

# Genomic regions influencing intramuscular fat in divergently selected rabbit populations

Sosa-Madrid, B.S., Hernández, P., Navarro, P., Haley, C.S., Fontanesi, L., Pena, R.N., Santacreu, M.A., Blasco, A., and Ibañez-Escriche, N.

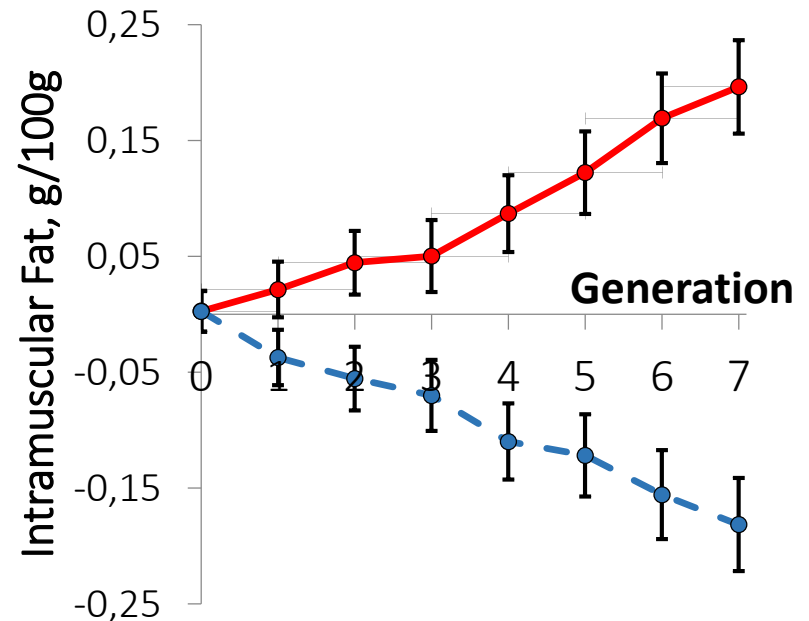
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**ICTA**



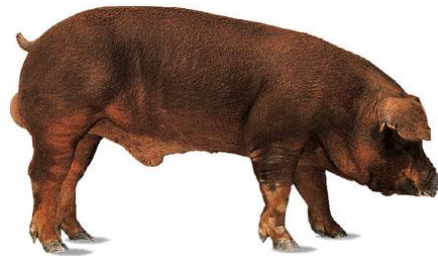
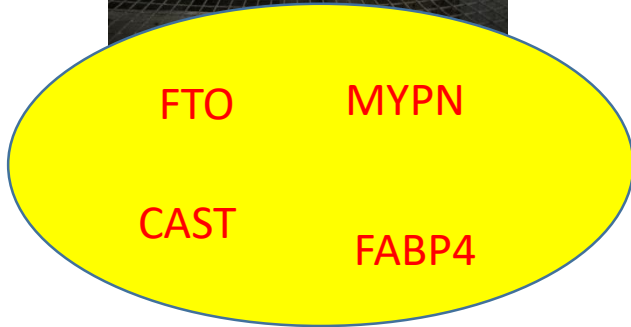
# INTRODUCTION

- Intramuscular Fat (IMF) -----> Meat Quality
- Control Mechanisms of IMF -----> Genomic
- Divergent Selection for IMF (9 generations)
- Selection Response = 3.1 SD



# INTRODUCTION

- Candidate Genes association study for IMF in rabbits.
- Relevant results in other livestock species: pigs (Duroc) and beef cattle (Japanese Black)



Pena et al. (2016)



Strucken et al. (2017)

Zhang et al. (2013); Wang et al. (2016),  
Migdał et al. (2018); Wang et al. (2017)

# OBJETIVES

- To identify SNPs and genomic regions associated with IMF in rabbits.
- To identify candidate genes related to IMF and located in the associated regions.



# Material and Methods

- 240 animals of the high line and 237 animals of low line.
- 4 full-sibs by female.
- IMF = grams / 100 grams of muscle.



# Material and Methods



High line



Low line



DNA samples



200,000 SNPs - Affymetrix

Genotyping and  
Quality Control

94,971 SNPs

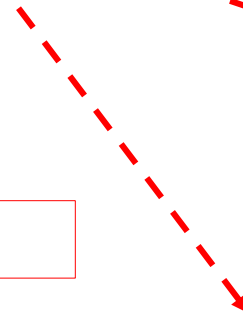
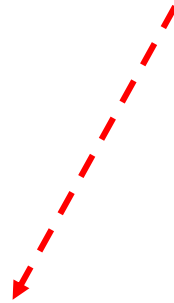
# Material and Methods: GWAS

- Three approaches:
  - Single marker regressions accounting for relatedness: genomic kinship matrix (SMR).
  - Single marker regressions accounting for relatedness: genomic kinship matrix + litter random effect (SMR –W)
  - Multi marker regressions (MMR: Bayes B) = SNPs o 1MB – windows.
- Functional analysis (DAVID y Enrichr).
- Analysis of linkage disequilibrium.

# Material and Methods: GWAS

- SMR

$$y = Xb + z_j \alpha_j + Zu + e$$



**SNP effects**

**Residual effect**

- **Mean**
- **Systematic effects:**
  - **Month-season**
  - **Sex**
  - **Parity order**

**Polygenic  
Random Effect  
(Genomic Matrix)**



# Material and Métodos: GWAS

- SMR - W

$$y = Xb + z_j \alpha_j + Zu + Wp + e$$

SNP effects

Residual effect

Random Litter  
Effect

- Mean
- Systematic effects:
  - Month-season
  - Sex
  - Parity order

Polygenic  
Random Effect  
(Genomic Matrix)

# Material and Methods: GWAS

- MMR

$$y = Xb + \sum_{j=1}^k z_j \alpha_j \delta_j + e$$

Residual effect

SNP effects

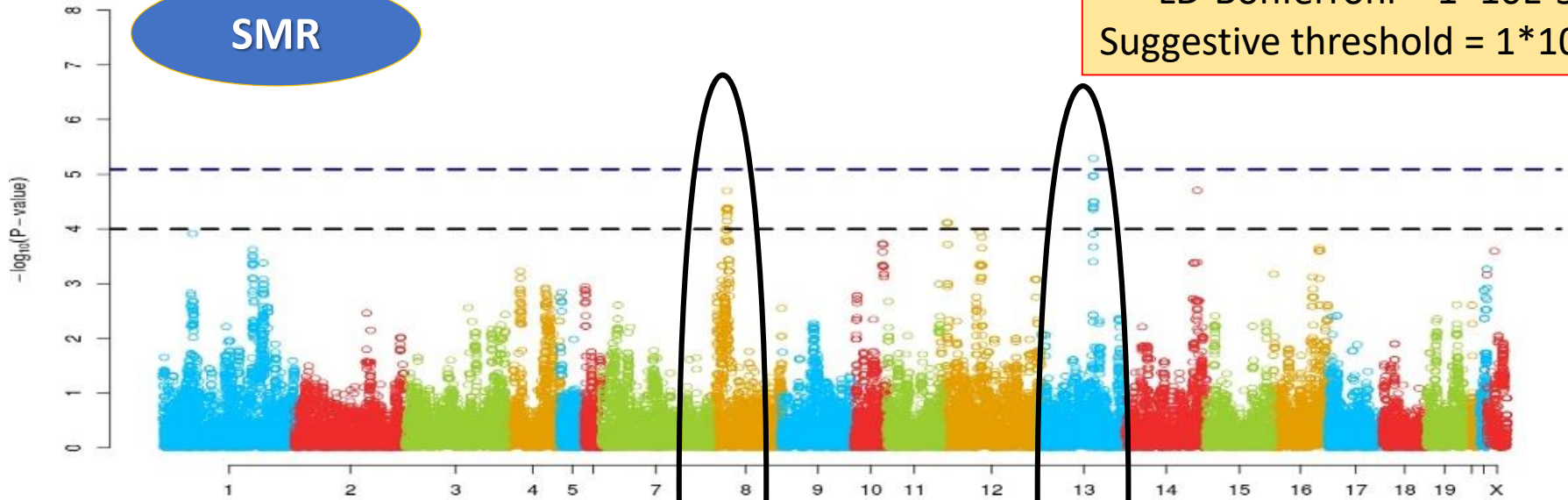
$\pi = 0,9988$

- Mean
- Systematic effects:
  - Month-season
  - Sex
  - Parity order
  - Line

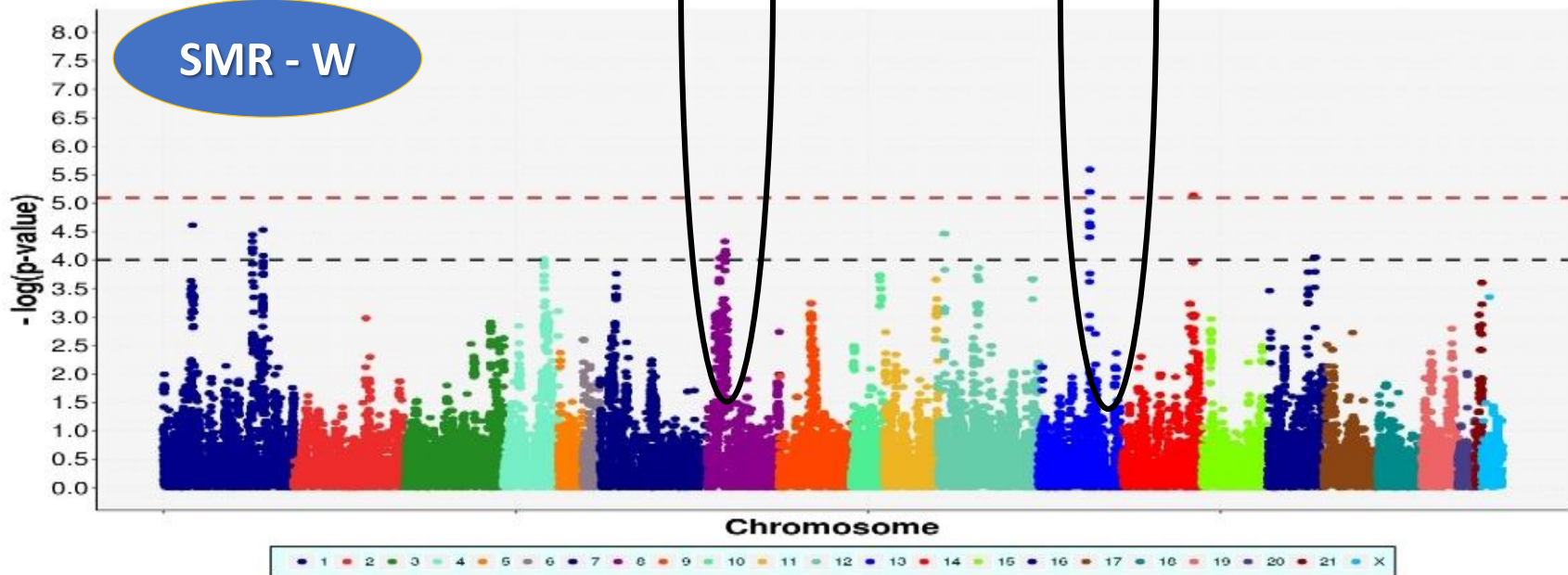
# Results y Discussion (manhattan plot)

SMR

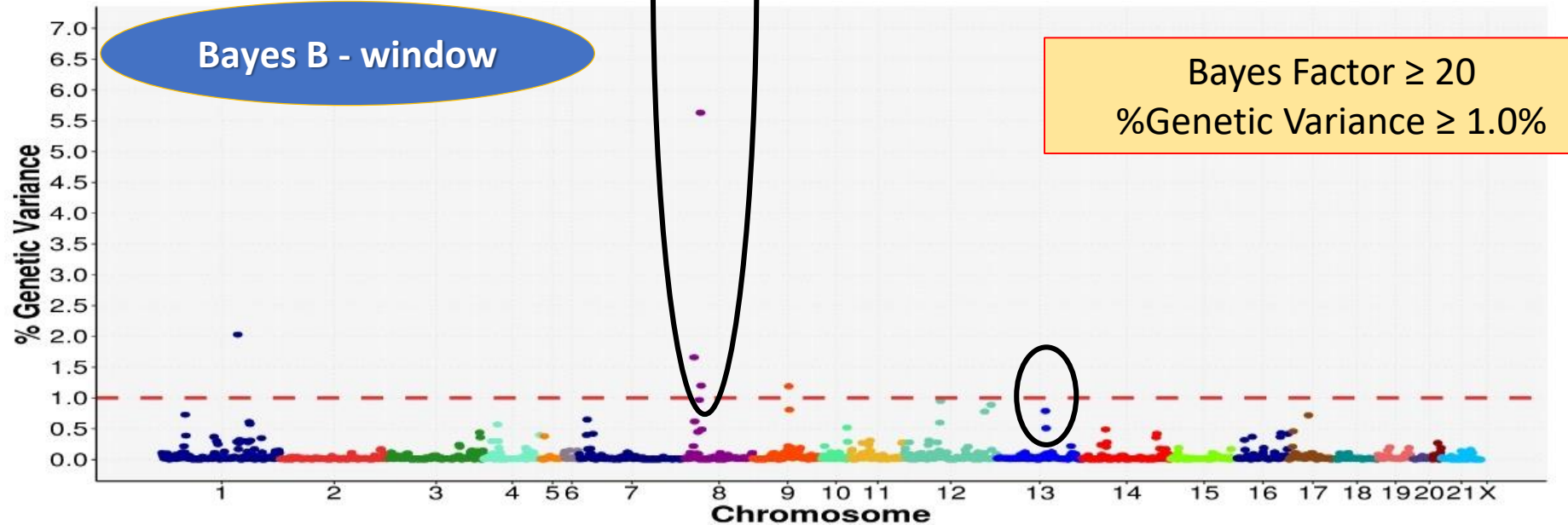
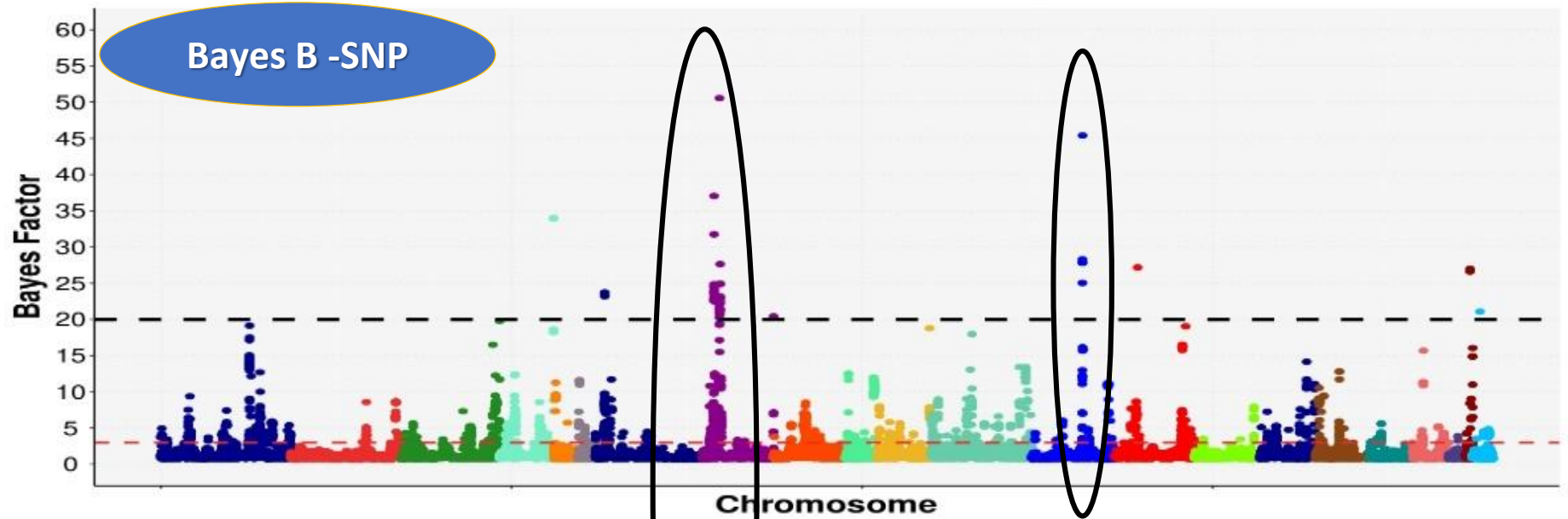
LD-Bonferroni =  $1 \times 10^{-5}$   
Suggestive threshold =  $1 \times 10^{-4}$



SMR - W



# Results y Discussion (manhattan plot)



# Results and Discussion

- Polymorphisms on the chromosomes 1, 8, 12, 13 and 14.
- 88 genes located in the associated regions.

Marker	OCU	Position (Mb)	SMR	SMR – W	BF	Nº of Window (%GV)
<b>Affx-151803947</b>	1	121.28	N.A	3.62E-05	N.A	118 (1.98%)
<b>Affx-151900210</b>	8	25.22	7.16E-05	4.75E-05	42.24	841 (5.47%)
<b>Affx-151808634</b>	8	25.86	4.15E-05	6.83E-05	23.98	841 (5.47%)
<b>Affx-151824236</b>	8	26.11	N.A	8.00E-05	21.08	842 (1.24%)
<b>Affx-151959973</b>	12	7.20	7.72E-05	3.48E-05	N.A	1167 (0.27%)
<b>Affx-151801561</b>	13	84.53	4.02E-05	6.43E-06	25.12	1380 (0.75%)
<b>Affx-151846540</b>	13	84.73	1.08E-05	6.38E-06	25.74	1380 (0.75%)
<b>Affx-151790364</b>	13	84.75	1.06E-05	6.43E-06	24.24	1380 (0.75%)
<b>Affx-151939801</b>	13	85.31	N.A	2.58E-06	44.27	1381 (0.54%)

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# Results and Discussion

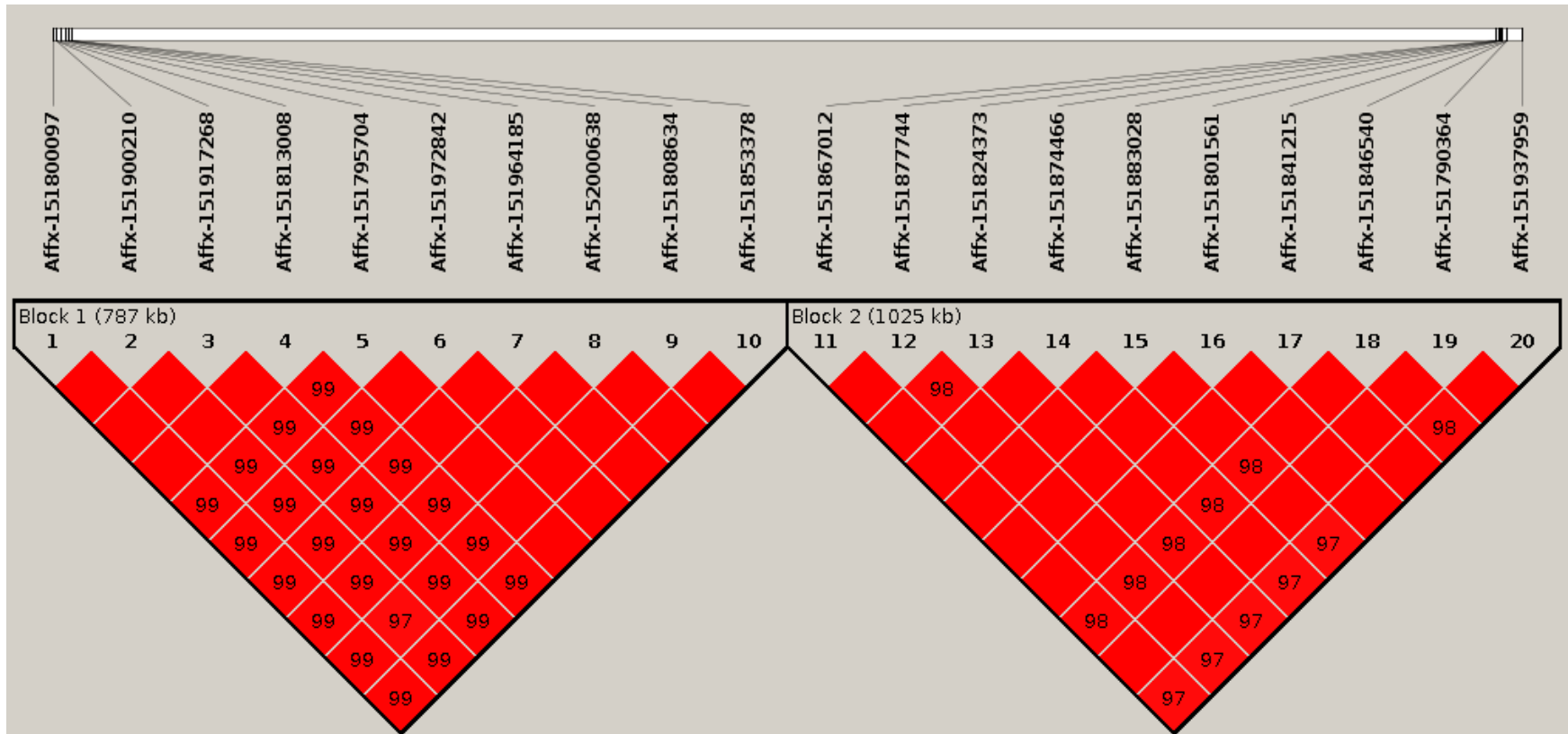
Relevant genes	OCU*	Functional Annotation
ARAP1	1	Lipid binding. Regulator of Molecular function.
STARD10	1	Lipid transport, binding and localization.
MTMR2	1	Lipid metabolic processes.
APOLD1	8	Lipid transport, binding and localization.
EWSR1	13	Brown adipocyte development (BAD).

\* Rabbit chromosome.



# Results and Discussion

- Linkage disequilibrium blocks.



OCU 8

OCU 13

# Conclusions

- The **GWAS** detected **SNPs** and **genomic regions associated** with intramuscular fat, mainly on **chromosome 8 and 13**.
- The genes **ARAP1, STARD10, APOLD1, MTMR2 y EWSR1** were related to **lipid metabolism and adipogenesis** (brown).
- The **intramuscular fat** has an important **polygenic** component.



# Acknowledgments

ICTA

igmm  
INSTITUTE OF GENETICS  
& MOLECULAR MEDICINE



Thank you for your attention!