

Unit of Animal Genomics

# Contribution à la gestion des défauts génétiques dans la race Blanc-bleu Belge



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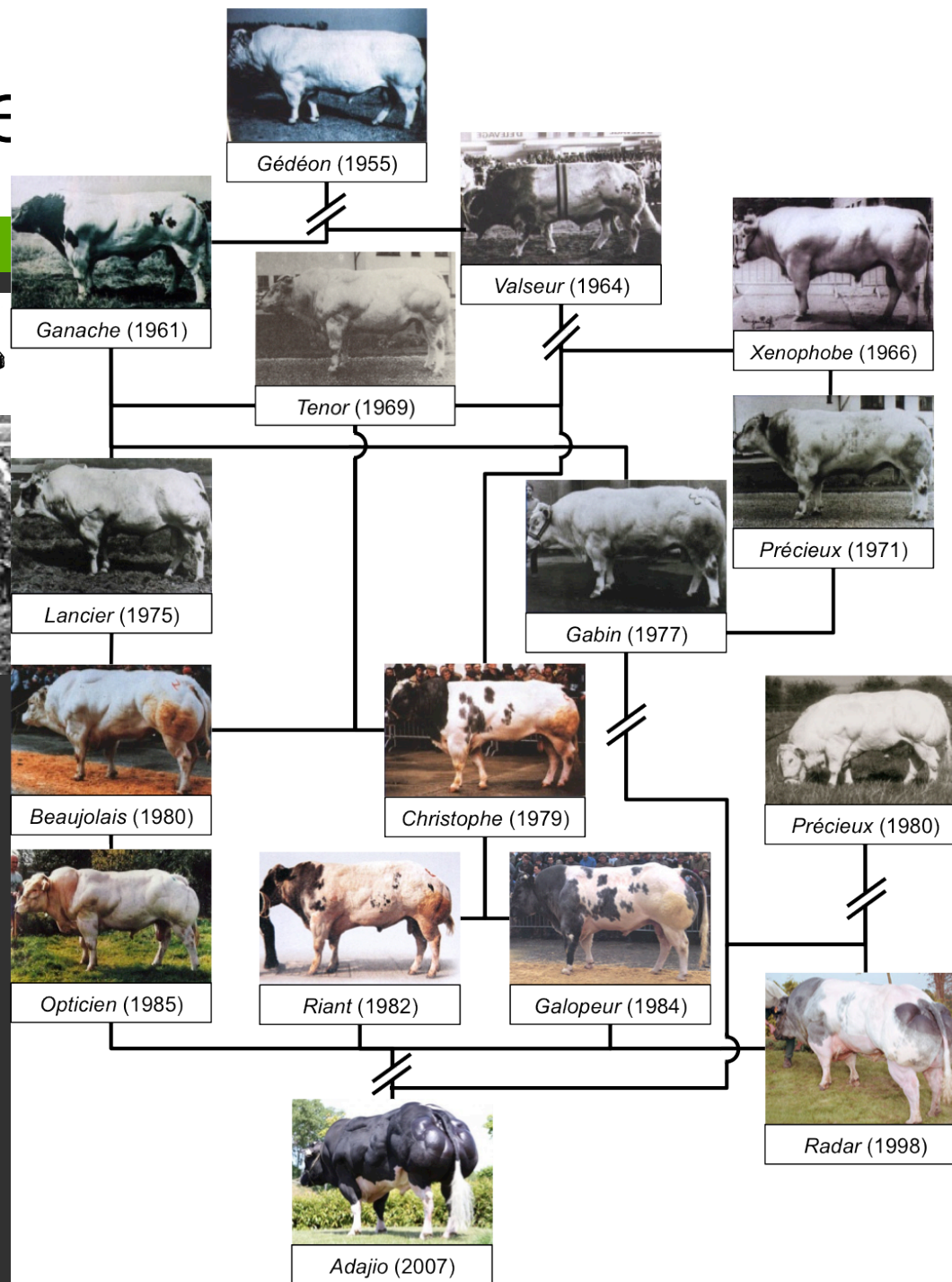
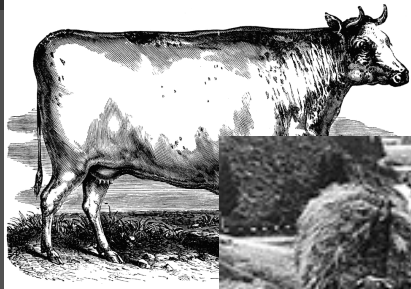
LE BLANC-BLEU BELGE,  
LA GENOMIQUE,  
& RILOUKE...



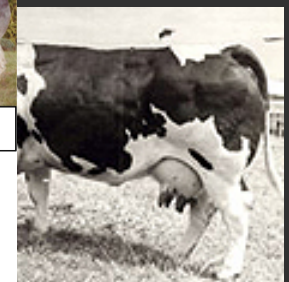


**LE BLANC-BLEU BELGE,  
LA GENOMIQUE,  
& RILOUKE...**





940





# Une robe Blanc-bleu Belge...

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Durkin et al., 2012



# Une musculature...

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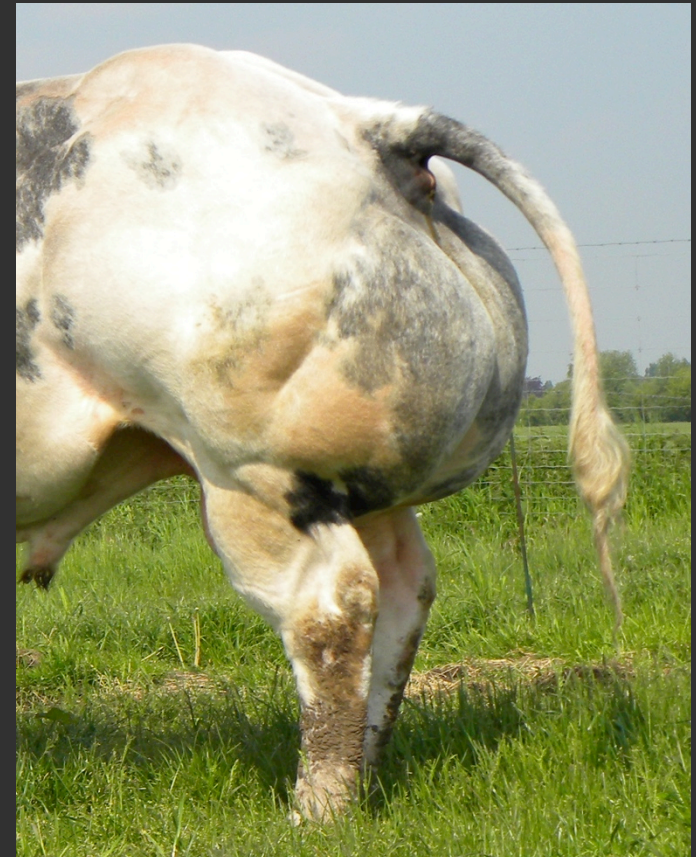
- ☐ Hyperplasie
- ☐ *Myostatine*
- ☐ ➔ 20 % musculature





# Une belle attache de queue...

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# Du devant...

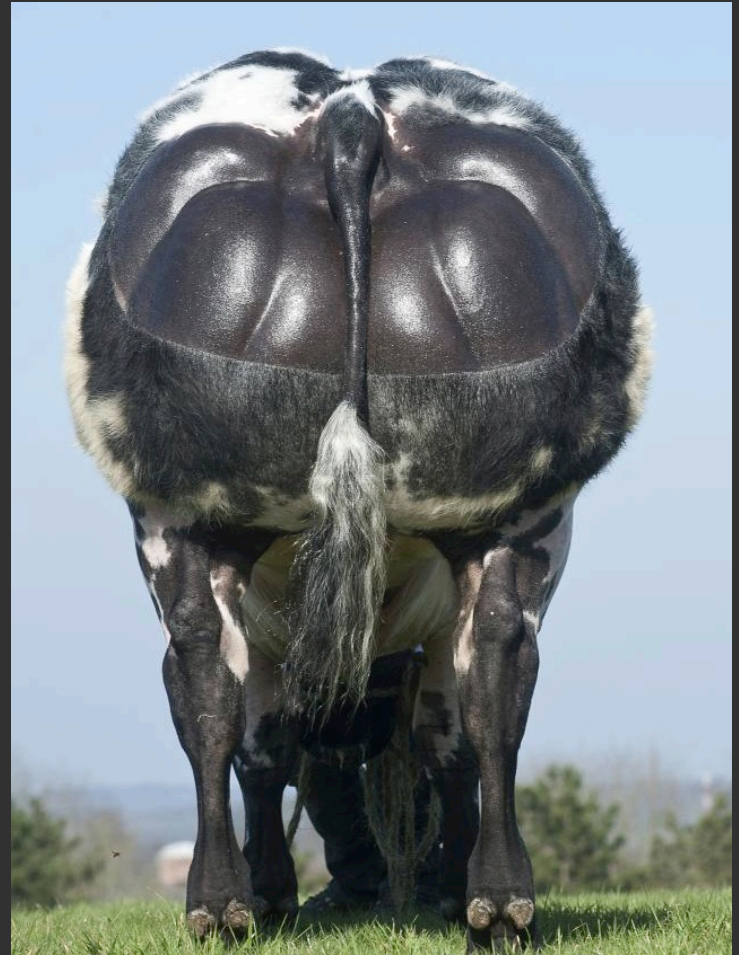
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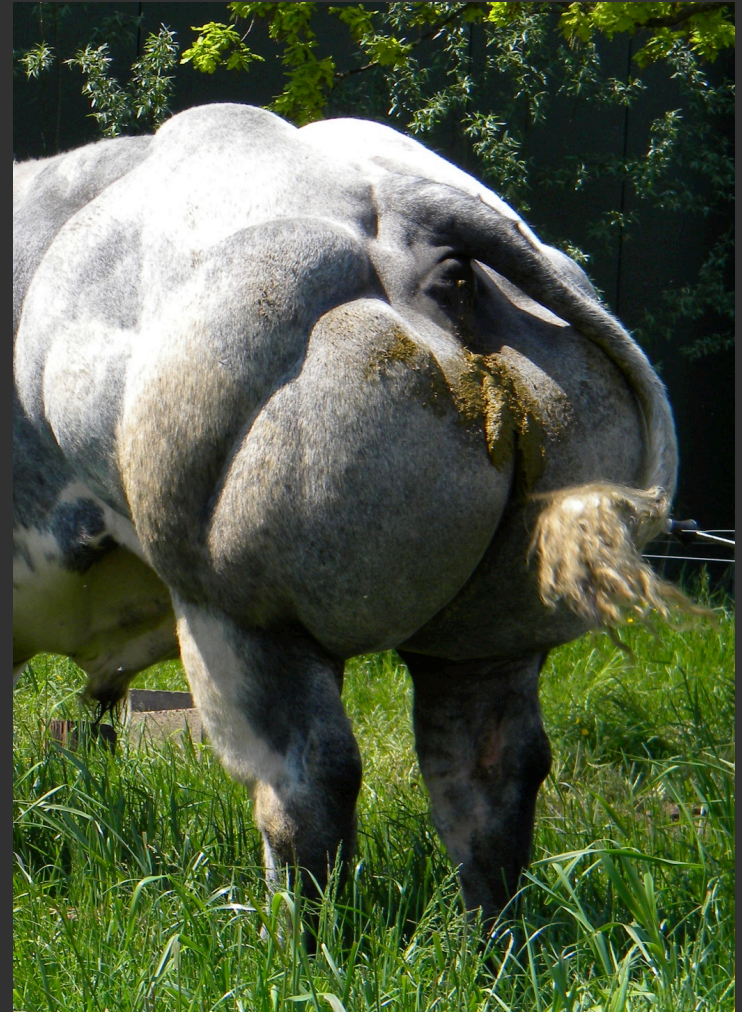
# De bons aplombs...

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# De la fesse...

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# Concours de beauté...

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# Blanc-bleu Belge

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- ❑ 50 % bovins & 95 % bovins viandeux
  - 1.300.000
- ❑ 17.000 troupeaux BBB / 25.000
- ❑ Carcasse = 70 % avec 80 % viande
- ❑ Sélection intensive pour la conformation
- ❑ Utilisation massive de l'IA (50 %)
- ❑ 99 % vêlage par césarienne



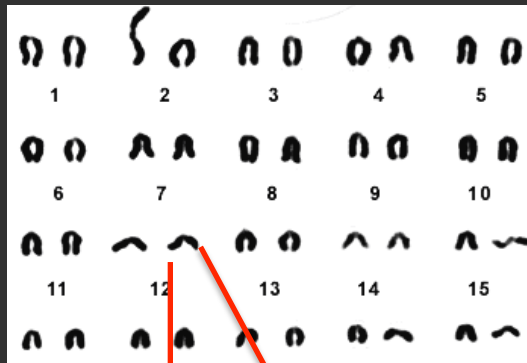


LE BLANC-BLEU BELGE,  
LA GENOMIQUE,  
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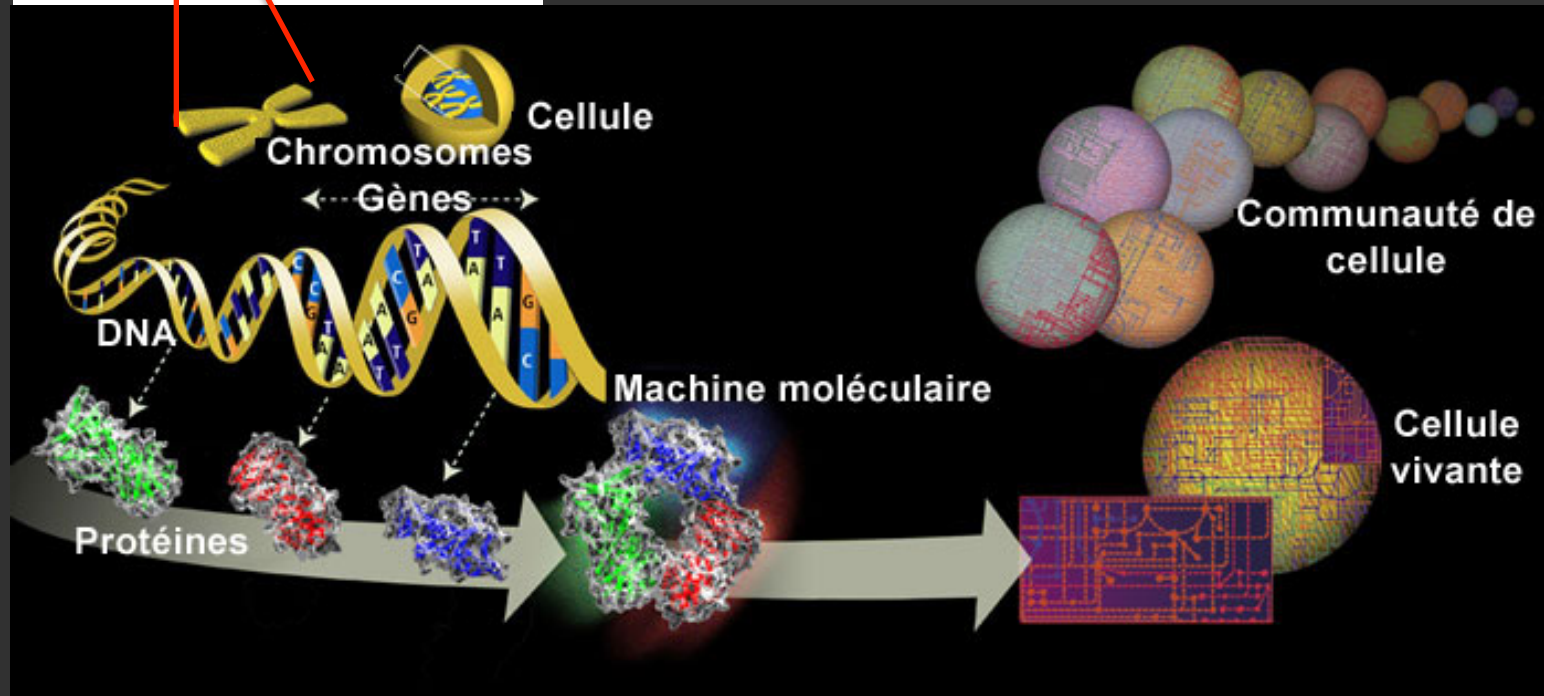


# Génome bovin

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- 3 Gb = 3.000.000.000 pb
- Taux de mutation = 1/100.000 pb
  - 1 à 5 mutations délétères
- Recombinaison





# Séquence bovine

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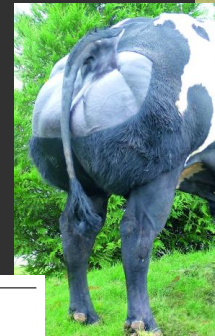
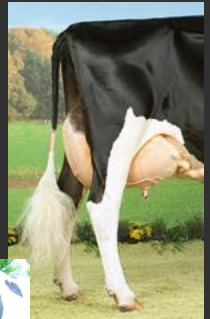


The Bovine Genome Sequencing and Analysis Consortium. *The Genome Sequence of Taurine Cattle: A Window to Ruminant Biology and Evolution*. Science, 2009

# Défauts génétiques chez les bovins

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- ❑ Sélection intensive
- ❑ Utilisation massive de l'IA
- EMERGENCE DE DÉFAUTS GÉNÉTIQUES
  - ❑ USA: BLAD (90') = 5 millions \$
- ❑ EVOLUTION DES OUTILS
  - ❑ Génotypage à haut-débit
  - ❑ Séquençage à haut-débit



### Highly effective SNP-based association mapping and management of recessive defects in livestock

Carole Charlier<sup>1</sup>, Wouter Coppieters<sup>1</sup>, Frédéric Rollin<sup>2</sup>, Daniel Desmecht<sup>3</sup>, Jorgen S Agerholm<sup>4</sup>, Nadine Cambisano<sup>1</sup>, Eloisa Carta<sup>5</sup>, Sabrina Dardano<sup>6</sup>, Marc Dive, Corinne Fasquelle<sup>1</sup>, Jean-Claude Frennet, Roger Hanset<sup>1,11</sup>, Xavier Hubin<sup>7</sup>, Claus Jorgensen<sup>8</sup>, Latifa Karim<sup>1</sup>, Matthew Kent<sup>9</sup>, Kirsten Harvey<sup>5</sup>, Brian R Pearce<sup>5</sup>, Patricia Simon<sup>1</sup>, Nico Tama<sup>1</sup>, Haisheng Nie<sup>1,10</sup>, Sébastien Vandeputte<sup>2</sup>, Sigbjorn Lien<sup>9</sup>, Maria Longeri<sup>6</sup>, Merete Fredholm<sup>8</sup>, Robert J Harvey<sup>5</sup> & Michel Georges<sup>1</sup>

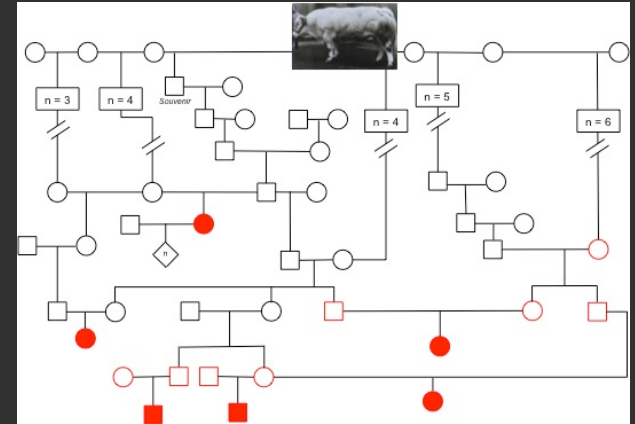
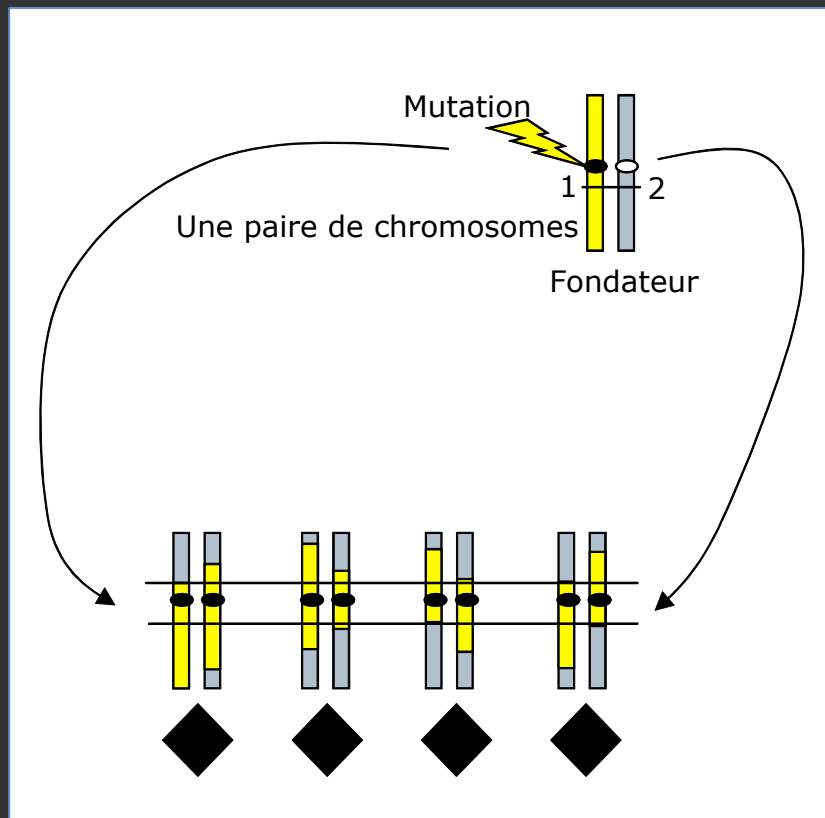
Charlier *et al.*, 2008



# Du phénotype...à la mutation

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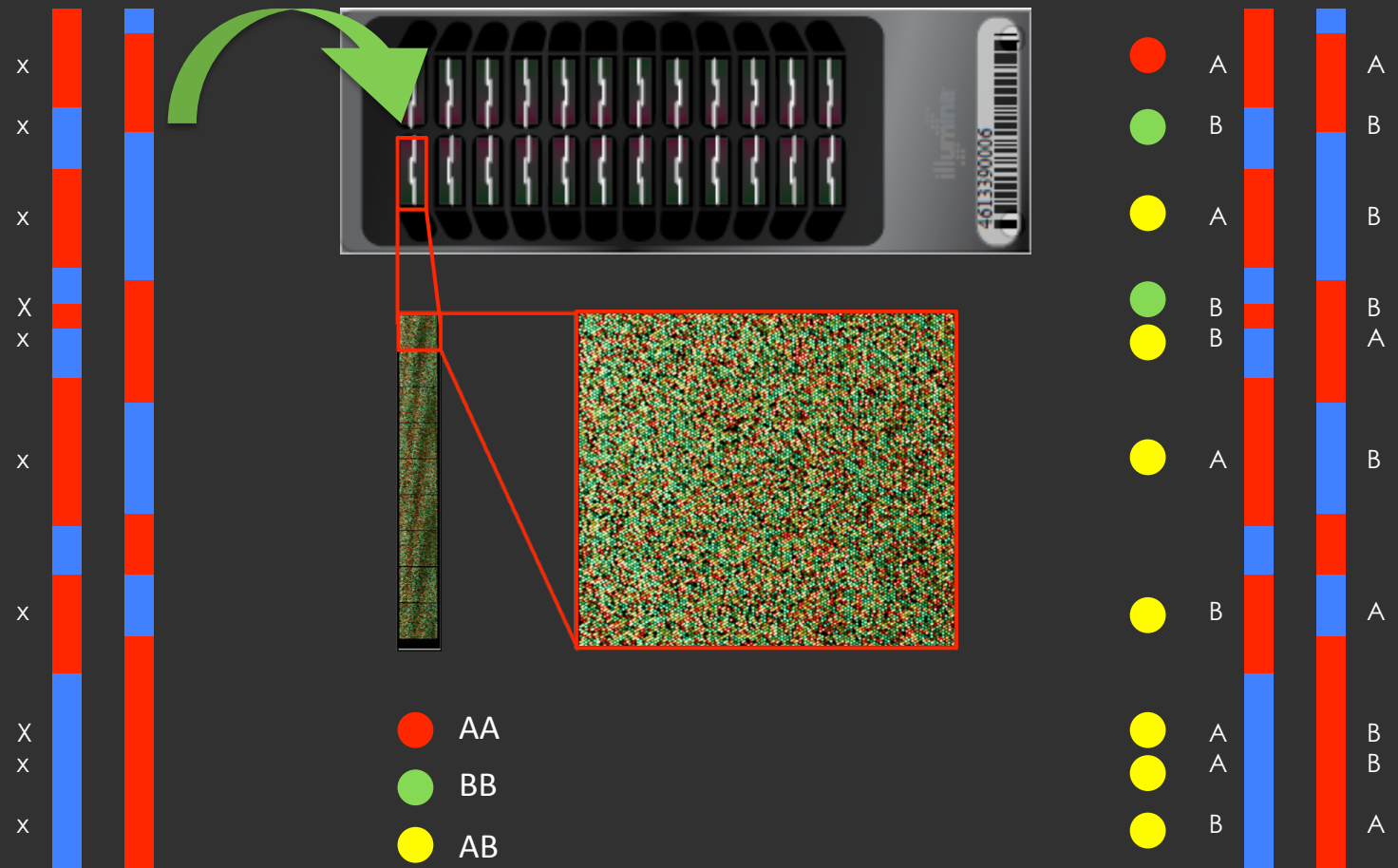
## □ Phénotypes & analyses épidémiologiques



# Du phénotype...à la mutation

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## ☐ Génotypage: Puces 50.000 SNPs

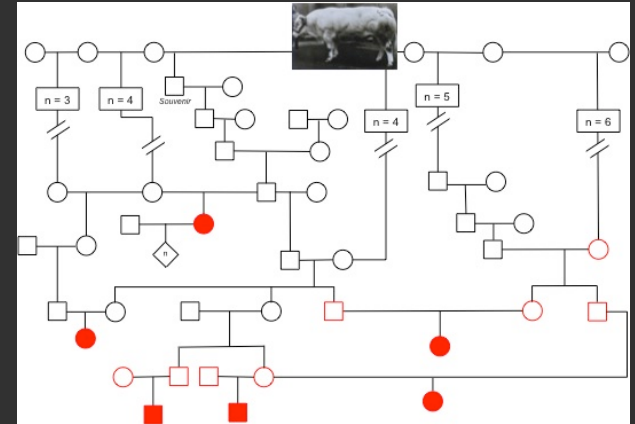




# Du phénotype...à la mutation

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□ Phénotypes & analyses épidémiologiques



□ Génotypage: SNP

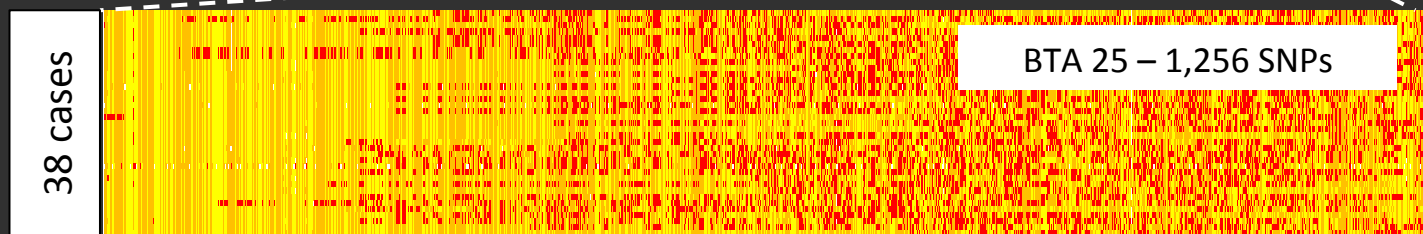
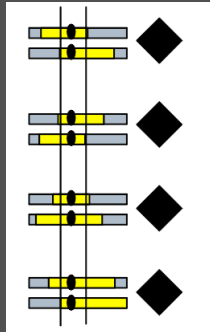
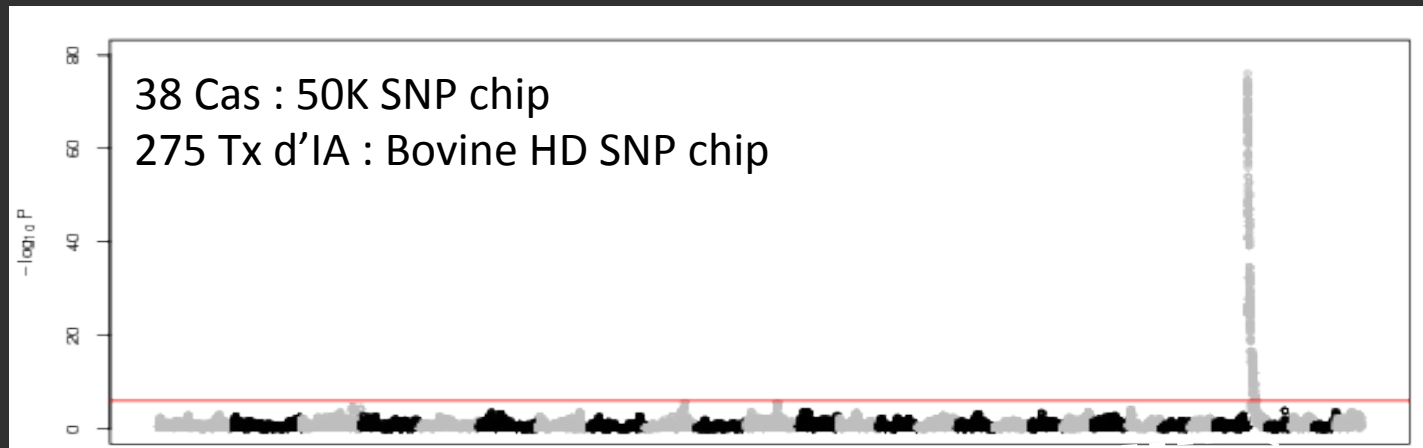


□ Etudes d'Association Génome Entier (GWAS)

# Du phénotype...à la mutation

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## □ Etudes d'Association Génome Entier



1,2 Mb



# Du phénotype...à la mutation

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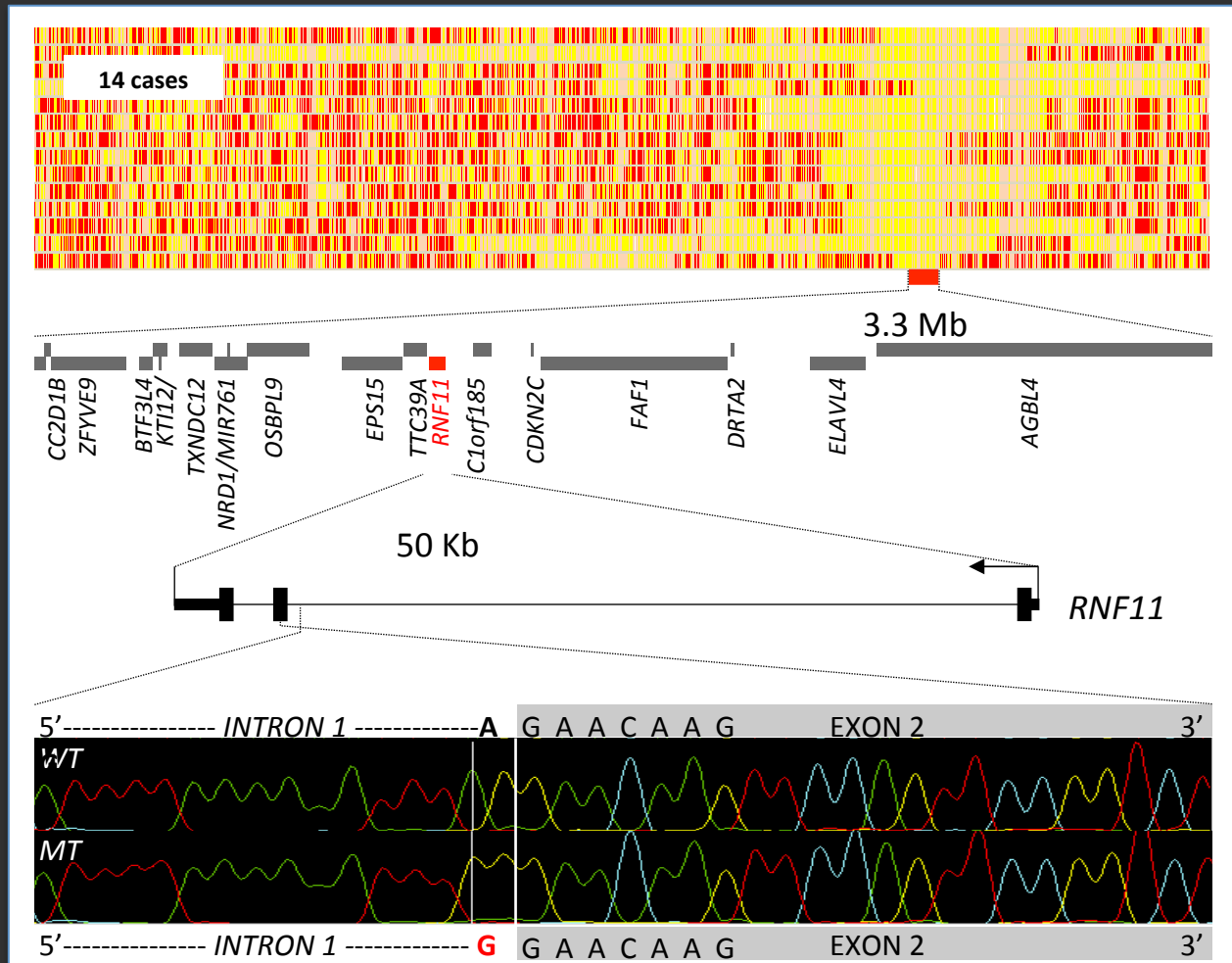
## □ Séquençage

- Gène candidat
- NGS : reséquençage du génome entier ou capture
- NGS : transcriptome

# Du phénotype...à la mutation

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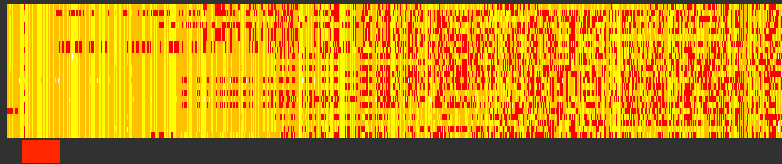
## □ Séquençage : Gène candidat



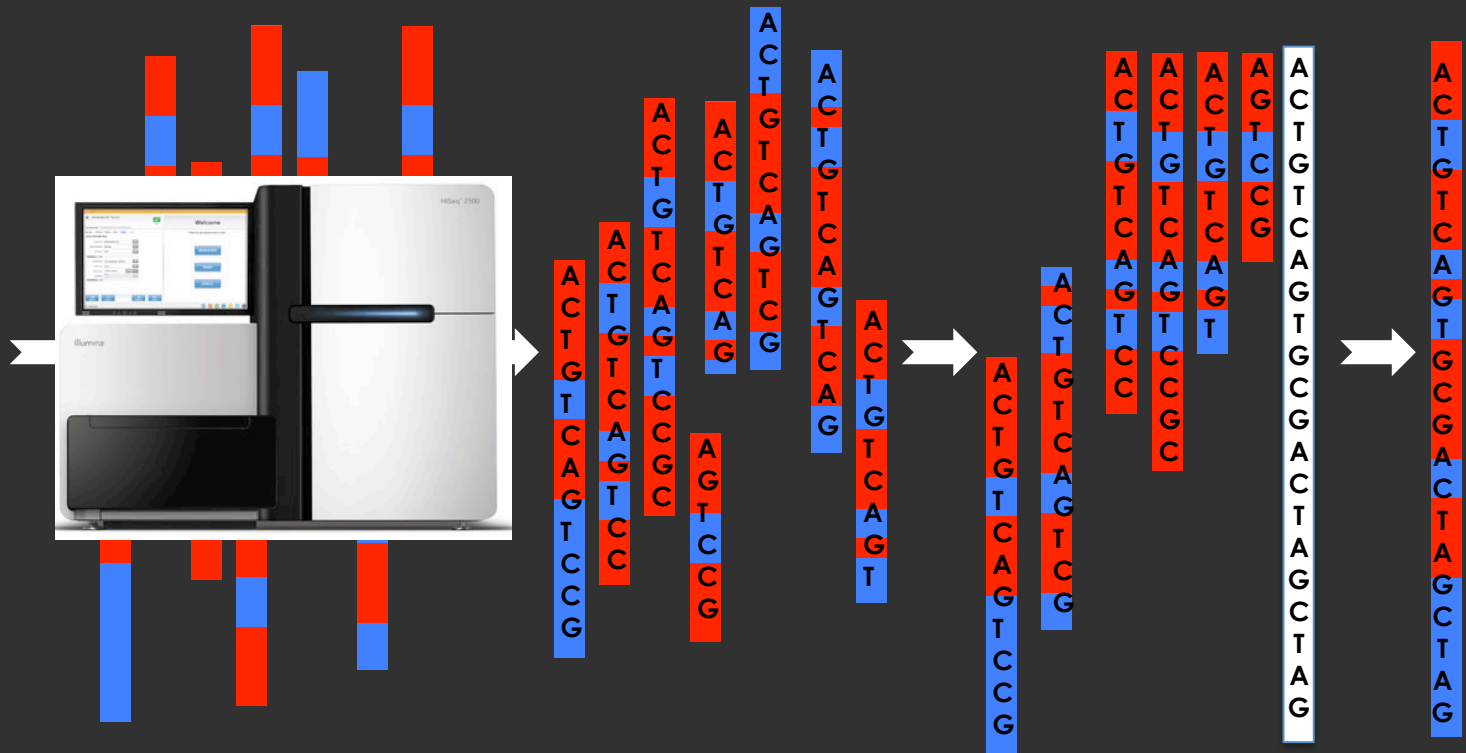
# Du phénotype...à la mutation

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## □ Séquençage : Reséquençage du génome



- nombreux gènes
- pas de gène candidat

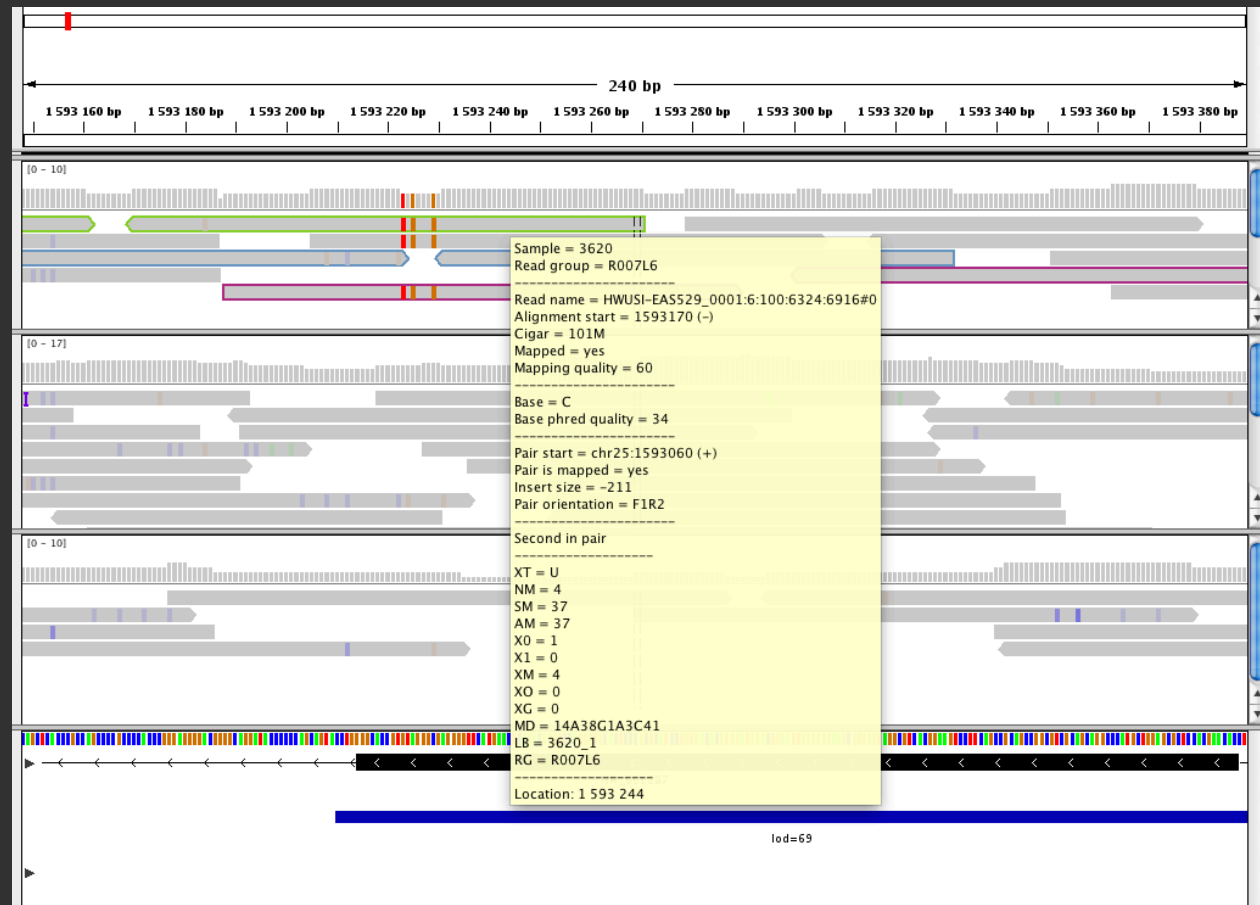




# Du phénotype...à la mutation

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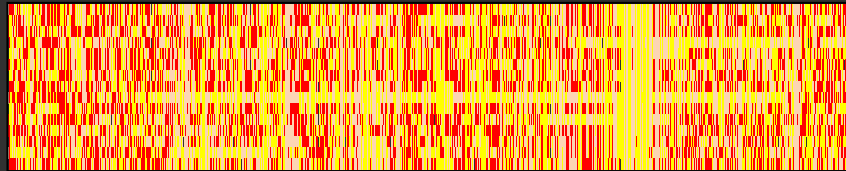
## □ Séquençage : Reséquençage du génome



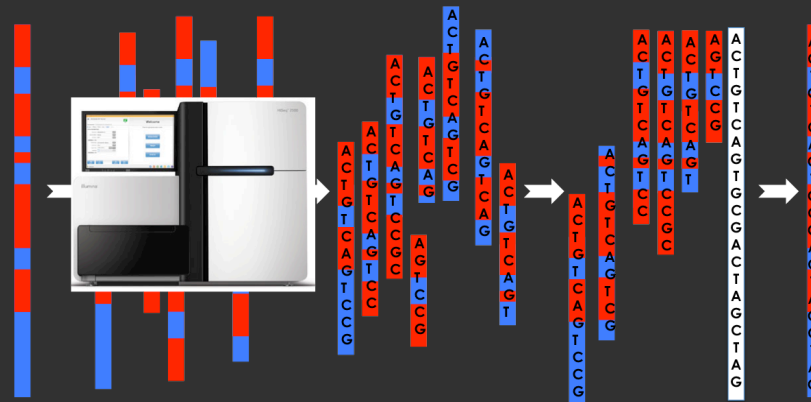
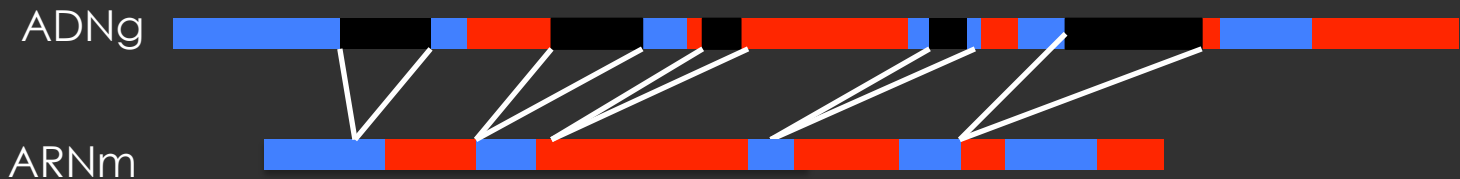
# Du phénotype...à la mutation

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## □ Séquençage : Transcriptome



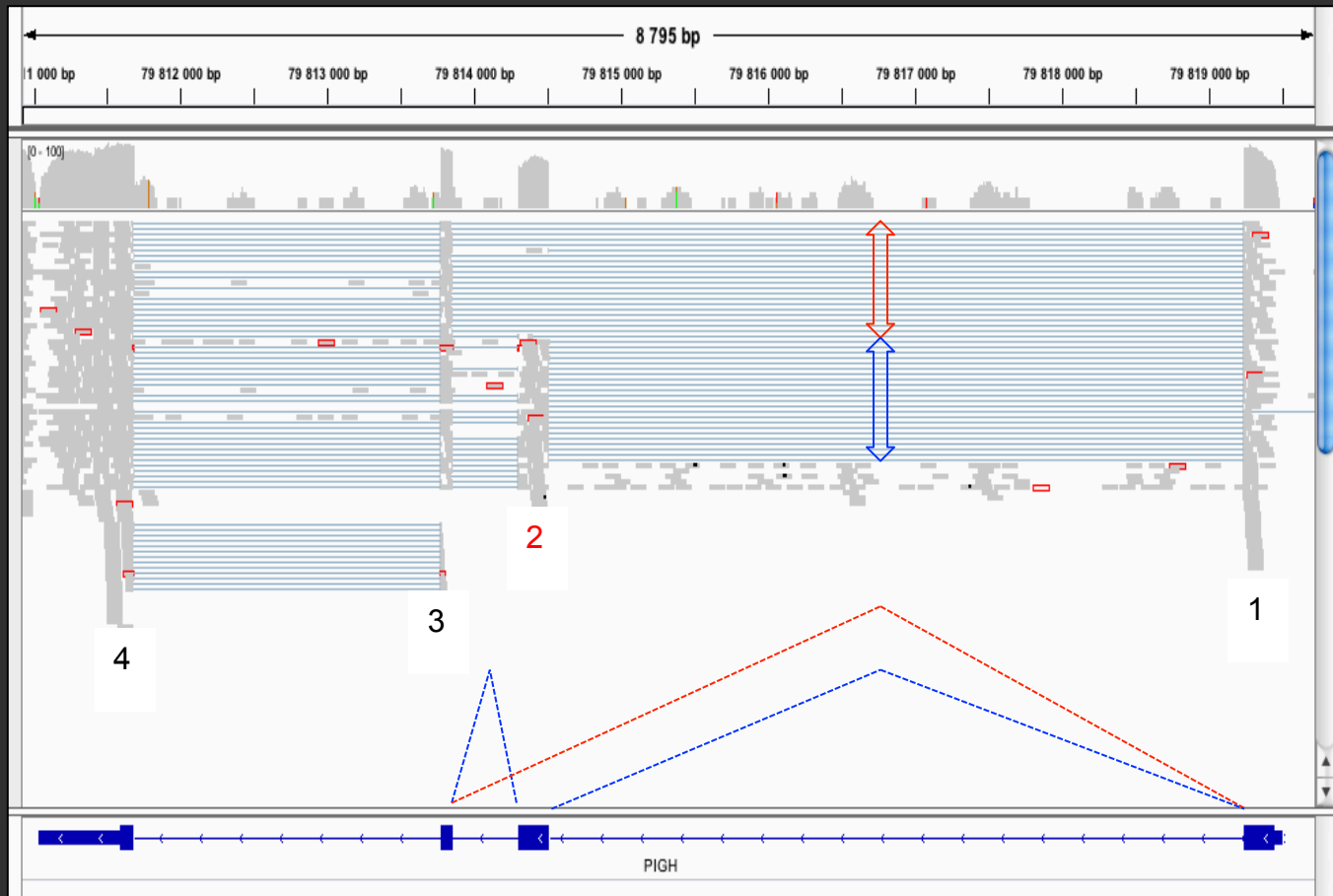
- Nombreux gènes
- Pas de gène candidat
- Pas de mutations candidates



# Du phénotype...à la mutation

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## □ Séquençage : Transcriptome

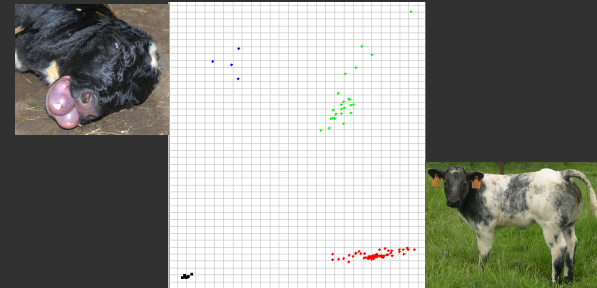




# Du phénotype...à la mutation

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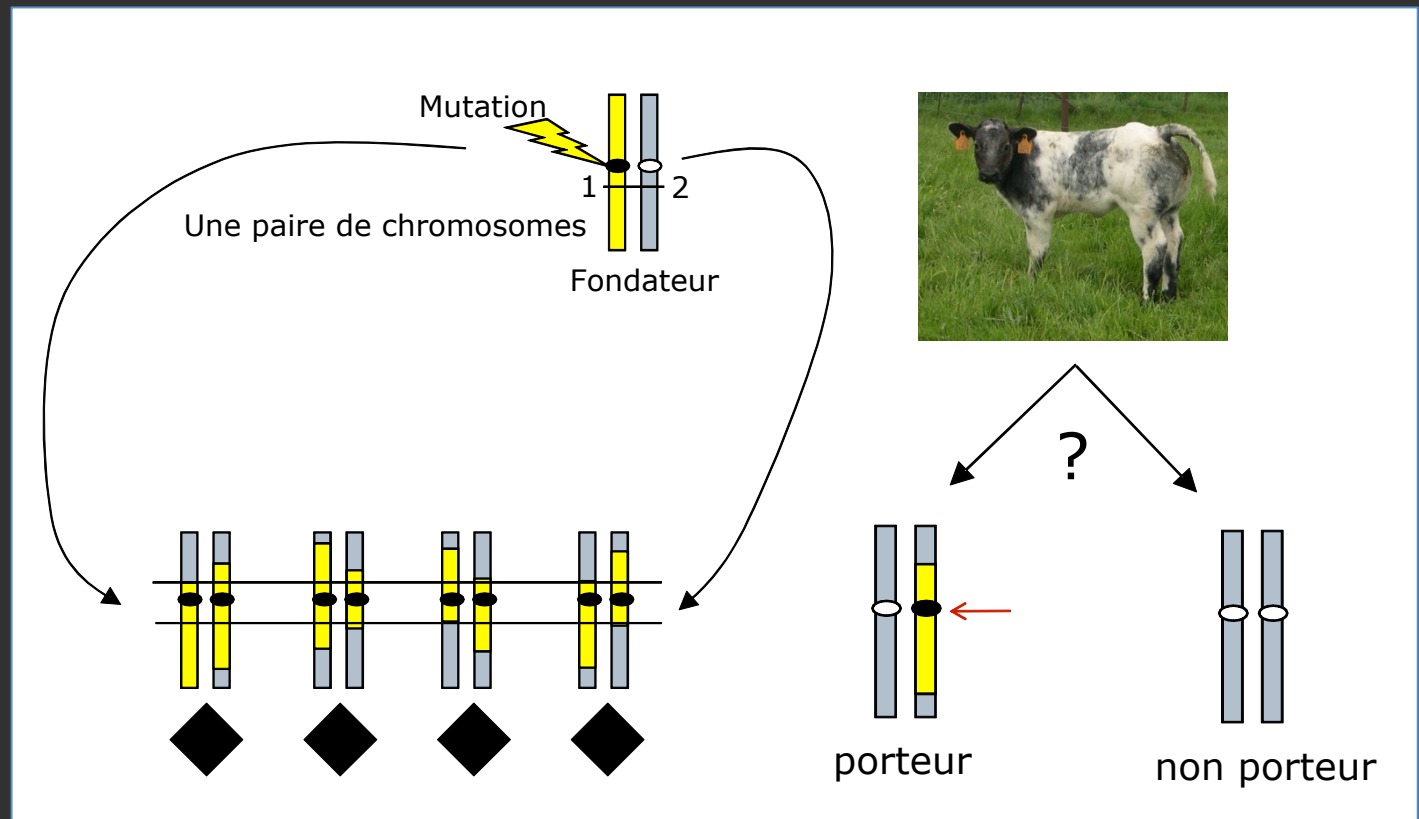
- ❑ Séquençage
  - Gène candidat
  - NGS : reséquençage du génome entier ou capture
  - NGS : transcriptome
- ❑ Validation de la mutation causale
  - Expression
  - Tests fonctionnels
- ❑ Tests diagnostiques
  - 5' exonuclease assay
  - Basé sur les haplotypes



# Tests diagnostiques

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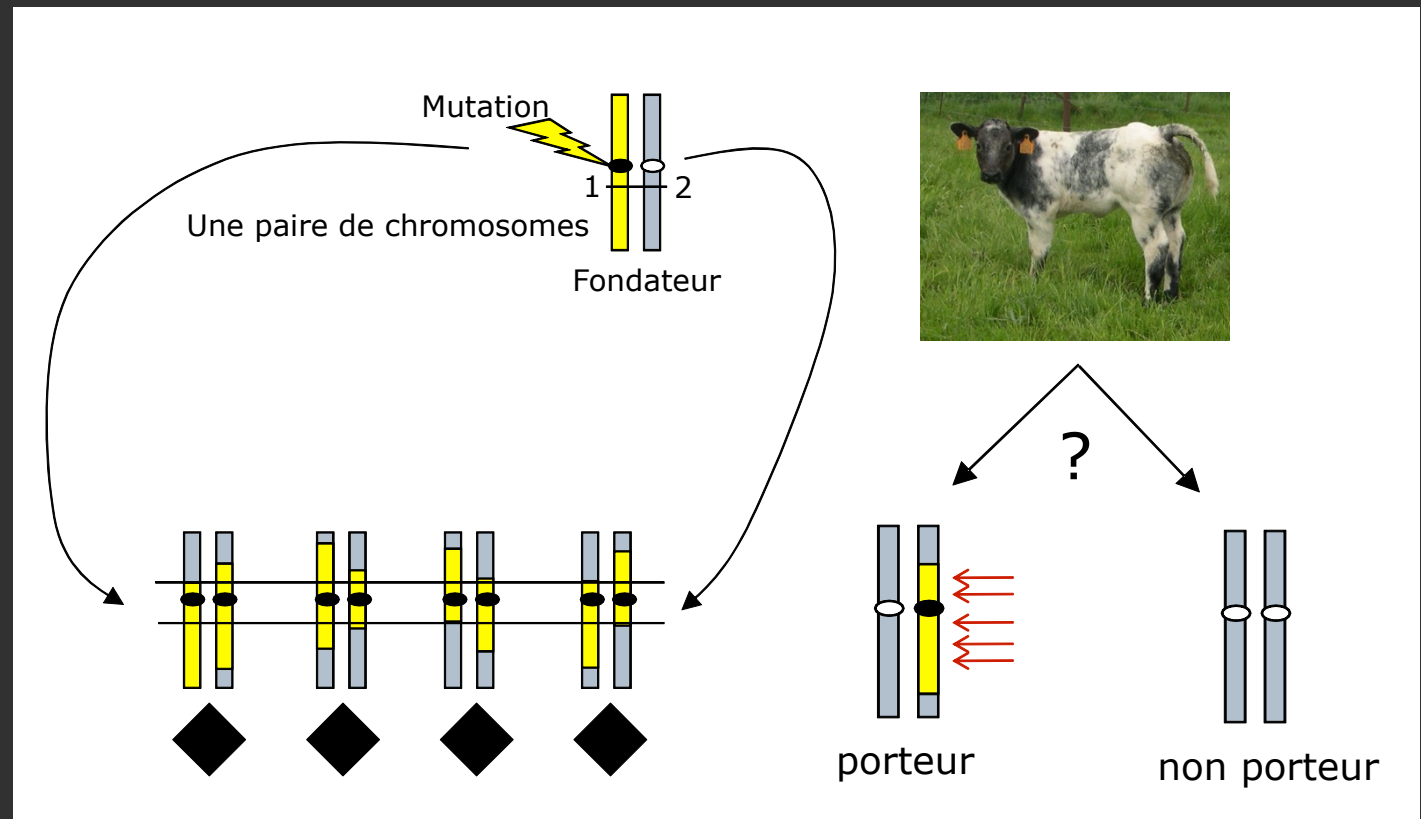
□ Tests directs : fiable à 100 %



# Tests diagnostiques

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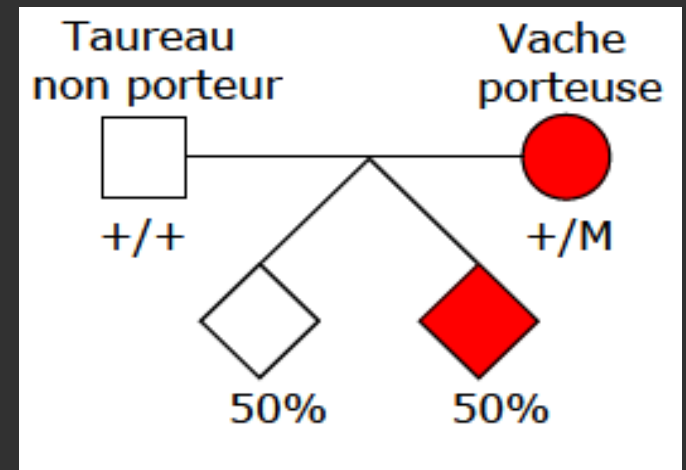
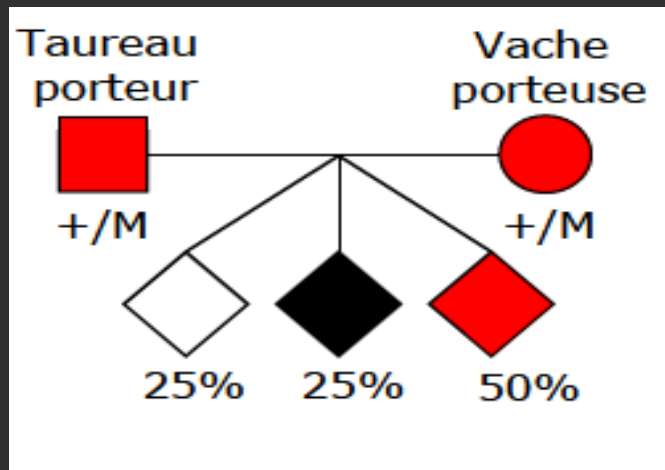
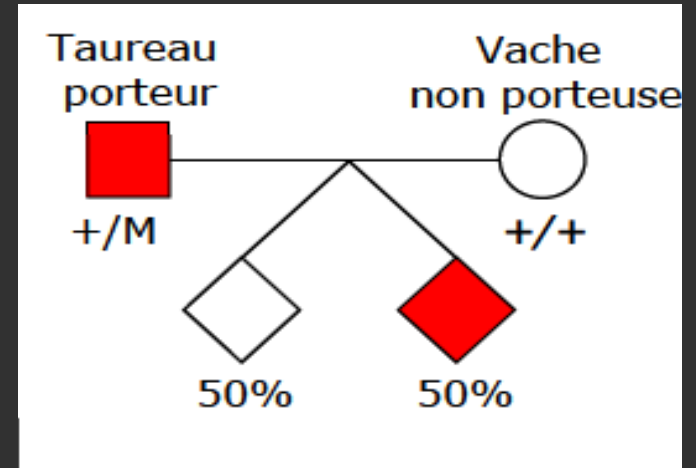
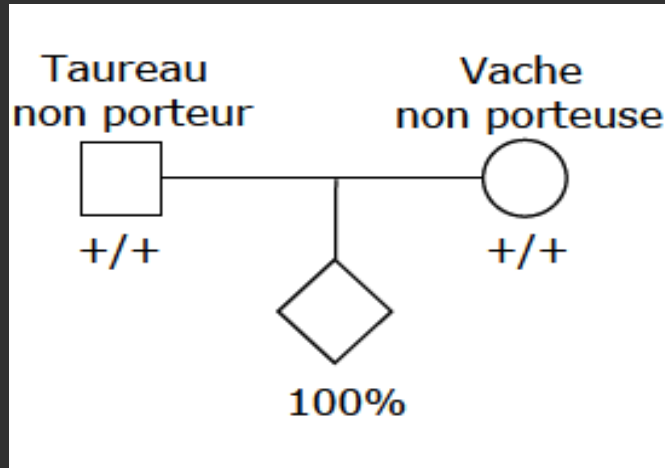
❑ Tests indirects : fiable à 95 %





# Sélection Assistée par Marqueurs

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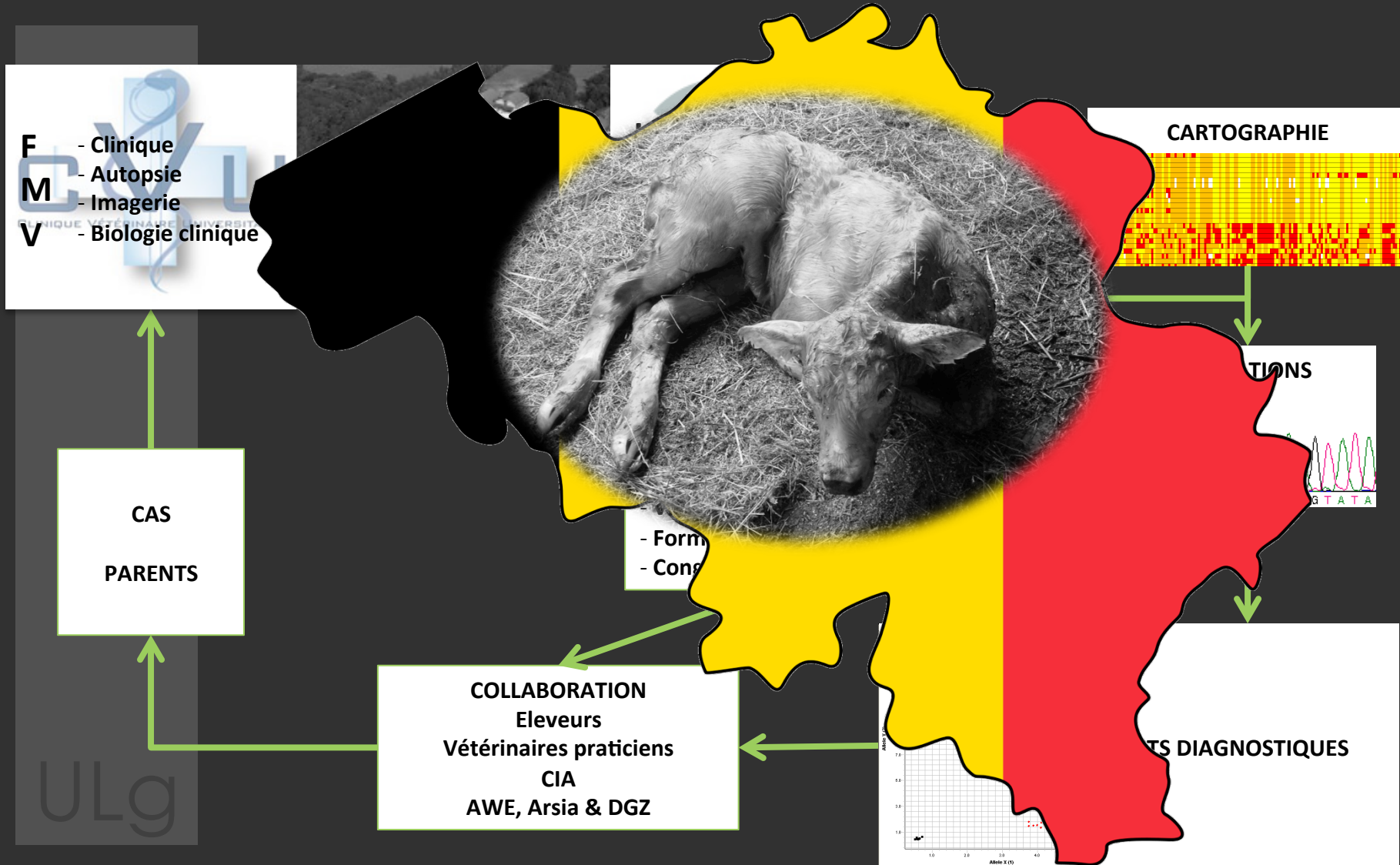




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LA GENOMIQUE,  
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# Hérédo-surveillance en BBB

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# Défauts génétiques en BBB

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- ☐ Dystonie Musculaire Congénitale 1 & 2
- ☐ Syndrome de la Queue Tordue
- ☐ Nanisme proportionné
- ☐ Hamartome gingival
- ☐ Syndrome létal d'arthrogrypose
- ☐ Gestation prolongée
- ☐ Maladie des génisses blanches



# Dystonie Musculaire Congénitale 1 & 2

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- ❑ DMC1 = SMA
- ❑ Sarcoplasme
- ❑ 10 - 15 % porteurs fin 2005
- ❑ *Christophe > Riant*

- ❑ DMC 2 = Electrique
- ❑ Jonction neuromusculaire
- ❑ 3 - 5 % porteurs fin 2006
- ❑ *Rieuse > Riant*



Charlier *et al.*, 2008

Prof. F. Rollin

# Syndrome de la Queue Tordue

Unit of Animal Genomics

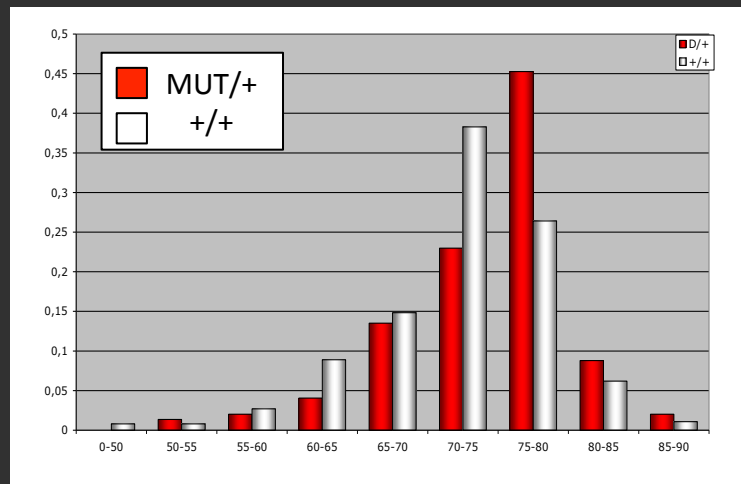
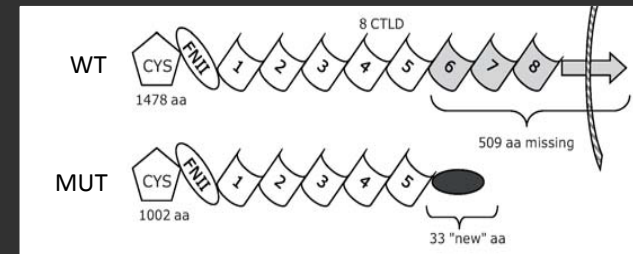


# Syndrome de la Queue Tordue

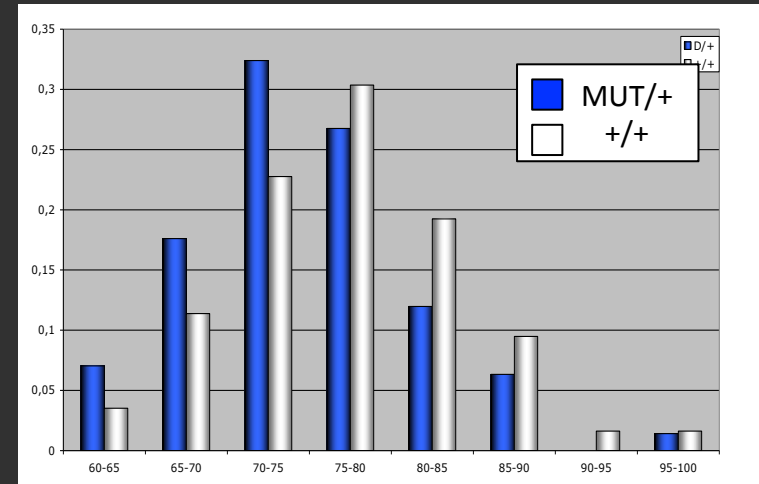
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- ❑ Endo 180: *Del-2pb MRC2*
- ❑ 25 % porteurs 2008
- ❑ *Précieux > ...*
- ❑ Sélection balancée



Musculature



Taille & aplombs



# Syndrome de la Queue Tordue

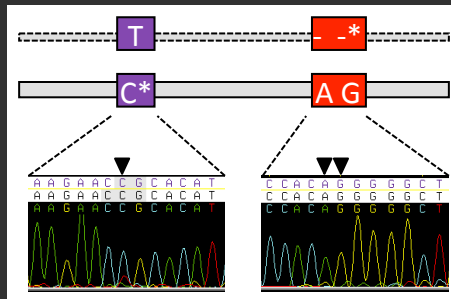
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MRC2 del 2bp  
+/+



MRC2 del 2bp  
MUT/+



MRC2 del 2bp  
MUT/+



MRC2 del 2bp  
MUT/MUT

- ❑ < 0,5 % porteurs 2010
- ❑ *Futur* > ... > *Colos* > ...
- ❑ Sélection balancée ?



# Nanisme proportionné

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- ❑ 147 cas
- ❑ *RNF11*:
  - Complexe A20 = régulation NF-KB
  - 40 % des cas
- ❑ *Oblat* > ... > *Galopeur* > ...
- ❑ 25 % porteurs 2009

# Nanisme proportionné

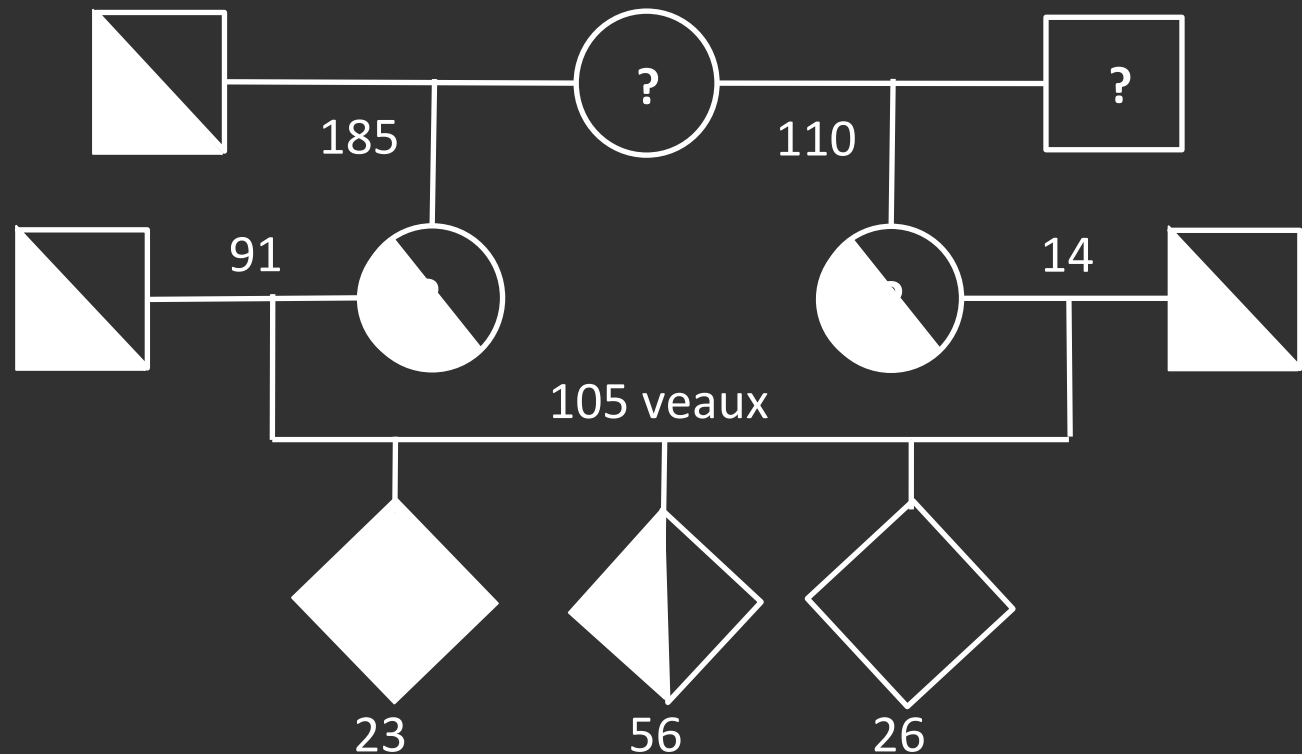
Unit of Animal Genomics



□ 25 % porteurs

➤ PEU DE CAS OBSERVES

➤ Etude prospective (105 MUT/+ x MUT/+)

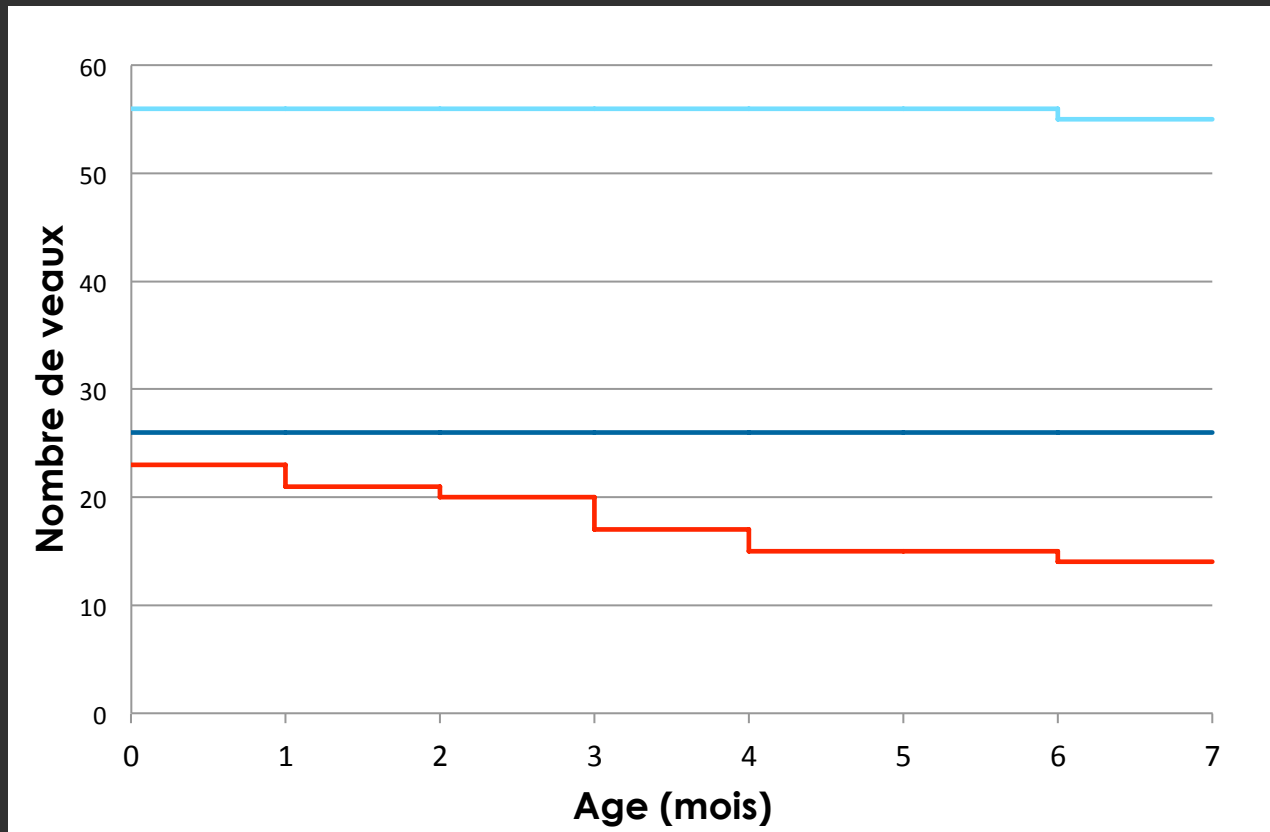


# Nanisme proportionné

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- Etude prospective (105 MUT/+ x MUT/+)
  - Mortalité et morbidité

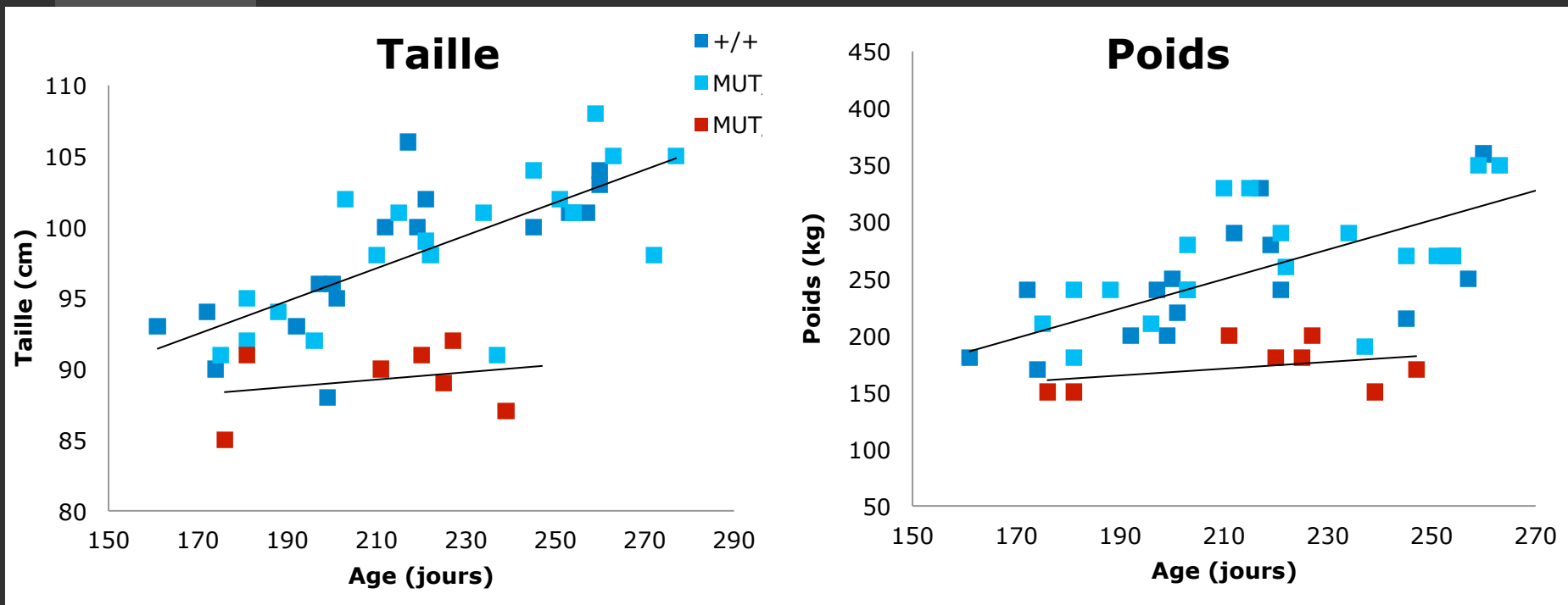


# Nanisme proportionné

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- Etude prospective (105 MUT/+ x MUT/+)
- Taille et poids



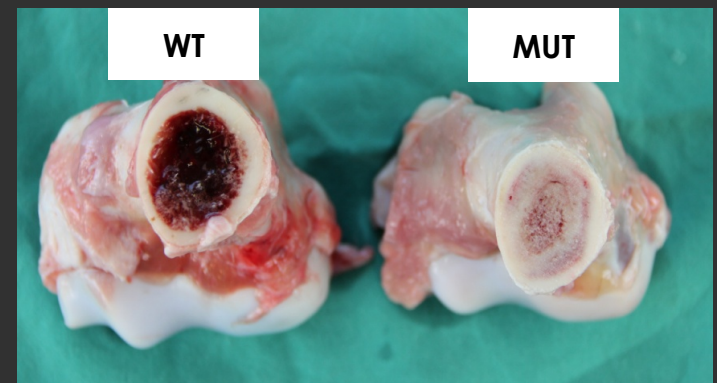


# Hamartome gingival

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- ❑ 68 cas
- ❑ NGS: *CLCN7*
- ❑ CIC-7 :
  - Ostéoclastes
  - Lysosomes
- ❑ 10 % porteurs fin 2010
- ❑ Gabin > ... > Osborne



# Syndrome Létal d'Arthrogrypose

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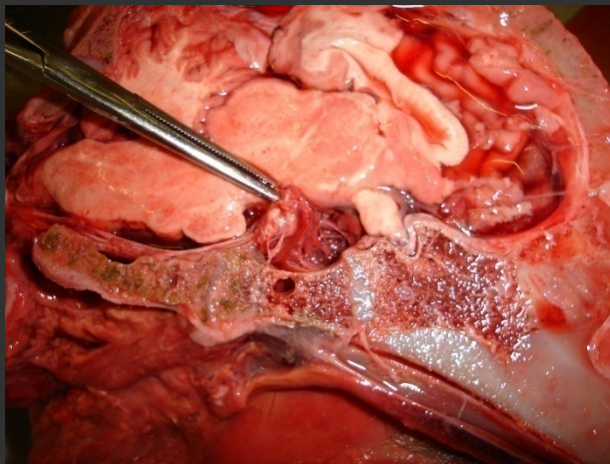
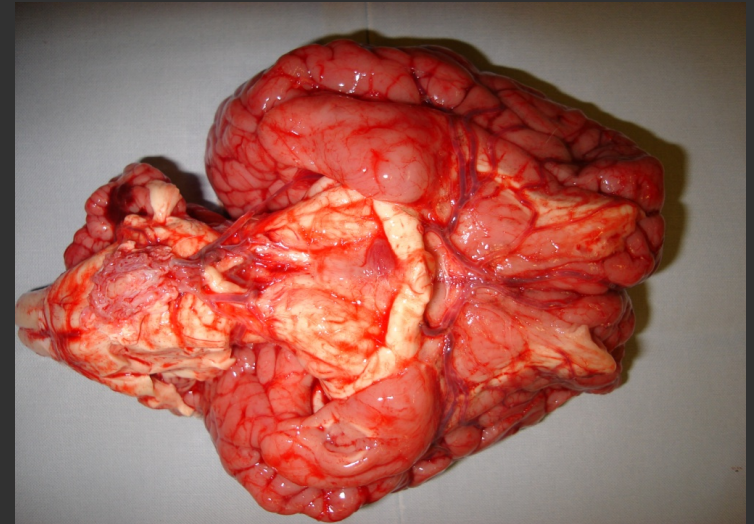


- ❑ 27 cas
- ❑ NGS ARNm : *PIGH*
- ❑ 5 % porteurs fin 2010
- ❑ Kalimine > ... > Ministre



# Gestation prolongée

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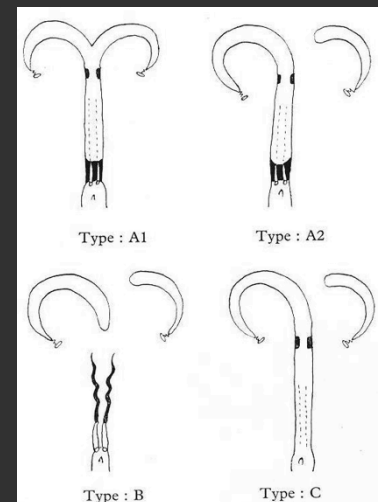
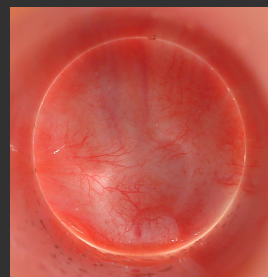
- ❑ 72 cas
- ❑ Gestation : 14 - 15 mois
- ❑ Hypoplasie adénohypophysaire  
(Cornillie et al., 2007)
- ❑ 10 % porteurs fin 2010
- ❑ Christophe > Riant > Bourgogne

# Maladie des Génisses Blanches

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## □ 206 WHDs

- Types (Hanset, 1969)
- Robes
- Pédigree



|       |   | Couleur de la robe |           |           | TOTAL      |
|-------|---|--------------------|-----------|-----------|------------|
|       |   | Blanche            | Pie-bleue | Pie-noire |            |
| TYPES | A | 150                | 11        | 0         | 161 (78 %) |
|       | B | 10                 | 0         | 0         | 10 (5 %)   |
|       | C | 32                 | 3         | 0         | 35 (17 %)  |
| TOTAL |   | 192 (93 %)         | 14 (7 %)  | 0         | 206        |

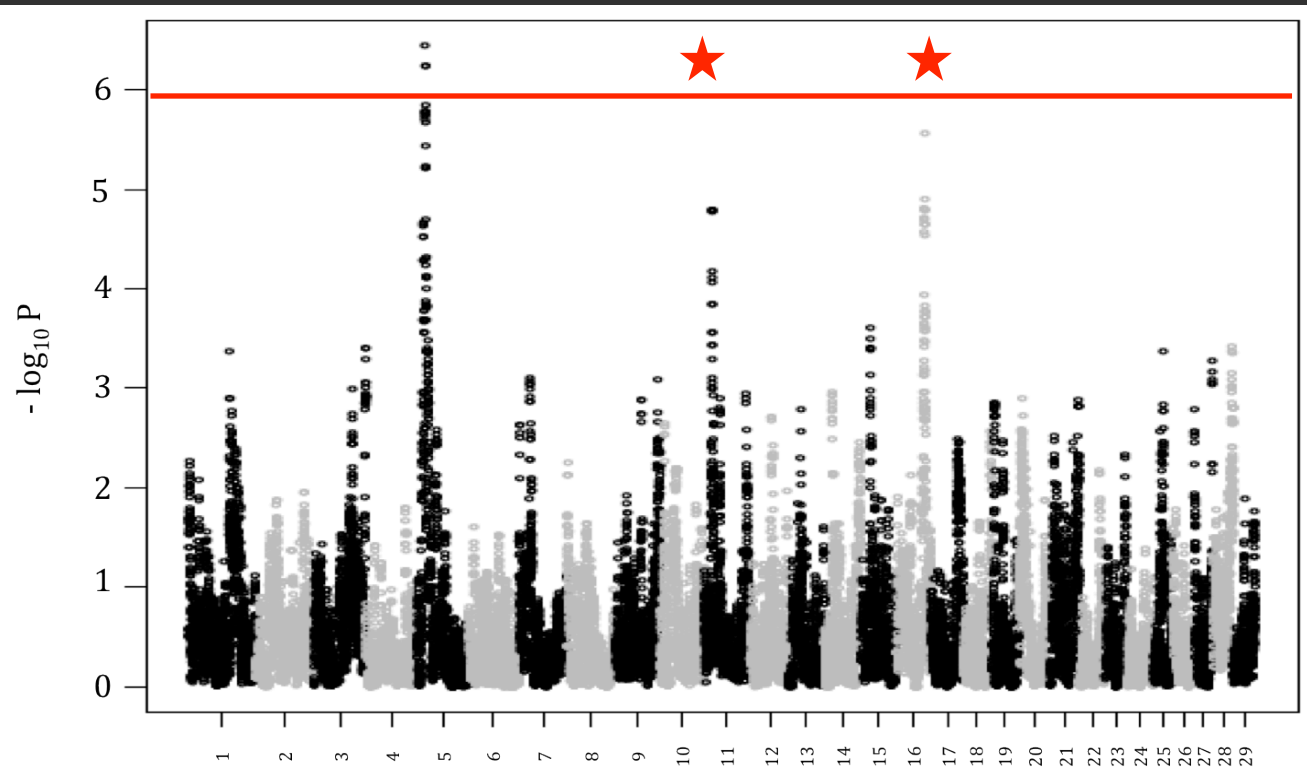


# Maladie des Génisses Blanches

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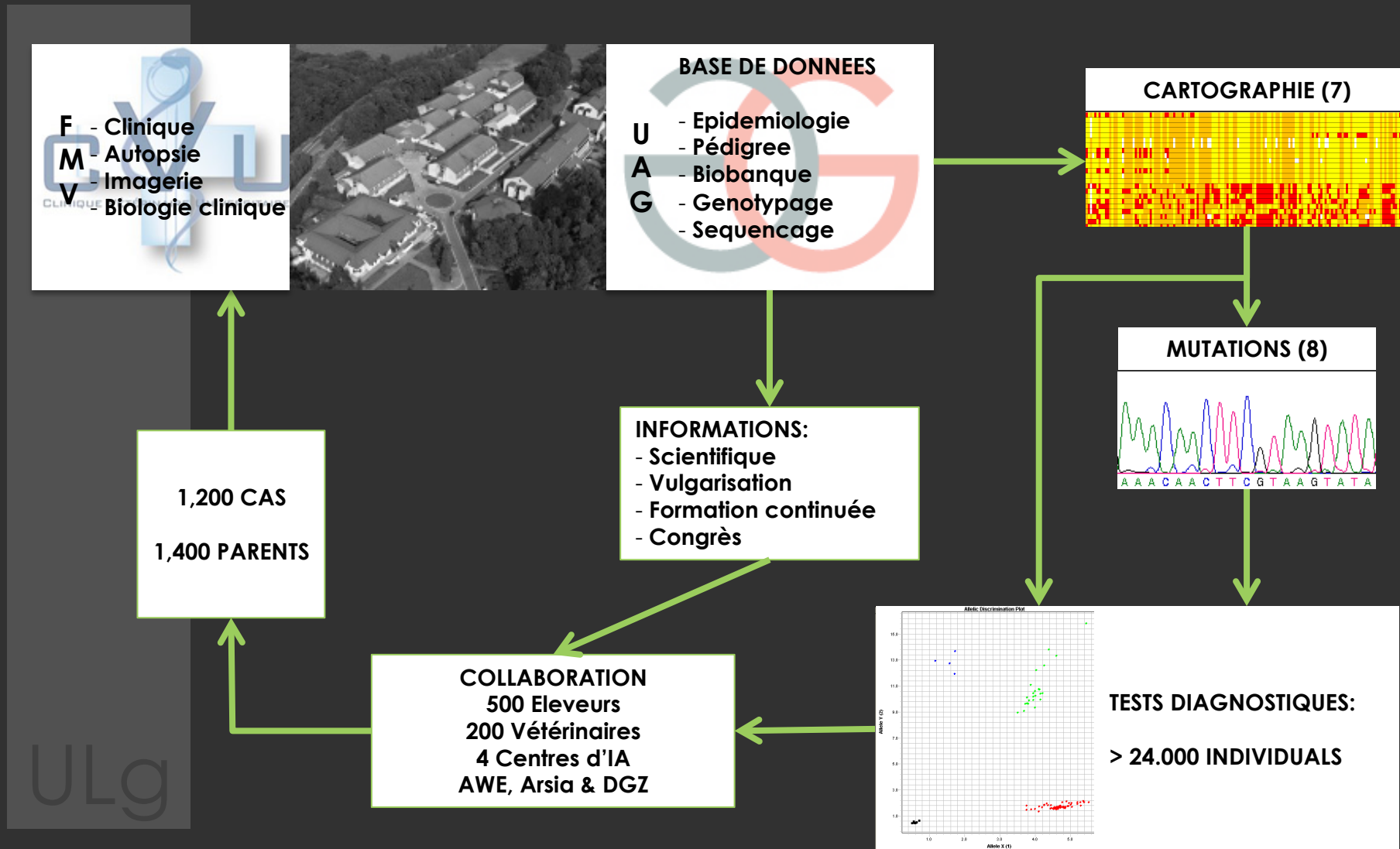
□ GWAS

| Robes          | Blanche | Pie-bleue | Noire |
|----------------|---------|-----------|-------|
| WHD (185)      | 171     | 14        | 0     |
| Taureaux (365) | 188     | 124       | 44    |



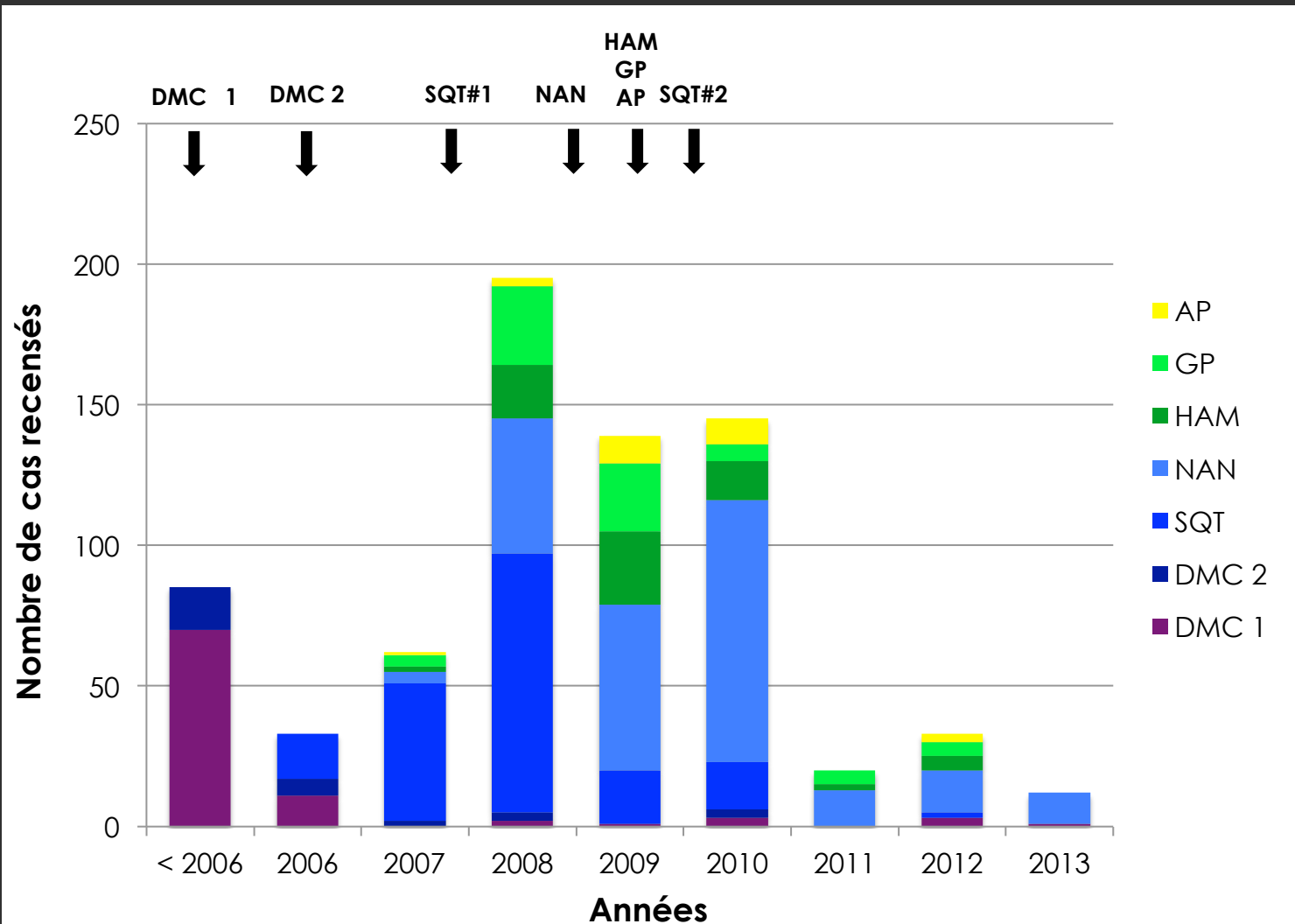
# Hérédo-surveillance en BBB

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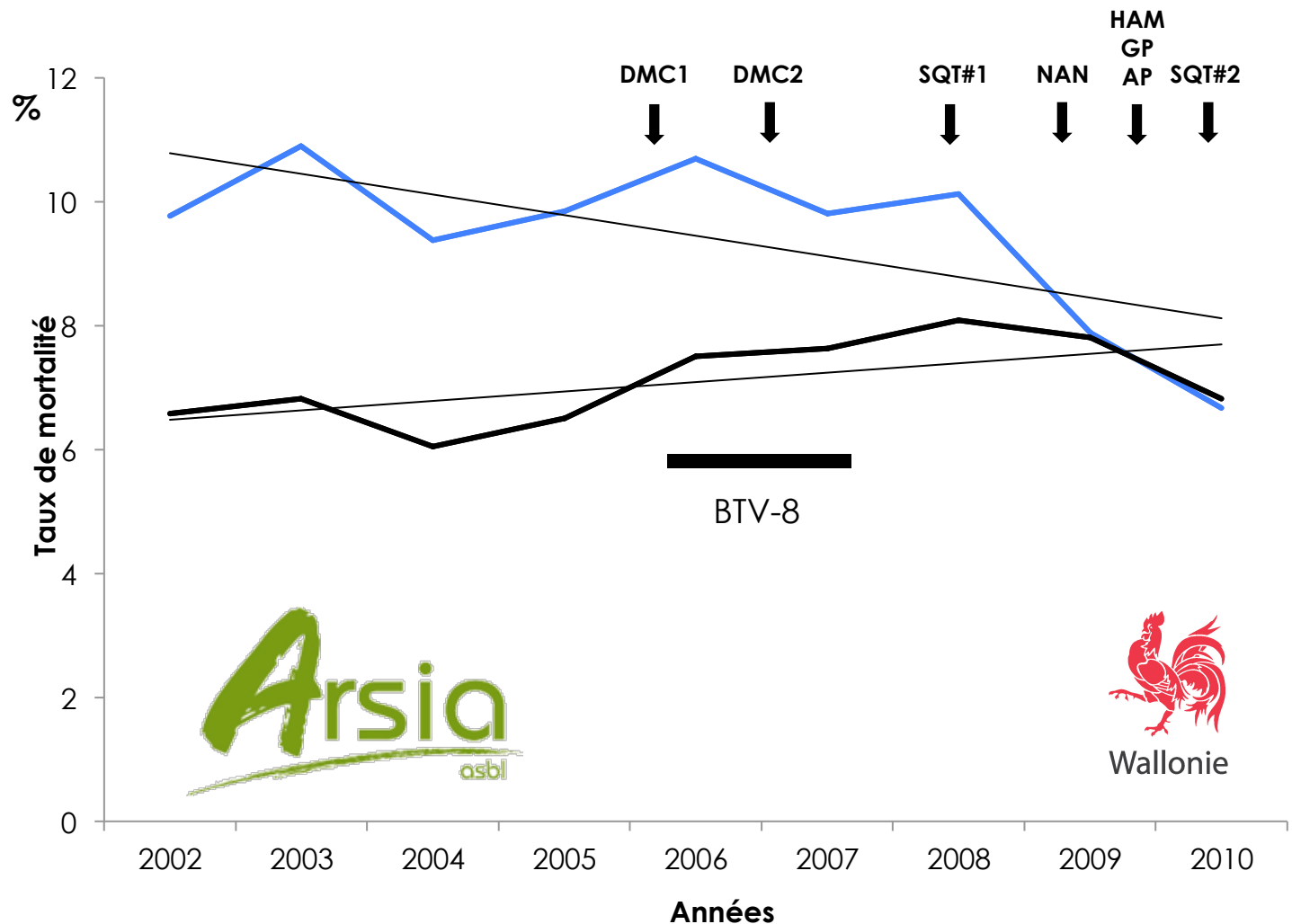
# Evolution du nombre de cas ?

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# Impact sur le taux de mortalité ?

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# Evolution du taux de porteurs Taureaux d'IA

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Défauts

ULg

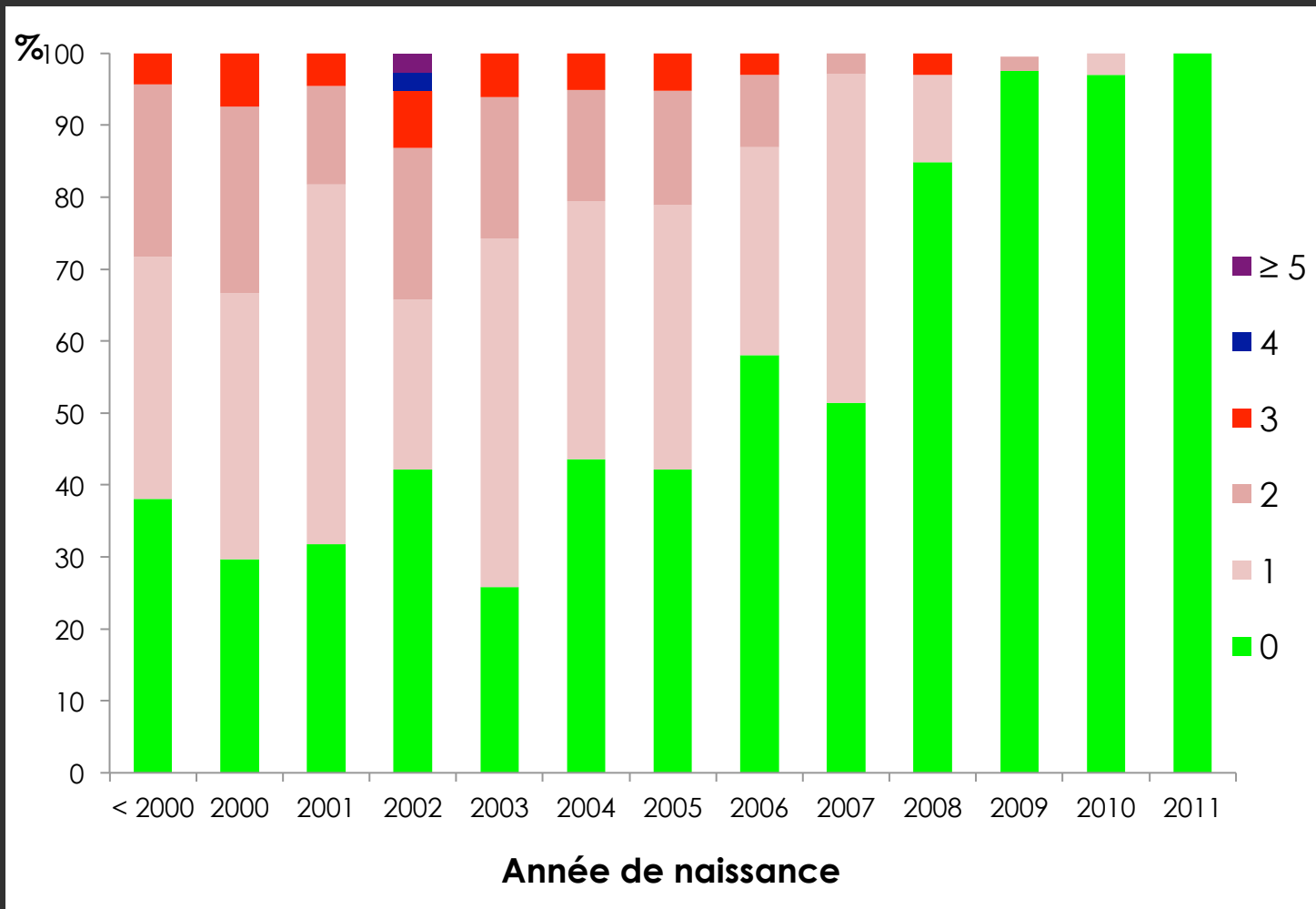
| Année de naissance | DMC 1<br>(559) | DMC 2<br>(556) | SQT<br>(539) | NAN<br>(528) | HAM<br>(532) | GP<br>(522) | AP<br>(521) |
|--------------------|----------------|----------------|--------------|--------------|--------------|-------------|-------------|
| < 2000             | 17             | 7              | 32           | 17           | 4            | 18          | 1           |
| 2000               | 10             | 3              | 41           | 36           | 7            | 11          | 0           |
| 2001               | 17             | 4              | 39           | 23           | 8            | 5           | 0           |
| 2002               | 14             | 5              | 46           | 28           | 15           | 8           | 5           |
| 2003               | 12             | 1              | 32           | 26           | 15           | 12          | 6           |
| 2004               | 2              | 5              | 29           | 24           | 11           | 10          | 2           |
| 2005               | 2              | 2              | 20           | 26           | 7            | 18          | 5           |
| 2006               | 0              | 0              | 13           | 33           | 5            | 5           | 5           |
| 2007               | 0              | 0              | 0            | 30           | 14           | 6           | 3           |
| 2008               | 0              | 0              | 0            | 6            | 9            | 6           | 3           |
| 2009               | 0              | 0              | 0            | 0            | 3            | 3           | 0           |
| 2010               | 0              | 0              | 0            | 0            | 0            | 0           | 0           |

TESTS

# Evolution du taux de porteurs Taureaux d'IA

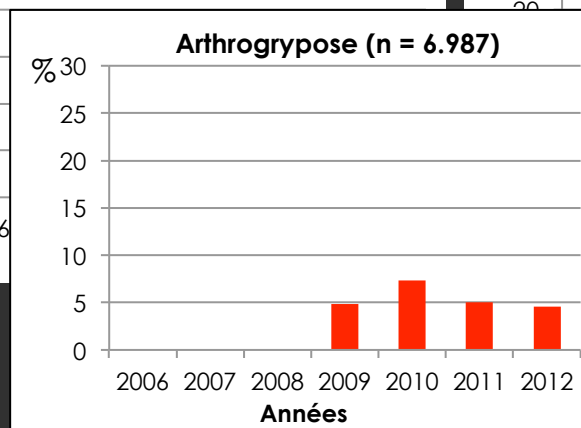
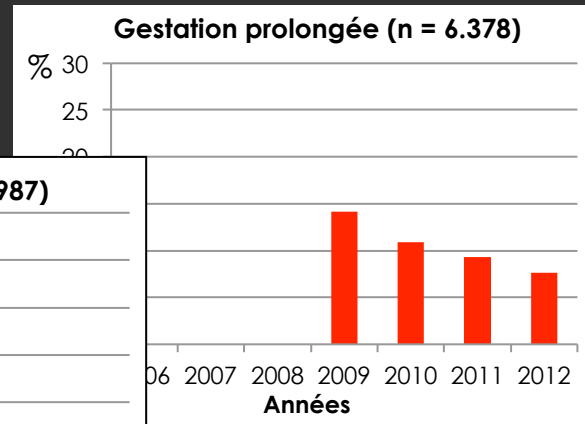
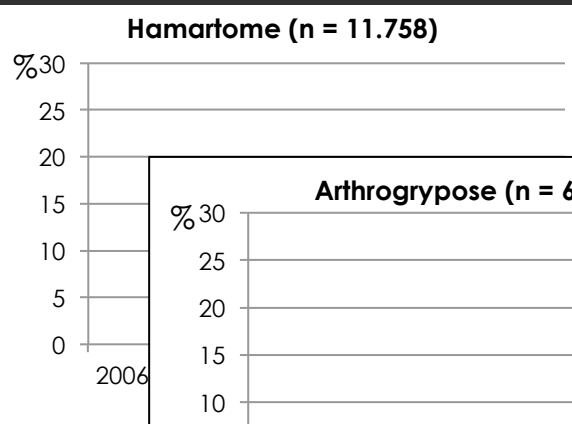
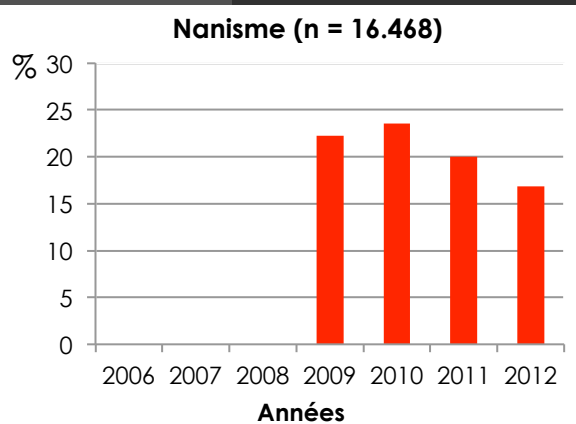
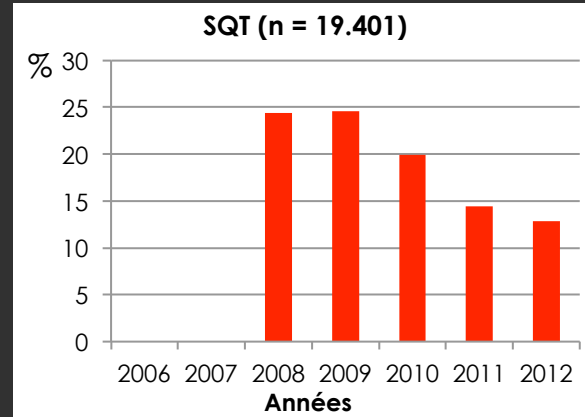
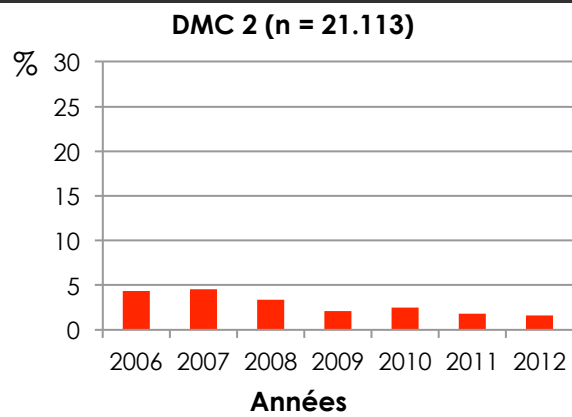
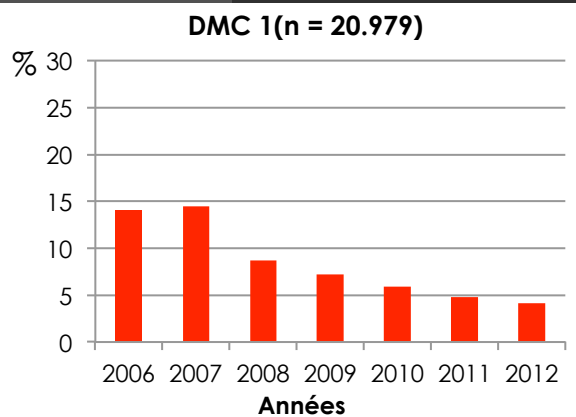
Unit of Animal Genomics

Nombre de mutations



# Evolution du taux de porteurs Population BBB

Unit of Animal Genomics



# L'hérédo-surveillance en BBB...

Unit of Animal Genomics

- ❑ Plateforme d'hérédo-surveillance
  - Nécessaire pour les races spécialisées
  - Collaboration & communication
  - Utile pour les maladies émergentes (FCO, SBV,...)
- ❑ Séquençage haut débit
  - accélération du processus
- ❑ Sélection des mâles
  - Eradication rapide & complète
  - Diminution lente des porteurs
  - Problématique
- ❑ BBB vers la sélection génomique....



# MUTATION DU BLANC-BLEU-BELGE

ÇA DEVAIT  
ARRIVER

