

histiocytic sarcoma research:

Chromosome 11 region corresponds to human chromosome 9p21 region (cancer region)

This region contains 4 genes with a role in cancer (Cyclin dependent kinase inhibitors)

-> exploration of this region (E. Ostrander) :

- No mutation in the 4 genes but change in expression in dogs with risk haplotypes
(*Shearin, Hedan et al. Cancer Epidemiol Biomarkers Prev 2012*)
- Work in progress (C. Andre and E. Ostrander)

Summary of the histiocytic sarcoma research:

- cancer impacting BMD life span
- polyfactoriel cancer -> involving genetic and environmental factors
(heritablity of 0,298)
- many regions are involved in HS predisposition of which CFA₁₁
 - > Needs of research to better understand development of this cancer to prevent and treat it

BUT data produced by research could be useful for breeders to help selection!

Collaboration with Antagene to develop a pre-test for BMD breeders

Development of a genetic 'Pre-Test'

- Selection of HS predisposing regions



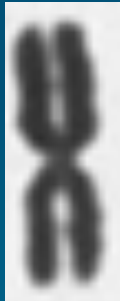
- Based of previous GWAS, we selected 140 markers across the genome
- 140 markers tested on 1081 BMDs from France :
256 affected BMDs/ 165 healthy dogs (>10 years old)
 - > selection of 9 markers from 5 chromosomes strongly involved in HS development
 - > These markers can discriminate affected and healthy dogs

Predisposing regions : impact on life-span

- Confirmation of Chromosome CFA11 region : on life span of 1081 french BMDs

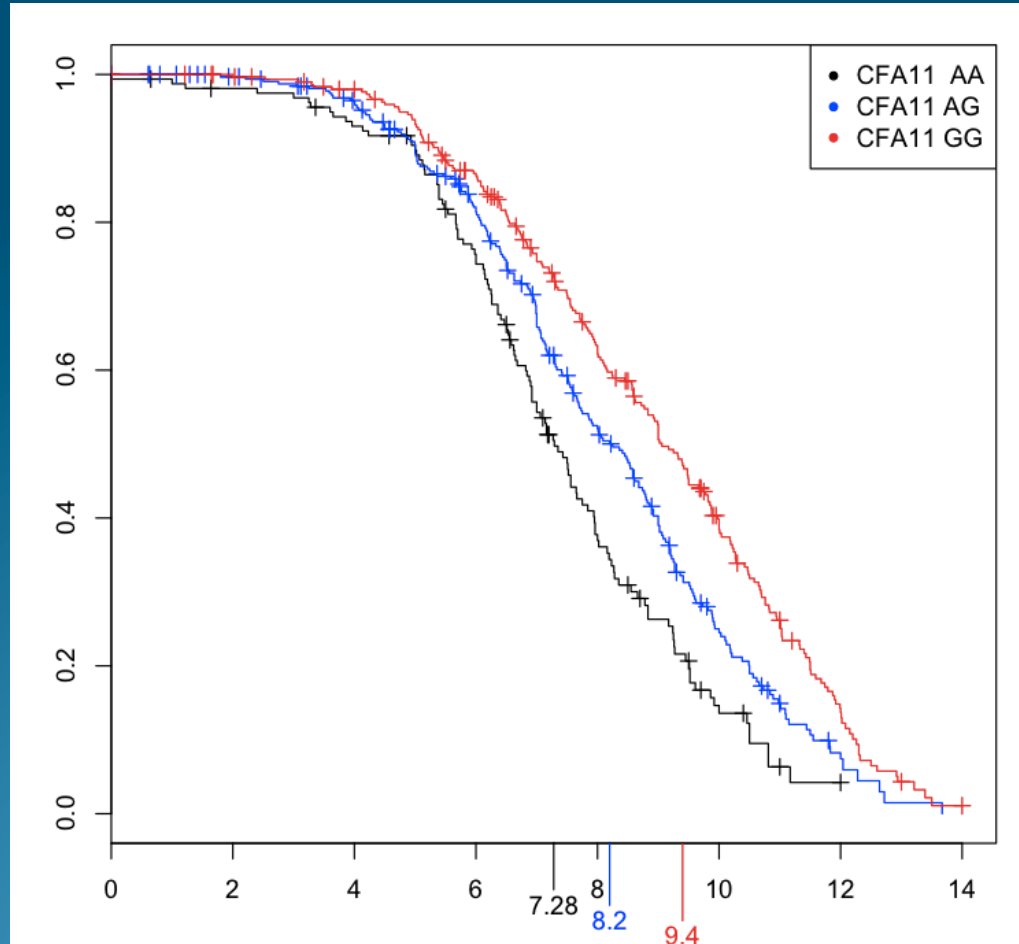


Risk chromosome



B
B
B

Percentage of dog living



Age



Protective chromosome



A
A
A

Predisposing regions : impact on life-span

- Correlation of chromosome 7FA11 region : on life span of 1081 french BMDs

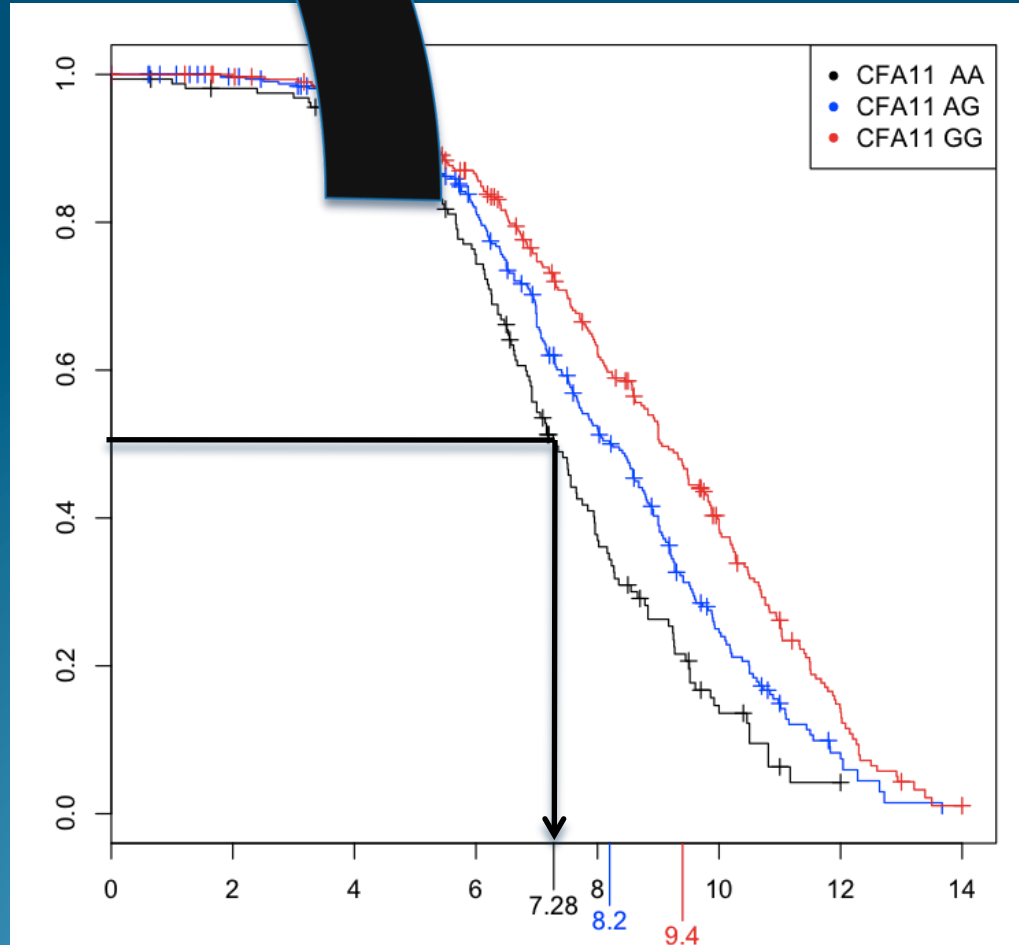


Risk chromosome



B
B
B

Percentage of dog living



Protective chromosome



A
A
A

Age

Predisposing region impact on lifespan

- Confirmation of chromosome CFA11 : on life span of 1081 Bernese Mountain Dogs

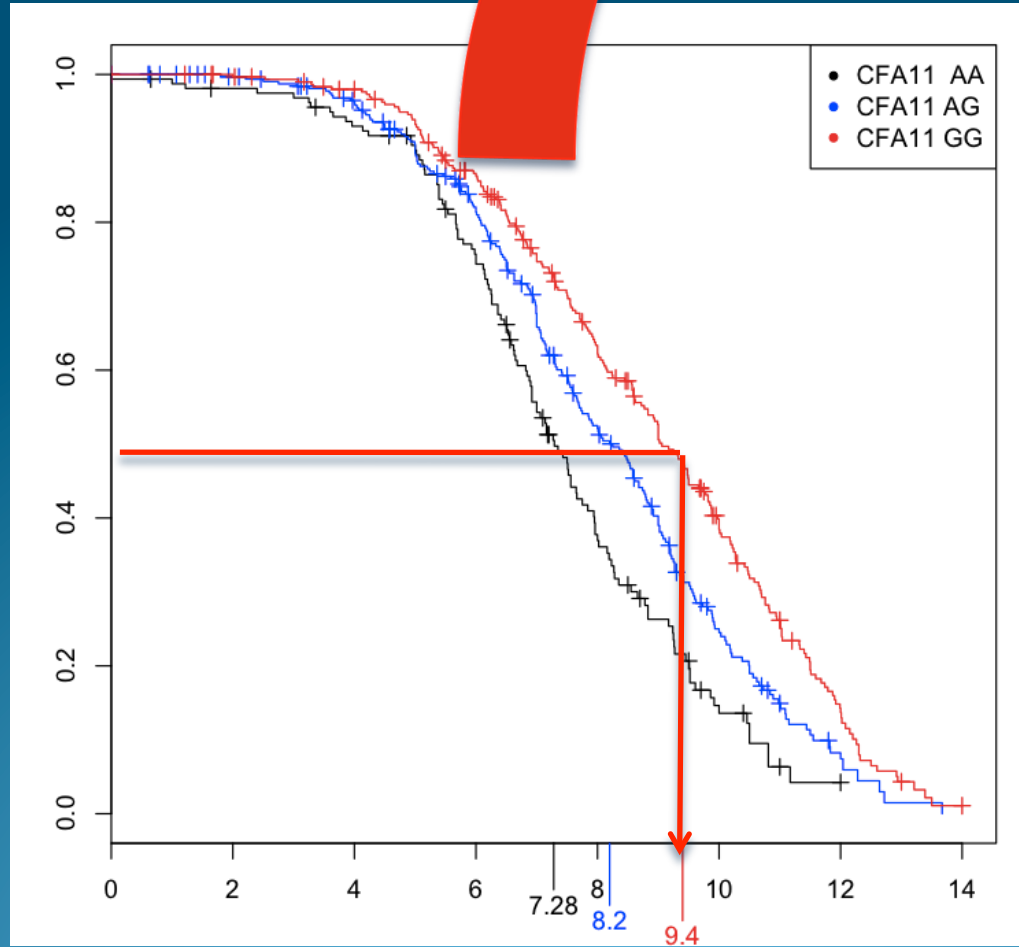


Risk chromosome

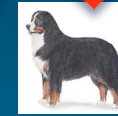


B
B
B

Percentage of dog living



Age



Protective chromosome



A
A
A

→ This chromosome influence life span of Bernese Mountain Dogs

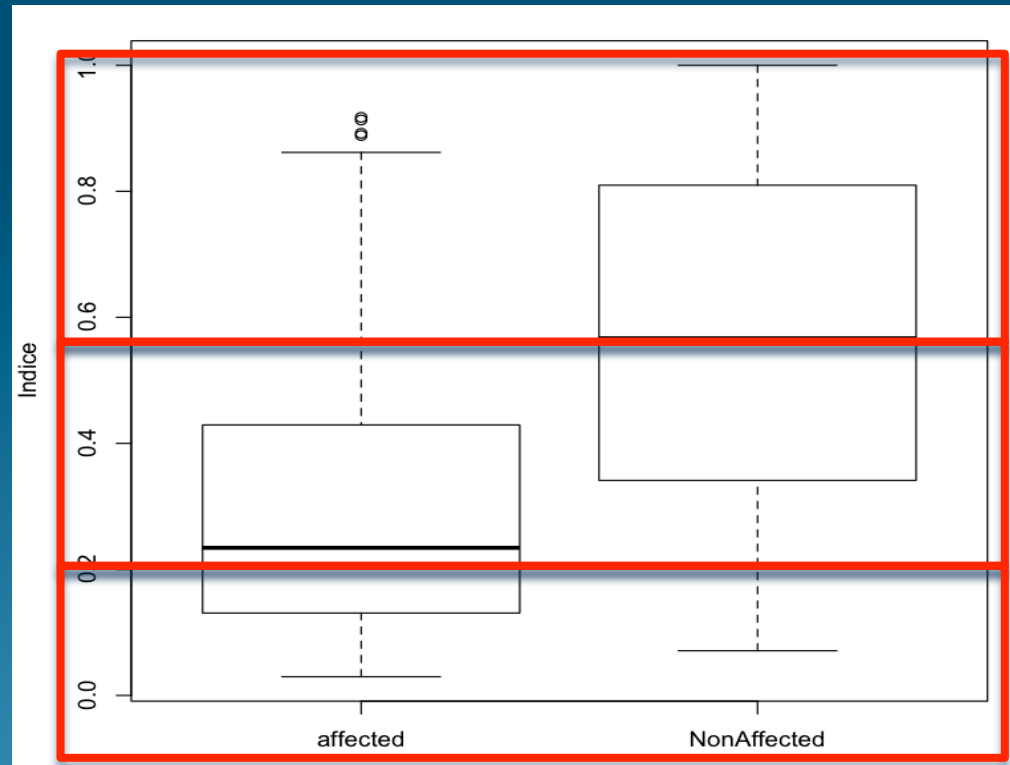
Estimation of the risk to develop HS : index values

With 9 markers -> development of an index link to probability of being a healthy dog

Index A :

Index B :

Index C :



47% of healthy
10 % of affected

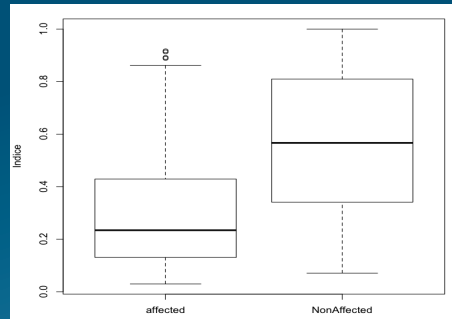
43% of healthy
50 % of affected

10% of healthy
40 % of affected

This index reflect a risk to develop and transmit histiocytic sarcoma

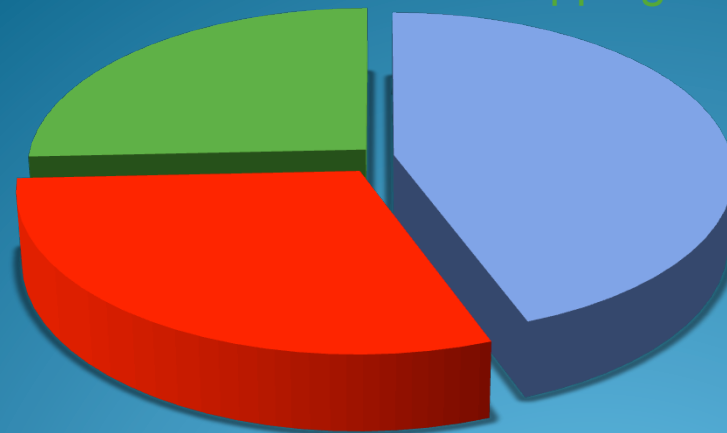
Estimation of the risk to develop HS : index values

With 9 markers -> development of an index link to probability of being a healthy dog



Repartition of the index values on the 1081 french BMDs :

4 times the chance of NOT developping HS

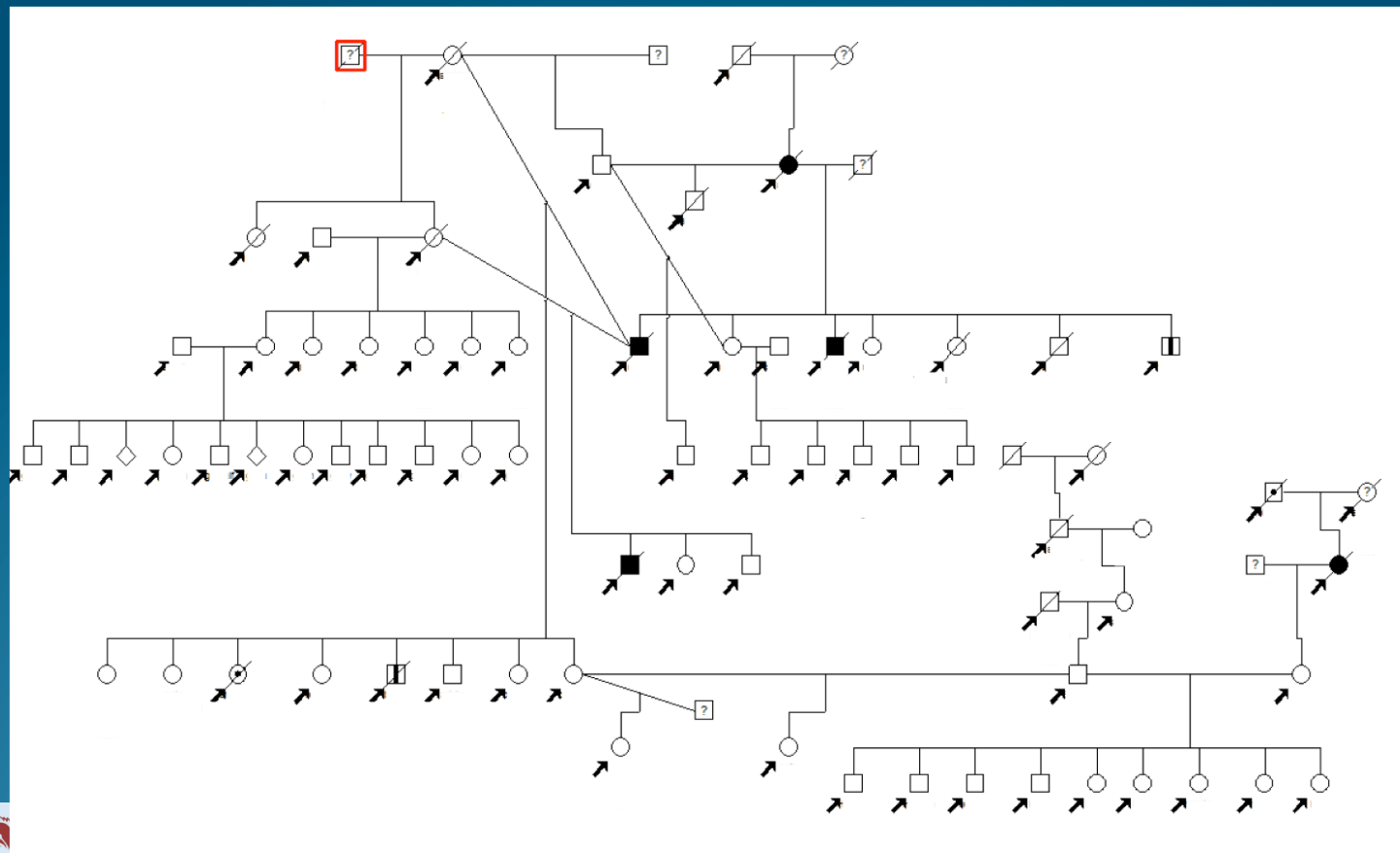


- index A (25,7%)
- index B (44,3%)
- index C (30,7%)

30% of dogs ⇔ have 4 times the risk of developping HS

Validation of the pre-test on the French population

In collaboration with the French BMD club (AFBS), we determined the index on two large families of 50 dogs each from over 4 generations : example of one family

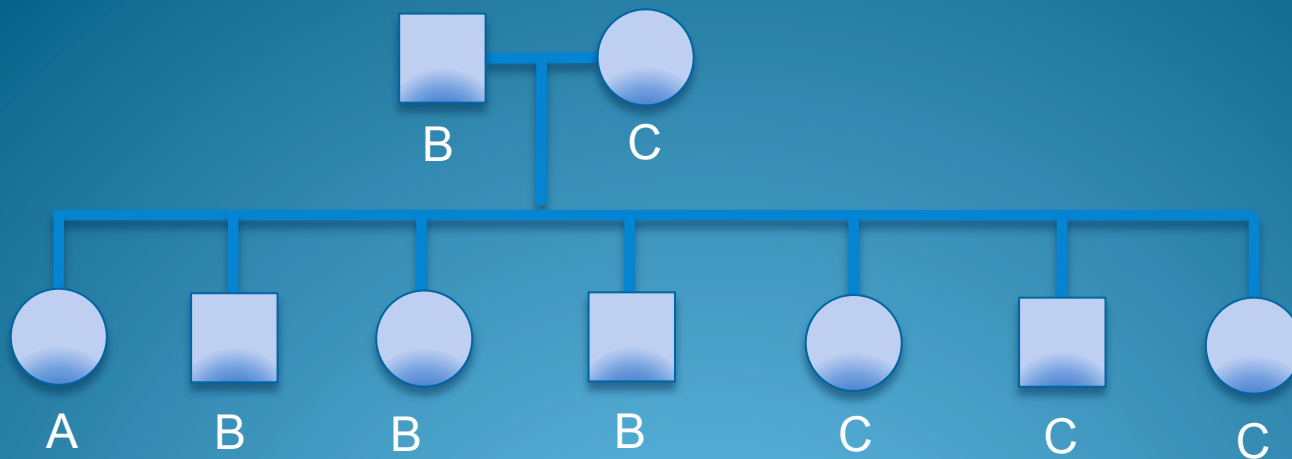


Validation of the pre-test on the French population

In collaboration with the French BMD club (AFBS), we determined the index on two large families of 50 dogs each from over 4 generations : example of one family

We observed :

- high variability of the index
- the index of a litter is concordant with the index of the parents



Avalability of the Pre-test

A TOOL FOR SELECTION

- ONLY available for Breeders
- ONLY validated on French Dogs
- NOT a diagnostic tool

It is a RISK test

- Not all dogs at risk (index C) will develop the cancer
- Not all dogs with a good index (index A) will be healthy BUT a majority will.

‘Pre -test’ : a test in development with expected advances from Research

Advice for breeders on how to use the pre test:

- This index should be just one of many selection criteria
- Breeders have to keep genetic diversity :

If a dog with C Index has a number of other positive qualities

- Mate it with Index A or B dogs
- Avoid C x C matings
- Select of future breeding dogs in the litter

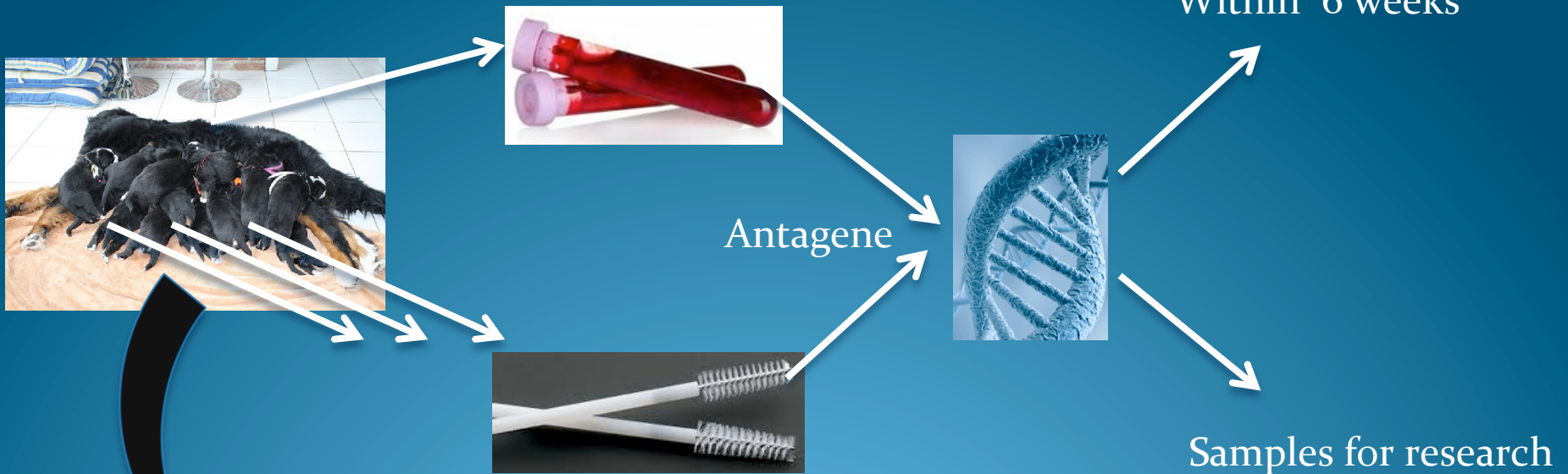
Avalability of the Pre-test

PROTOCOL AND CONDITIONS

- Breeders have to
- sign a memorandum of agreement
 - send a sample of the dog to be tested
 - send samples of dog family for research
 - provide an online follow up of the dogs

ANTAGENE

Index send to breeder
Within 6 weeks



One line follow up of sampled dogs
(every year/suspicion of cancer)

30/08/13 – 9th International Health Symposium
C ANDRE and B HEDAN

Next step

To use this pre-test on other BMD populations :

1. It is important to validate the pre test on different BMD populations: for that each Club can collect and send blood samples on EDTA to Antagene

from 30 affected dogs

30 old unaffected dogs

-> part of the research work : no charge

2. European breeders can order a pre-test for their dogs but they need to be aware that the pre-test is only validated on the French BMD population .

Aknowledgments

For the research part :

- Catherine Andre's lab and collaborators, UMR6290 (Rennes FRANCE)

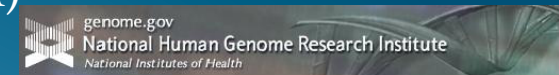
- Catherine Andre
- Jerome Abadie, professor of veterinary pathology
- Patrick Devauchelle, cancerology veterinarian
- Edouard Cadieu



- Matthew Breen's lab and collaborators (NCSU, Raleigh, USA)



- Elaine Ostrander's Lab and collaborators (NIH, Bethesda, USA)



- Funded by AKC, Italian SIBB, German DCBS, French AFBS and CNRS

- BMD Clubs, breeders and owners (AFBS, bernese garde, SCIABS-SIBB, belgium and swiss club...) and IWG

For the pre-test development : collaborations between CNRS and ANTAGENE
Anne THOMAS and Caroline DUFAURE DE CITRES



www.antagene.com/en/commander/pre-test-histiocytic-sarcoma