Management of Inherited Disorders in Belgian Blue Cattle Breed

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Inherited defects in cattle

- 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)

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

Charlier et al., Nature genetics, 2008
Belgian blue cattle breed

- 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%)
Heredo-surveillance in BBCB

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Collaboration:
- 500 Breeders
- 200 Vet practitioners
- 4 semen providers
- AWE, Arsia & DGZ

1,200 CASES
1,400 RELATED

Data:
- Epidemiology
- Pedigree
- Genotyping
- Sequencing
- Biobank

Informations:
- Scientific
- Vulgarisations
- Continuing education
- Congress

Diagnostic Tests:
> 22,000 INDIVIDUALS

Mapping (7)

Mutations (7)
From the phenotype...

- Phenotyping & epidemiological analysis

- Genotyping: SNP technologies

- Genome Wide Association Study
Genome-wide Haplotype-based Association Study

38 Cases: 50K SNP chip
275 AI sires: Bovine HD SNP chip

BTA 25 – 1,256 SNPs

1.2 Mb
... to the causative mutation

- 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

14 cases

3.3 Mb

50 Kb

CC2D1B
ZFYVE9
K1122/1XNDC12
RAB3B
OSBP9
EPS15
TTC39A
RNF11
Clorf185
CDKN3C
FAE1
DRTA2
ELAVL4
AGBL4

G G

Wild-type

Mutant
Whole Genome Sequencing

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Inherited defects in BBCB

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

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

- SLC6A5
  - Na/Cl dependent glycine transporter
- Death within few hours
Crooked Tail Syndrom

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Crooked Tail Syndrome

- MRC2: Extracellular matrix remodelling
- 25\% carriers
- Selective sweep
- 2\textsuperscript{nd} loss-of-function
Dwarfism

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

![Graph showing the relationship between age and height or number of calves.](image)
Hamartomas & osteopetrosis

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

- PIG-H: GPI-anchor
- NGS: transcriptomic
- 5% carriers
Prolonged gestation

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

Years

Mortality rate

% 12

10

8

6

4

2

0

2002 2003 2004 2005 2006 2007 2008 2009 2010

BTV-8

ULg

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Management of carriers (AI sires)

Year of birth

% ≥ 5 4 3 2 1 0

ULg
Management of carriers
(BBCB population)

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CMD 1 (n = 20,979)

CMD 2 (n = 21,113)

CTS (n = 19,401)

Dwarfism (n = 16,468)

Hamartoma (n = 11,758)

Prolonged gestation (n = 6,378)
Heredo-surveillance in cattle...

- 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
THANK YOU...

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