grip Strength
Acoustic Starte/PPI
Awake ECG / Echo
Calorimetry
Intraperitoneal Glucose Tolerance Test
Challenge Whole Body Plethsmography
Body Composition (lean/fat) QNMR
Auditory Brain Stem Response
Slit Lamp
Opthalmoscope
9
10
11
12
13
14
15
Terminal
Multiplex analysis
Hematology
Clinical Blood Chemistry
Insulin Blood Level
FACS spleen/BM
Organ and Heart Weight
Gross Pathology (7+7)
Block Banking
Histopathology (2+2) - from blocks where required
X-ray (5 + 5)
Whole mount LacZ staing
16
7 M + 7 F Mutant Adult Mice

phenomin

TECH DEVELOPMENT

Cardiovascular

Behavior and cognition

Nutrition, metabolism

Neuromuscular system

Embryology and Reproduction

Immunology and Inflammation

Respiration, allergy

Imaging

immune responses to pathogens

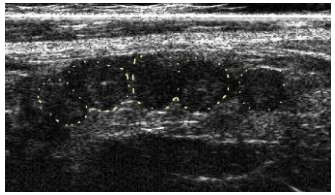
Skeleton, Tooth and Craniofacial morphology

Cytometry by time-of-flight mass spectrometry

Electrophysiology

Scientific Experts: Block-Zupan A., Chambon P., Chan S., Fiore F., Frossard N., Gorvel J.-P., Grenot P., Hérault Y., Kieffer B., Laporte J., Lepape A., Malissen B., Malissen M., Mark M., Metzger D., Monassier L., Ouagazzal A.M., Pourquié O., Ricci R., Romand R., Roux M., Spitz F., Ugolini S., Vivier E., …

O. Wendling,
M. Mark



Gestation at E7

Follow gestation by micro-ultrasonography at E5 and E8 (count the deciduas)

No or few (less than 40 %) resorptions

High level of resorptions

Collect fetuses at E18.5

Collect embryos at E10.5

Externally malformed fetuses

Externally normal fetuses

Fix 2 litters in paraformaldehyde

Fix 3 litters in Bouin's solution

Fix 3 litters in Klotz's solution

β-galactosidase expression by optical tomography

Genotyping

No mutant detected

Mutants detected

No mutant detected

Genotyping

Collect embryos at E10.5

Collect embryos at E10.5

Mutants detected

No mutant detected

Fix 2 litters in Bouin's fluid

Autopsy (Klotz) or Serial sections (Bouin)

Serial sections

End of analysis
(Death must occur around implantation or gastrulation)

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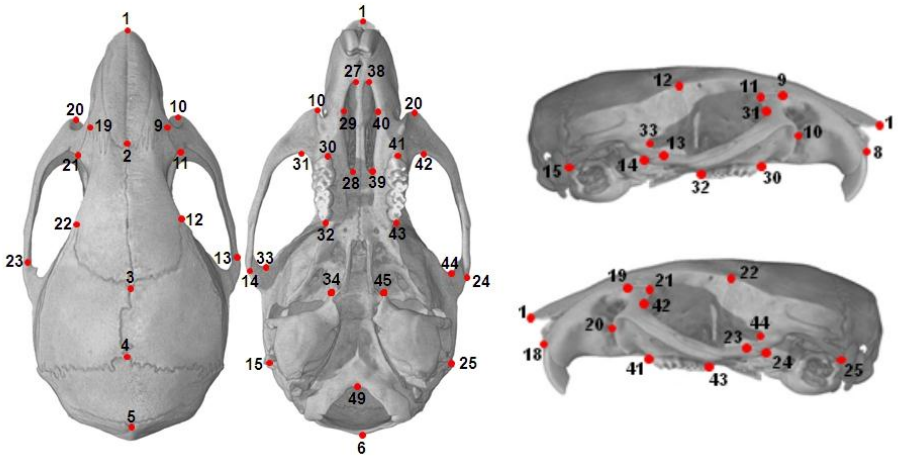
Landmark and methodologies for craniofacial analysis

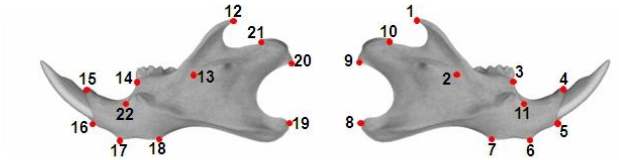
A

LANDMARKS Right	LANDMARKS Median	LANDMARKS Left	Description
	1		Nasale
	2		Nasion
	3		Bregma
	4		Parietals-occipital junction
	5		Midline of the interparietal-occipital junction
	6		Dorsal midpoint of the foramen magnum
8		18	Dorsal-most point of the incisor alveoli
9		19	Parietal-premaxillar-maxillar junction
10		20	Anterior-most point of the zygomatic spine
11		21	Posterior-most point of the frontal-maxillary dorsal junction
12		22	Anterior-most point of the squamosal-parietal junction
13		23	Anterior-most point of the zygomatic-squamosal junction
14		24	Posterior-most point of the zygomatic-squamosal junction
15		25	Tip of the post-tympanic hook.
27		38	Anterior-most point of the anterior palatine foramen
28		39	Posterior-most point of the anterior palatine foramen
29		40	Ventral-most point of the premaxillar, maxillar and anterior palatine foramen junction
30		41	Mesial-most point of the first upper molar cervix
31		42	Point of greatest curvature of the posterior margin of malar process
32		43	Distal-most point of the third upper molar cervix
33		44	Point of greatest curvature of the squamosal retroversus process
34		45	Antero-medial projection of ectotympanic in basicranial
	49		ventral midpoint of the foramen magnum



B

LANDMARKS Right	LANDMARKS Left	Description
1	12	Tip of the coronoid process
2	13	Distal-most point of the third lower molar cervix
3	14	Mesial-most point of the first lower molar cervix
4	15	Dorsal-most point of the incisor alveoli
5	16	Inferior-most point of the incisor alveoli
6	17	Inferior-most point on border of ramus inferior to incisor alveolar
7	18	Superior-most point on inferior border of mandibular ramus
8	19	Tip of the mandibular angle
9	20	Ventral-most point of the mandibular condyle
10	21	Anterior-most point of the mandibular condyle
11	22	Mandibular foramen



L. Viriot, P. Lopes, E. Velot, S. Lerondel, Y. Herault

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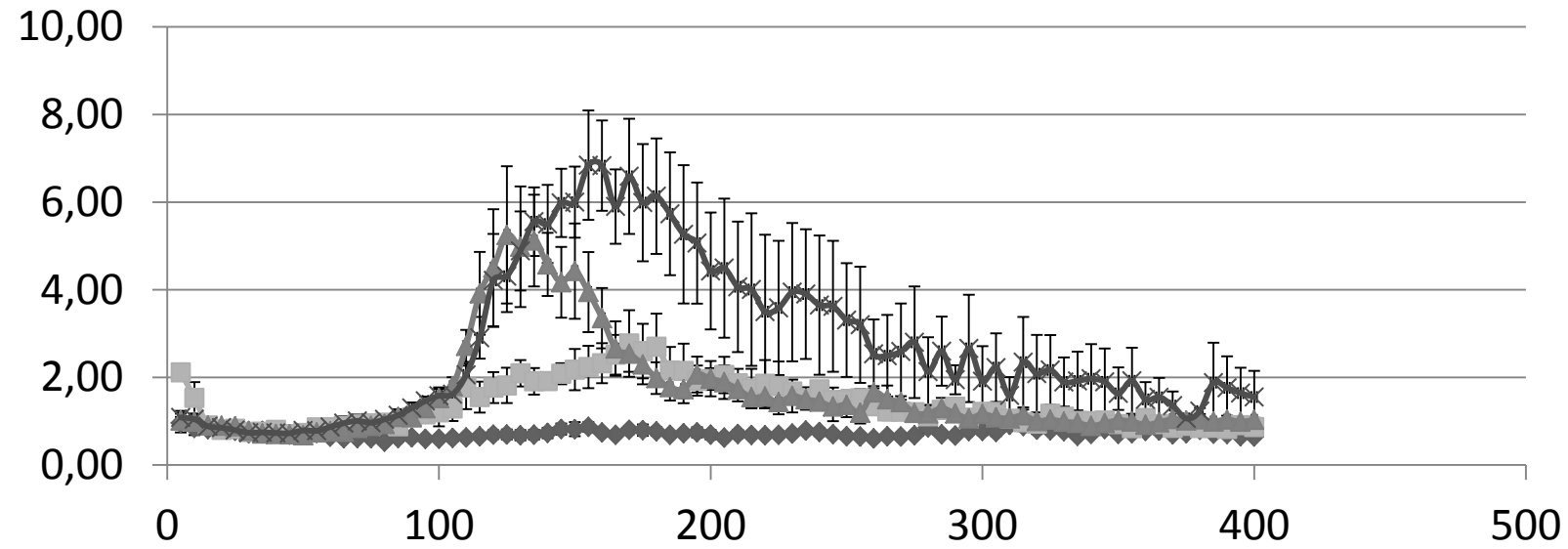
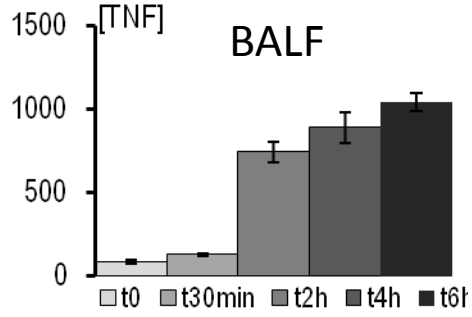
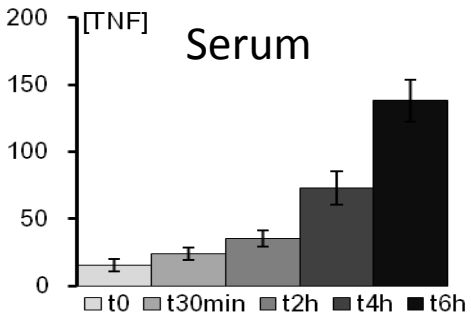
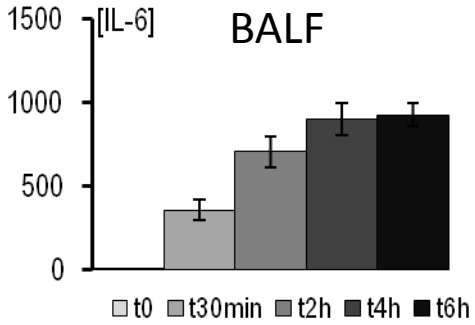
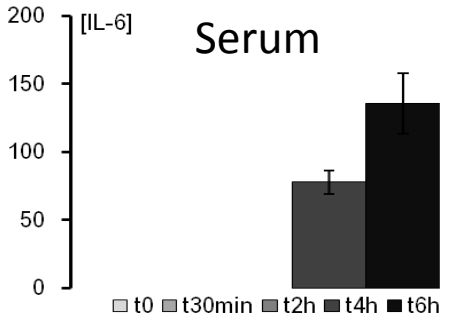
Lipopolysaccharide (LPS) challenge







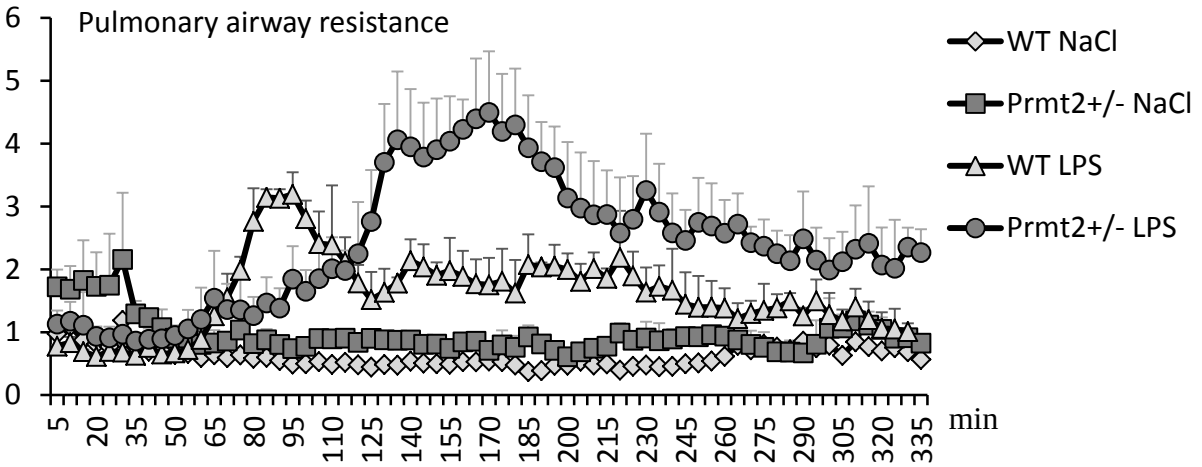


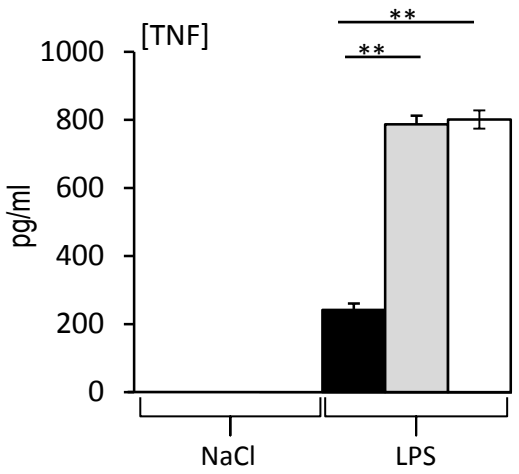


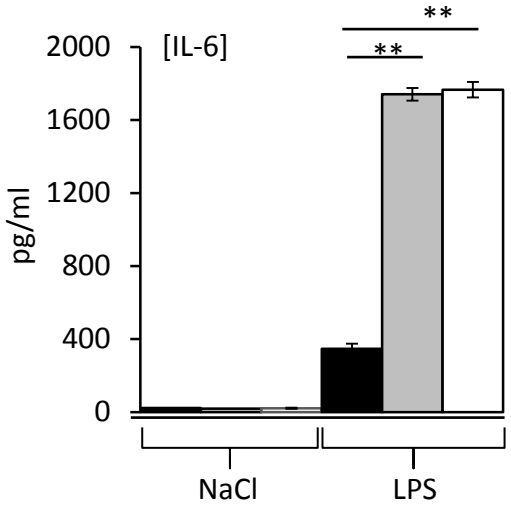
Pulmonary and inflammatory Function (6h)

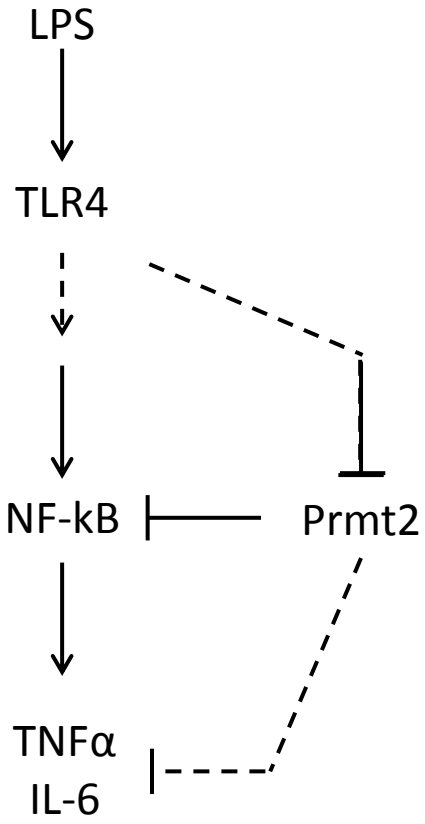
E. Dalloneau, J. Becker, Y. Herault

Lipopolysaccharide (LPS) challenge









E. Dalloneau, J. Becker, Y. Herault (J. Immunol in press)

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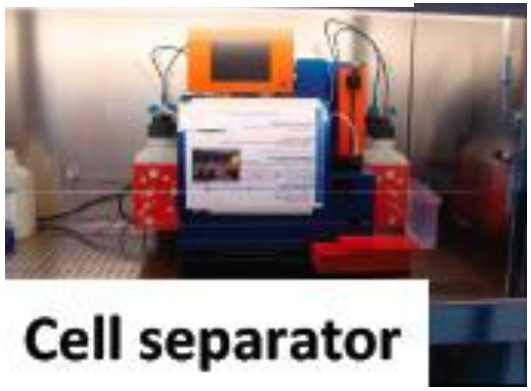
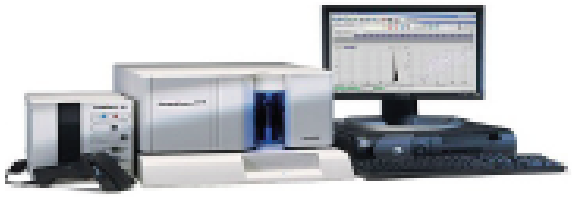
Iphe
immunity profiler

Profiling of the mouse innate and adaptive immune system under normal and confined (BSL3) conditions via the quantitative analysis of over 200 parameters.



Cell separator

Cell sorter



Luminex CBA

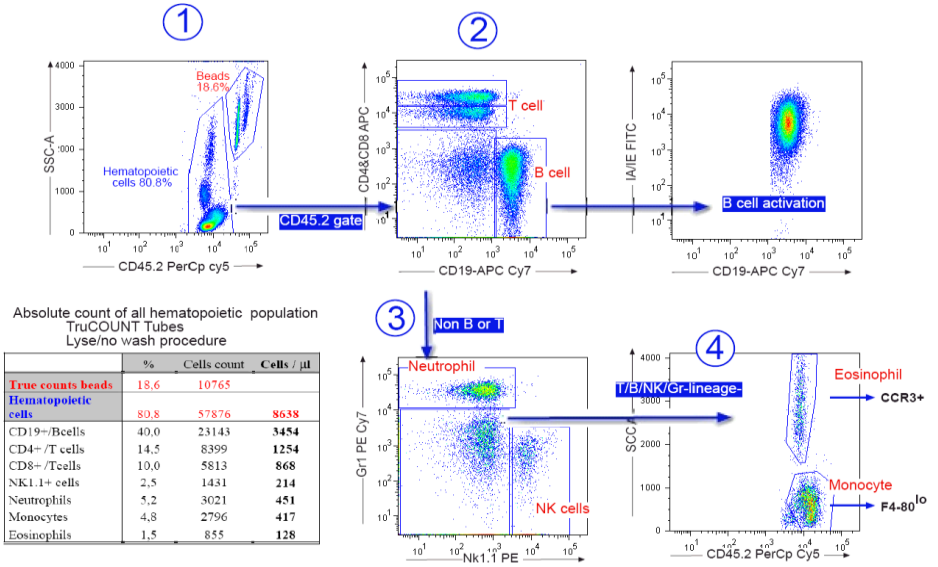
Mass Cytometer

Cell analyzer

BSL3 live imaging

phenomin

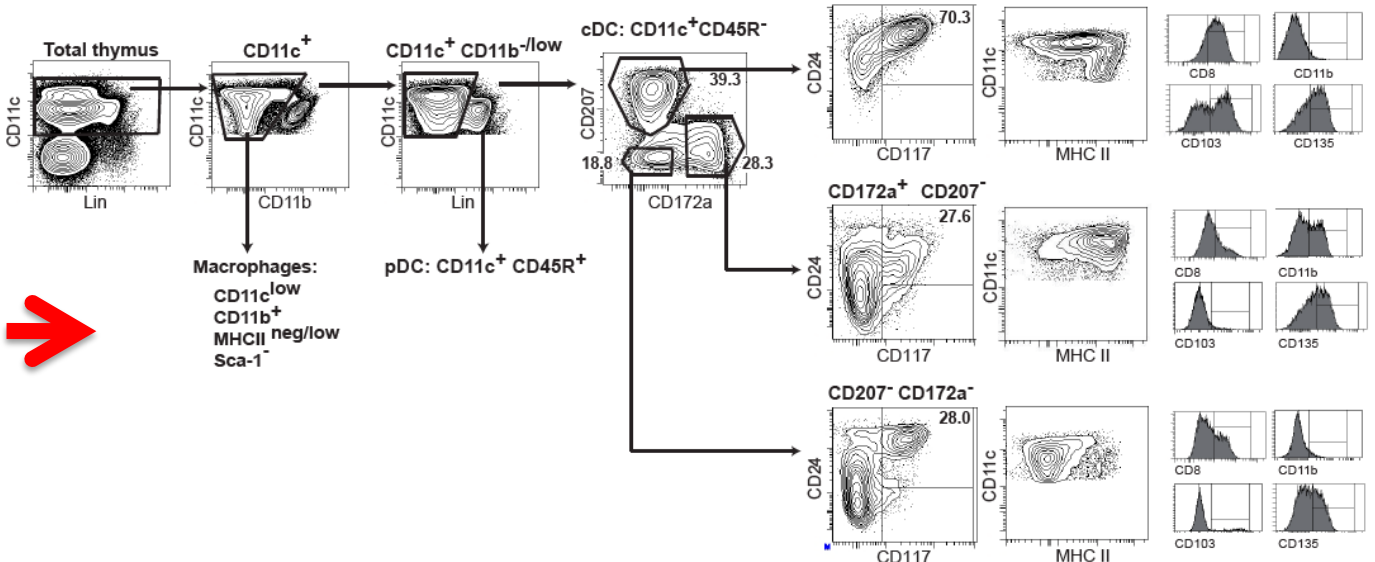
Standard operating procedure for quantitative analysis of the lymphoid and myeloid cells present in small blood samples.



Absolute count of all hematopoietic population
TruCOUNT Tubes
Lyse/no wash procedure

	%	Cells count	Cells / µl
True counts beads	18.6	10765	
Hematopoietic cells	80.8	57876	8638
CD19+/Bcells	40.0	23143	3454
CD4+ /T cells	14.5	8399	1254
CD8+ /Tcells	10.0	5813	868
NK1.1+ cells	2.5	1431	214
Neutrophils	5.2	3021	451
Monocytes	4.8	2796	417
Eosinophils	1.5	855	128

Standard operating procedure for quantitative analysis of dendritic cells.



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> 1000 Lab Users

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iCS

Ciphe immunity profiler

Ciml IMMUNOLOGY

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UZUN	Ibrahim
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