Generation of animal models (mouse or rat) of rare diseases at PHENOMIN-ICS

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Animal models to study human disease have experienced a boom in recent decades. These remain essential models for validating or not the safety part of medicines for their Marketing Authorization. At PHENOMIN-ICS, we can generate the model of choice for your research and assist you with the phenotypic validation of your line.

Genetic Engineering and Genome Editing

Expert advice

Strategy discussed with the collaborator in order to propose the best possible approach

"À la carte" projects / new tools

Technical and scientific expertise- Highly competent teams

Validation of ES cell clones by long PCR and Southern blot (IMPC and internal clones)

> 1,500 targeted mutagenesis projects using ES cells

>200 CRISPR projects

> 300 transgenesis projects by random insertion

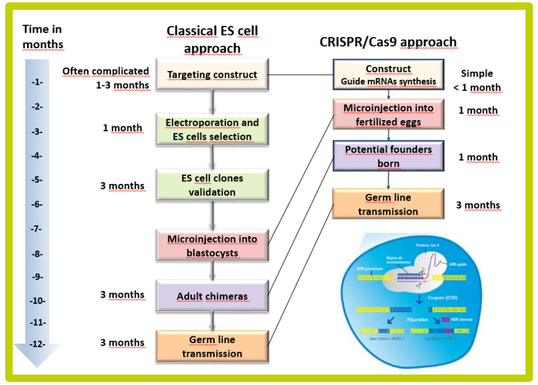
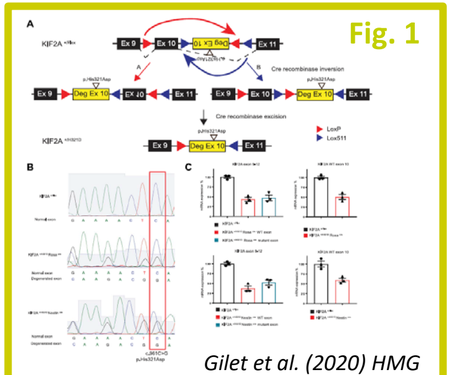
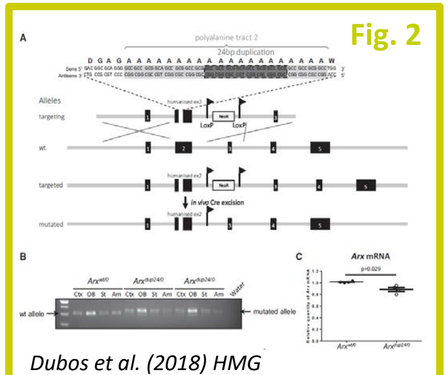


Fig. 1



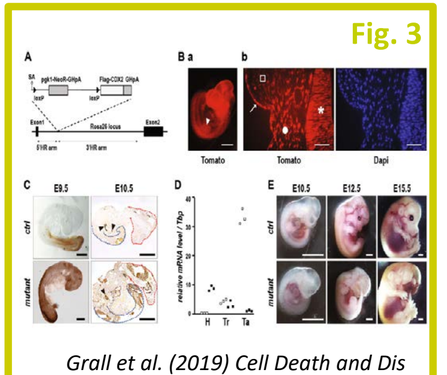
Gilet et al. (2020) HMG

Fig. 2



Dubos et al. (2018) HMG

Fig. 3



Grall et al. (2019) Cell Death and Dis

Types of models

- Constitutive Knock-out (loss of function)
- Conditional knockout
- Knock-In (including Point Mutation)
- Humanization
- Conditional mutation
- Targeted transgenesis (Rosa26)
- Duplication, deletion, region
- Inversion Flex2 type models

Some examples of mouse models of human diseases obtained at the Institut Clinique de la Souris

- ***Malformations pathogéniques congénitales***

TUBG1: modèle de mutation ponctuelle transformable en KO *(Ivanova et al., 2019 Nat Comm)* ; KIF2A: modèle Flex2- mutation conditionnelle *(Gilet et al., 2020, HMG; Fig.1)*

- ***Désordre neuro-développemental***

ARX: duplication d'une expansion de polyalanine (c.428_451dup24) *(Dubos et al, 2018 HMG, Fig.2)*

CDX2: Surexpression conditionnelle *(Grall et al., 2019; Cell Death and Disease. Fig.3)*

- ***Angiopathie héréditaire avec néphropathie, anévrismes et crampes musculaires (AHNAC)***

Col4a1^{G498V} mutants *(Chen et al., 2016, J Am Soc Nephrol; Guiraud et al., 2017, Am J Path)*

- ***Syndrome de Bardet-Biedl***

BBS12: souris perte de fonction (Marion et al., 2012, Cell Meb)

- **Sclérose latérale amyotrophique**

FUS: delta NLS inductible *(Scekic-Zahirovic et al., 2016, EMBO J Fig.4); Scekic-Zahirovic et al., 2017, Acta Neuropath, ; Piccharelli et al., 2019, Nat Neurosci)*

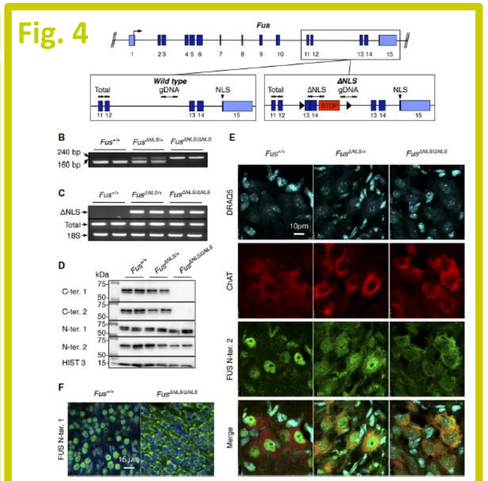
- **Syndrome de Costello**
- **Syndrome LEOPARD**

PTPN11: mutation ponctuelle T468S *(Tanjan et al., 2014, PNAS)*

- **Modèles de 'Copy Number Variations'**

Modèles de Trisomie 21 (*Birling et al., 2017, Sci Rep*; Fig.5), 17q21.31Bis; 17q21.31-Koolen-deVries *(Arbogast et al., 2017, PLOS genetics)*; 16p11.2 *(Arbogast et al., 2016, PLOS genetics)*

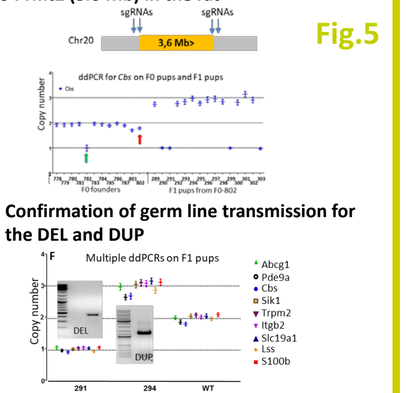
Fig. 4



Scekic-Zahirovic et al. (2016) EMBO J

CRISPR/Cas9 Deletion and duplication of a HSA21 synthenic region ranging from Umodl1 to Prmt2 (3.6 Mb) in the rat

Fig.5



Confirmation of germ line transmission for the DEL and DUP

Birling et al. (2017) Sci Rep

To summarize

We routinely modify the genome of mice or rats to generate relevant models that best reproduce the different aspects of the human disease of interest. Thanks to CRISPR technology, it is now possible to quickly generate almost any type of pattern or mutation.

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EXCELLENCE IN MOUSE PHENOGENOMICS