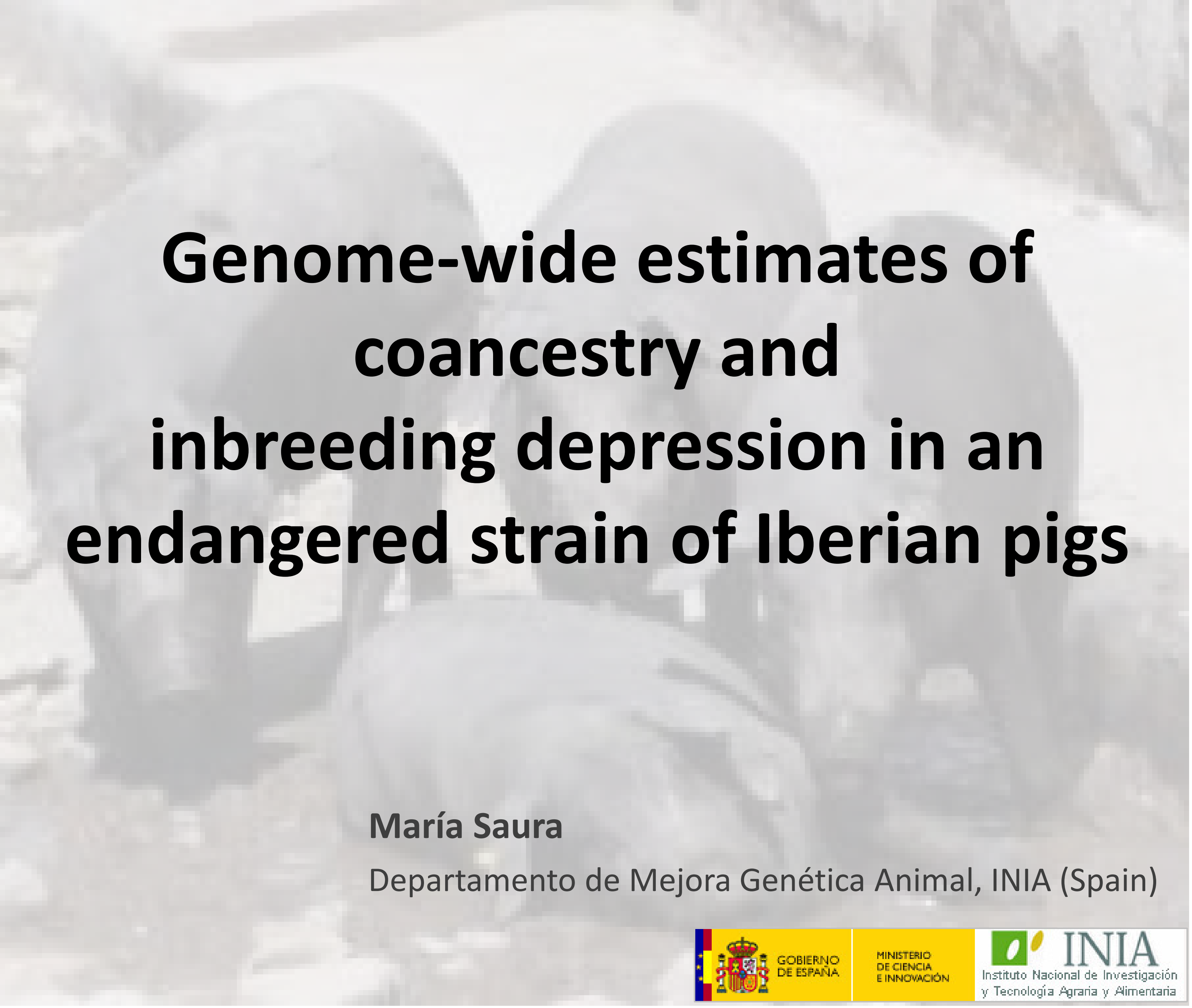

Genome-wide estimates of coancestry and inbreeding depression in an endangered strain of Iberian pigs

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Background

- Aims of a conservation program
  - Maintain genetic variation
  - Control the increase in inbreeding [avoid inbreeding depression]

  - Maintain genetic variation → important parameter: **coancestry** [*f*]
  - Avoid inbreeding depression → important parameter: **inbreeding** [*F*]

- Traditionally *f* and *F* computed from pedigree information

- High throughput genotyping methods
  - Overcome limitations of classical markers
  - Obtain more detailed information (genomic regions)

Objectives

- **Evaluate the use of dense SNP panels for:**

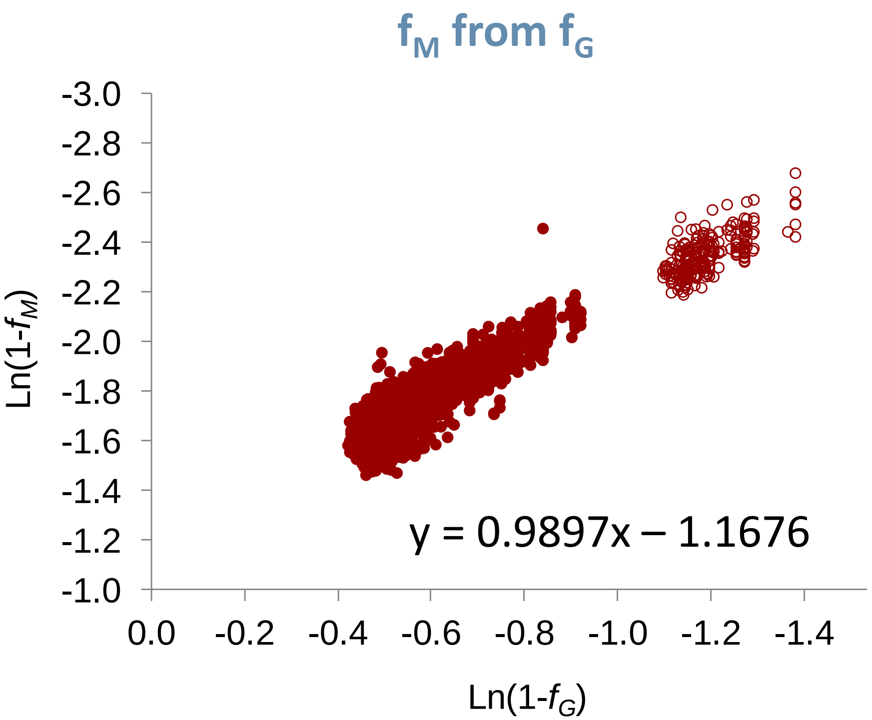
  1. Estimating coancestry → use in management
  2. Detecting genomic regions involved in inbreeding depression

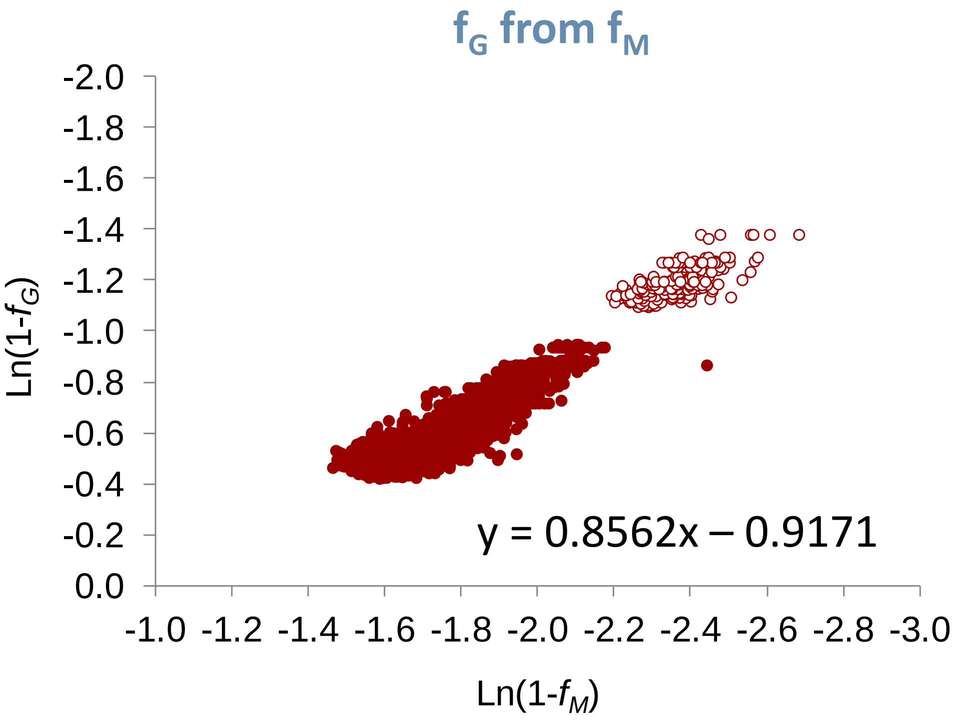
In a highly inbred strain of Iberian pigs

Guadyerbas strain

- Material for this study
- One of the most ancient strains of Iberian pigs
- Isolated since 1944 in a closed herd
- Now in serious danger of extinction
- Complete and accurate pedigree since foundation of herd
  [25 generations - 1178 records]
- Genotypes for 219 individuals → Porcine 60K SNP Beadchip

Coancestry predictions


f_M from f_G


f_G from f_M

f_G is a very good predictor of f_M

Well known

f_M is a very good predictor of f_G

Contrast with previous results

$\boldsymbol{\rho} = 0.9$

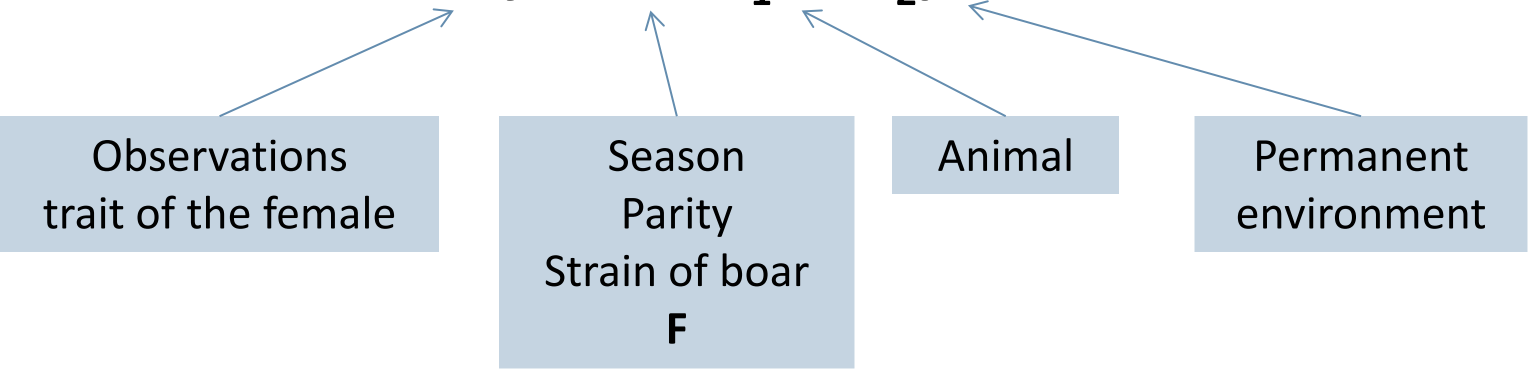
Inbreeding depression analysis

- **Inbreeding depression** → Reduced performance as a result of inbreeding: well known, particularly for fitness-related traits

- **Traits analyzed**
  - **TNB:** total number of piglets born
  - **NBA:** number of piglets born alive

- **Mixed animal model** → genealogical and molecular analyses

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}_1\mathbf{a} + \mathbf{Z}_2\mathbf{p} + \mathbf{e}$$



Observations
trait of the female

Season
Parity
Strain of boar
F

Animal

Permanent
environment

Inbreeding depression: Genealogical analysis

- Genealogical inbreeding coefficients F_G were obtained using all pedigree information since the foundation of the herd
- 832 sows with data
- Average F_G: 0.19 [Range: 0 - 0.5]

Significant inbreeding depression in both TNB and NBA:

-0.2 piglets per 10% increase in F

Can we gain insight into regions causing depression using the information contained in the 60K chip?

Inbreeding depression: Molecular analysis

- **Inbreeding coefficients used:**
  - F_{snp}: defined as the genomic marker-by-marker inbreeding, i.e. the proportion of homozygous genotypes
  - F_{roh}: defined as the proportion of the genome in Runs Of Homozygosity
    - Long segments of homozygous SNPs (> 500 Kb, > 30 SNPs)
    - Gives a more accurate measure of autozygosity (IBD genomic segments) → autozygous genotypes are not evenly distributed by the genome but distributed in runs

- **Analyses performed:**

1. Average coefficients **over the whole genome**
2. Average coefficients **for each chromosome**
3. Average coefficients **for specific regions within chromosomes**

Results

- F_{snp} and F_{roh} for 109 genotyped sows

Analysis 1 [whole genome]

→ Not significant effect

Analysis 2 [chromosome]

→ **Significant effect on chromosome 13**

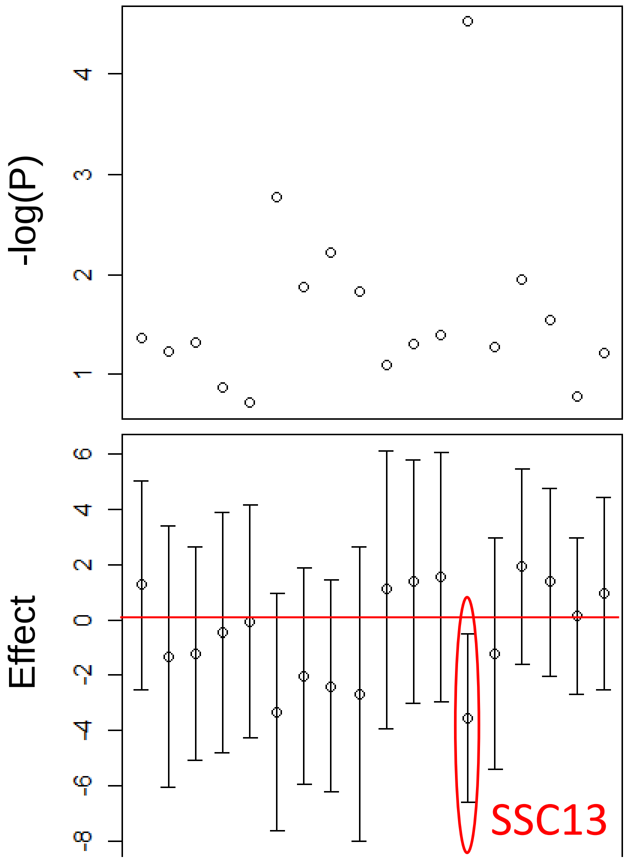
Analysis 3 [region]

→ **Significant effect on chromosome 13 region 27.6 - 53.9 Mb**

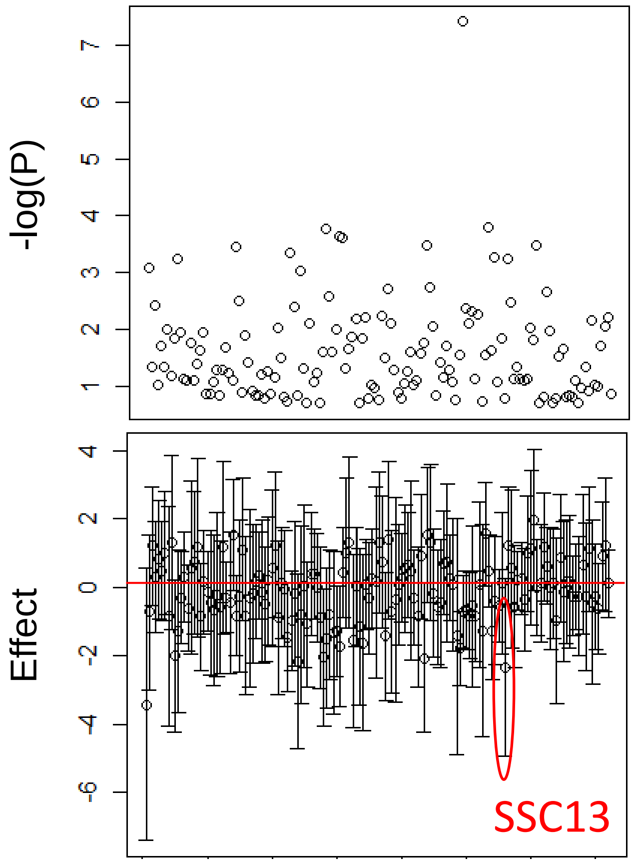
$r(F_{snp}, F_{roh}) > 0.97$

Analysis 3: specific regions SSC13

Results **per chromosome**



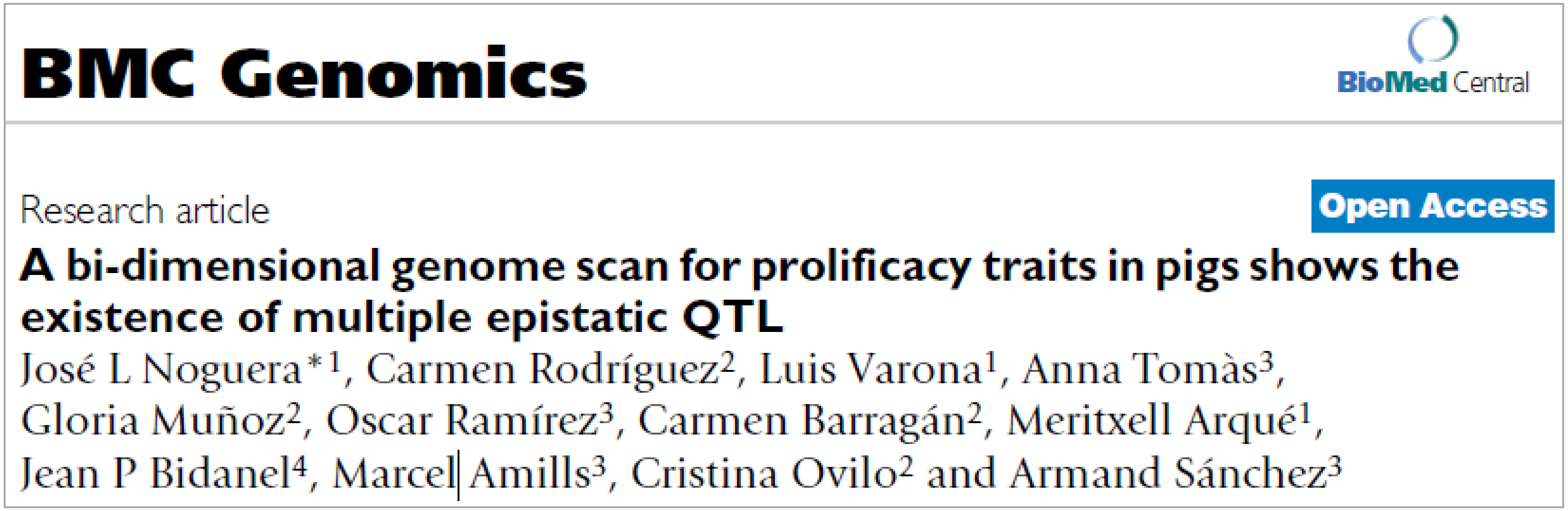
Split SSC13 in 3, 5 and **8 segments**



Significant effect in region 27.6 – 53.9 Mb

Comparing with previous QTL studies

- Few QTL studies on genomic analysis of reproductive traits in pigs
- First study genome-wide scan for prolificacy traits



BMC Genomics

BioMed Central

Research article

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A bi-dimensional genome scan for prolificacy traits in pigs shows the existence of multiple epistatic QTL

José L Noguera*[1], Carmen Rodríguez[2], Luis Varona[1], Anna Tomàs[3], Gloria Muñoz[2], Oscar Ramírez[3], Carmen Barragán[2], Meritxell Arqué[1], Jean P Bidanel[4], Marcel Amills[3], Cristina Ovilo[2] and Armand Sánchez[3]

Iberian x Meishan F_2 intercross

QTL region on SSC13 → Affecting both TNB and NBA
Overlaps with the inbreeding depression region detected

Noguera et al. (2009)

Comparing with previous QTL studies

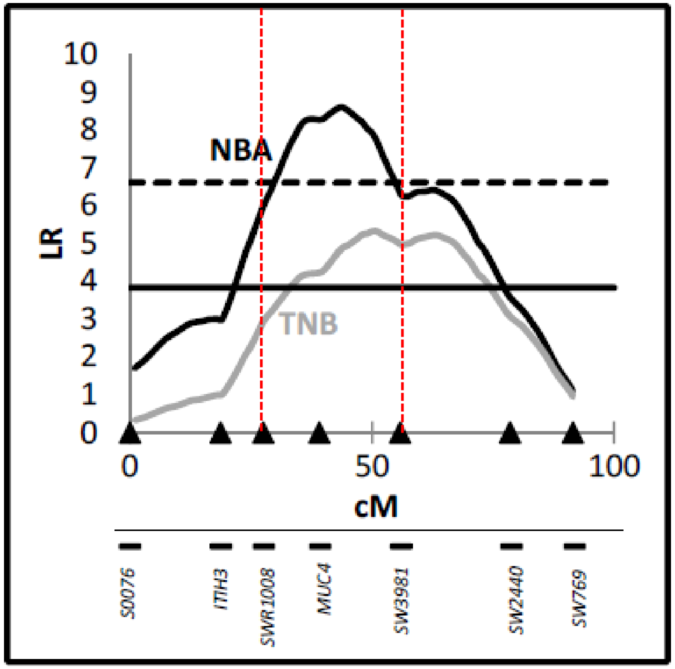


Figure 1 QTL profiles on SSC13 for NBA and TNB showing the likelihood ratio test statistic. The horizontal lines set at 3.84 and 6.63 show the 0.05 and the 0.01 significance levels respectively.

Position (27.57 – 53.88 Mb) coincides with QTL region

271 genes in common region

ITIH1, ITIH3, ITIH4

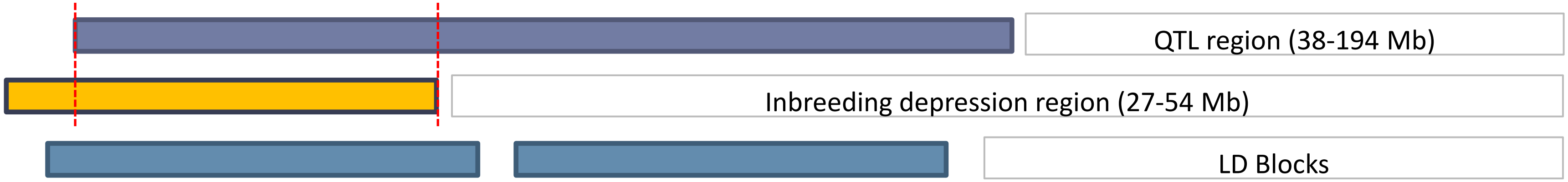
Inter-α-trypsin inhibitor, heavy chains 1, 3, 4

↓

Associated with TNB and NBA

Positions markers *Sscrofa10.2*

s0076- NA ***ITIH3***-38.10 ***swr1008***-58.92 ***MUC4***-143.78 ***sw3981***-194.99 ***sw2440***-206.65 ***sw769***-212.03 Mb



QTL region (38-194 Mb)

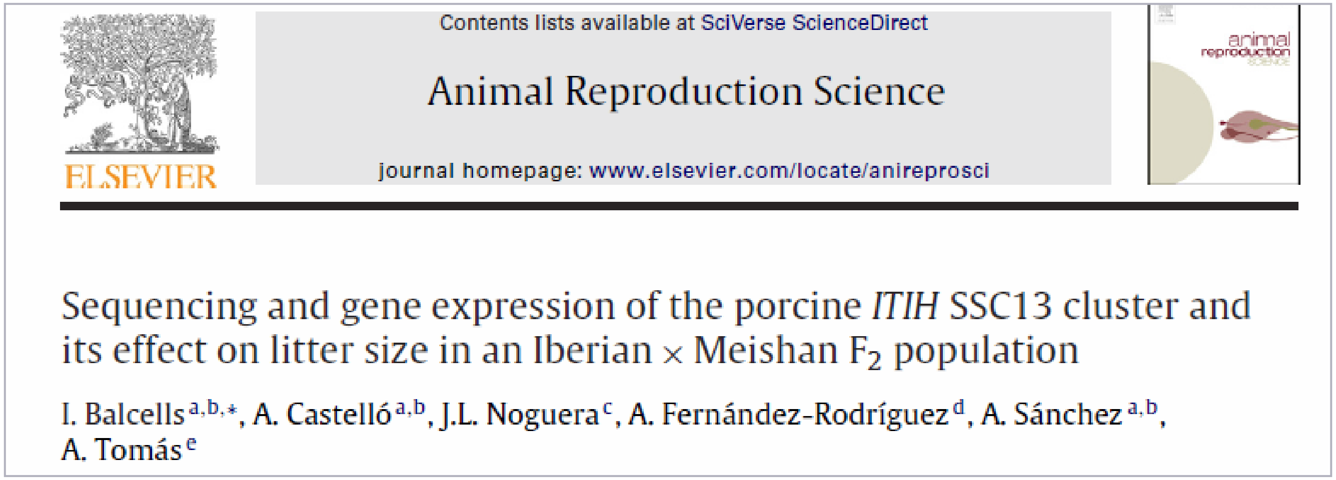
Inbreeding depression region (27-54 Mb)

LD Blocks

ITIH cluster

Inter- α -trypsin inhibitor, heavy chains (ITIH)-1, -3, -4

May play an important role in embryo implantation



Contents lists available at SciVerse ScienceDirect

Animal Reproduction Science

journal homepage: www.elsevier.com/locate/anireprosci

Sequencing and gene expression of the porcine *ITIH* SSC13 cluster and its effect on litter size in an Iberian × Meishan F_2 population

I. Balcells[a,b,*], A. Castelló[a,b], J.L. Noguera[c], A. Fernández-Rodríguez[d], A. Sánchez[a,b], A. Tomás[e]

- Identified polymorphisms → analyzed endometrial gene expression of porcine ITIH-1, -3 and -4 genes → explain **differences in prolificacy of sows**
- Significant associations with **NBA**
  - ITIH-1 [2 SNP]
  - ITIH-3 [4 SNP]
  - ITIH-4 [4 SNP]

Conclusions

Genetic variation

- High correlation between f_G and f_M computed from SNP
- f_M is a very good predictor of f_G and *vice versa*

SNP chip is a useful tool for managing the loss of genetic variability, particularly when pedigree is unavailable

Inbreeding depression

- Significant inbreeding depression for NBA and TNB in chromosome 13

Region 27-54 Mb

  - Overlaps with a previously detected **QTL region**
  - ITIH cluster → important role in embryo implantation

SNP chip is a useful tool for detecting genome regions associated to inbreeding depression

Acknowlegments

INIA
Instituto Nacional de Investigación
y Tecnología Agraria y Alimentaria

Dr Beatriz Villanueva

Dr Almudena Fernández

Dr Ana Fernández

Dr Carmen Rodríguez

Carmen Barragán

UNIVERSIDAD POLITECNICA MADRID

Prof Miguel Ángel Toro

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GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

Ministerio de Economía y Competitividad, INIA (RZ2010-00009-00-00 and JCI-2011-10896)

Advantages of genomic F rather than pedigree-based F

- It measures directly homozygosity (and potentially, the actual % of the genome that is autozygous), whereas pedigree-based F is only an expectation of such percentage

- It allows to estimate autozygous and inbreeding depression in specific genomic regions

- It is able to capture autozygosity arising from very distant common ancestors which is ignored by pedigree-based F because it refers to a relatively recent base population where all individuals are assumed to be non-inbred and unrelated.

- It can be estimated in populations whre pedigree recording is very difficult or impossible

Molecular inbreeding coefficients

- F_{snp}: defined as the genomic marker-by-marker inbreeding obtained based on the excess of SNP homozygosity

$$F_{snp\ (i)} = [OH_{(i)} - EH)/(n - EH)]$$

F for individual (i)

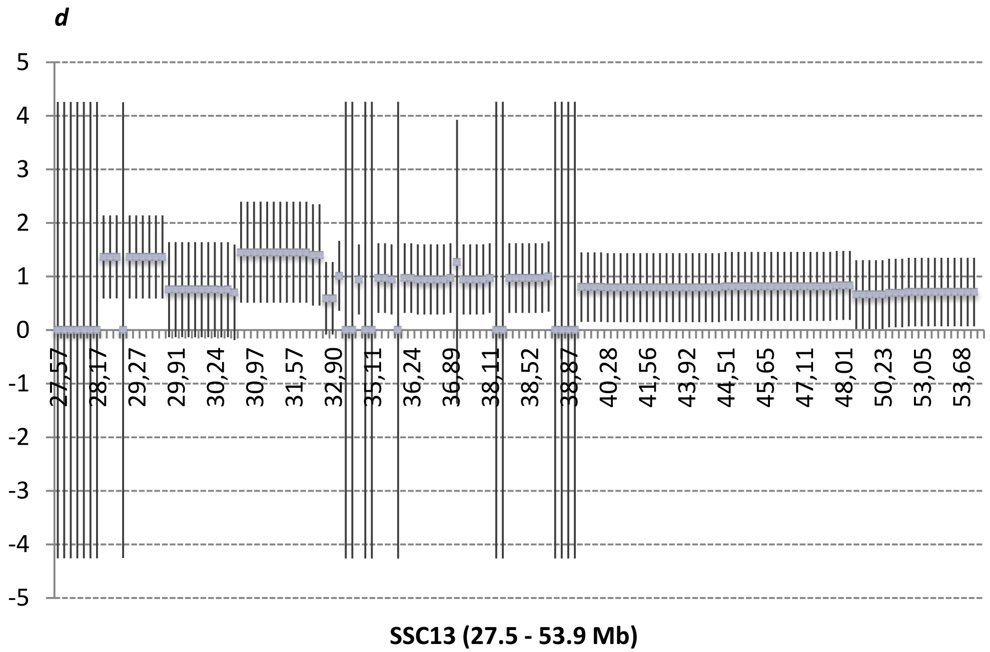
Observed homozygosity across all n SNP for individual i

Expected homozygosity across all SNP for the population

- F_{roh}: defined as % of the genome in Runs Of Homozygosity → length of the genome that is ROH for the individual

$$F_{roh\ (i)} = \pounds ROH_{(k)} / \text{length genome}$$

GWAS



- d > 0 → 7 blocks of SNPs showing significant dominance effects and non significant additive effects

Gen coefficients << Mol coefficients

- Relationship f_M and f_G

$$(1 - f_M) = (1 - f_G)\overbrace{(1 - \sum p_i^2)}^{\text{Heterozygosity of the base population}}$$

$\downarrow$ Log transform

$$\mathrm{Ln}(1 - f_M) = \mathrm{Ln}(1 - f_G) + \mathrm{Ln}(1 - \sum p_i^2)$$

$$\mathrm{Ln}(1 - f_G) = \mathrm{Ln}(1 - f_M) + \mathrm{Ln}(1 - \sum p_i^2)$$

$$y = \beta_1 x + \beta_0$$

Expectation > the slope of the regressions has to be the same (=1)