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Pig QTL mapping research in France - Recent results

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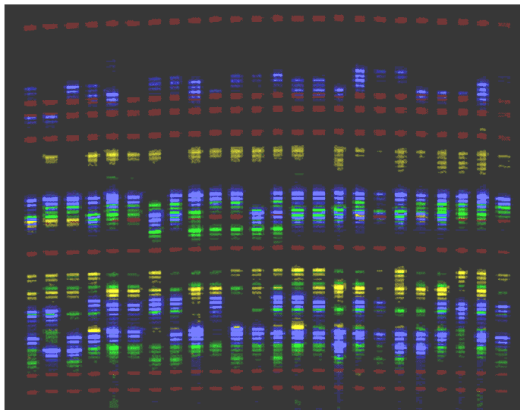
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Pig QTL mapping research in France - recent results -

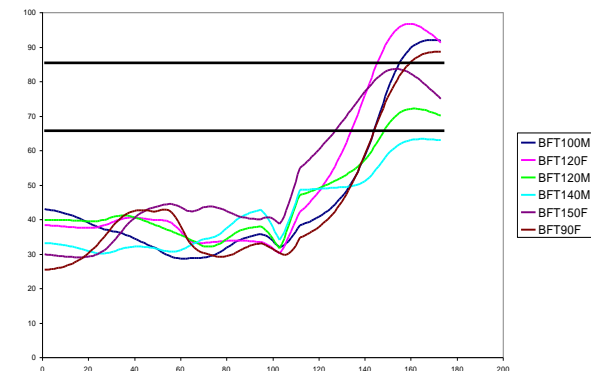


J.P. Bidanel

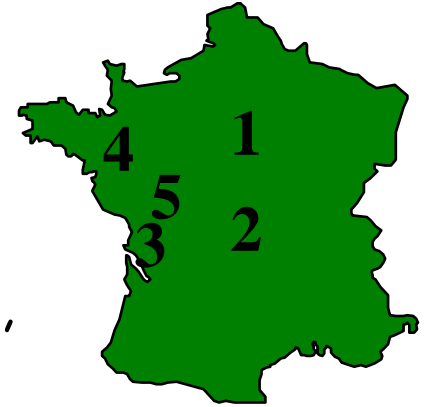


Nanchang
China

13 October 2005



The pig genetic group in Jouy-en-Josas (SGQA)



- * **The SGQA team :**

- P. Sellier (DR, few %), J.P. Bidanel (DR, 50%),
- C. Larzul (CR), H. Gilbert (CR),
- T. Tribout (IR), M.P. Sanchez (IE), H. Lagant (AI, 50%),
- L. Canario (PhD), A. Rosendo (PhD), F. Ytournel (PhD)

- * **4 experimental herds**

- 2. Bourges (J. Gogué et al., 9 P),
- 3-5. GEPA (S. Deretz et al., 19 P),
- 4. Le Rheu (M. Bouffaud et al., 7 P),

The pig genetic group in Jouy-en-Josas – current research programs

1. Polygenic variation

Selection experiment on residual feed intake (HG)

Canalising selection experiment on meat ultimate pH (CL)

Looking for meat quality predictors using transcriptomics (D116) (PLR)

In vivo prediction of IMF (CL)

Characterisation of sow maternal abilities (LC)

2. QTL mapping

Meat quality QTL (MPS)

Feed intake and behaviour QTL (HG)

Melanoma QTL (HG)

QTL in selected populations (TT)

Close collaboration
with Denis Milan
and his team

3. Fine mapping

Fine mapping of the IGF2 region (MPS)

Fine mapping of 4 chromosomal regions (MPS)

Fine mapping of SSC1 melanoma QTL (HG)

4. Management of livestock populations

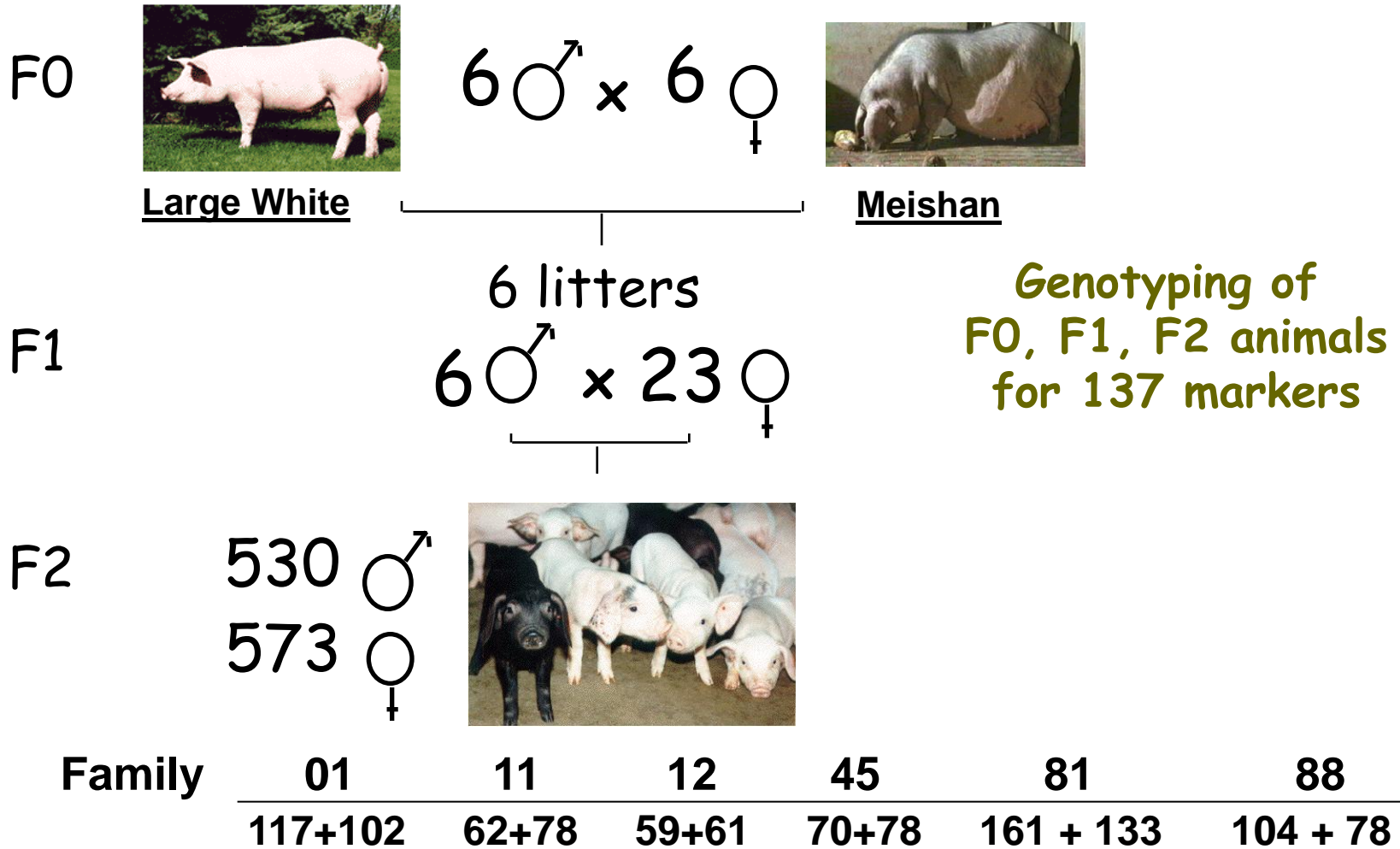
Genetic evaluation of pigs

Management of diversity

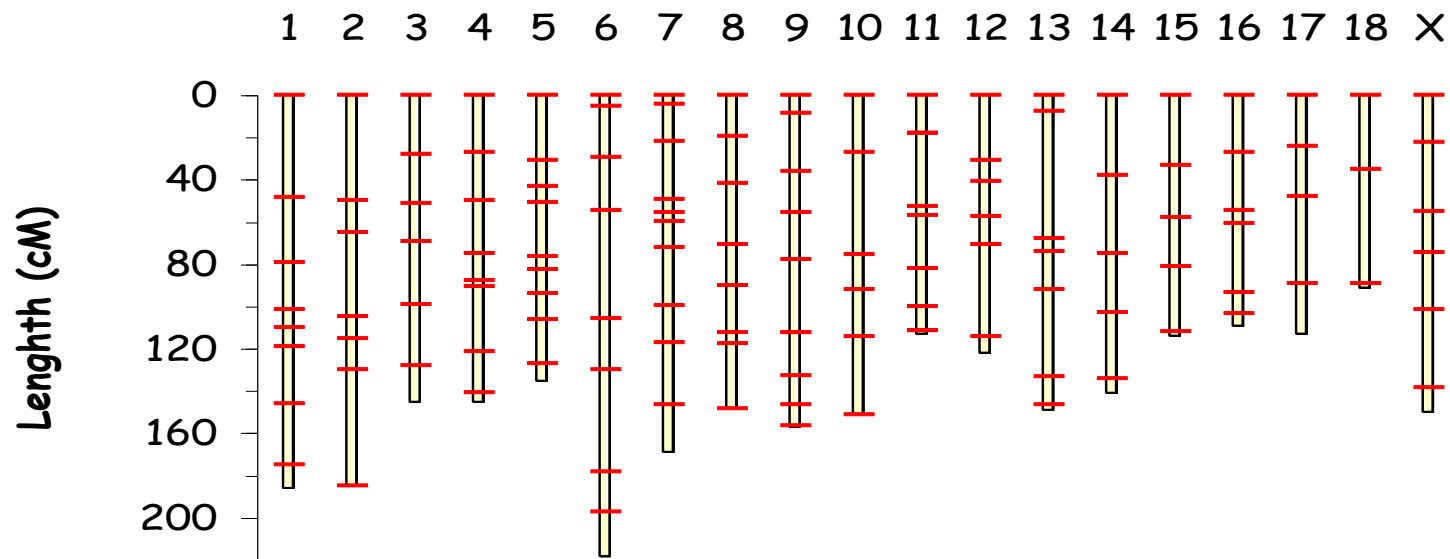
Optimisation of breeding schemes including GAS/MAS

Pig QTL mapping in France

- The PORQTL programme (F2 MS x LW)
- Grand-sire design (LW & LR)
- Meat quality QTL (F2 DU x LW)
- Feed consumption & behaviour QTL
(PI x LW) x LW
- Melanoma QTL
- BIOMARK project
- TRANSPORC project
- Statistical developments



- 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

- **Data pre-corrected for environmental effects**

- Contemporary group, sex, ...
- Age or weight, ...



- **Two models used for QTL detection**

- A Line-cross model (LC)

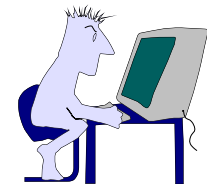
assuming QTL alleles fixed in grand-parental populations.
Use of QTL express (Seaton et al., 2002)

- A half-full sib model (HFS)

Estimating within-family QTL effects.
Use of QTLMAP (Le Roy et al., 1998)

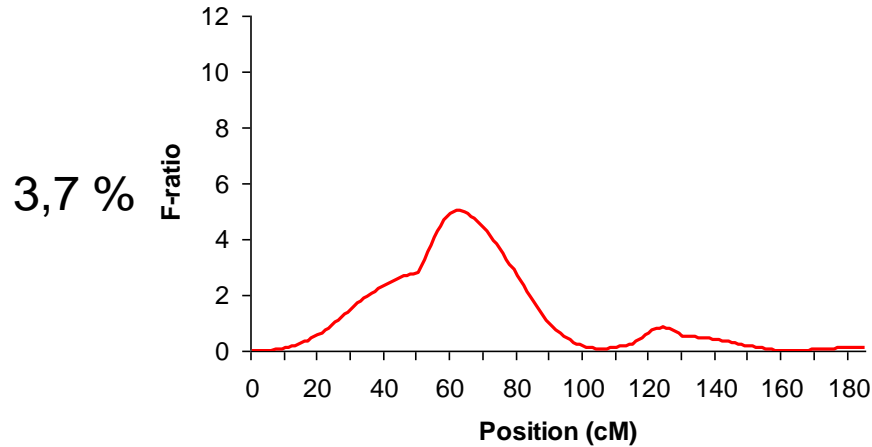
- Significance threshold determined by :
 - Data permutation (LC model)
 - Churchill and Doerge (1994)
 - Sampling from a normal distribution (HFS model)

- Chromosome & genome wise thresholds
 - Expected number of false positive
 - 100 traits => 40 independent traits
 - 5% CW => 35-40 false positive results
 - 5% GW => 1-2 false positive results

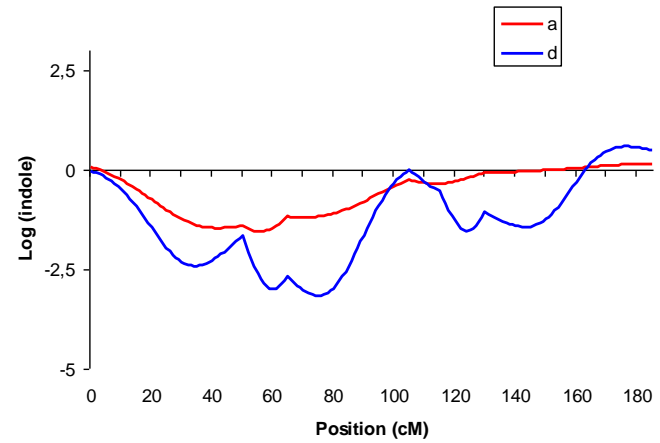


Latest results : fat skatole & indole levels (1/2) **PORQTL**

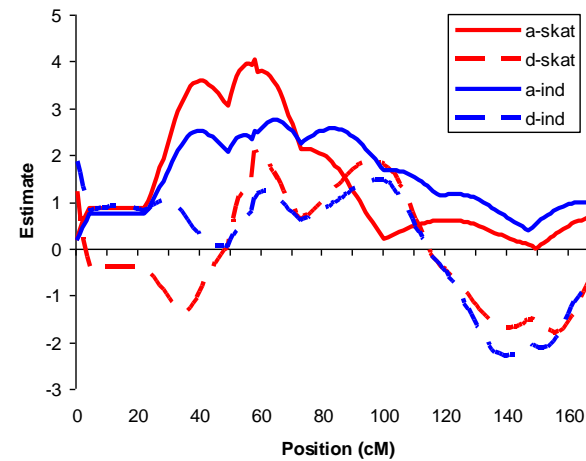
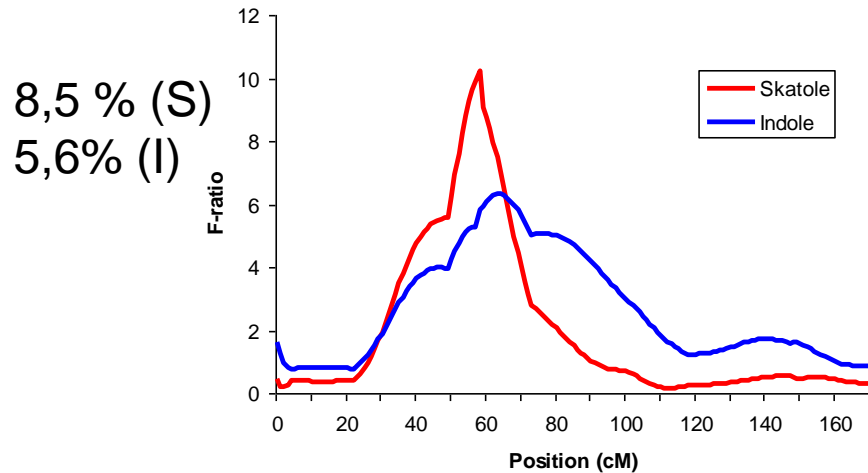
Indole - SSC 2 - F-ratio



Indole - SSC2 - Estimates

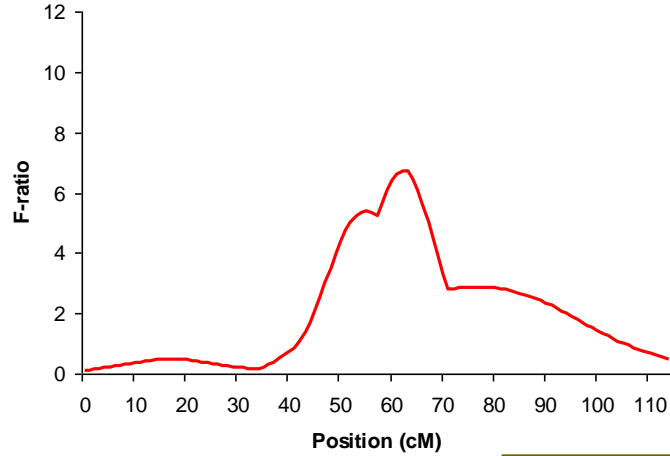


Skatole - SSC7 - F-ratio

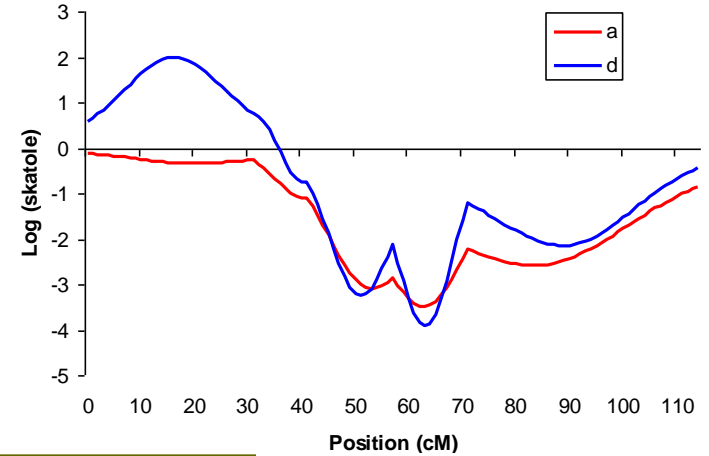


Latest results : fat skatole & indole levels (2/2) **PORQTL**

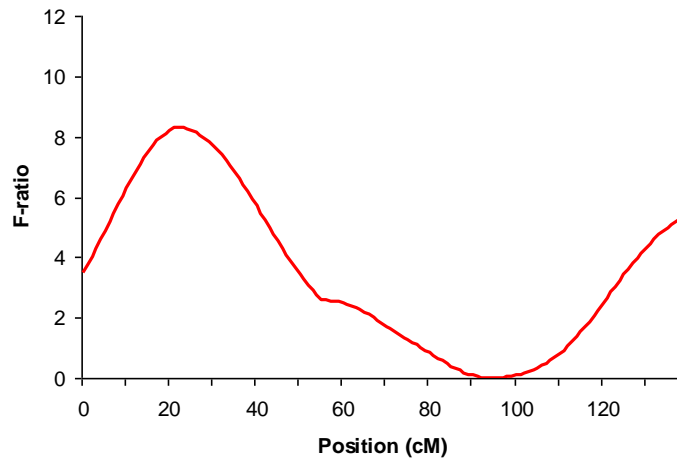
Skatole - SSC12 - F-ratio



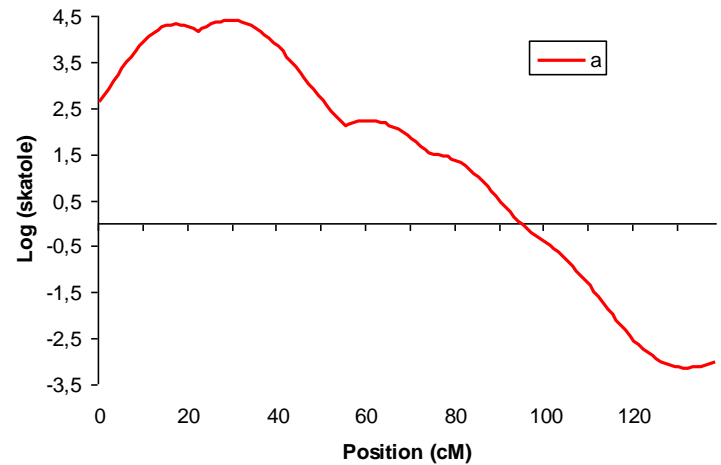
Skatole - SSC12 - Estimates



Skatole - SSCW - F-ratio



Skatole - SSCX - Estimates



Latest results : reproductive traits



=> Part of Rosendo's Thesis

Teat number

SSC	Loc	F-ratio	a	se(a)	d	se(d)	h^2_Q
3	78	6.8 +	0.19	0.07	-0.22	0.12	2.6
4	5	5.7+	-0.21	0.07	-0.06	0.11	1.2
7	112	9.1 *	-0.26	0.06	0.10	0.10	2.0
8	94	9.3 *	0.24	0.06	-0.08	0.09	1.8
11	114	5.9 +	0.08	0.06	0.28	0.09	1.3
16	44	9.1*	0.28	0.07	-0.01	0.11	2.3

- 6 relatively « small » QTL explaining <3% phenotypic variance
- 4 QTL with favourable effects of MS alleles, 2 with favourable effects of LW alleles

Age at puberty

SSC	Loc	F-ratio	a	se(a)	d	se(d)	h^2_Q
1	169	6.4 +	3.7	1.2	-2.7	1.8	2.8
4	67	7.1 +	-4.2	1.2	-2.18	1.78	3.8
6	174	7.7 +	-4.5	1.2	3.1	2.0	4.6
7	57	6.7 +	3.7	1.0	1.5	1.4	2.9
13	46	16.3 ***	-6.3	1.1	1.9	1.7	8.9

- Five QTL explaining from 3 to 9 % of phenotypic variance
- 3 QTL with favourable effects of MS alleles, 2 with favourable effects of LW alleles

Latest results : reproductive traits

PORQTL

Ovulation rate

Trait ^a	SSC	Loc ^b	F-ratio ^c	a ^d	s.e.(a)	d	s.e.(d)	h^2_{eQ}
OR	4	74	10.8 *	-0.66	0.17	0.53	0.24	3.2
OR	5	106	(67.0) *	0.28	-	-	-	2.6
OR	7	54	8.8 +	0.70	0.17	0.30	0.25	3.4
OR	9	127	7.9 +	0.67	0.19	-0.54	0.31	3.1
OR _W	9	127	7.1 +	0.56	0.18	-0.57	0.29	2.9
OR	13	46	6.5 +	0.74	0.23	0.73	0.49	4.0
OR _W	13	49	8.0 +	0.79	0.21	0.48	0.43	3.9

- 5 QTL regions explaining 2.6 to 4% of phenotypic variance
- 4 QTL with positive (favourable) effects of Meishan alleles

Latest results : reproductive traits

PORQTL

Number of embryos -embryo survival

Trait ^a	SSC	Loc ^b	F-ratio ^c	a ^d	s.e.(a)	d	s.e.(d)	h ² _Q ^e
NVE	6	106	6.5 +	-0.81	0.25	-0.45	0.34	2.7
NVE	9	36	(56.7) +	0.71	0.28	0.58	0.51	1.6
ES	9	36	(66.9) *	4.6	1.6	3.9	2.9	2.0
NVE	12	31	6.5 +	-0.81	0.25	-0.45	0.34	2.4
NVE	18	89	5.4 +	0.5	0.24	0.85	0.34	2.3

- 4 QTL regions explaining 1.6 to 2.7 % of phenotypic variance
- 2 QTL with positive (favourable) effects of Meishan alleles

Backcross MS x LW designs

2 designs

- Reproductive traits

- field design
- 250 litters
- Currently analysed in Rosendo 's thesis

- Production and meat quality traits

- Backcross animals used for fine mapping
- Confirmation of F2 QTL in a BC genetic basis
- New suggestive QTL on SSC 1 and 2

=> Paper by Sanchez et al to be published in JAS

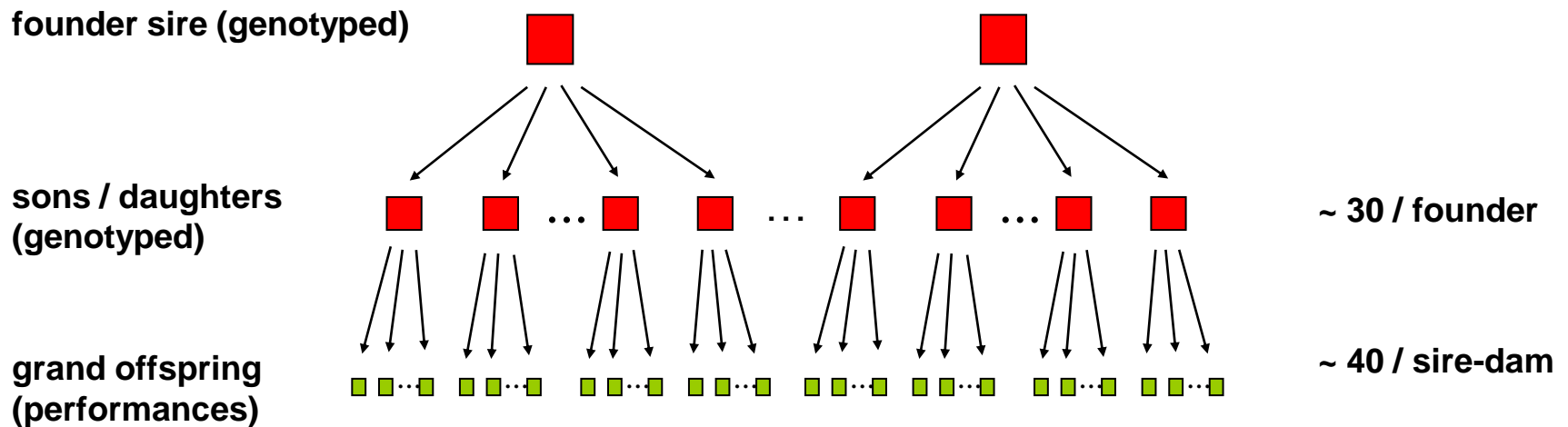
Backcross MS x LW designs

Results of Sanchez et al (JAS, 2006)

SSC	Trait	S1 boar (Het 1, Het 2, rec 4, hom 7)			S2 boar (Het 1, Het 2, rec 4, hom 7)			S3 boar (Het 1, Het 2, rec 4, hom 7)			S4 boar (Het 1, Het 2, rec 4, hom 7)		
		Location (cM)	Sign. level ^a	Additive value ^b	Location (cM)	Sign. level	Additive value	Location (cM)	Sign. level	Additive value	Location (cM)	Sign. level	Additive value
1	pH-add	169	+	0.14	-	ns	-	-	ns	-	-	ns	-
1	pH-gs	167	+	0.12	-	ns	-	-	ns	-	-	ns	-
1	pH-ld	168	+	0.16	175	+	-0.21	-	ns	-	-	ns	-
1	pH-bf	167	***	0.19	156	+	0.094	-	ns	-	-	ns	-
1	a* gs	-	ns	-	-	ns	-	-	ns	-	165	+	0.88
1	L* bf	-	ns	-	175	+	5.34	-	ns	-	155	+	2.2
1	WHC-gs (10s)	-	ns	-	-	ns	-	-	ns	-	155	+	21.5
2	pH-add	-	ns	-	0	+	0.070	-	ns	-	-	ns	-
2	pH-bf	1	+	0.076	-	ns	-	-	ns	-	-	ns	-
2	b* bf	-	ns	-	-	ns	-	0	+	0.48	-	ns	-
2	L* bf	-	ns	-	-	ns	-	4	*	-2.25	-	ns	-
7	a* gs	-	ns	-	101	+	0.81	-	ns	-	-	ns	-

Use of a grand-sire design for QTL mapping in France (1/2)

In French Large White and Landrace populations Data analyses : T Tribout



- Use of the national central database
- Use of a DNA bank for AI boars

Use of a grand-sire design for QTL mapping in France (2/2)

- **8 grand-sire families**
- **traits investigated**
 - growth, carcass and meat quality traits (farm & central station)
 - reproduction traits : litter size at birth and weaning weaning-oestrus interval, ...
- **Preliminary results**
 - Age at 100 kg : no QTL found
 - Backfat thickness
 - SSC2 BF100 (13 cM) + BF_{rum} + BF_{neck}
 - SSC3 BF100 (5 cM) + BF neck
 - SSC13 (111 cM)
 - SSC17 (22 cM) + BF back

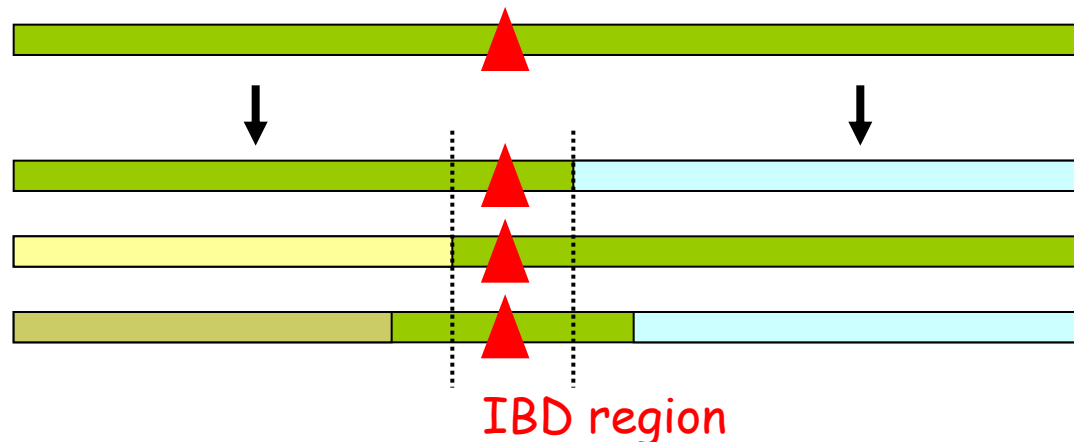
- Duroc x Large White F2 pigs
 - Resp. : M.P. Sanchez
 - ~ 500 pigs - 6 large families
 - Focused on meat quality traits, but growth and carcass traits also investigated
 - Animals genotyped for a first set of ~ 50 markers. Second set in 2006 (?)
 - Results to be analysed in 2006

- (Piétrain x Large White) x Large White BC pigs
 - Resp : H Gilbert
 - ~ 550 pigs - 12 families
 - Focused on feed consumption and behaviour traits (measured using ACEMO electronic feeders), but growth and carcass traits also investigated
 - Part of SABRE integrated European project
 - Animals to be genotyped in 2007 (?)
 - Results to be analysed in 2007-2008

- **Main model = hereditary cutaneous melanoma in pigs**
 - Use of a pig line (Libechov) spontaneously developing melanoma
 - Backcross programme with coloured (Duroc) pigs
 - Clinical and histological characterisation of the tumour
 - Genetic characterisation of predisposition
 - Several QTL / candidate regions found (SSCr 1, 2, 6, 7, 8)
 - Comparative genomic hybridisation => gain and loss of genetic material => consensus regions of chr gains (SSCr 3, 12, 14) and loss (SSCr 13)

BIOMARK project (1/2)

- ❑ "A thorough evaluation of several QTL segregating in commercial pig lines for fine QTL mapping and the setting up of marker assisted selection"
- ❑ Funded by "Genanimal" project
- ❑ D Milan - JP Bidanel - MJ Mercat (ITP)
- ❑ Objectives :
 1. Use of data from as many well-characterized (for the QTL investigated) families from a maximum number of different pig populations for the fine mapping of 6 QTL regions



❑ Objectives (following):

2. Confirm QTL effects in commercial pig populations

❑ Methods

- ❑ Investigated haplotype diversity and effects in ~ 5000 animals

- ❑ Production of new families from commercial populations
 - ❑ 15 sire families with progenies of ~100 pigs
 - ❑ Measured for a large number of traits
 - ❑ Growth, carcass, meat quality
 - ❑ Immune reponse
 - ❑ Used for new whole genome scans (?)

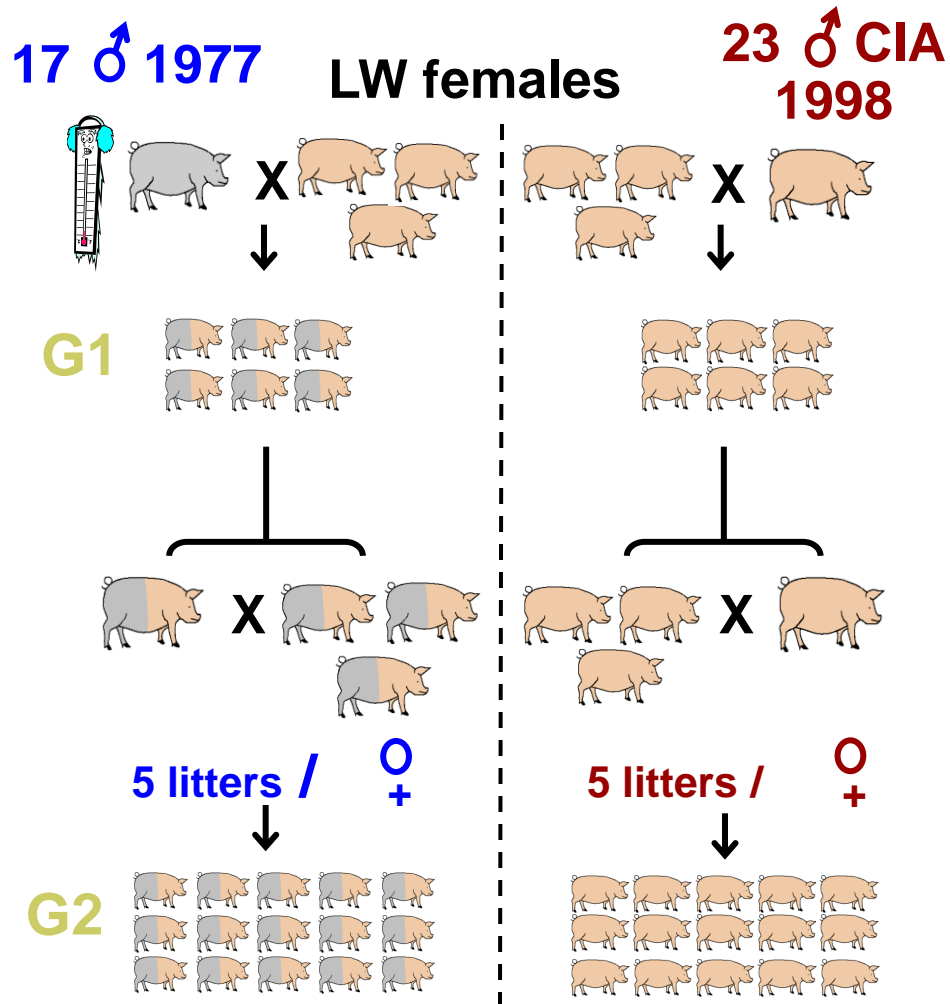
- ❑ Design also used to test known genes / markers polymorphisms

TRANSPORC project (1/2)

- F Lefèvre (VIM) – L Flori – P Chardon – C Rogel-Gaillard (LREG)
JP Bidanel (SGQA)
- Investigating host pathogen interactions in pigs using transcriptomics tools
- Pathogen model = Aujeszky virus
- Innate response
 - In vitro response
- Vaccinal response
 - In vivo response
- Investigating the effects of selection on immune response



TRANSPORC project (2/2)



□ QTLMAP software

■ Analysis of :

- half sibs
- half/full sib designs
- Line cross designs

■ Univariate analyses

- Variety of distributions (Normal, discrete, survival)

■ Multivariate analyses

- Based on discriminant analysis
- Increased power
- Test of pleiotropy / linkage

=> Software available upon request

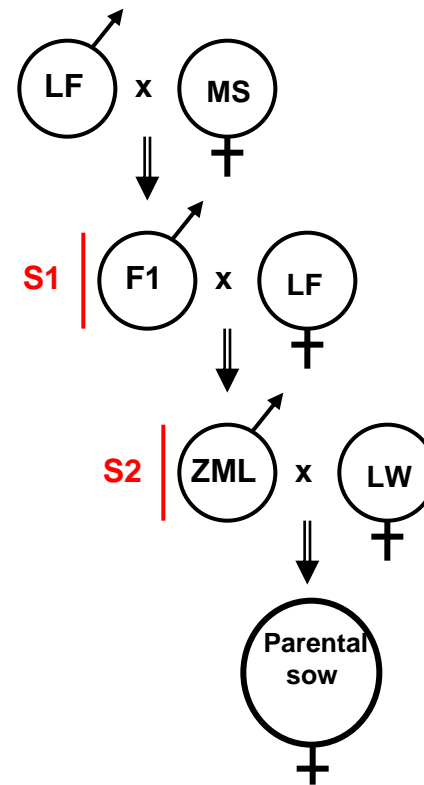
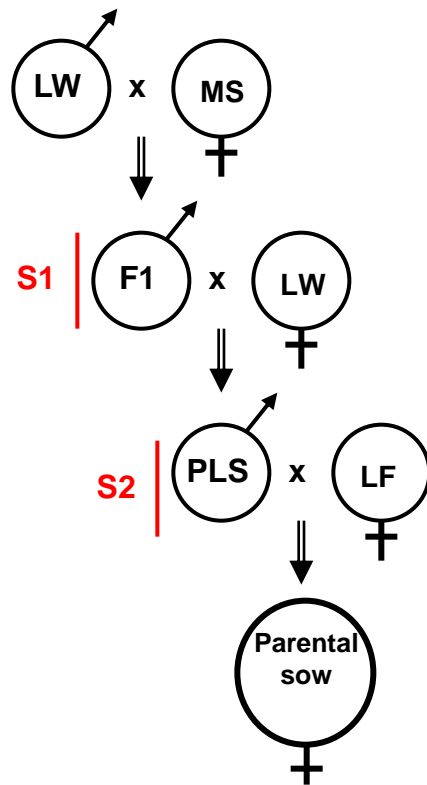
- Use of population linkage disequilibrium
 - Development of a software based on the method developed by Meuwissen and Goddard
 - Comparison of different methods for linkage disequilibrium analyses (F Ytournel PhD thesis)
 - Meuwissen and Goddard
 - Pérez-Enciso
 - Hernandez-Sanchez
 - Method developed at INRA (Biometry – Toulouse) based on Terwilliger
 - Applications to the fine mapping in dairy cattle and pigs
- Analysis of expression data

Genotype / Marker assisted selection (GAS / MAS)

- Development of simulation models for « practical » pig breeding schemes
 - Large populations
 - small closed populations
- **Objectives**
 - Genetic / economic interest of GAS / MAS
 - Optimisation of GAS/MAS
 - Which animals to genotyped ?
 - Genetic evaluation method ?
 - M then Ph, Ph then M, P and M
 - Application to real situations
 - HAL in Pietrain populations
 - MAS in Chinese x Western composite lines

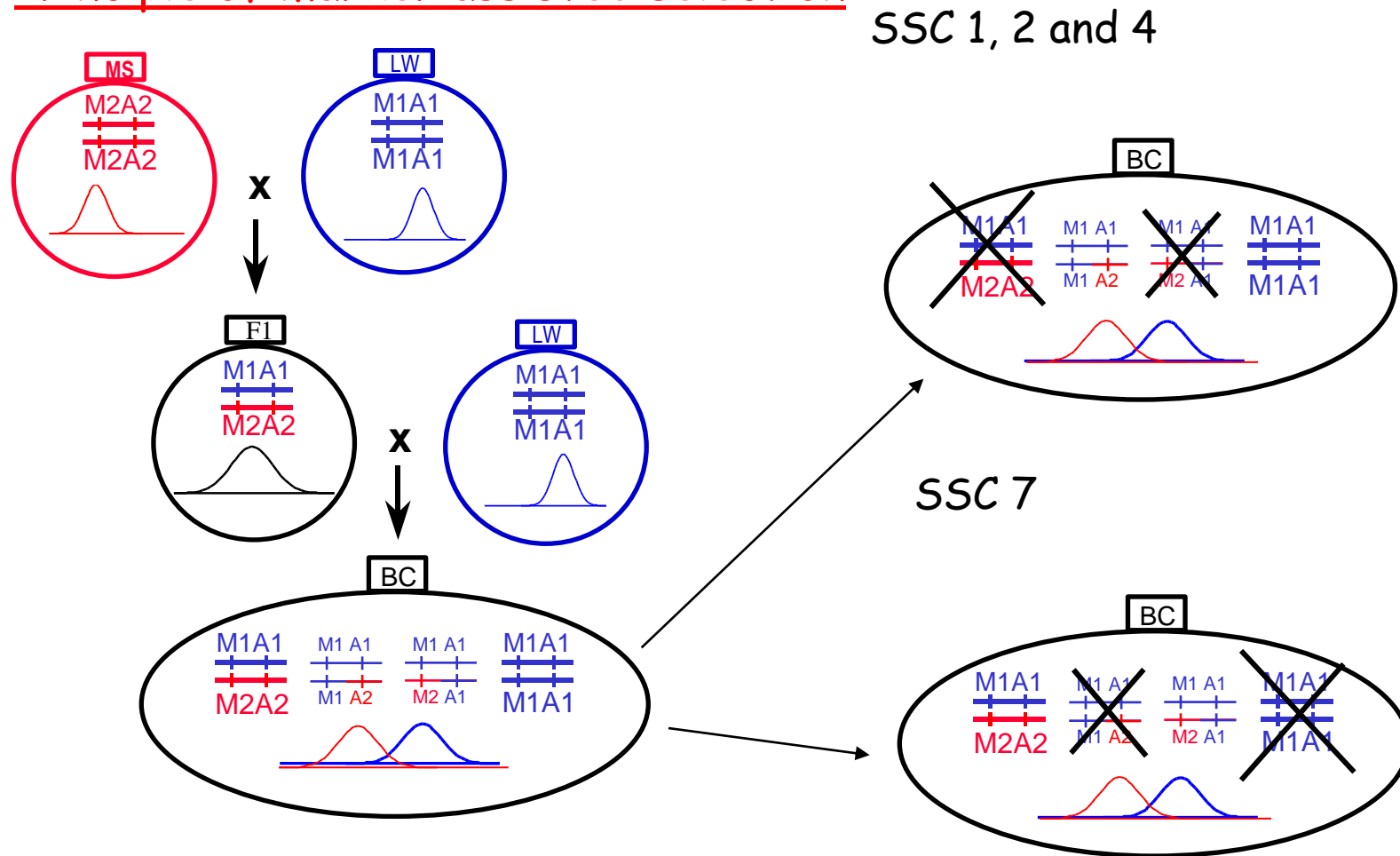
Marker assisted selection in backcross (LW*MS)*LW boars

Crossbreeding plan used



Marker assisted selection in backcross (LW*MS)*LW boars

Principle of marker assisted selection



Computation of a molecular score, then a global index

$$MS = \sum(P(\text{hapl}) \cdot HW)$$

$$GI = \alpha MS + \beta PI$$