GENETICS

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COMMUNAUTÉ EUROPÉENNE

Fonds européen
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Wallonie

Université
de Liège

Unit of Animal Genomics

Management of Inherited Disorders in Belgian Blue Cattle Breed

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ECBHM resident Workshop – Nantes, 2013

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Inherited defects in cattle

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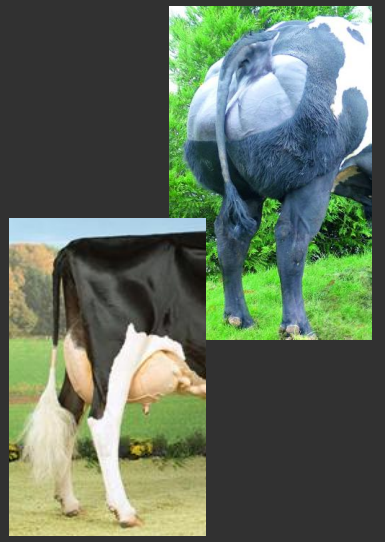
- Intensive selection
- Extensive use of AI



- ➢ OUTBURSTS OF INHERITED DEFECTS
  - BLAD (90') = $5 million in US
- Genomic tools improvement
  - High throughput genotyping
  - Next-generation sequencing (NGS)

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

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

Charlier *et al.*, Nature genetics, 2008

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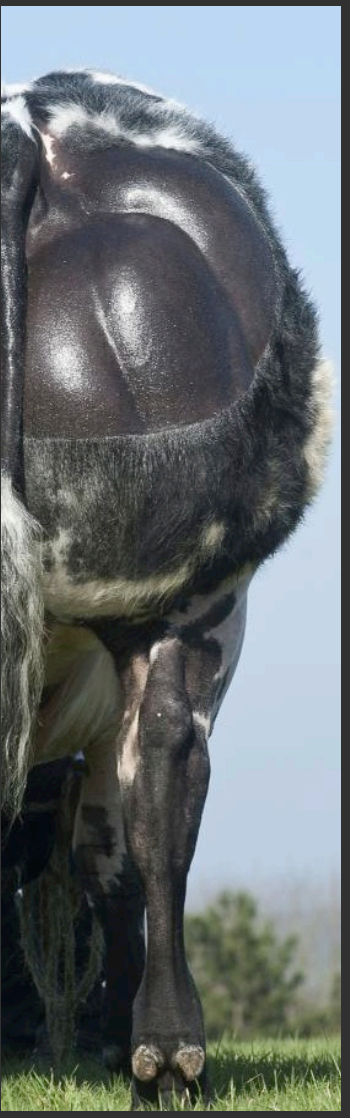
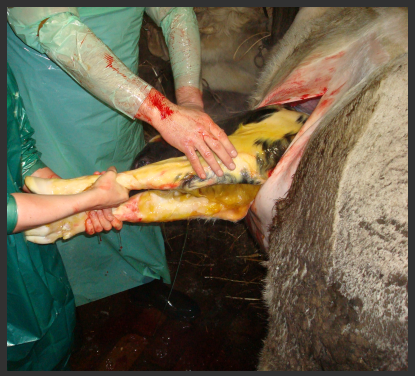
Belgian blue cattle breed

Unit of Animal Genomics



- 50 % belgian cattle & 95 % beef cattle
  - 1.300.000
- 17.000 BBCB herds / 25.000 herds
- Carcass yield = 70 % with 80 % meat
- 99 % calvings by C-section



- Intensive selection for meat production
- Extensive use of AI (50 %)

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Heredo-surveillance in BBCB

Unit of Animal Genomics

F - Clinic
- Necropsy
- Imaging

M - Biochemestry

V

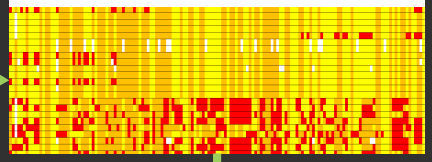
DATA

U - Epidemiology
- Pedigree

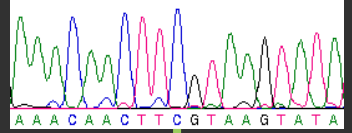
A - Genotyping

G - Sequencing
- Biobank

MAPPING (7)



MUTATIONS (7)

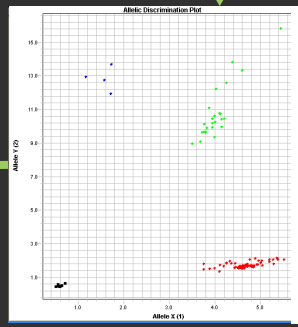


INFORMATIONS:
- Scientific
- Vulgarisations
- Continuing education
- Congress

1,200 CASES

1,400 RELATED

COLLABORATION
500 Breeders
200 Vet practitionners
4 semen providers
AWE, Arsia & DGZ



DIAGNOSTIC TESTS:

> 22.000 INDIVIDUALS

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From the phenotype…

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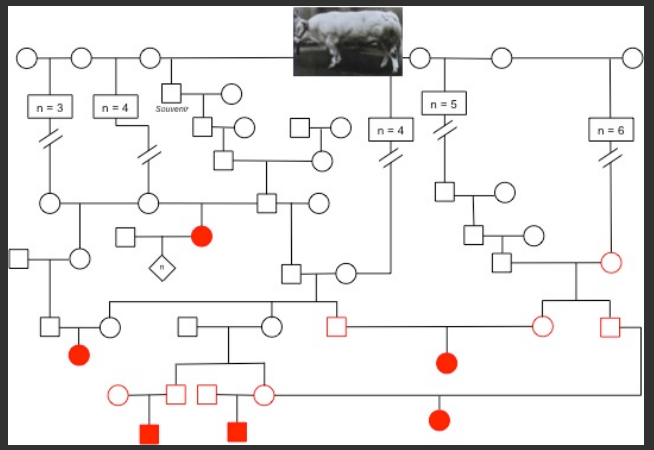
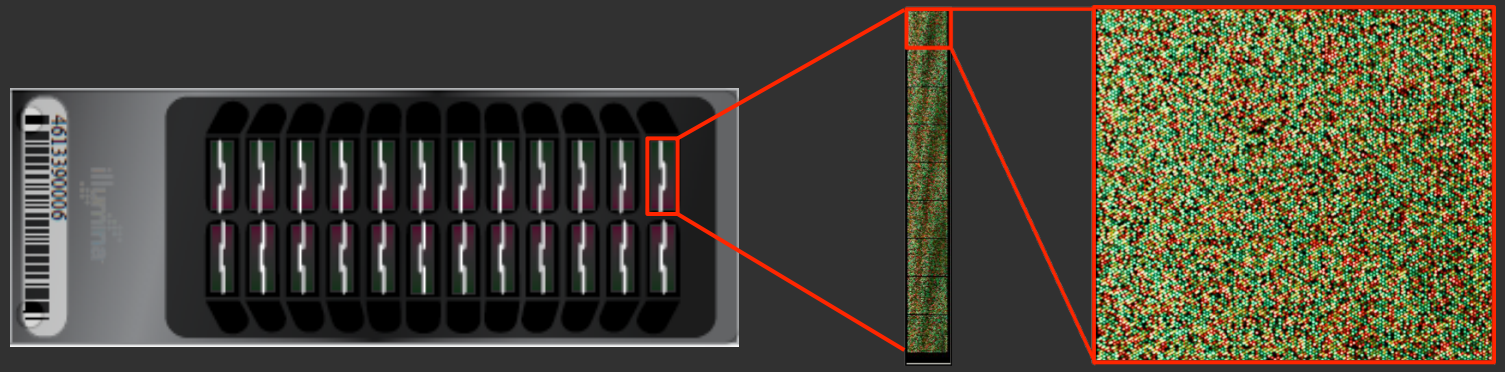
- Phenotyping
  & epidemiological analysis



- Genotyping: SNP technologies



- Genome Wide Association Study

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Genome-wide Haplotype-based Association Study

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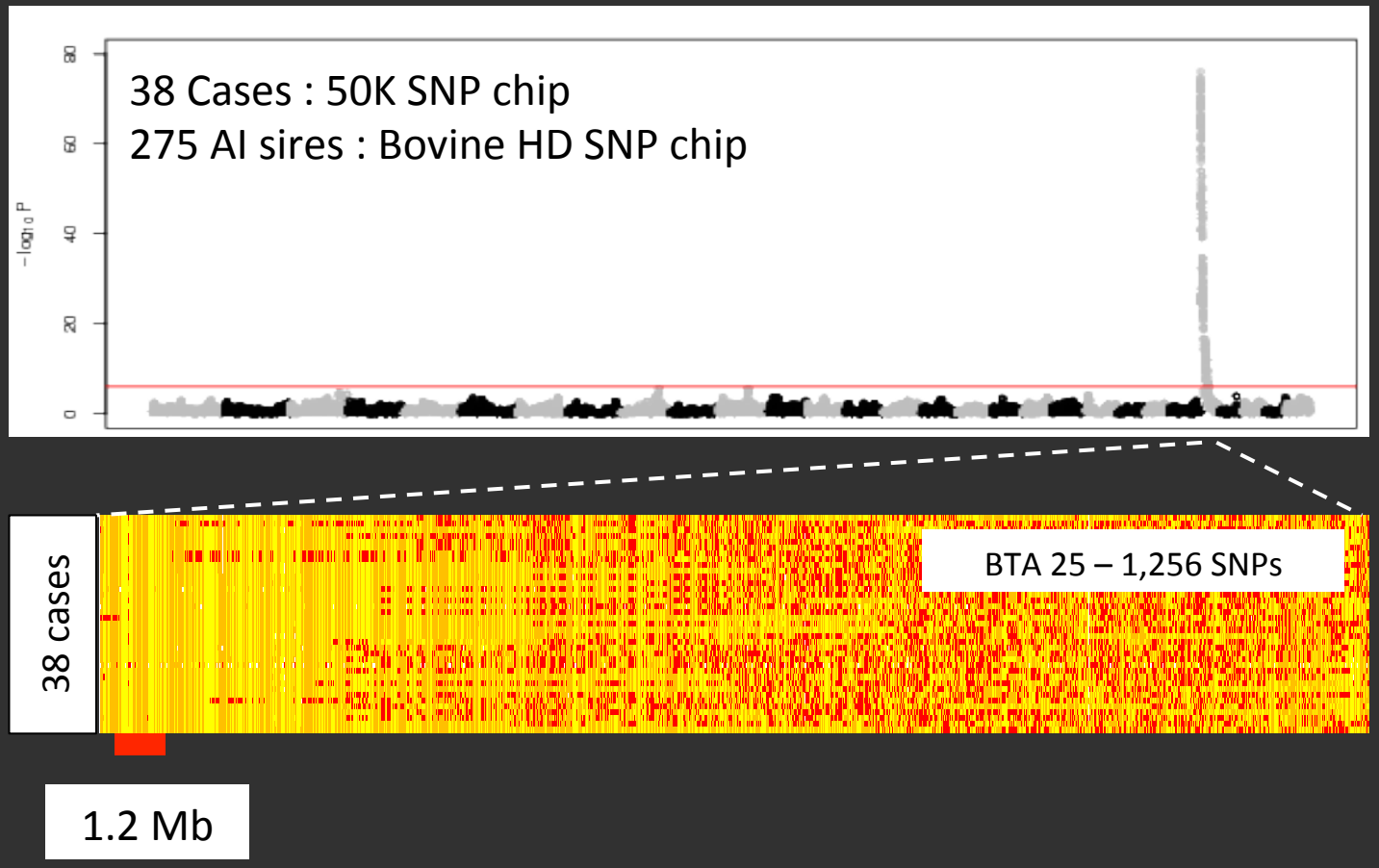

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… to the causative mutation

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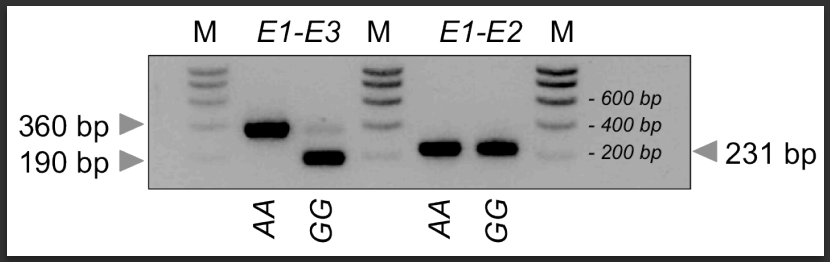
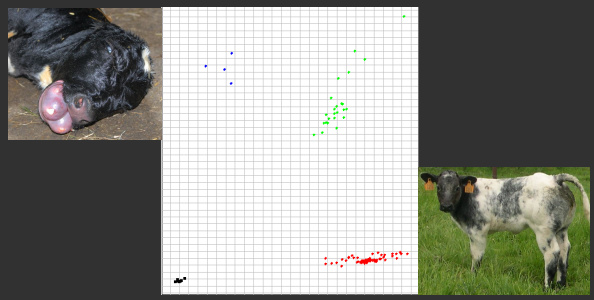
- Sequencing
  - Candidate gene = Sanger sequencing
  - NGS : whole genome sequencing or capture
  - NGS: transcriptome
- Causative mutation validation
  - Expression analysis
  - Functional tests



- Diagnostic tests
  - 5’ exonuclease assay
  - Haplotype-based



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Sanger sequencing for candidate gene

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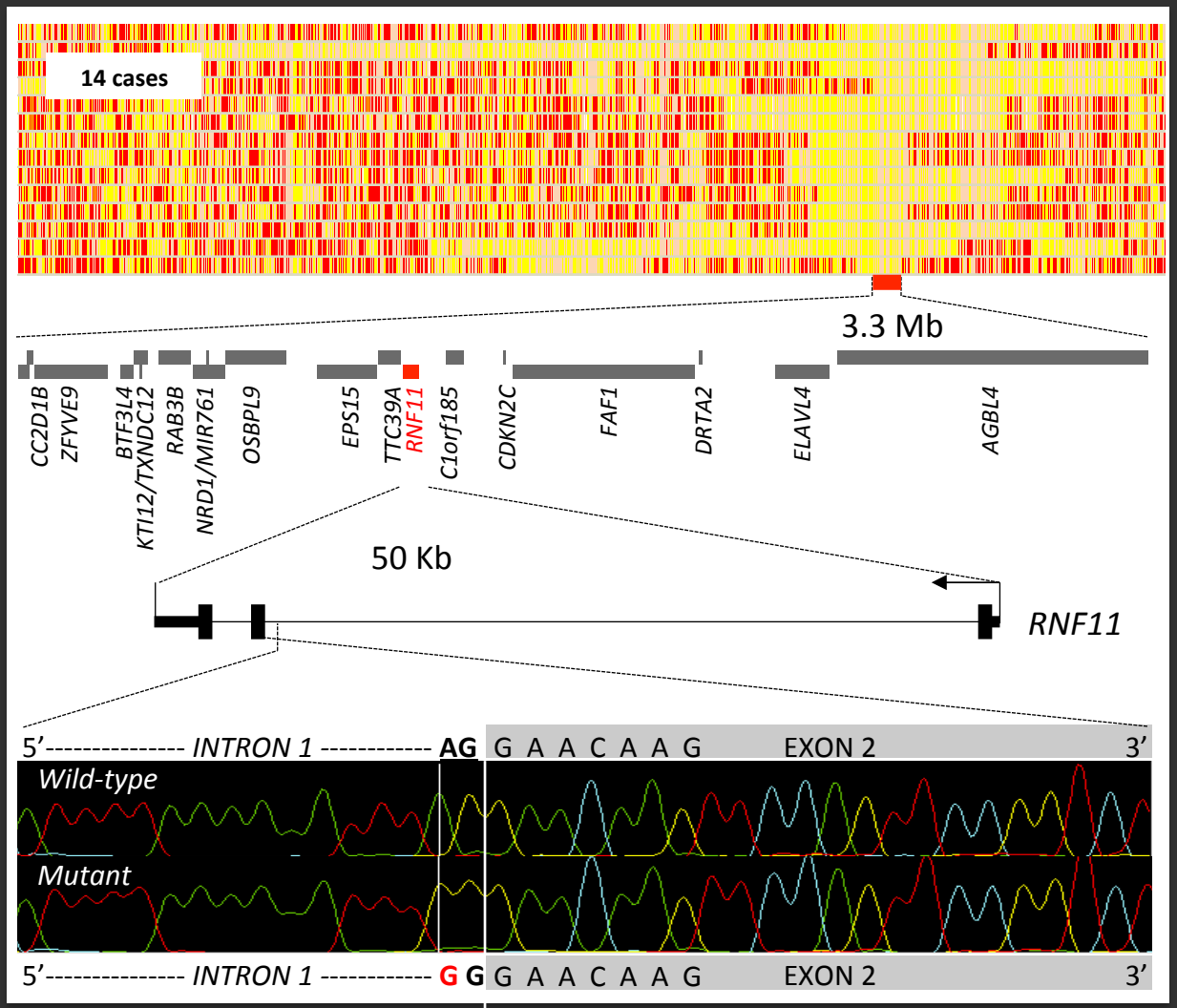

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Whole Genome Sequencing

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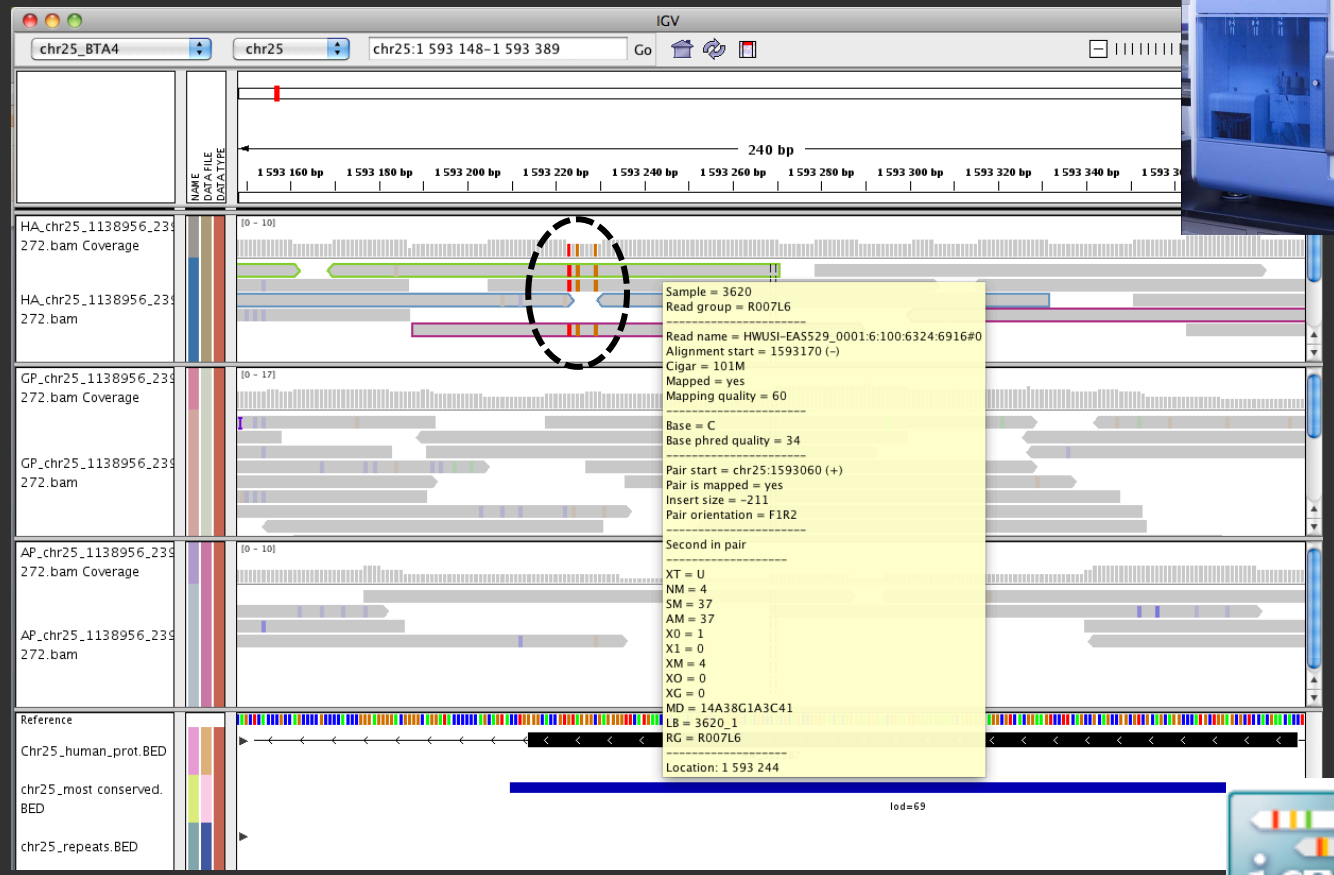

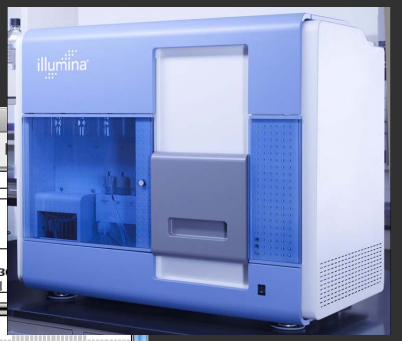

Integrative Genomics Viewer

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Inherited defects in BBCB

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- Congenital Muscular Dystonia 1 & 2
- Crooked tail syndrom
- Dwarfism
- Hamartoma and osteopetrosis
- Lethal arthrogryposis syndrom
- Prolonged gestation

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Congenital muscular dystonia 1 & 2

Unit of Animal Genomics

- *ATP2A1* or *SERCA*
  - Sarcoplasmic Ca pump
- Death in few weeks
  - Bronchopneumonia

- *SLC6A5*
  - Na/Cl dependent glycine transporter
- Death within few hours

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Crooked Tail Syndrom

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Crooked Tail Syndrom

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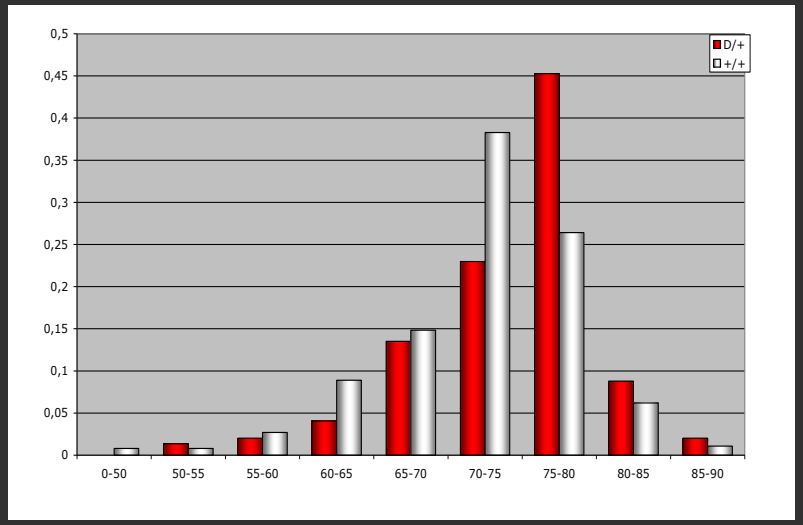
- *MRC2*: Extracellular matrix remodelling
- 25 % carriers
- Selective sweep



- 2nd loss-of-function

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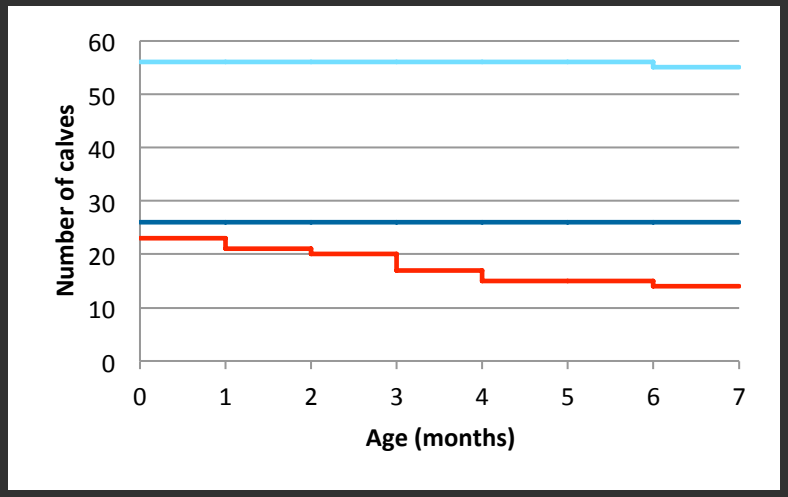
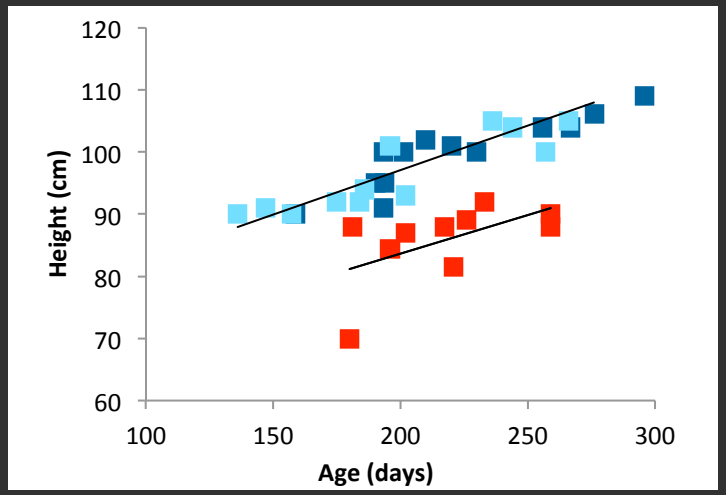
Dwarfism

Unit of Animal Genomics

- *RNF11* : A20 complex
  - Growth
  - Inflammation control
- 40 % stunted growth
- 25 % carriers
- Selective sweep





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Hamartomas & osteopetrosis

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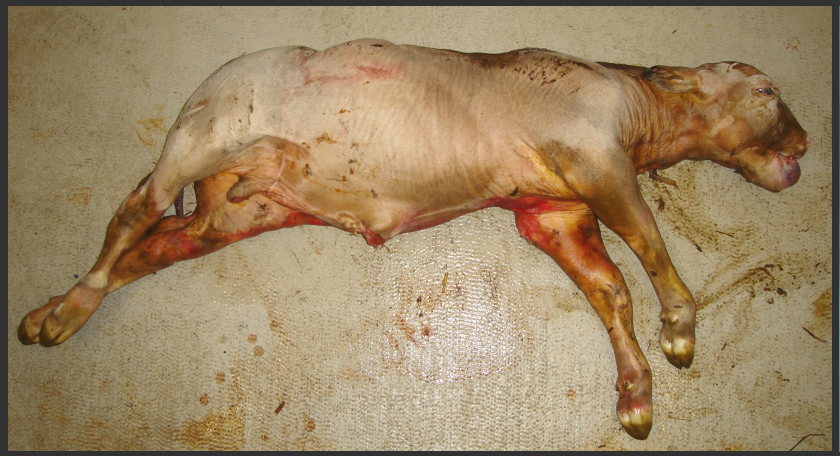

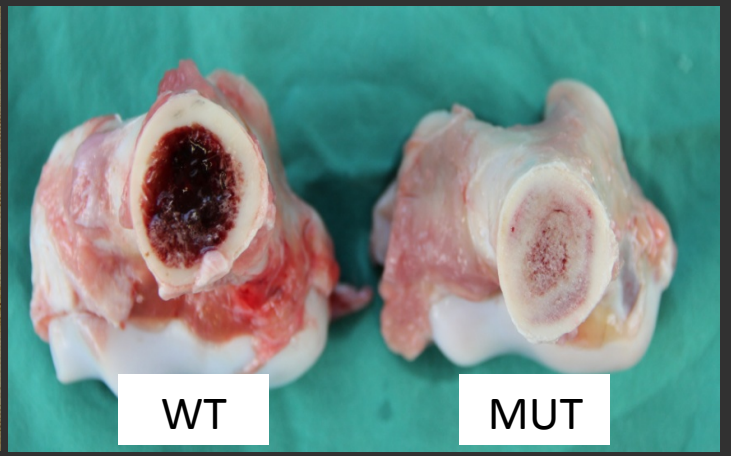

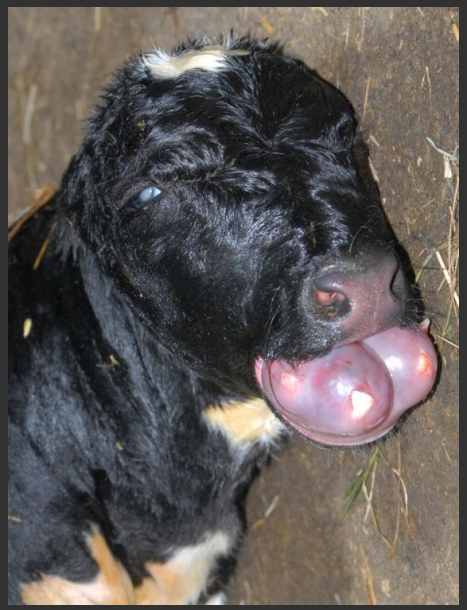

- *CLCN7* : Bone resorption /osteoclasts
  - Ostropetrosis
  - Lysosomal storage disease
- NGS : 3 private mutations
- « Fast mutant »
- 10 % carriers

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Lethal arthrogryposis syndrom

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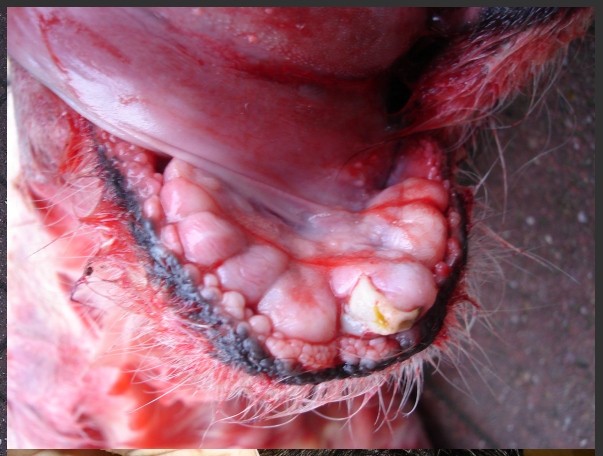

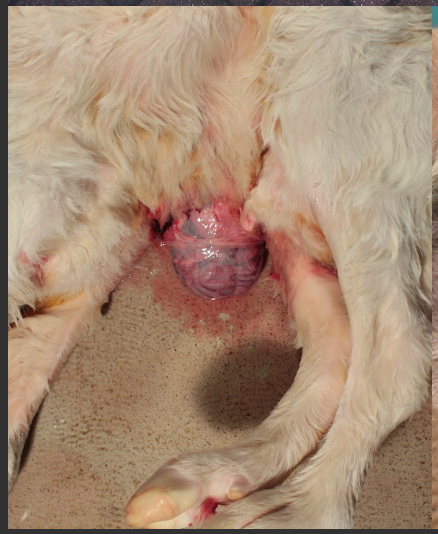

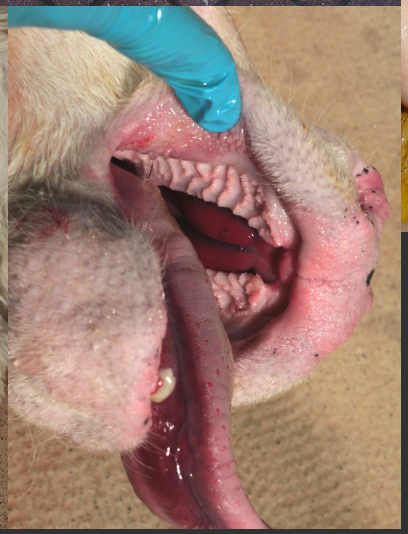

- *PIG-H* : GPI-anchor
- NGS : transcritpomic
- 5 % carriers

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Prolonged gestation

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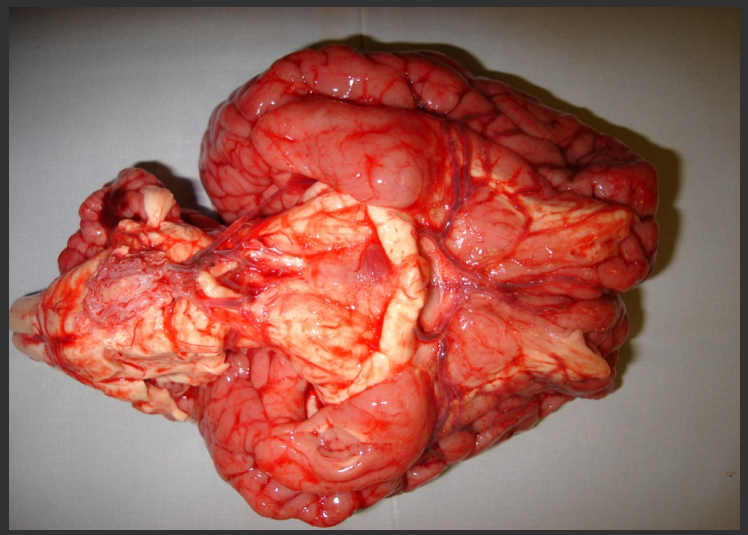

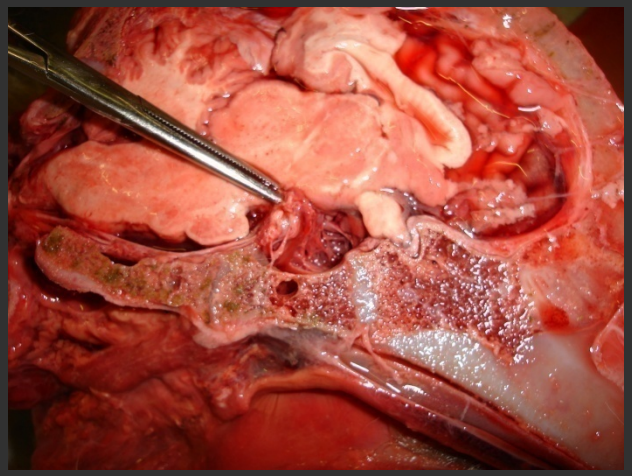

- Gestation length : 14-15 m
- Adenohypophyseal hypoplasia
- Mapping IBD – BTA 18
- Haplotype based test
- In progress....

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Management of mutant cases

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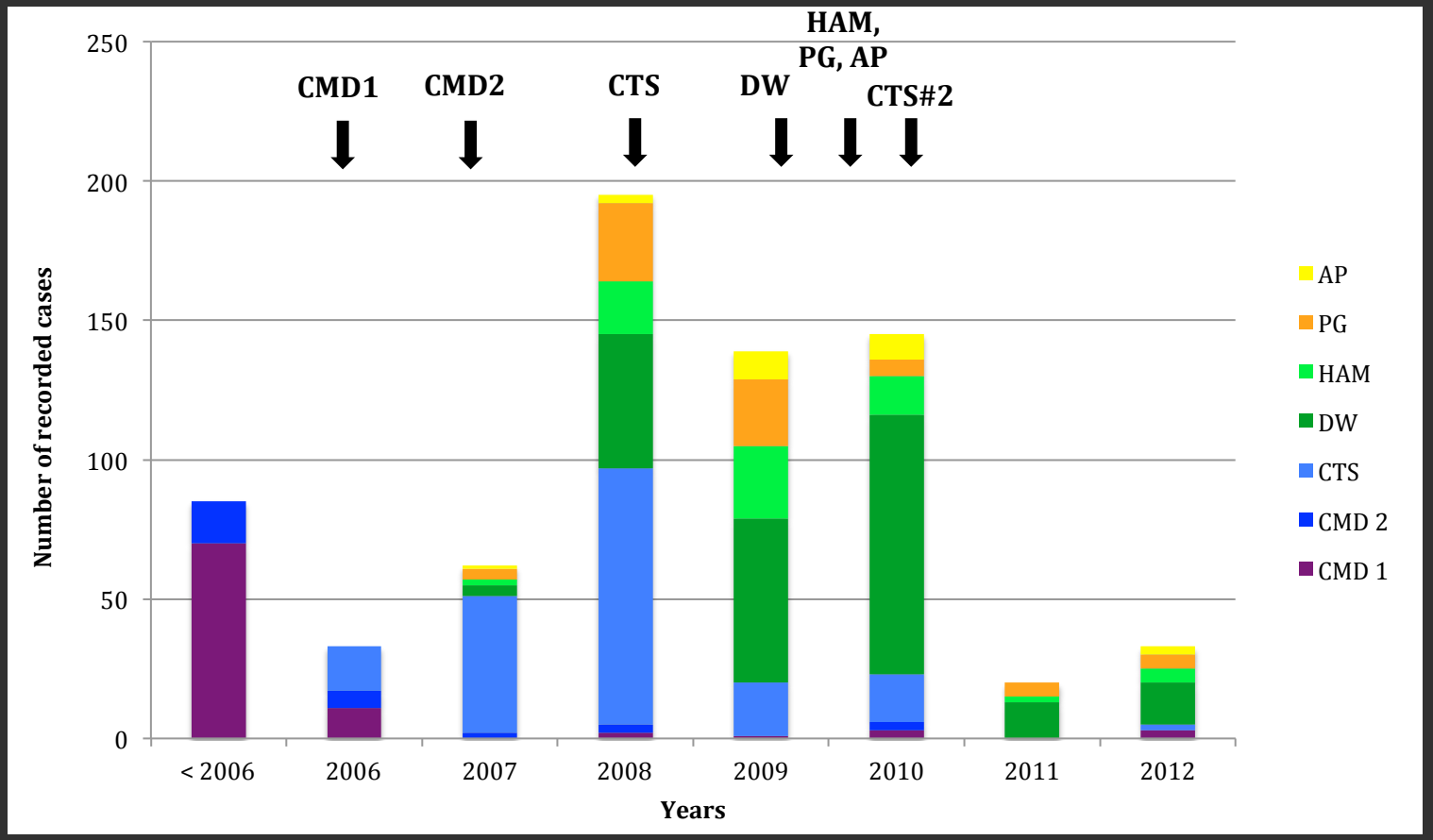

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Walloonian mortality rate

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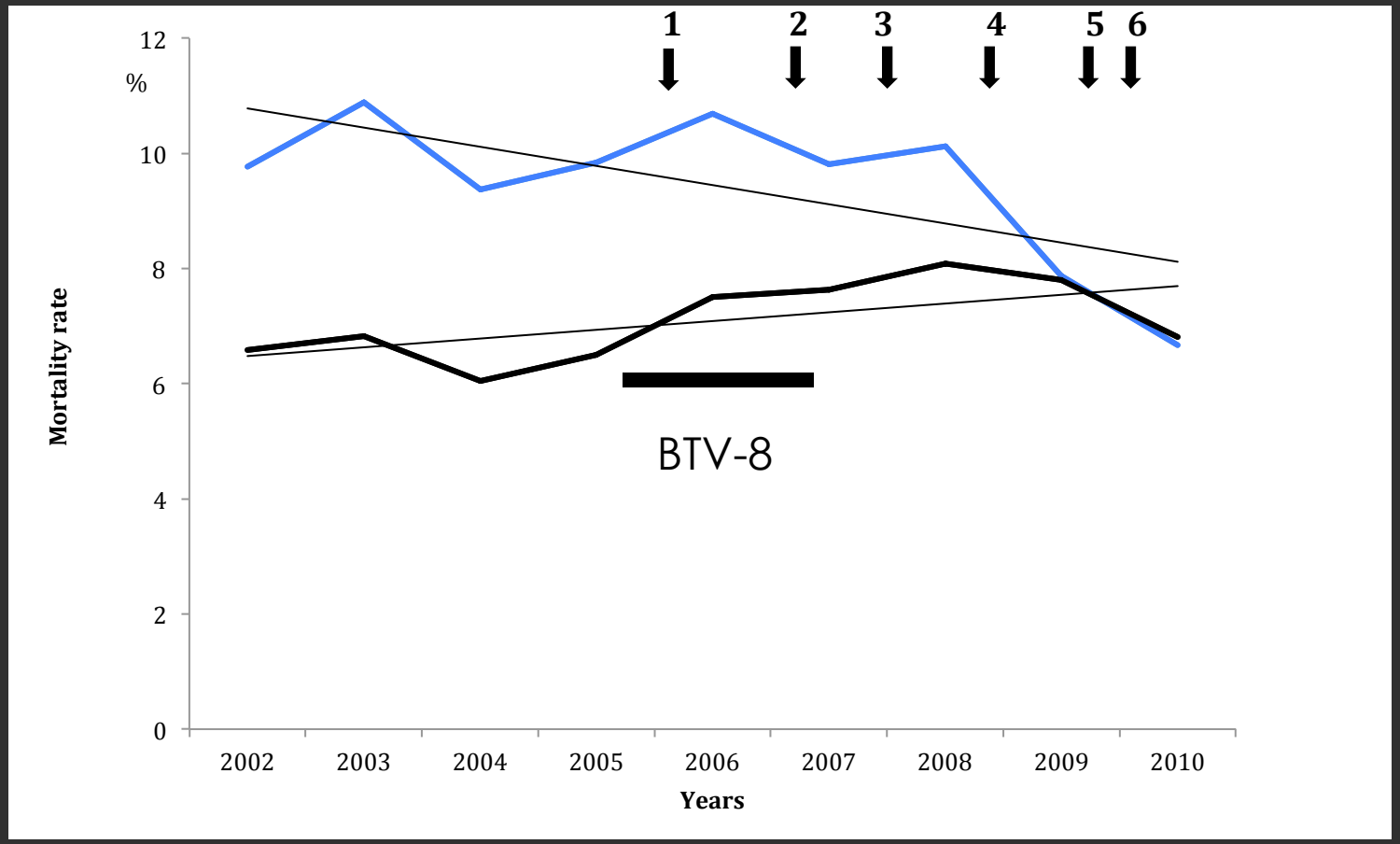

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Management of carriers (AI sires)

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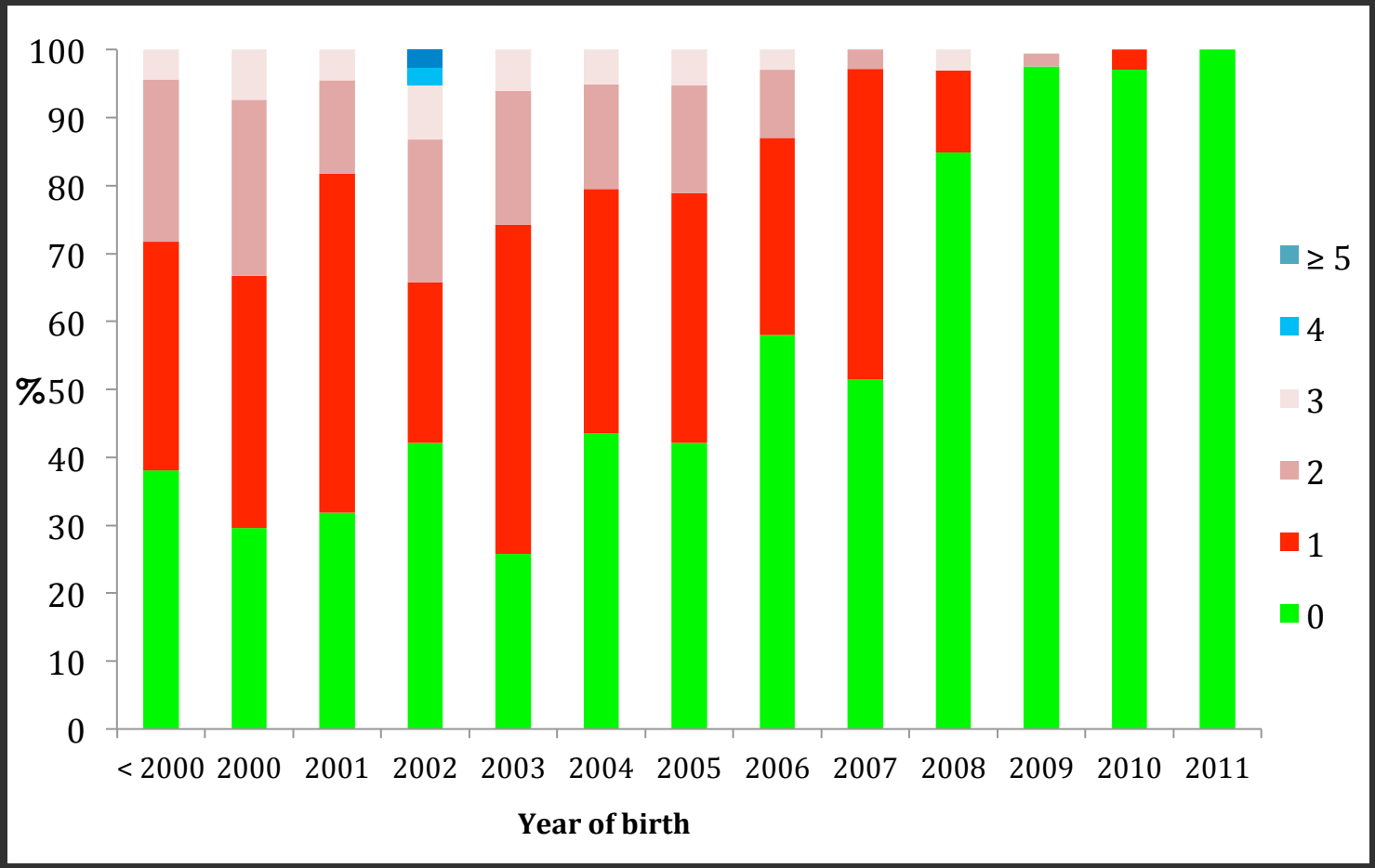

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Management of carriers (BBCB population)

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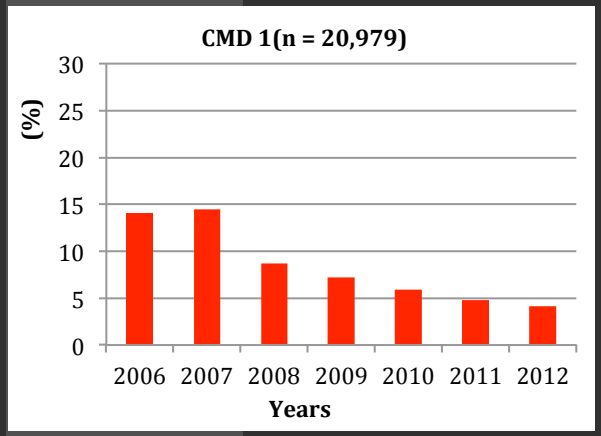

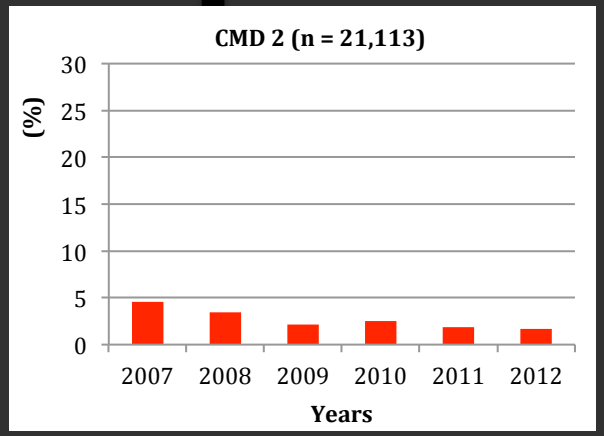

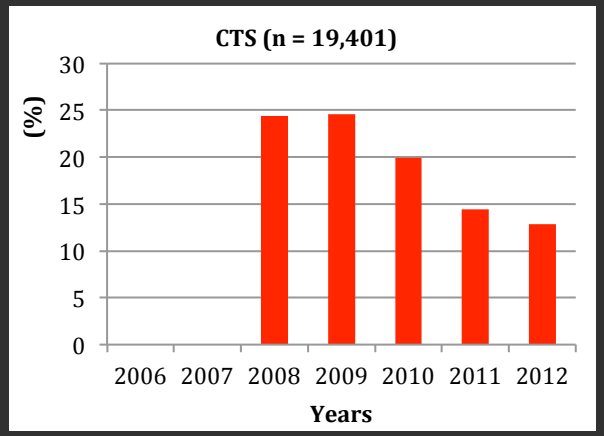

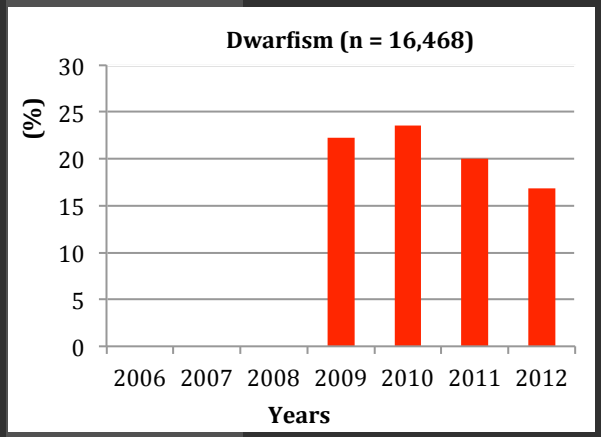

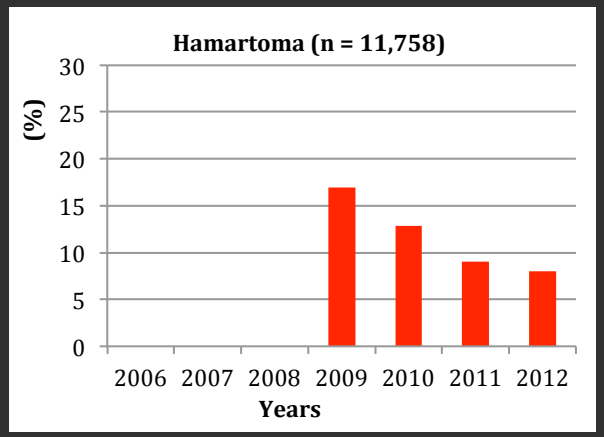

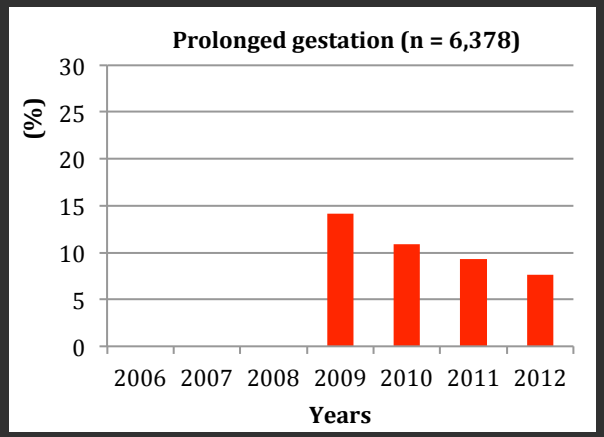

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Heredo-surveillance in cattle…

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- Heredo-surveillance platform
  - Useful tool for highly selected breeds
  - Efficiency of the collaboration
  - Useful for emerging diseases (BTV, SBV, …)
- NGS accelerates causative mutation identification process
- Selection based on males
  - Complete & rapid disease eradication
  - Slight carrier frequency decrease
  - Problematic in case of:
    - High carrier frequencies
    - High number of defect

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THANK YOU...

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