GEroNIMO and RUMIGEN Joint Final Event

Breeding the Future

Genomics, Epigenomics & Societal Acceptability for Sustainability in Livestock

Perspectives on the use of the EpiChip for breeding and animal husbandry purposes

Oscar González-Recio *and RUMIGEN partners*

THE UNIVERSITY *of* EDINBURGH
The Royal (Dick) School
of Veterinary Studies

ROSLIN

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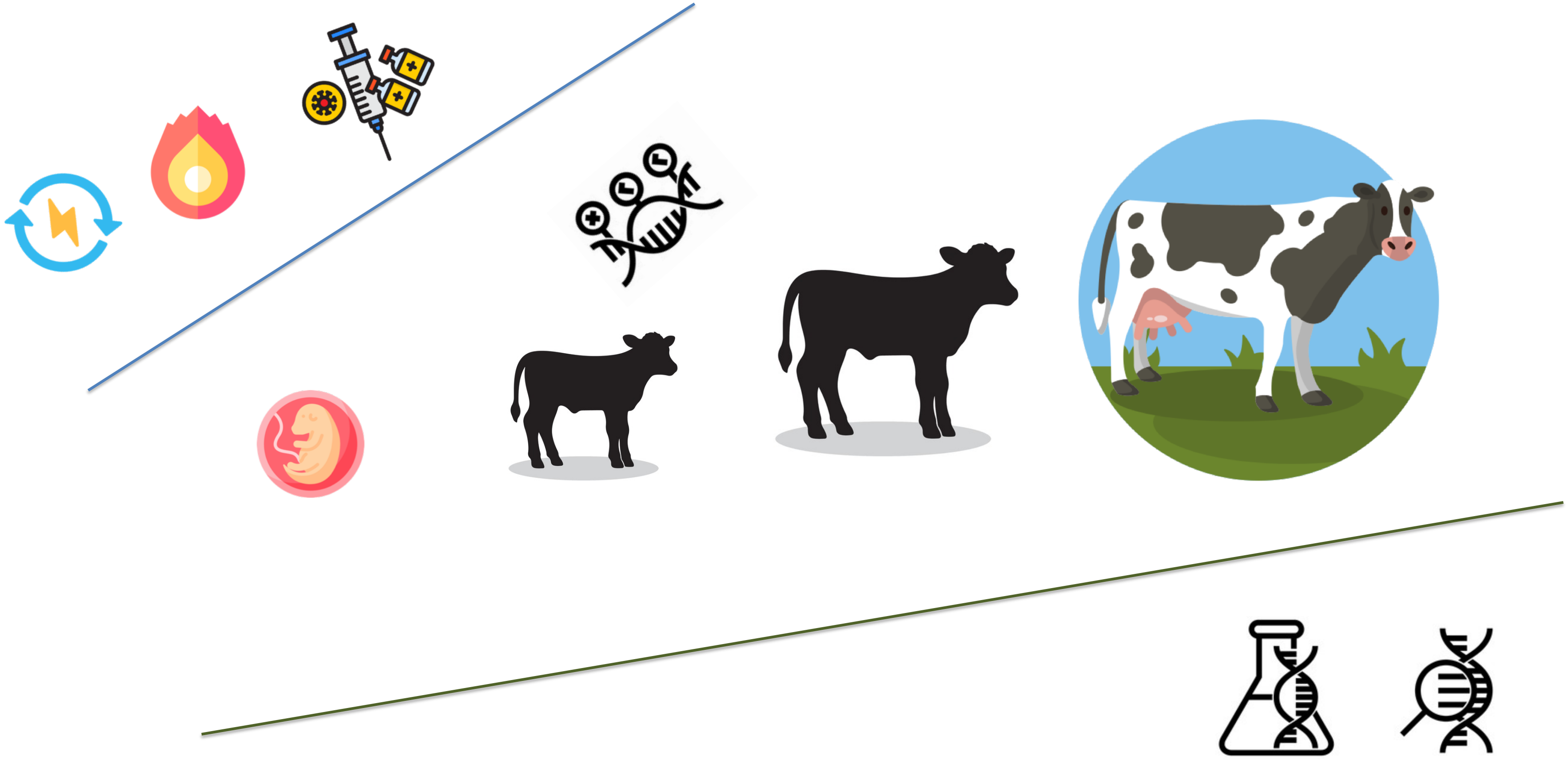
Rumigen

TOWARDS IMPROVEMENT OF **RUMI**NANT BREEDING
THROUGH **GEN**OMIC AND EPIGENOMIC APPROACHES

Why same genetics perform different in different environment?



01 What we learnt in RUMIGEN about epigenetics

02 What challenges we did not fully solve

03 What role will epigenetics play in future cattle breeding programs

04 Final message

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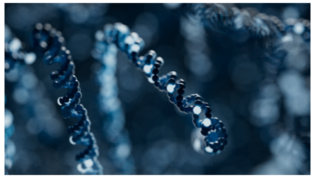
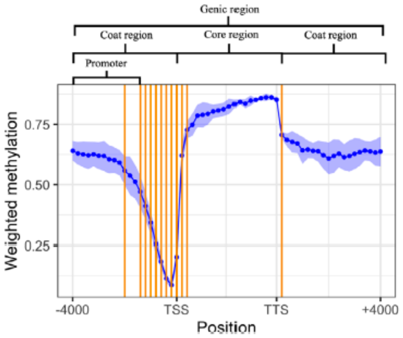
What we have learnt

New sequencing and genotyping technologies



Oxford Nanopore Technologies

Direct methylation sequencing



Select CpG for EpiChip

methylation status ~54,000 CpGs

RRBS + WG-BiS

What we have learnt

ENVIRONMENT

- The environment plays a crucial role in modelling the epigenome in dairy cattle
- From embryo development to adulthood
- Although mainly dynamic, some of these epigenetic changes remain for a substantial period of time

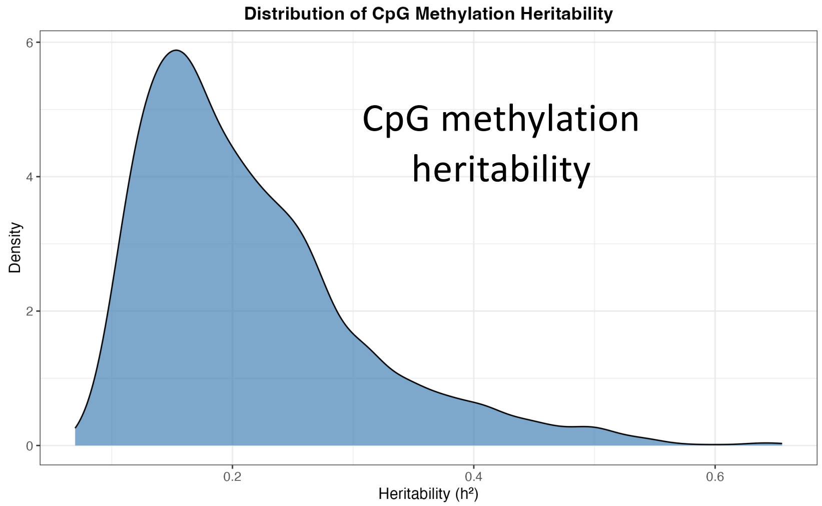
GENETICS

- Susceptibility to methylation at birth is heritable
- This is different from epigenetic inheritance or transgenerational epigenetics 🚫

○ 450 newborn calves

○ Single Step GBLUP

$$\mathrm{CpG\_Methylation}_j = \mu + \mathrm{birth\_season} + u + e$$



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- Epigenetic information needs to be treated accordingly in statistical models / mediator trait

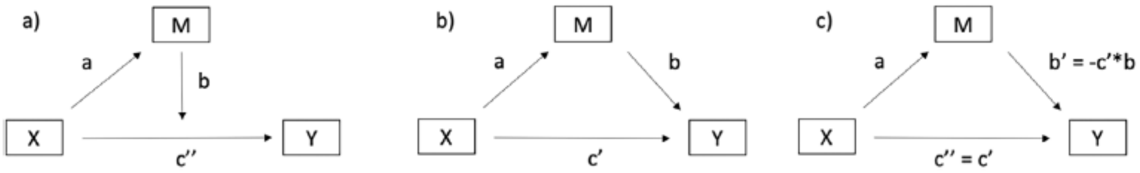

FIGURE 2 | Scheme of how recursive effects of methylation over the phenotype are proposed in the generator (a) and statistical models (b). These models can be reparametrised to prove recursiveness (c), where (b) is impacted by (c') creating an effect of methylation marks on the phenotype combined with the animal's direct genetic effect.


Journal of Animal Breeding and Genetics

WILEY

ORIGINAL ARTICLE OPEN ACCESS

A Recursive Model Approach to Include Epigenetic Effects in Genetic Evaluations Using Simulated DNA Methylation Effects

Adrián López-Catalina[1,2,3] | Mohamed Ragab[1] | Antonio Reverter[3] | Oscar González-Recio[1]

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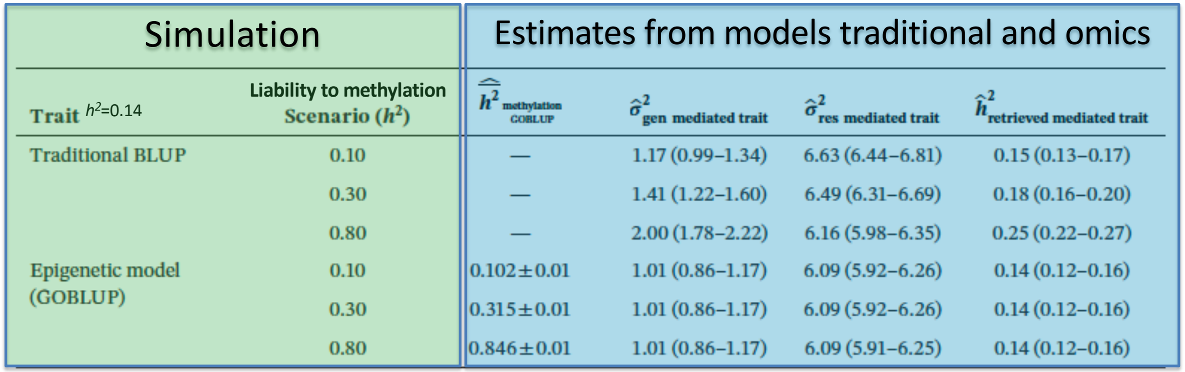
- Additive variance in traditional models captures part of epigenetic variance (in simulations)



Simulation		Estimates from models traditional and omics			
Trait h^2=0.14	Liability to methylation Scenario (h^2)	$\widehat{h^2}_{\text{methylation GOBLUP}}$	$\hat{\sigma}^2_{\text{gen mediated trait}}$	$\hat{\sigma}^2_{\text{res mediated trait}}$	$\hat{h}^2_{\text{retrieved mediated trait}}$
Traditional BLUP	0.10	—	1.17 (0.99–1.34)	6.63 (6.44–6.81)	0.15 (0.13–0.17)
	0.30	—	1.41 (1.22–1.60)	6.49 (6.31–6.69)	0.18 (0.16–0.20)
	0.80	—	2.00 (1.78–2.22)	6.16 (5.98–6.35)	0.25 (0.22–0.27)
Epigenetic model (GOBLUP)	0.10	0.102 ± 0.01	1.01 (0.86–1.17)	6.09 (5.92–6.26)	0.14 (0.12–0.16)
	0.30	0.315 ± 0.01	1.01 (0.86–1.17)	6.09 (5.92–6.26)	0.14 (0.12–0.16)
	0.80	0.846 ± 0.01	1.01 (0.86–1.17)	6.09 (5.91–6.25)	0.14 (0.12–0.16)

Note: The variances and h^2 estimates and their HPD intervals (95%) across scenarios for the epi-moderated traits are presented in the third, fourth and fifth columns as well as the estimated average heritability and their standard deviations across the 13 windows in the GOBLUP model in the second column.

What we have learnt

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- The environment plays a crucial role in modelling the epigenome
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- Although mainly dynamic, some of these epigenetic changes remain for a substantial period of time

GENETICS

- Susceptibility to methylation at birth is heritable
- This is different from epigenetic inheritance or transgenerational epigenetics
- Epigenetic information needs to be treated accordingly in statistical models / mediator trait
- Additive variance in traditional models captures part of epigenetic variance (in simulations)
- No relevant increase in predicting true breeding value using omics models (in simulations)

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What challenges remain

ENVIRONMENT

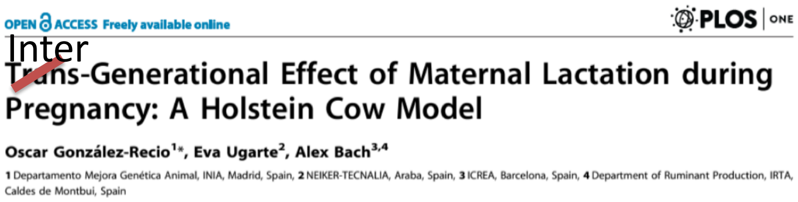
- Strategies to reverse methylation status
- Other factors affecting the methylation – **exposome - phenomics**

GENETICS

- In depth study of stability of methylation marks across life stages and their heritability
- Impact on important productive traits
- Genetic correlation between liability to methylation and relevant traits
- Performance of developed statistical method models on real data

What role will epigenetics play in breeding programs

Replacement born from primiparous cow – better epigenetic profile



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Inter
~~Tra~~ns-Generational Effect of Maternal Lactation during Pregnancy: A Holstein Cow Model

Oscar González-Recio[1]*, Eva Ugarte[2], Alex Bach[3,4]

1 Departamento Mejora Genética Animal, INIA, Madrid, Spain, 2 NEIKER-TECNALIA, Araba, Spain, 3 ICREA, Barcelona, Spain, 4 Department of Ruminant Production, IRTA, Caldes de Montbui, Spain

What role will epigenetics play in breeding programs

Replacement born from primiparous cow – better epigenetic profile

Primiparous cows – lower EBV reliability

- **Genomic information** becomes more relevant to **plan replacement**

- **Genomics → Epigenetics**

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➢**Genomic information** becomes more relevant to **plan replacement**

➢**Genomics → Epigenetics**

Tips:

✓Promote genomic selection in underdeveloped breeding programs

✓**Stablished breeding programs →Early stage for adoption. Need further research for commercial implementation (high TRL)**

Rumigen

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- **Genomic information** becomes more relevant to **plan replacement**
- **Genomics → Epigenetics**
- **Epigenetics → Novel traits**
  - ✓ **Liability to methylation in genomic regions associated to traits of interest**
  - ✓ **Epigenetic age: functional longevity and welfare**

What role will epigenetics play in breeding programs

Final message:

Start creating a reference population with epigenetic information with the RUMIGEN Epichip

or

begin the path, and learn from our mistakes


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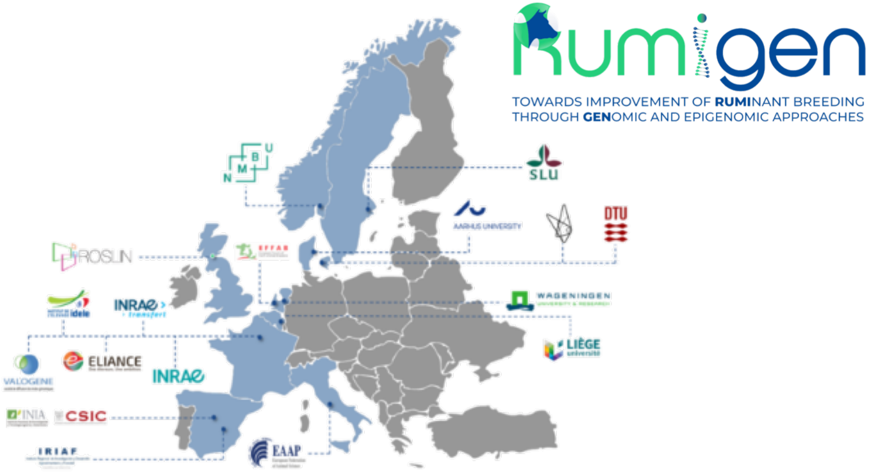
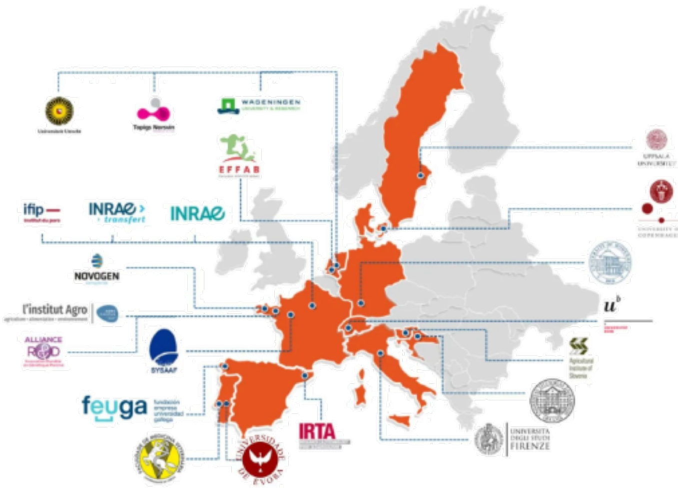
THANK YOU





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