



Fine QTL mapping of pig QTL in France

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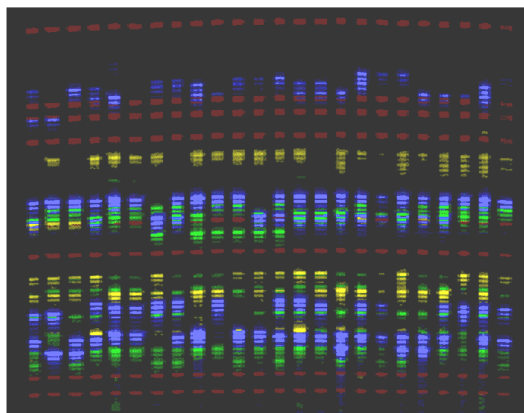
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Fine mapping of pig QTL in France

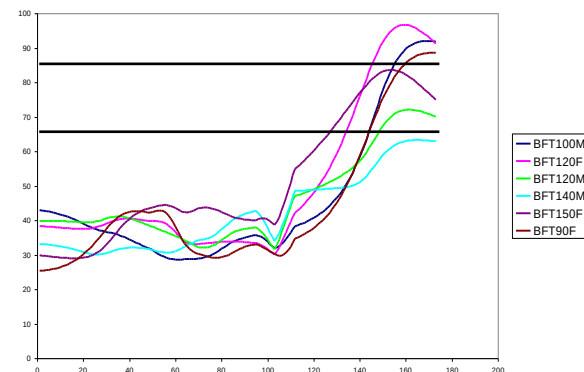


J.P. Bidanel
D. Milan



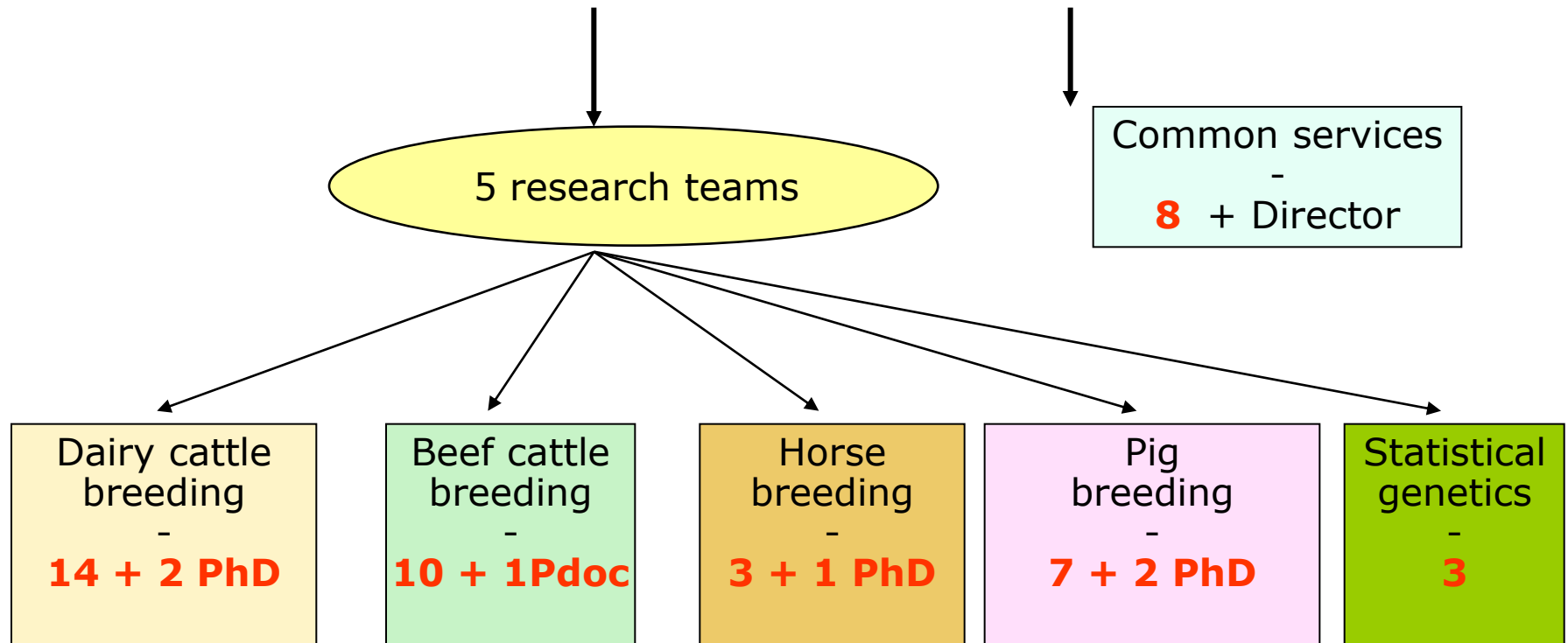
Animal Technology
Institute Taiwan

December 2, 2004



SGQA - Organisation

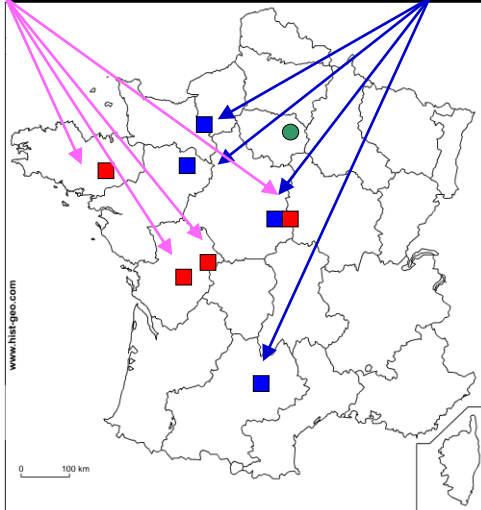
Staff : 51 (36 INRA permanent positions)



SGQA Research facilities & collaborations

Station de Génétique quantitative et appliquée

8 experimental units



■ UE bovine ■ UE porcine ● SGQA

Staff : 76
Support : 245 k€ + salaries
250 DC, 520 BC
360 S, 2400 pig pl.

1 service unit: (computing center)

Management
of national
genetic
databases

Work-
stations,
mainframe

Genotyping laboratory Labogéna

DNA
banks

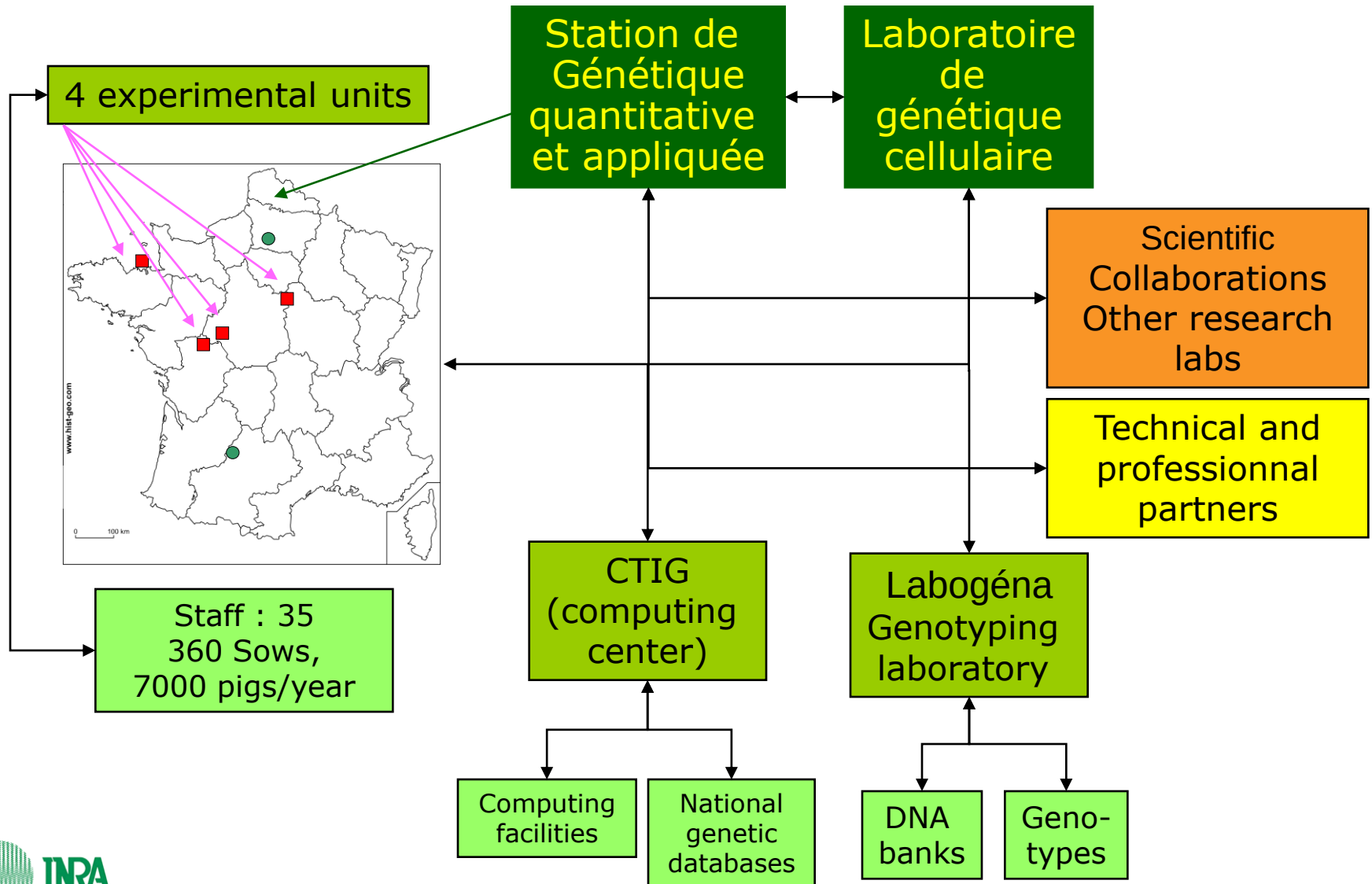
Geno-
types

Scientific
Collaborations
SAGA
LGC
LGBC
...

Technical and
professional
partners

Pig QTL mapping at INRA

Research facilities & collaborations



□ Main collaborators

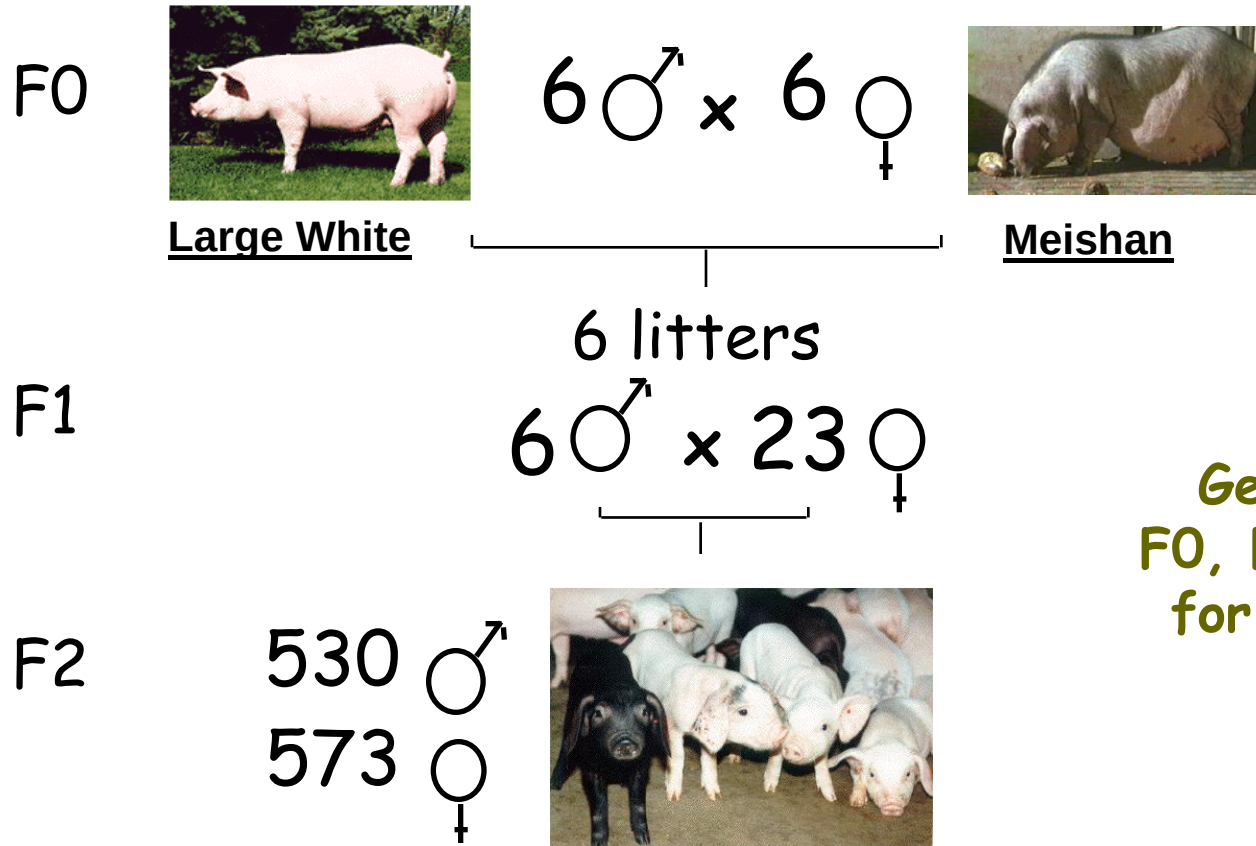
J.P. Bidanel , D. Milan, C. Chevalet, N. Woloszyn, F. Bourgeois, J.C. Caritez, J. Gruand, P. Le Roy, M. Bonneau, L. Lefaucheur, J. Mouroto, A. Prunier, C. Désautés, P. Mormède, C. Renard, M. Vaiman, A. Robic, J. Gellin, L. Ollivier

□ INRA research units

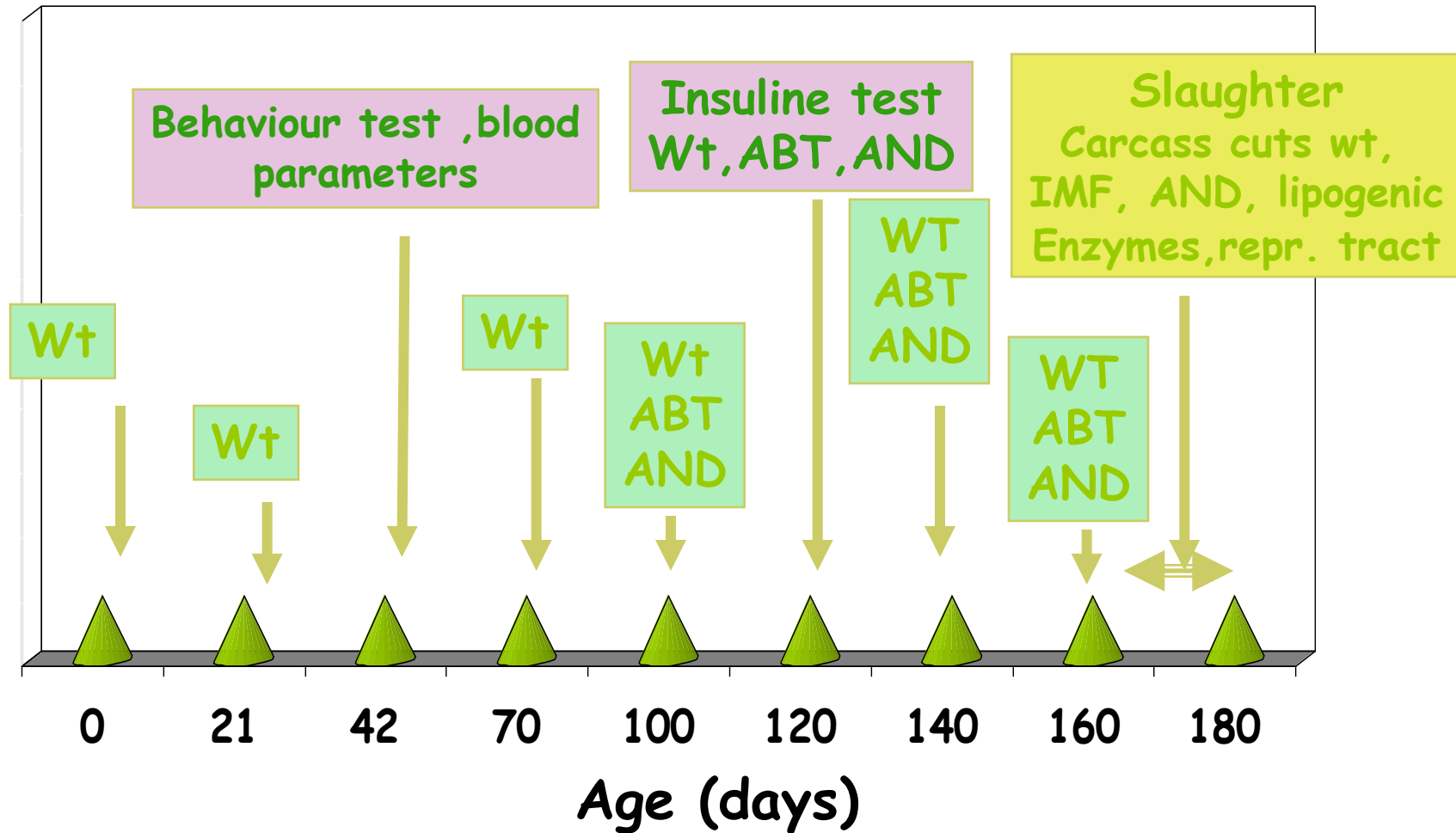
Station de Génétique Quantitative et Appliquée, Laboratoire de Génétique Cellulaire, Domaines expérimentaux du Magneraud et de Rouillé, Labogéna, Unité Mixte de Recherche sur le Veau et le Porc, Laboratoire de Radiobiologie et d 'étude du génome, Laboratoire de Génétique du Stress

□ Funded by :

European Union(Bridge, Biotech+)
INRA incitative action "Structure of genomes"
Animal Genetics Department
Ministry of Research (GREG)



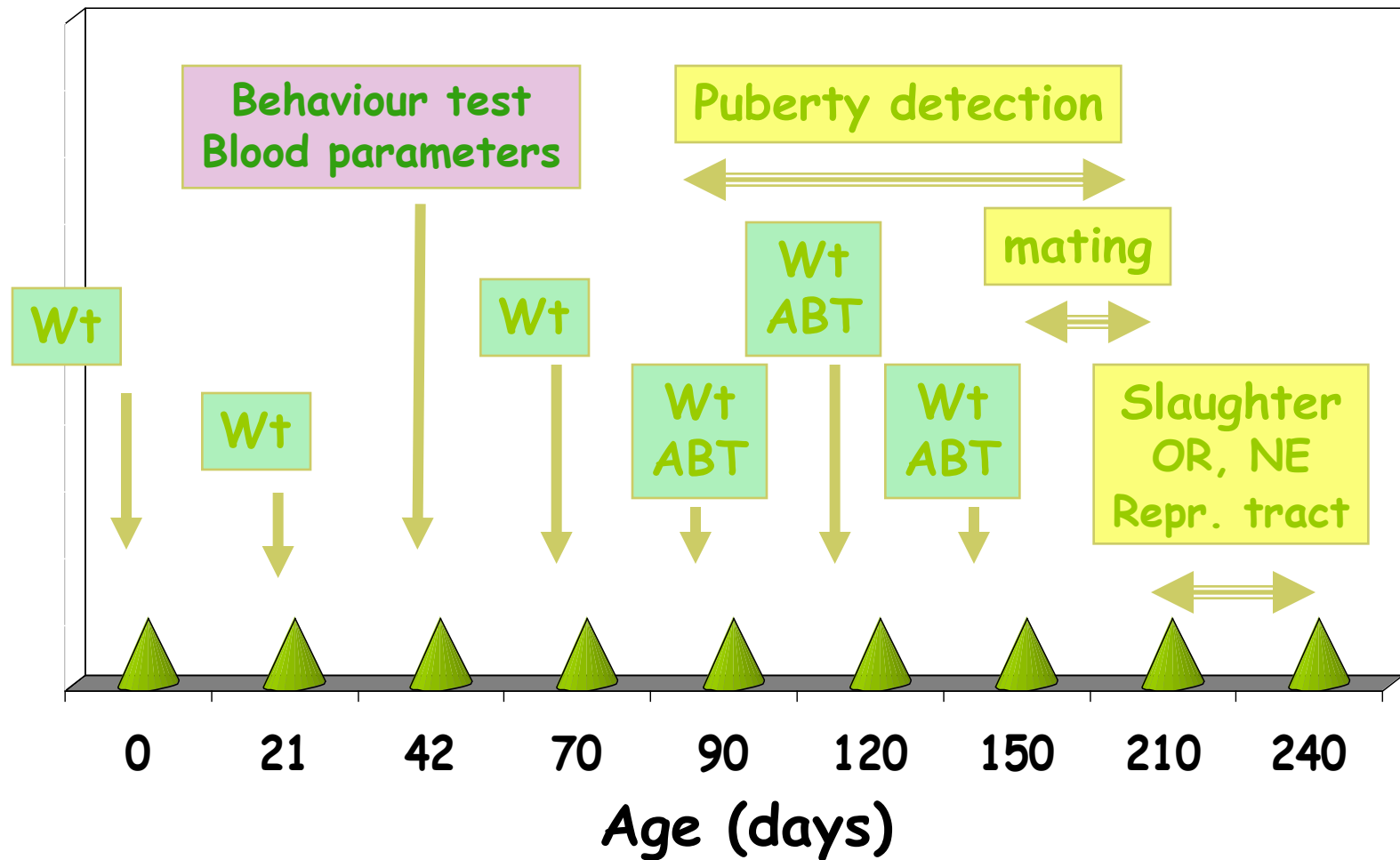
**Genotyping of
F0, F1, F2 animals
for 137 markers**



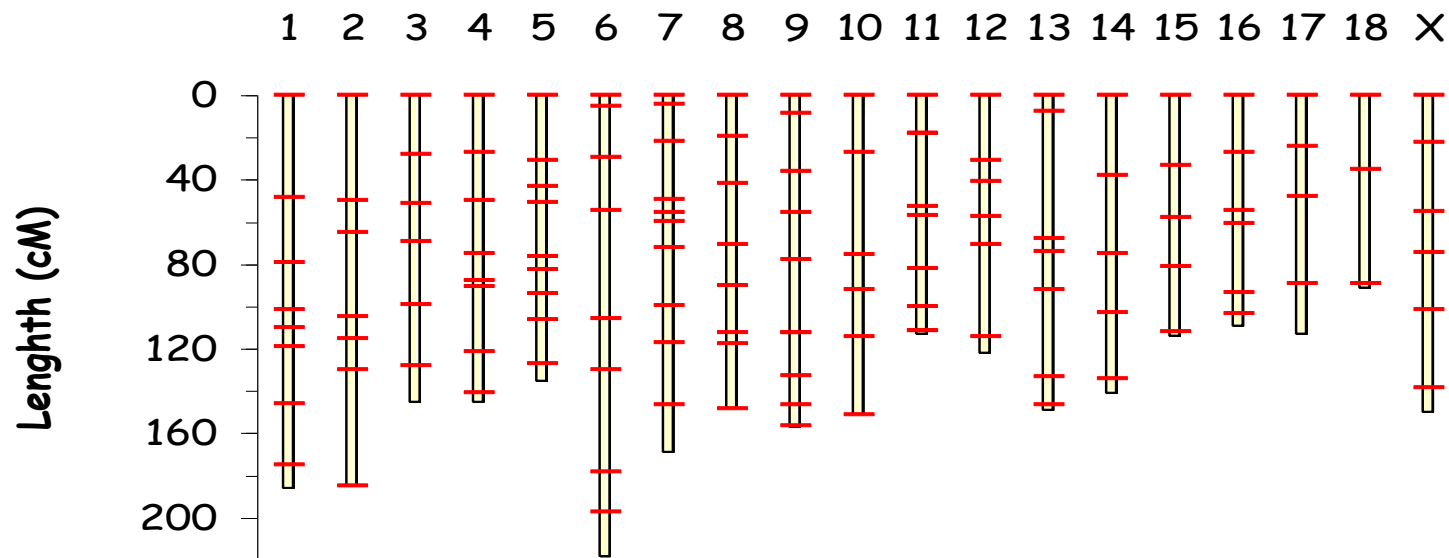
Traits measured - females



PORQTL



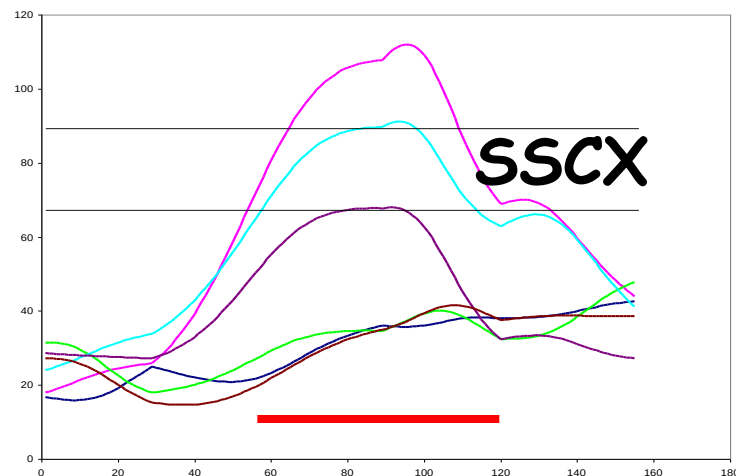
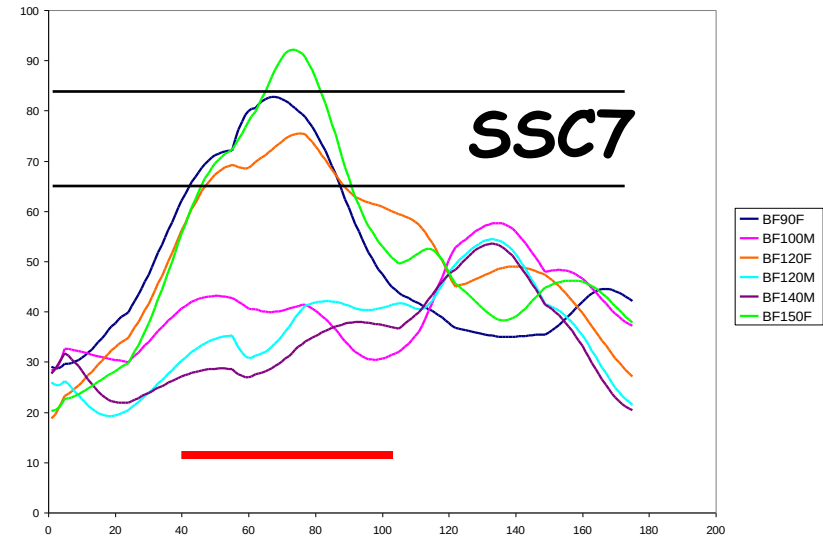
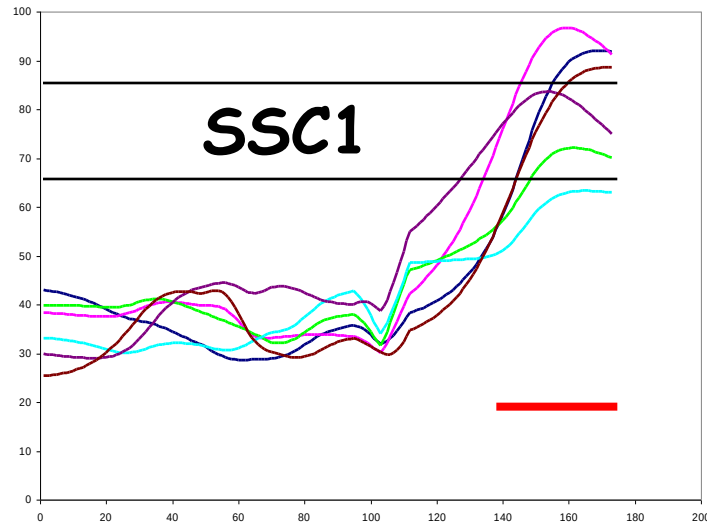
- Panel of 136 microsatellite markers + SLA
- Genotyping on automated sequencers
- Map built using Crimap software



- 3 to 12 markers / chromosome
- Average marker interval : 22 cM

Results : example - backfat thickness

PORQTL



Low accuracy of QTL position

QTL fine mapping

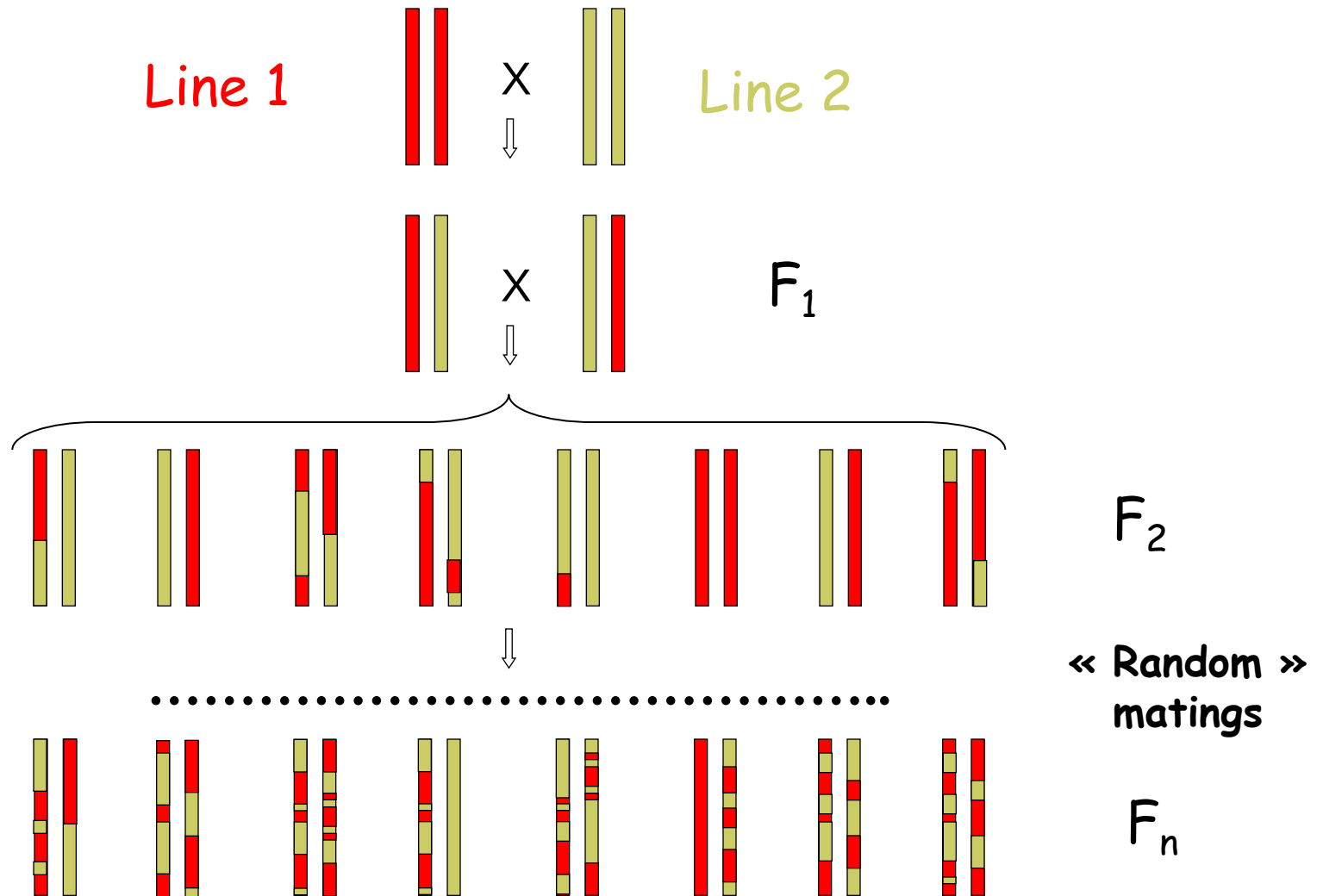
Many experimental designs available in plants and mice ...

- Recombinant inbred lines
- Recombinant inbred segregation test
- Selective phenotyping
- Interval specific congenic strains
- ...

... but only some of them can be used for farm animals

- Advanced intercross lines
- Recombinant progeny testing

Advanced Intercrossed Lines (AIL)



Advanced Intercrossed Lines (AIL)

- Characteristics

- 1 individual = « Mosaïc » of genome fragments from founder populations

- Interests

- Increase in genome « length »

$$c_t = \frac{1 - (1 - c_1)^{t-2} (1 - 2c_1)}{2}$$

Generation $\nearrow$ c_t $\nwarrow$ Recombinaison rate

- Can be used for non inbred populations

Advanced Intercrossed Lines (AIL)

Synthetic breeds can be used as AIL

Readily available material in many livestock species:

Cattle

Zebu x cattle: Brangus, St Gertrudis, ...

INRA 95

Sheep

INRA401 = Romanov x Berrichon du Cher

Pigs, rabbits

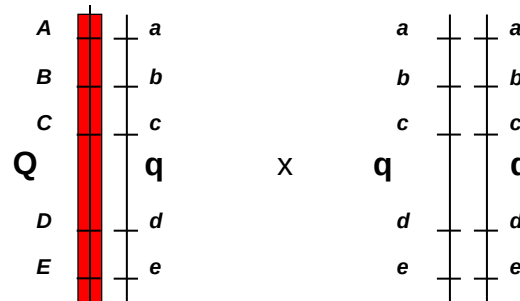
Laconie = Pietrain x LW x Hampshire

Tiameslan = Meishan x Laconie

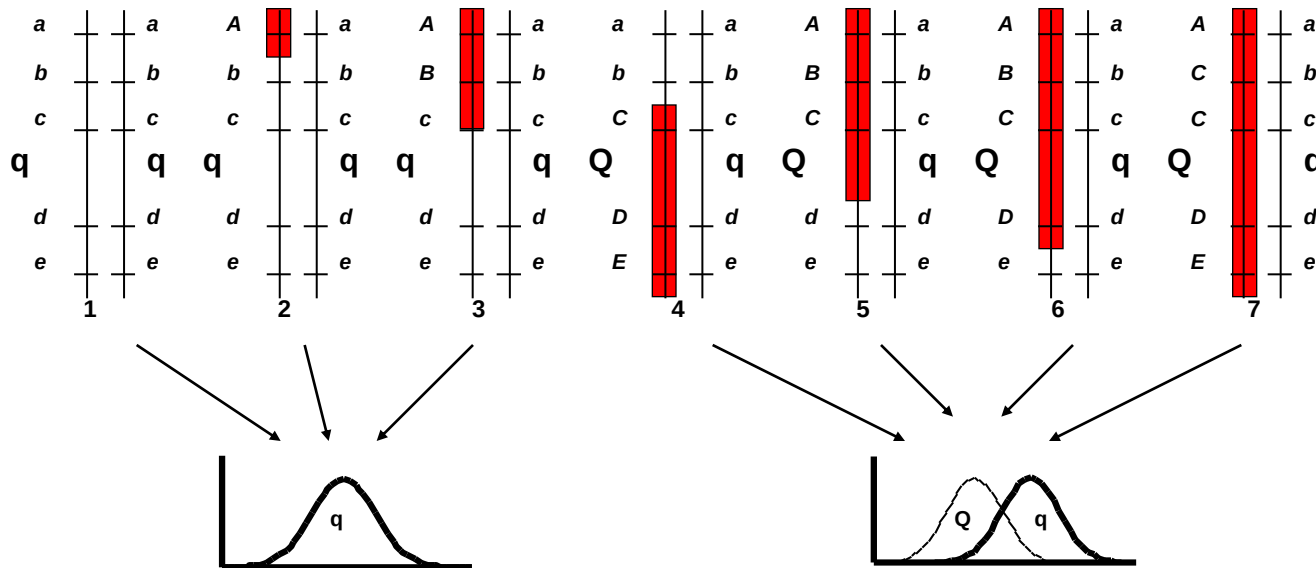
Taizumu = Meishan x Large White

Creole livestock

Recombinant progeny testing (RPT)



- Selection of recombinant individuals
- Progeny test



Recombinant progeny testing (RPT)

- Interests

- **Sequential design:**

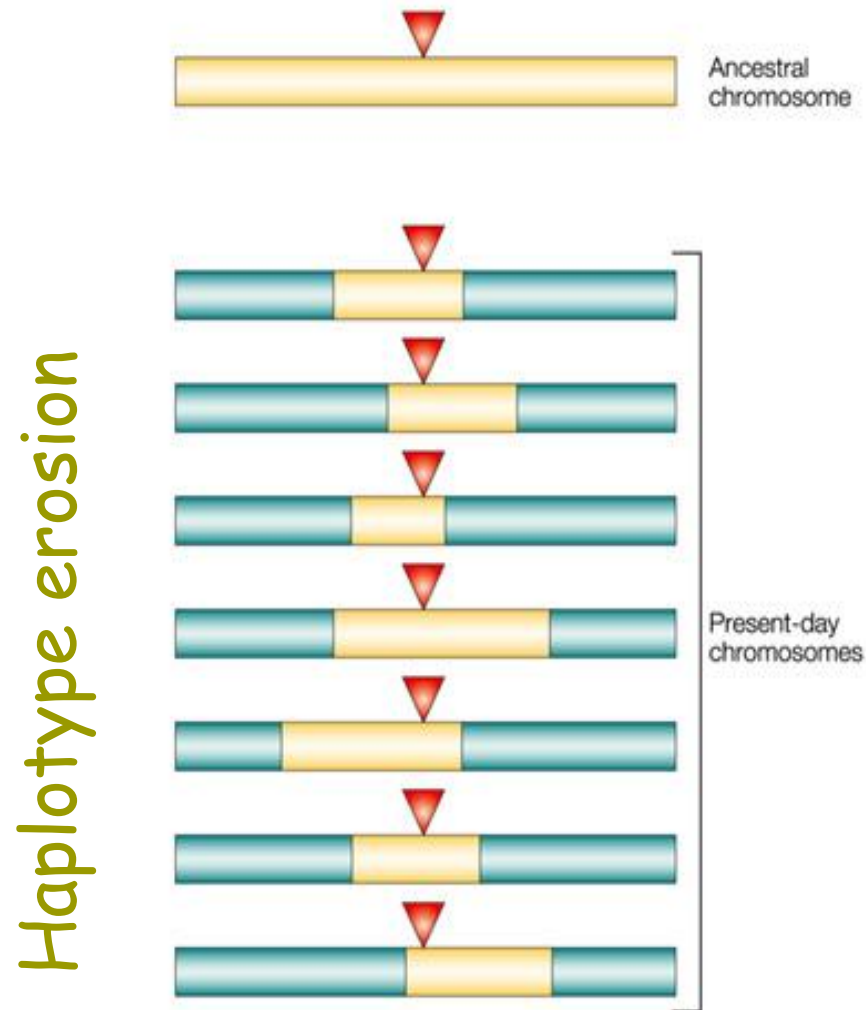
- allows the QTL mapping interval to be progressively reduced

- **Can be used in noninbred populations**

- Disadvantage

- Important number of individuals to be phenotyped and genotyped

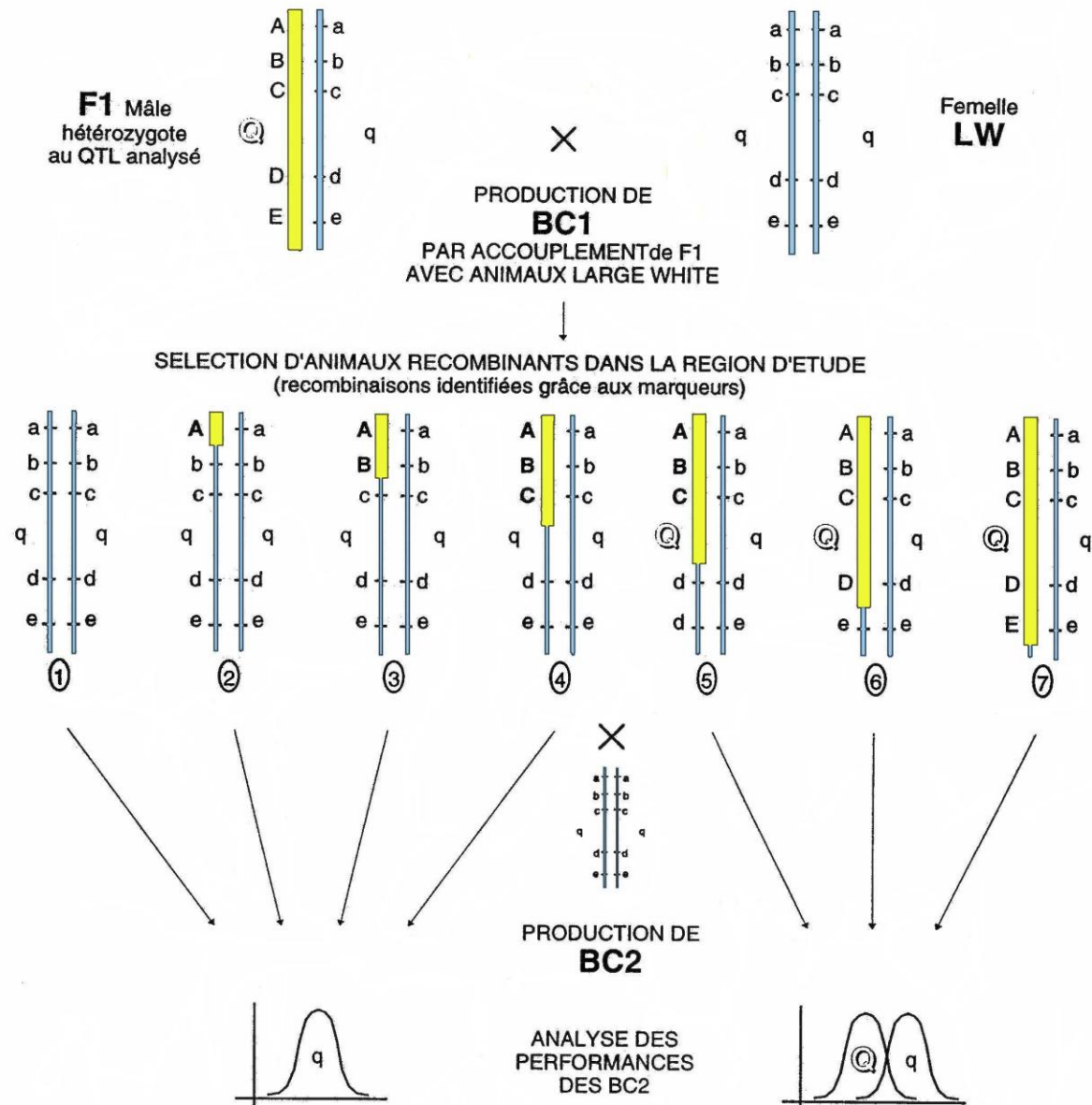
Use of linkage disequilibrium / « historical » recombinations



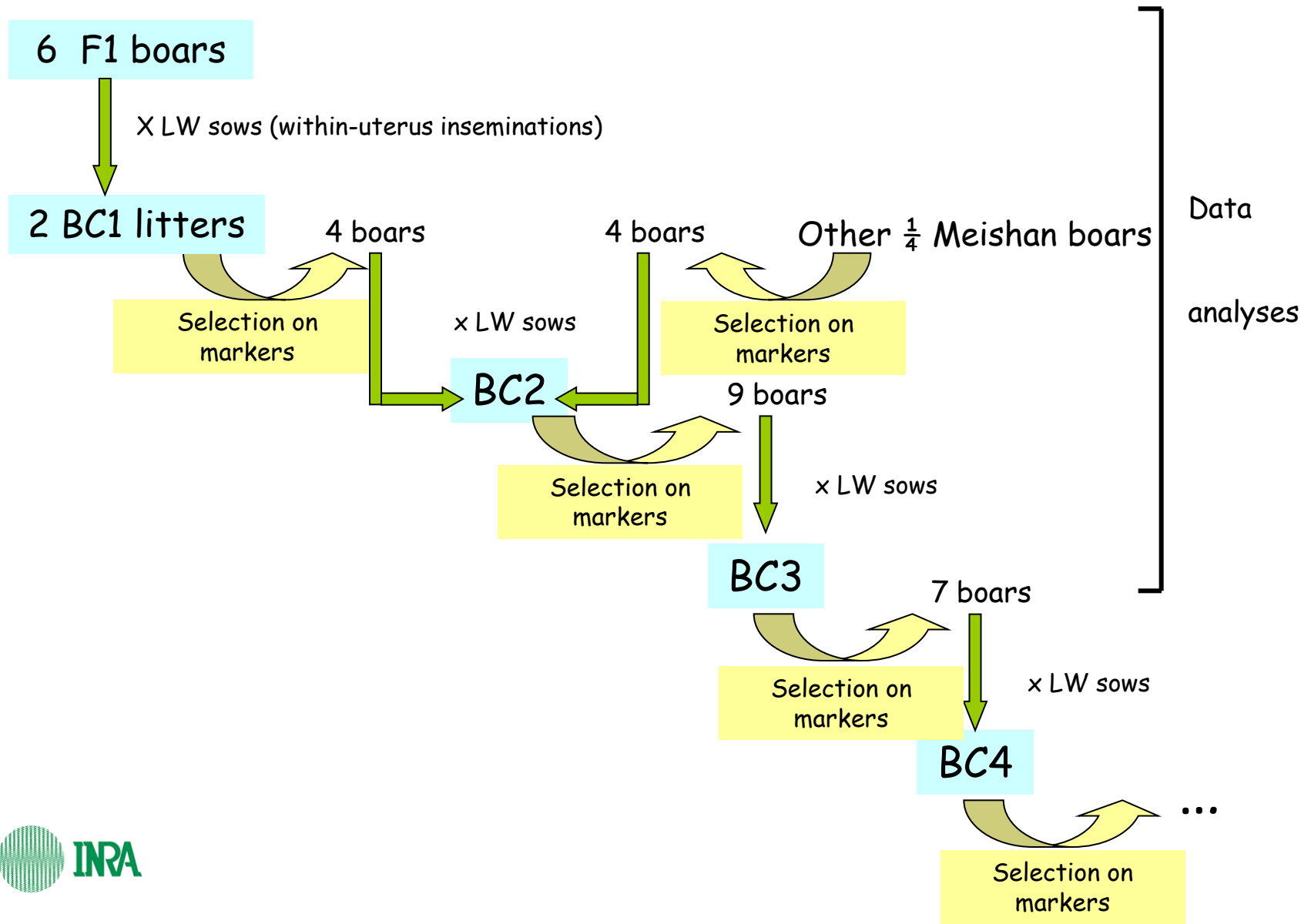
Nature Reviews | Genetics

Ardlie et al. 2002

Fine mapping of QTL using backcrosses



Fine mapping through successive generations of backcrosses



Traits measured

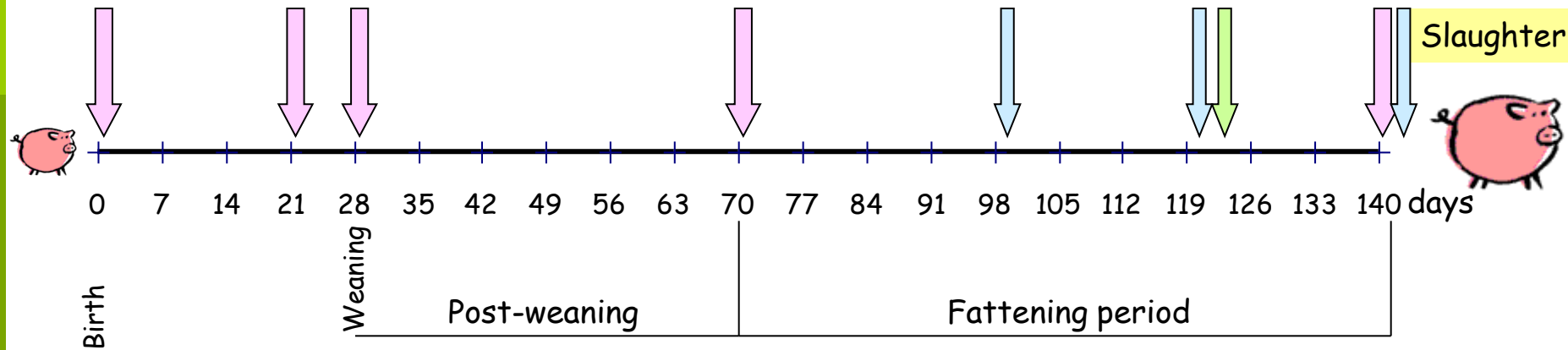
Weights

US backfat thickness

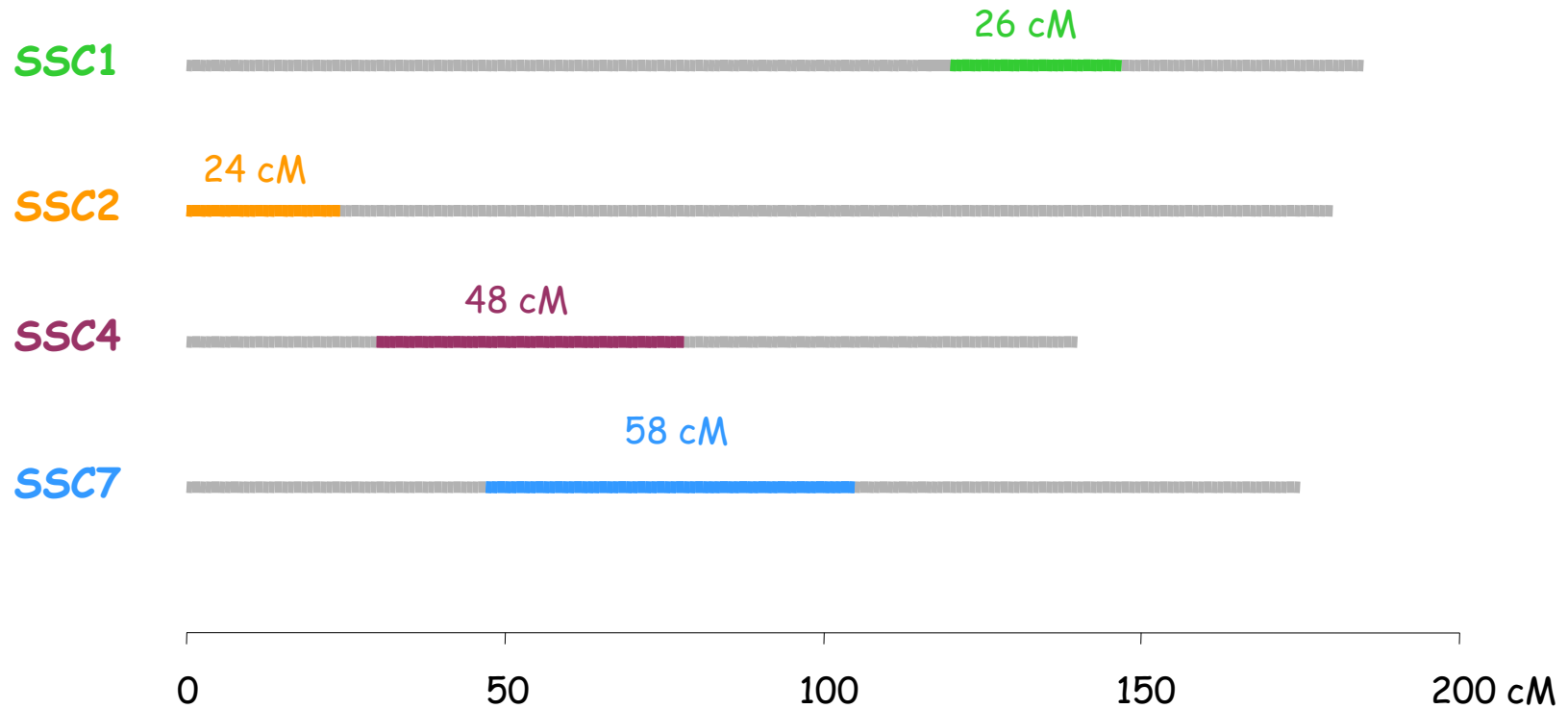
Biopsies of fat (androstenone) and muscle (IMF)

At slaughter:

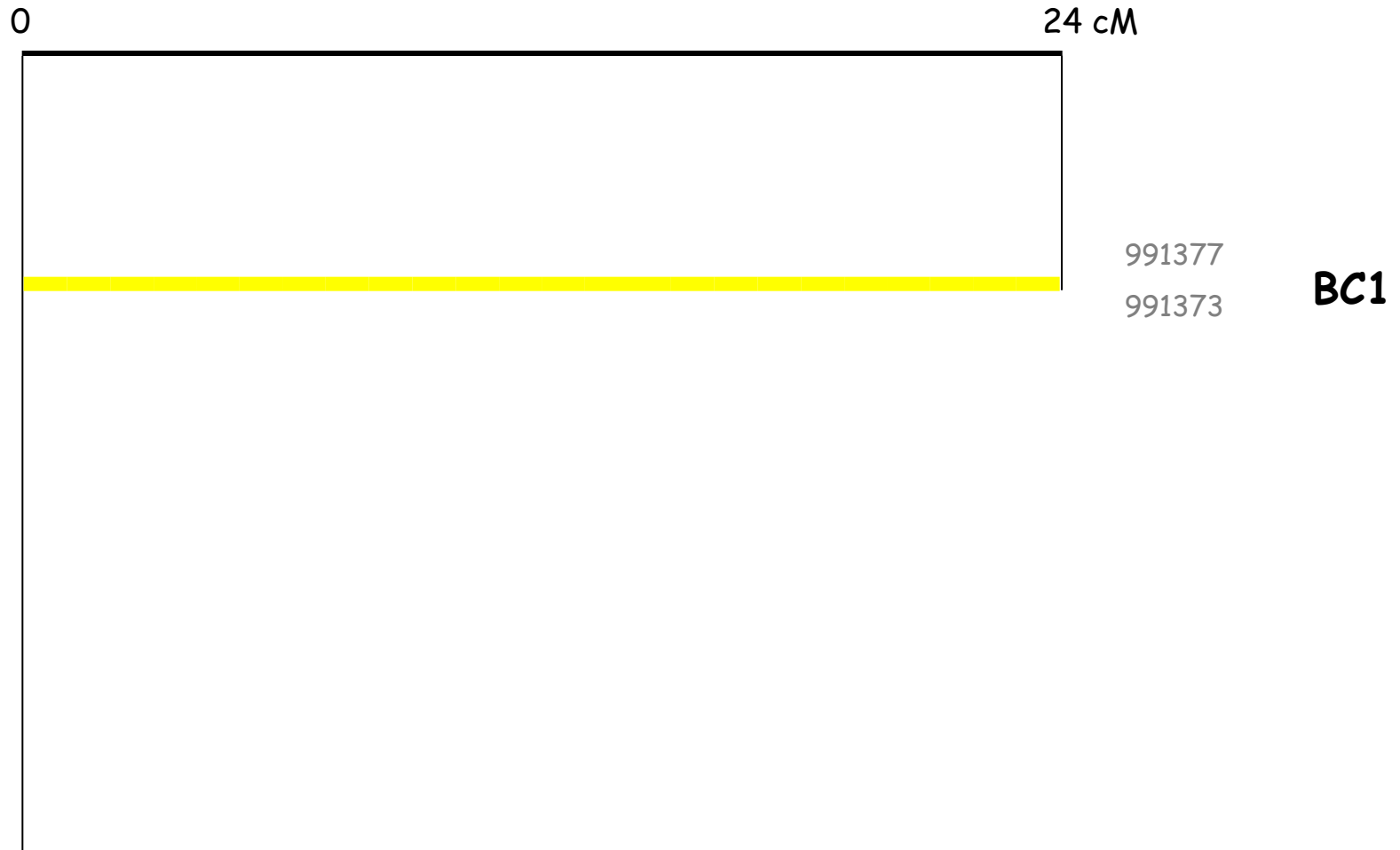
- Carcass cuts weights
- Carcass fat and lean depths
- pH 24h of Adductor femoris, Gluteus superficialis, Longissimus dorsi, semi membranous, semi spinalis
- Wetting time of Gluteus superficialis
- Reflectance (L^* a^* b^*) of Gluteus superficialis



Chromosomal regions investigated



Example : SSC2

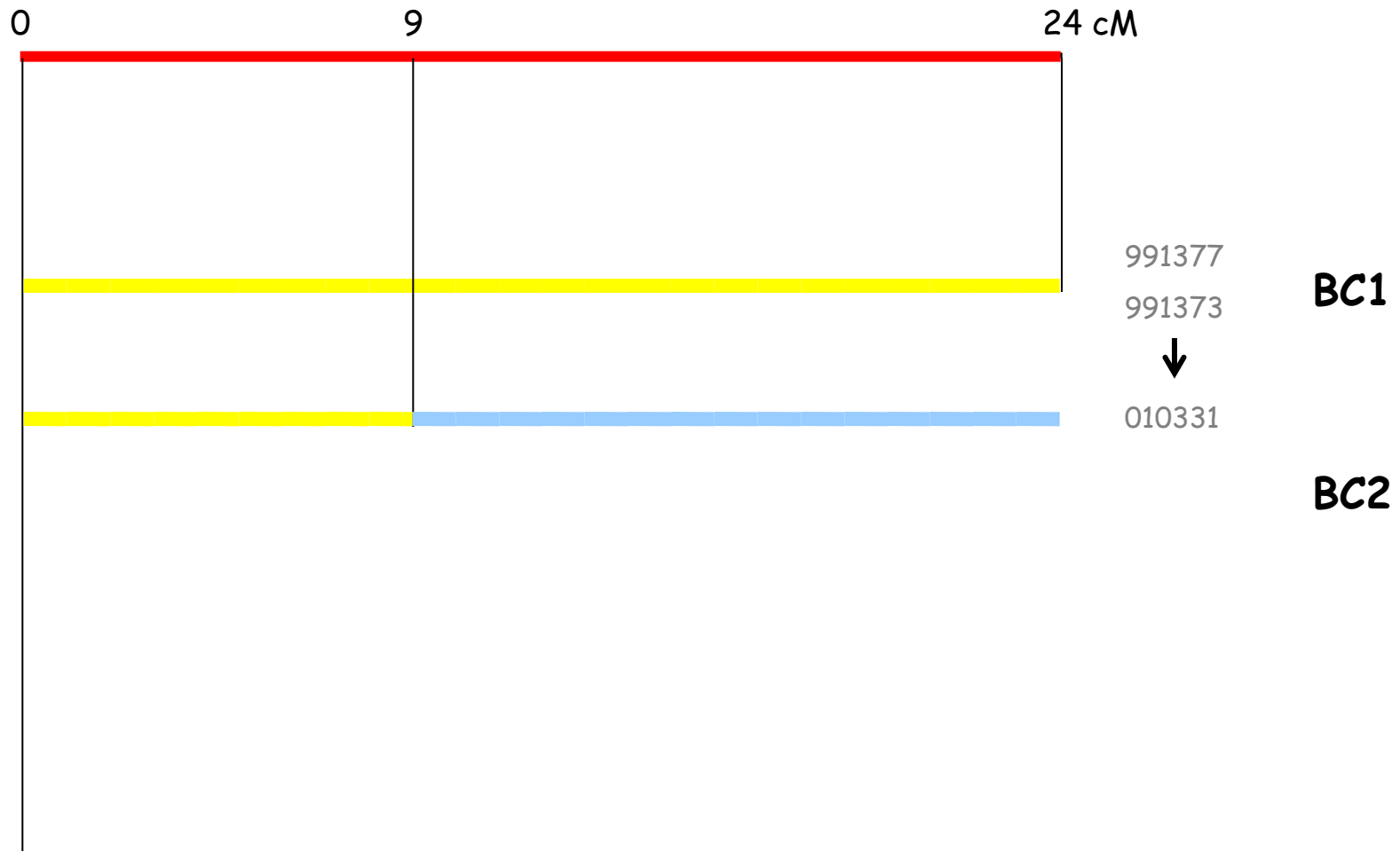


SSC2: progeny testing of BC1 boars

Generation	Boar	Growth	Carcass composition	Meat quality
BC1	991373	**	***	*
	991377	*	***	*

NS: non significant - * $P < 0.05$ - ** $P < 0.01$ - *** $P < 0.001$
(at the chromosome level)

Example : SSC2

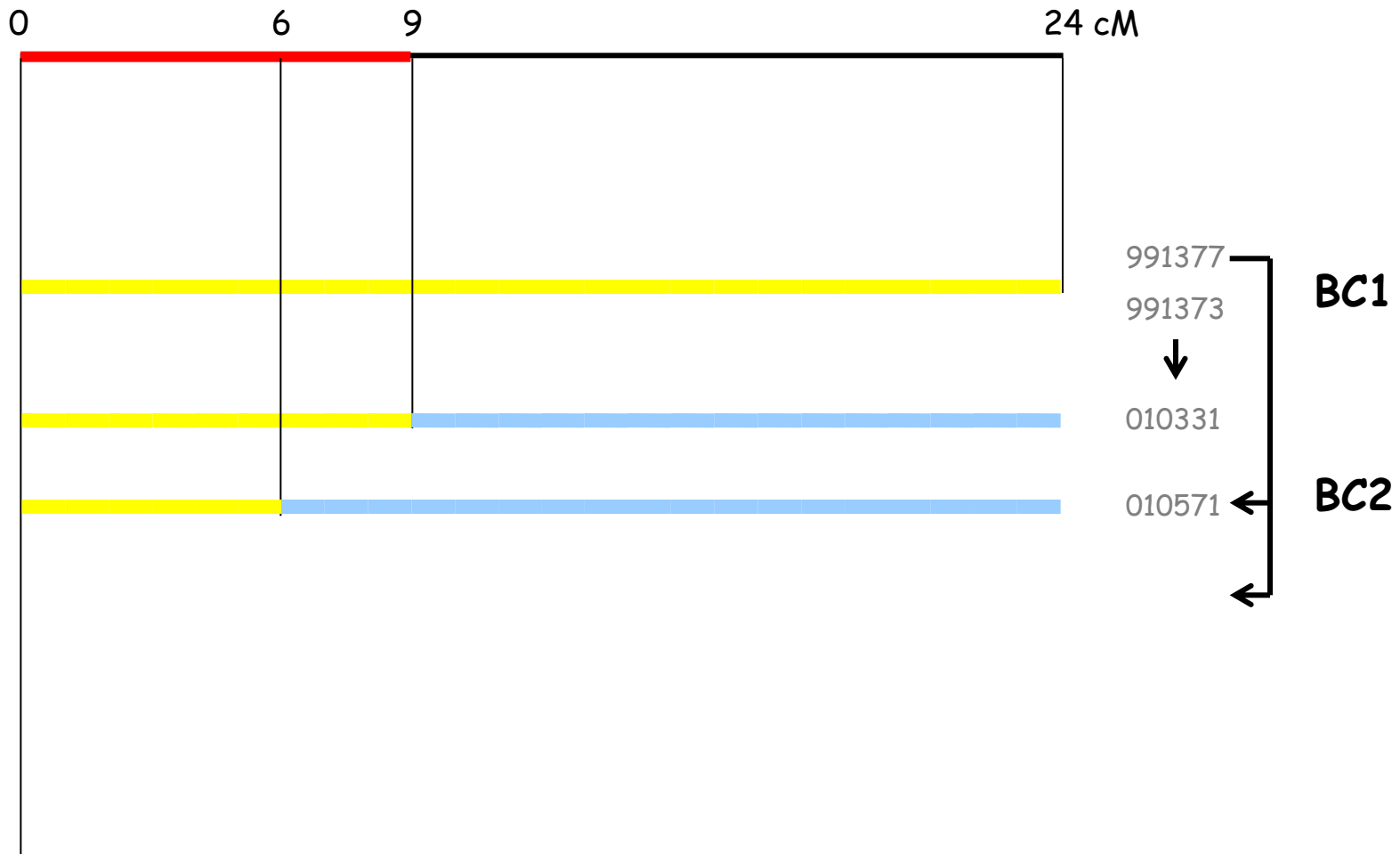


SSC2: progeny testing of BC2 boars

Generation	Boar	Growth	Carcass composition	Meat quality
BC1	991373	**	***	*
	991377	*	***	*
BC2	010331	**	***	NS

NS: non significant - * $P < 0.05$ - ** $P < 0.01$ - *** $P < 0.001$
(at the chromosome level)

Exemple : SSC2

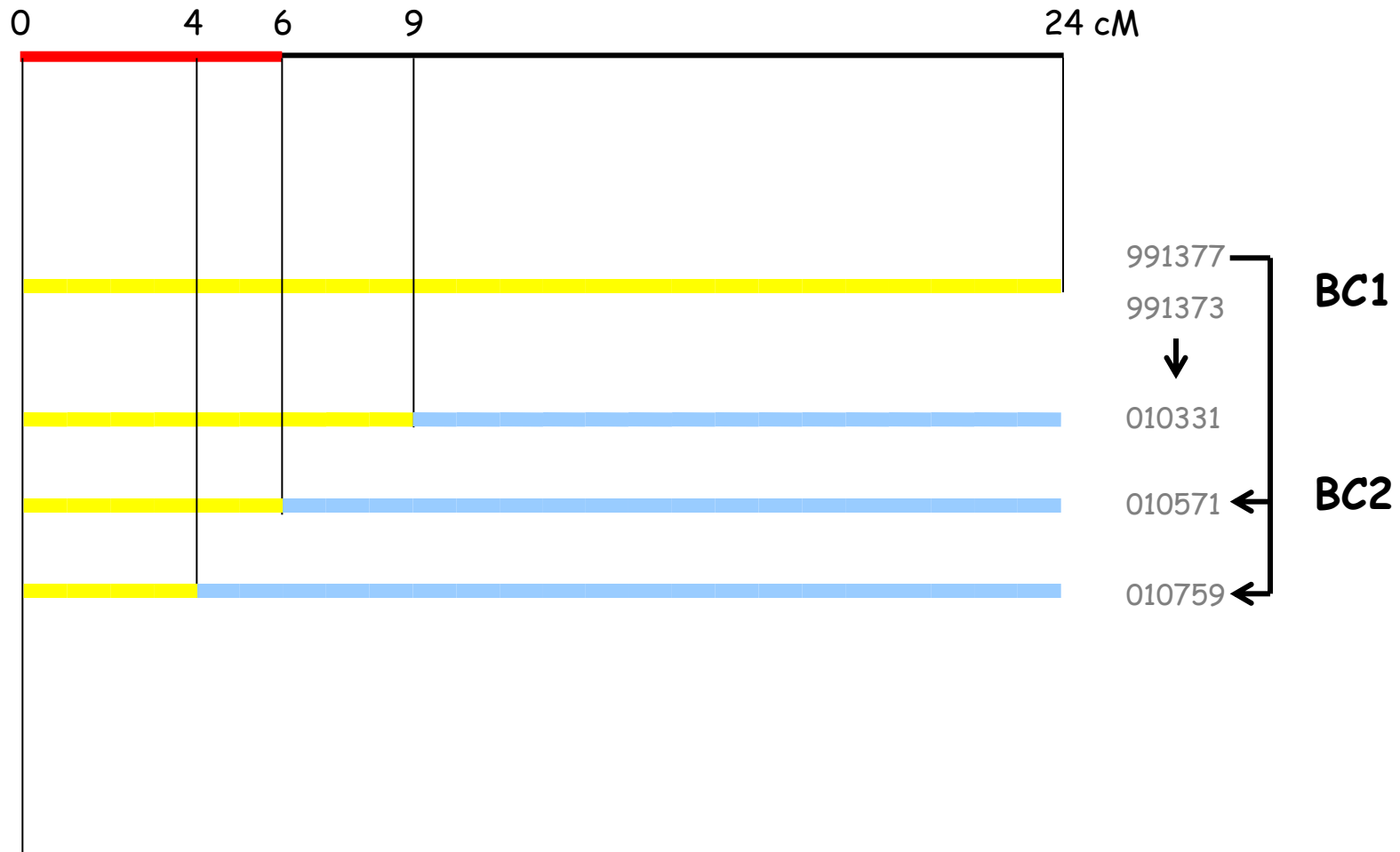


SSC2: progeny testing of BC2 boars

Generation	Boar	Growth	Carcass composition	Meat quality
BC1	991373	**	***	*
	991377	*	***	*
BC2	010331	**	***	NS
	010571	***	***	*

NS: non significant - * $P < 0.05$ - ** $P < 0.01$ - *** $P < 0.001$
(at the chromosome level)

Exemple : SSC2



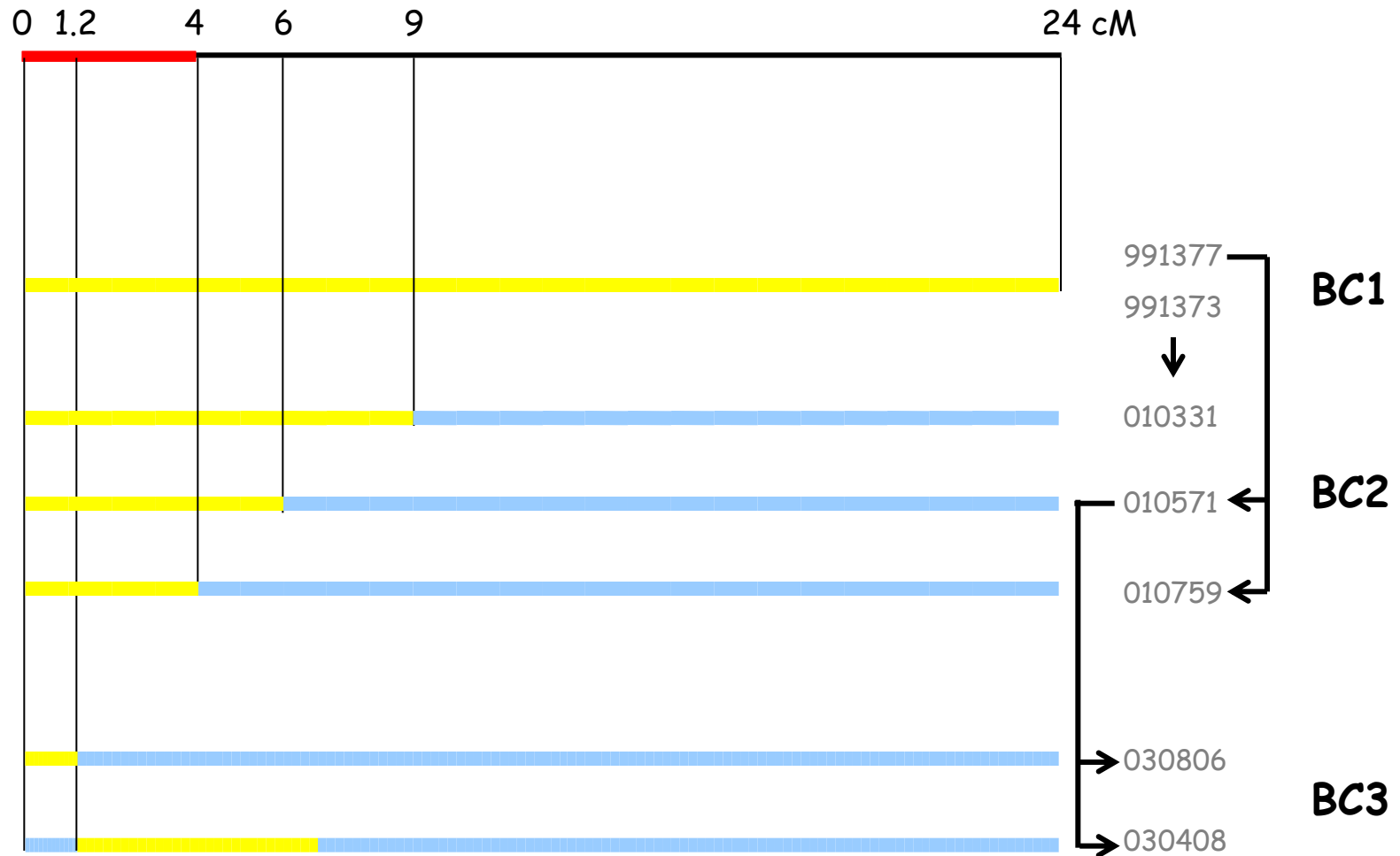
SSC2: progeny testing of BC2 boars

Generation	Boar	Growth	Carcass composition	Meat quality
BC1	991373	**	***	*
	991377	*	***	*
BC2	010331	**	***	NS
	010571	***	***	*
	010759	NS	***	**

NS: non significant - * $P < 0.05$ - ** $P < 0.01$ - *** $P < 0.001$

(at the chromosome level)

Exemple : SSC2



Conclusion (fine mapping)

Mapping interval has been reduced to :

SSC2 : 4 cM

SSC7 : 6 cM

For **SSC1** & **SSC4**: BC2 boars will be analysed soon

→ Much work remain to be done

Other traits:

IMF

ANDROSTENONE: fat samples remain to be analysed

Additional analyses: Transcriptome
SSC2 imprinting

Use of « historical » recombinations

Founder
individual

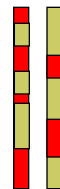
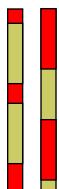


X
↓



Line 2

•
•
•
•



« Random »
matings

F_n

- ❑ Development of methods and a software for QTL primary detection => QTLMAP software
 - Analysis of half-sib (HS) and mixtures of half and full-sib families (HFS)
 - ❑ HS well suited for dairy cattle data
 - Extended to take into account the information of maternal grand-sires
 - ❑ HFS well suited for pig data
 - Within – population or in crosses between divergent lines
 - No assumption concerning the fixation of QTL alleles in parental populations
 - Compute the probability of different possible phases
 - Heterogeneity of sire family variances can be accounted for (e.g. when another QTL is segregating)

=> QTLMAP available upon request

- Multiple trait – multiple QTL (Gilbert, 2003)
 - Use of discriminant analysis in order to reduce the number of parameters
 - Increases detection power
 - Different models (pleiotropic vs linked QTL)
 - Implemented in QTLMAP software
- Traits with specific distribution (Moreno, 2003)
 - Discrete traits, survival traits
 - Implemented in QTLMAP software
- Use of population linkage disequilibrium
 - Development of a software based on the method developed by Meuwissen and Goddard
 - Comparing different methods :
 - Meuwissen and Goddard
 - Fernando et al.
 - Applications to fine mapping in dairy cattle and pigs

Multiple trait / QTL : an example on SSC7

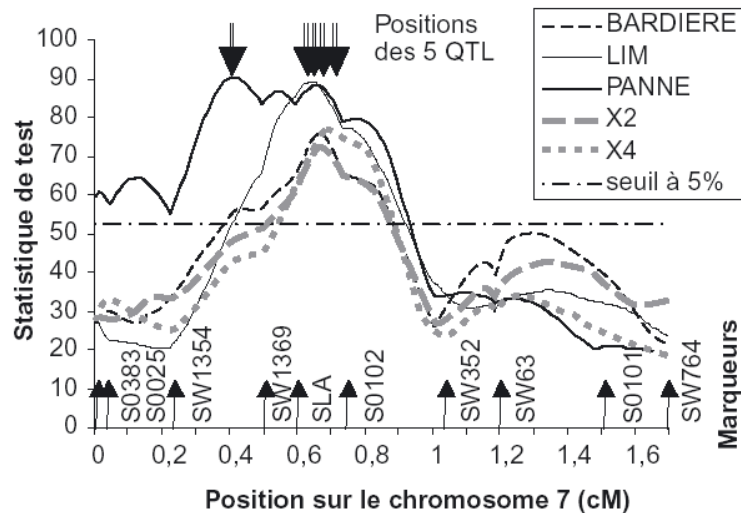


Figure 1 - Résultats des analyses "unicaractère" et "uniQTL"

Tableau 5 - Synthèse des résultats : positions et effets additifs¹ des 5 QTL détectés

Caractères Position (cM)	BARDIERE	PANNE	X2	X4	LIM
66	-0,58				
0	-0,22				
66		-0,59			0,83
18			-0,27	-0,28	
68			-0,32	-0,36	

¹ En unité d'écart type phénotypique

Gilbert et al (2004)