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FONDAZIONE  
INVERNIZZI | Centro di ricerca Romeo ed Enrica Invernizzi  
per le produzioni lattiero-casearie sostenibili

# Il contributo della genetica all'incremento della produttività in zootecnia e alla soluzione dei problemi ambientali causati dall'intensificazione

*Paolo Ajmone Marsan*

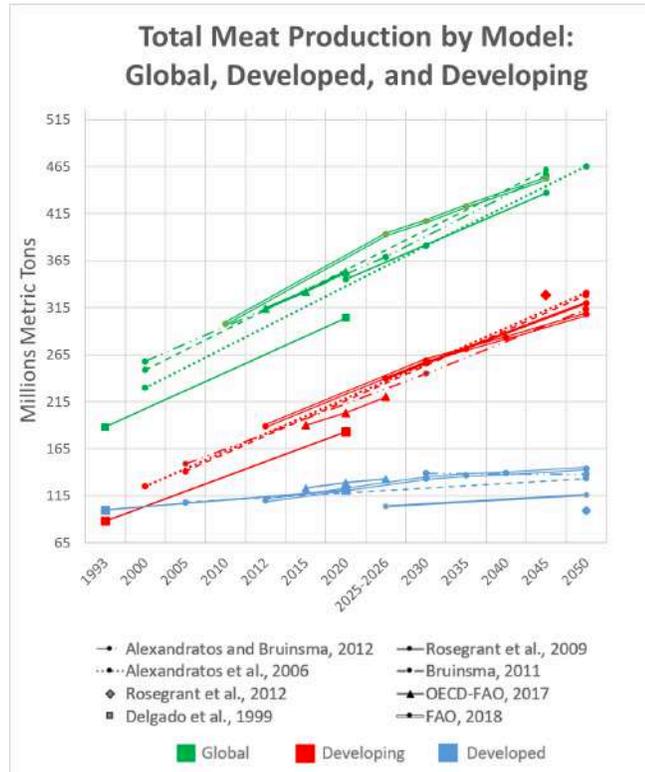
*Dipartimento di Scienze Animali della Nutrizione e degli Alimenti - DIANA*

*Centro di Ricerca Romeo ed Enrica Invernizzi sulle produzioni lattiero-casearie sostenibili – CREI*

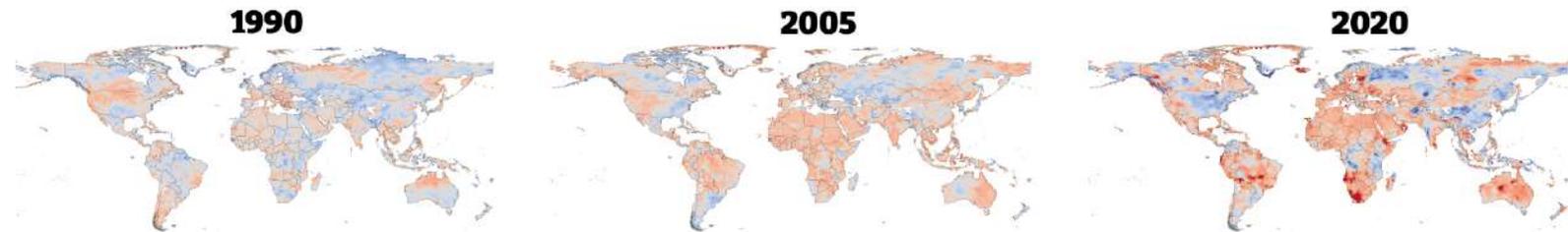
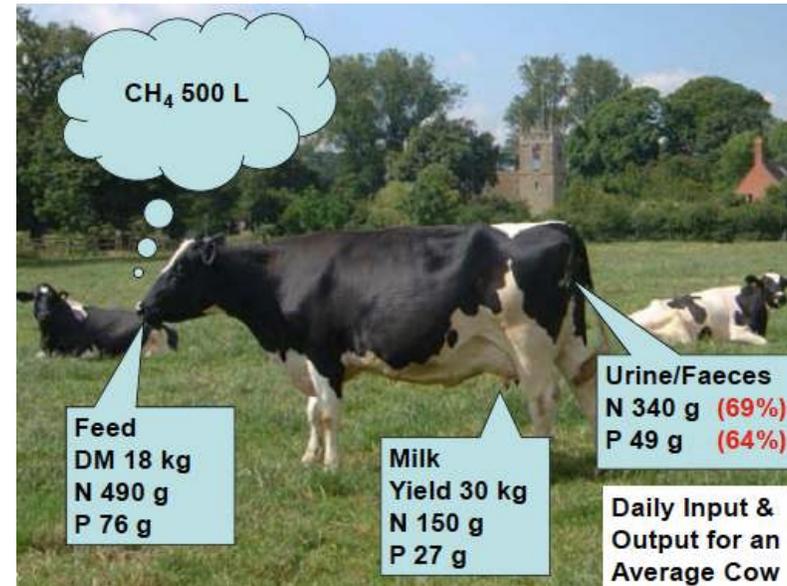
*Università Cattolica del S. Cuore*

# Sfide che la zootecnia deve affrontare

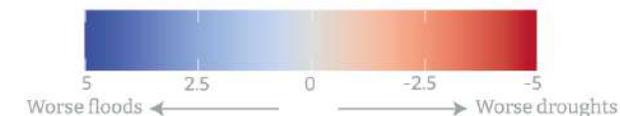
Soddisfare una domanda in crescita



Mitigare i cambiamenti climatici



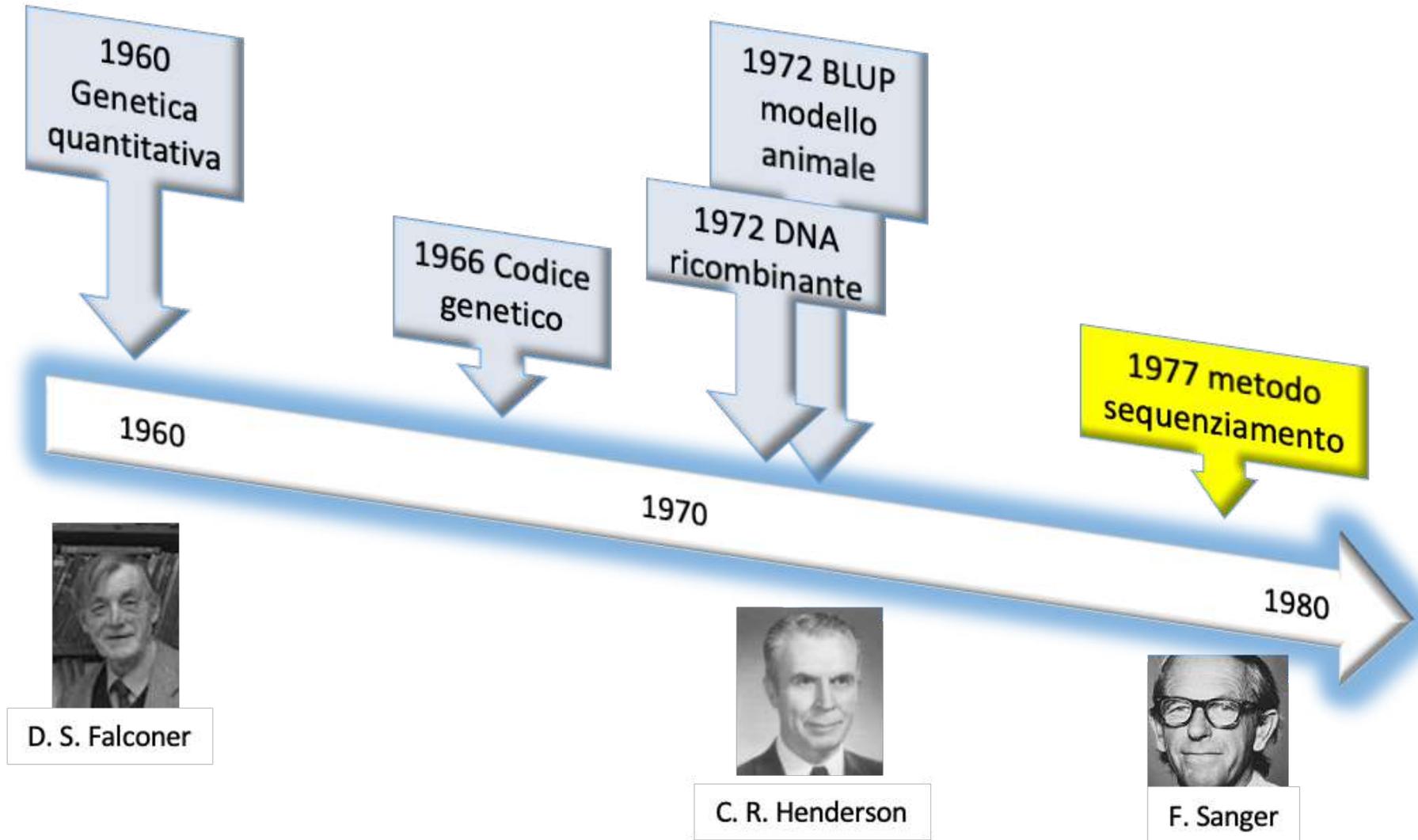
Adattarsi ai cambiamenti climatici





Genetica: da dove siamo partiti

# Verso l'utilizzo del DNA

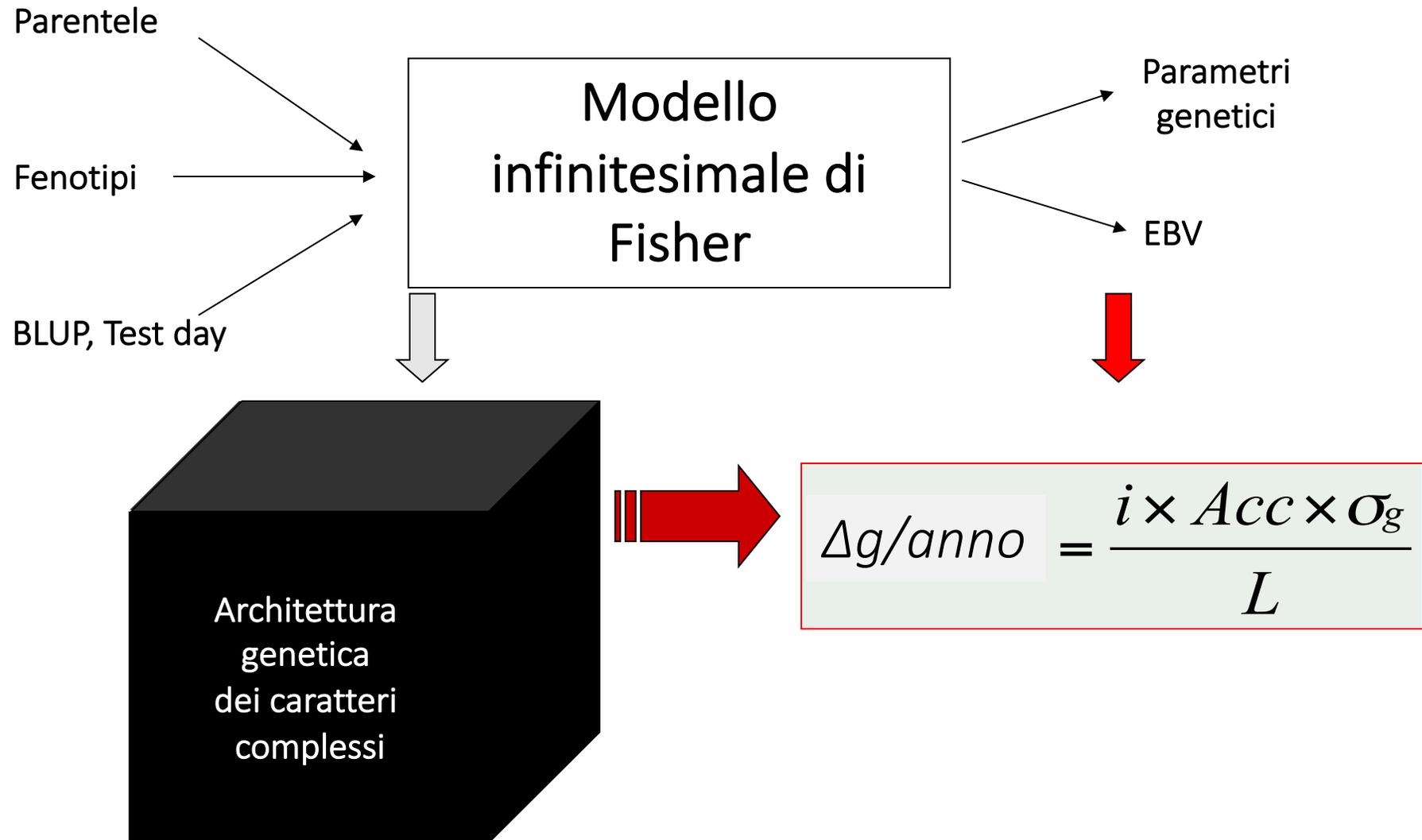


# Valutazione genetica

$$P = G + E$$

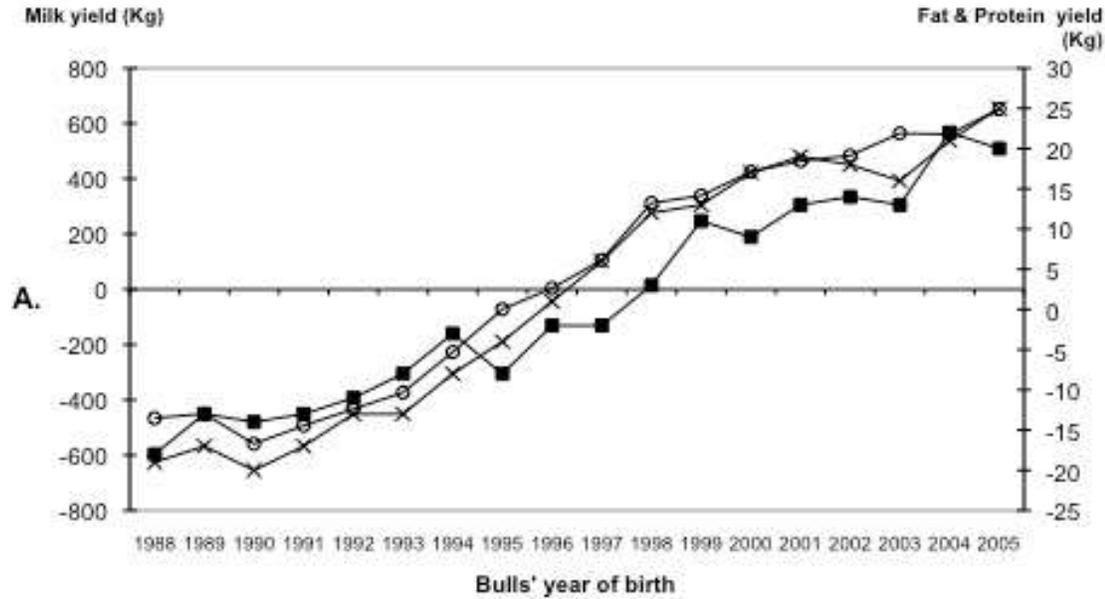


# Selezione tradizionale

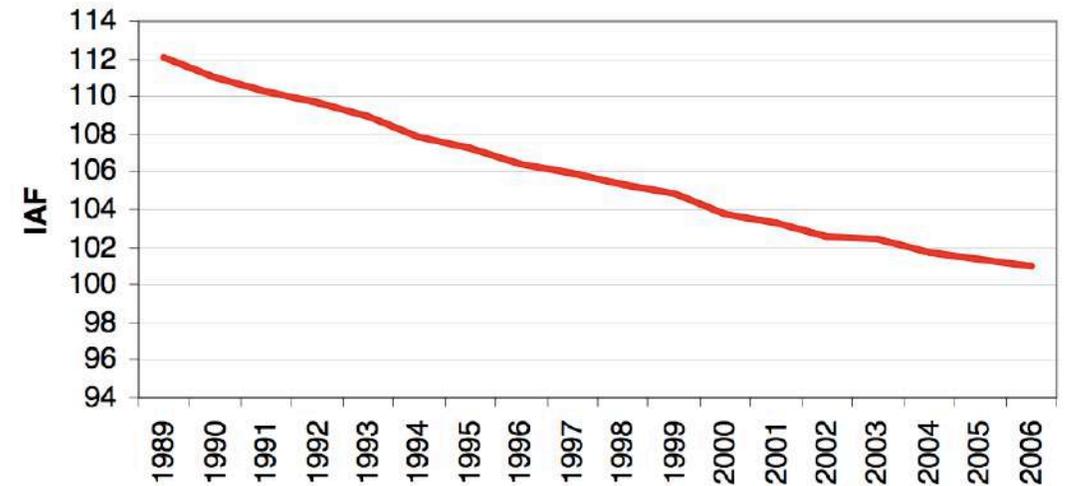


# Selezione tradizionale

Trend genetici per latte, grasso e proteina



Trend genetico per fertilità



# Evoluzione dell'indice di selezione nella Frisone Italiana



<b>Carattere</b>	<b>ILQ 1989-1990</b>	<b>ILQ 1991-1993</b>	<b>ILQM</b>	<b>PFT 2002-2009</b>	<b>PFT 2009-</b>
Latte kg	0	-27	-21	0	0
Grasso kg	33	6	5	12	8
Proteina kg	67	67	54	42	36
Grasso %	0	0	0	2	2
Proteina %	0	0	0	3	3
Tipo	0	0	0	4	4
Mammella	0	0	20	13	13
Arti e Piedi	0	0	0	6	6
Cellule	0	0	0	10	10
Longevità	0	0	0	8	8
Fertilità	0	0	0	0	10



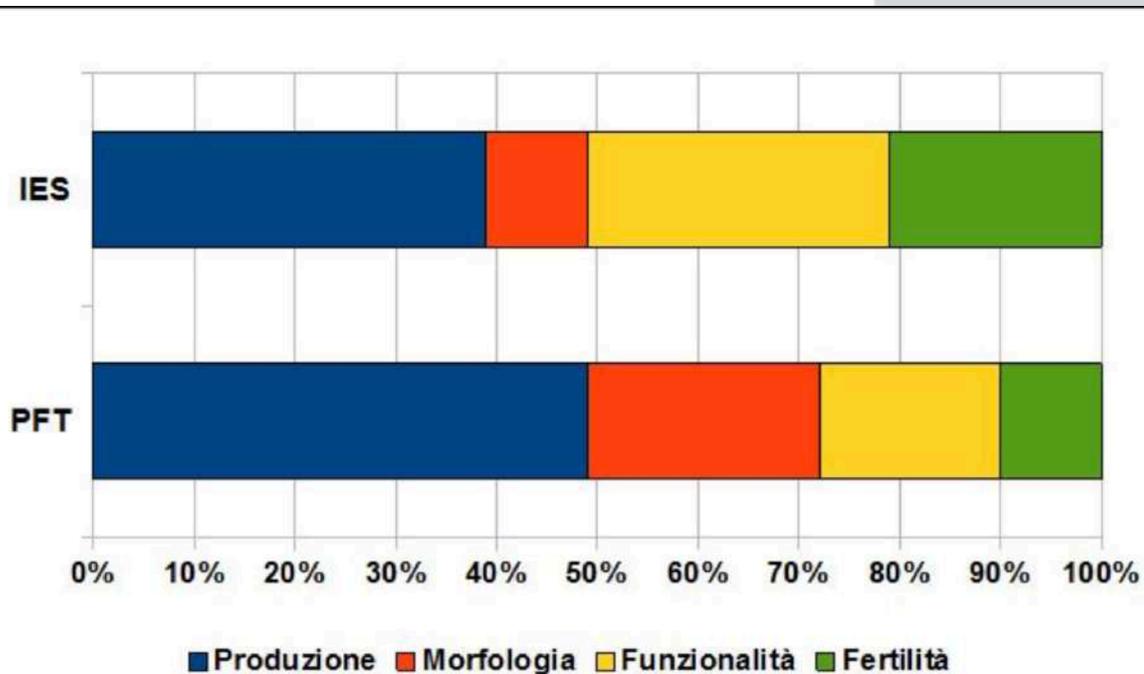
Dove siamo

# Frisona, Indice Economico Salute (IES) (2016)

$$\text{IES} = 0,32 * \text{grasso kg} + 1,37 * \text{proteina kg} + 0,043 * \text{grasso\%} * 100 + 0,0188 * \text{proteina} * 100 - 5 * \text{statura} + 4 * \text{locomozione} + 1 * \text{profondità mammella} + 20,51 * (\text{longevità} - 100)/5 + 6 * ((\text{scs}-100)/5,7) + 18 * (\text{fertilità} - 100)/5 + 3,35 * ((\text{bcs}-100)/5) + 3,51 * ((\text{facilità parto materna} - 100)/5)$$

che determina un rapporto tra produzione, morfologia e funzionalità pari al 39:10:51

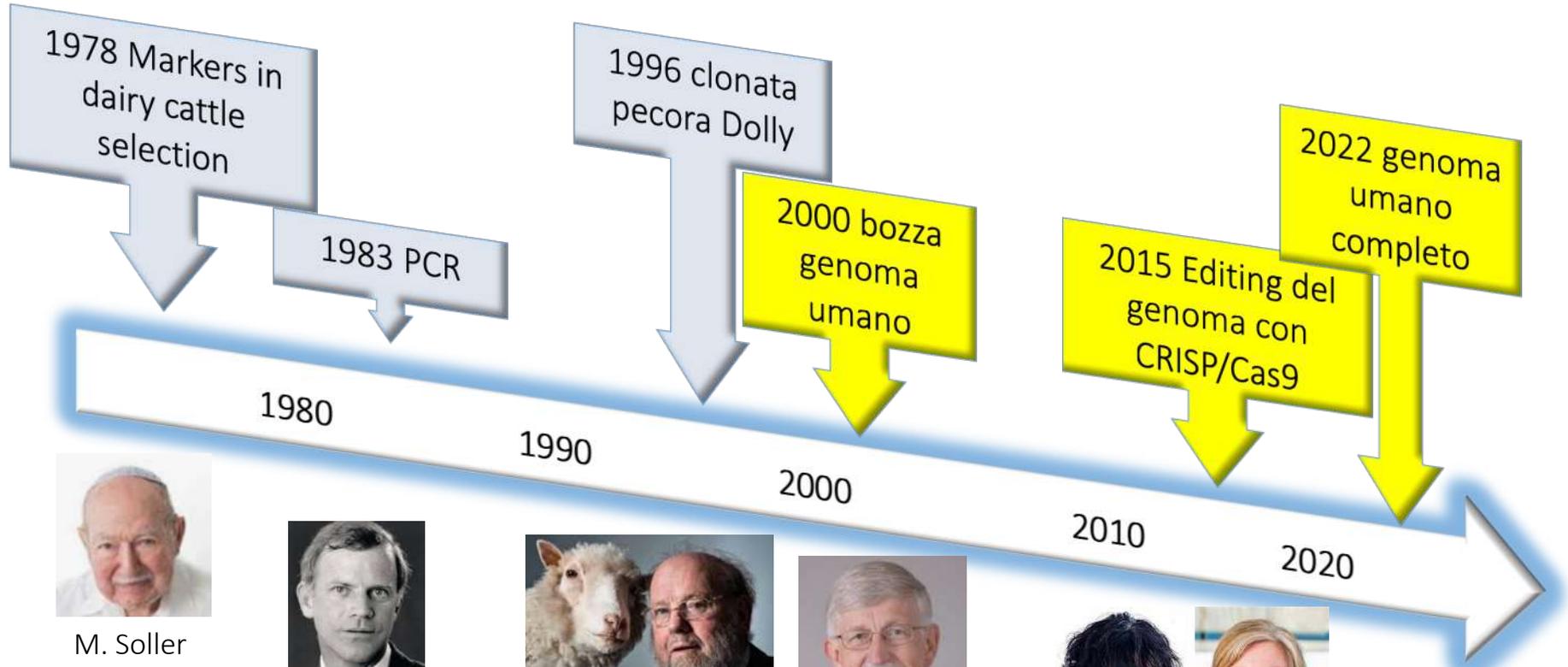
PRODUZIONE	PESO	MORFOLOGIA	PESO	FUNZIONALITÀ	PESO
Grasso	8	Statura	-5	Longevità	20,51
Proteina	27,62	Locomozione	4	Cellule Somatiche	6
Grasso %	1	Profondità Mammella	1	Facilità Parto Vacca	3,51
Proteina %	2			Fertilità	18
				Body Condition Score	3,35



IES 39:10:51

PFT 49:23:28

# Nuovo millennio: era del DNA



M. Soller



C. Mullis



I. Wilmut



F. Collins



C. Venter

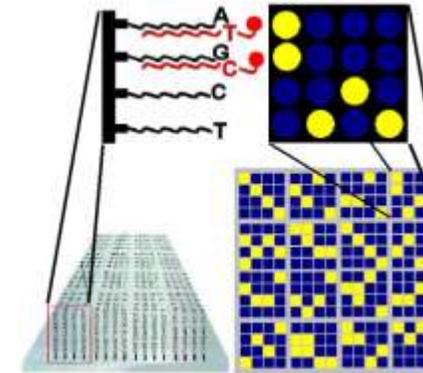
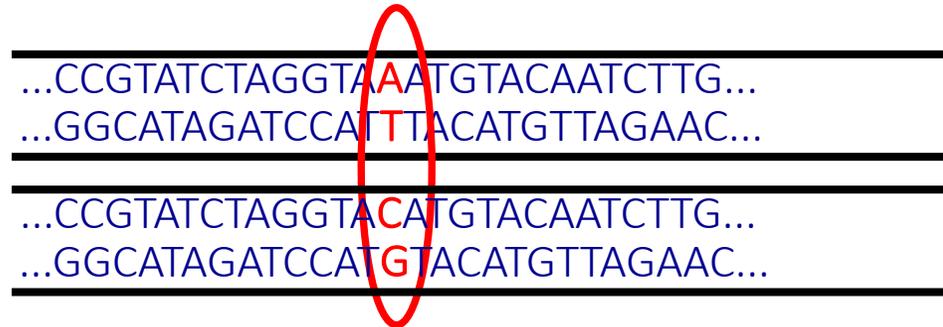


E. Charpentier, J.A. Doudna

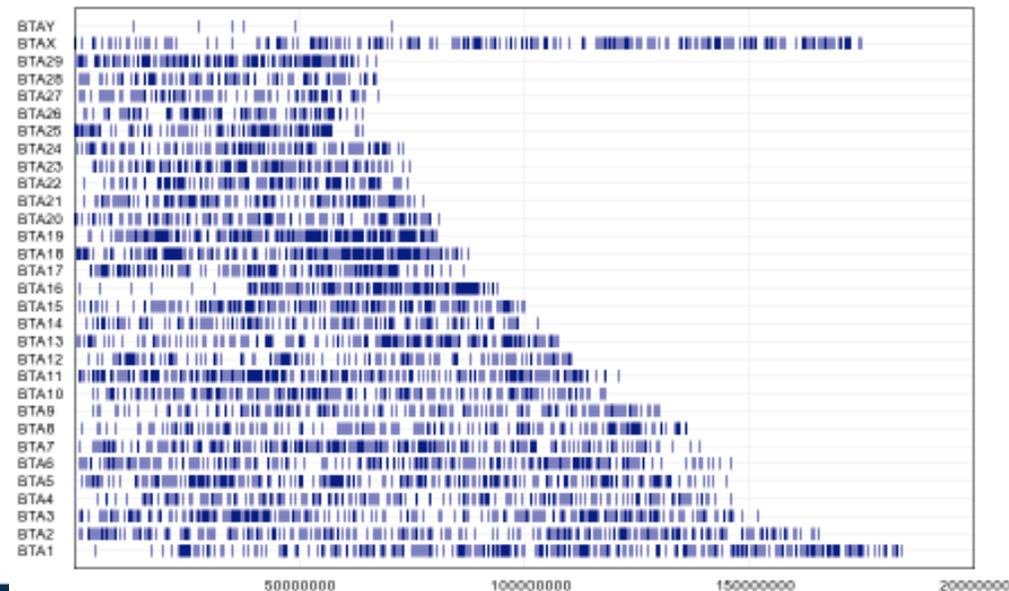
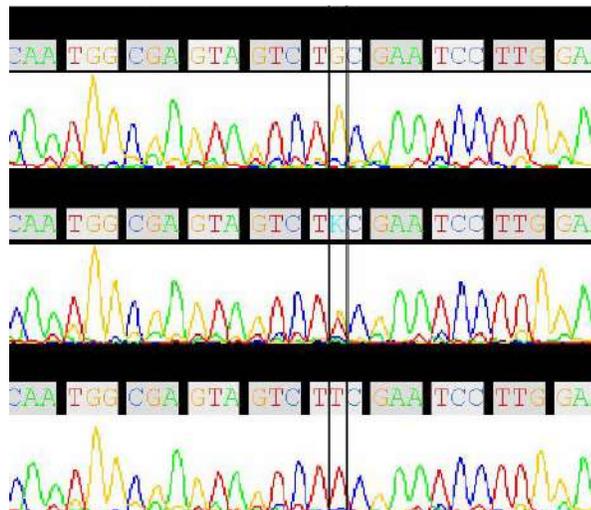


# Single Nucleotide Polymorphisms (SNPs)

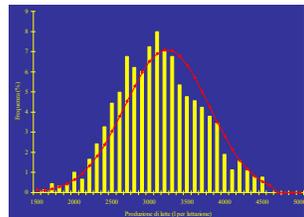
Mutazioni puntiformi in specifiche posizioni lungo il genoma



Analisi su chip/microarray



# Selezione genomica: un cambio di paradigma



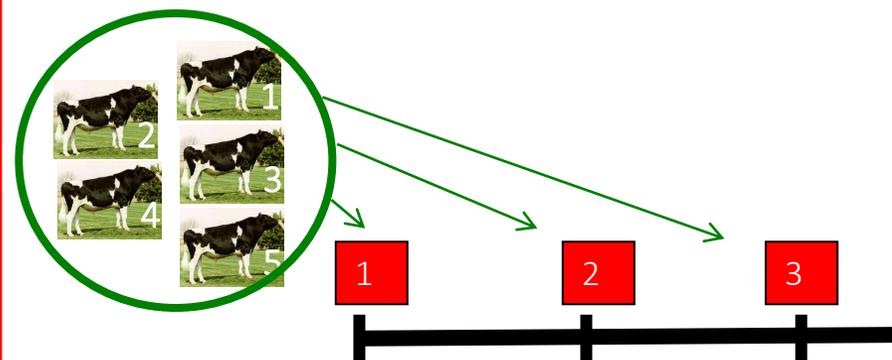
**Selezione tradizionale:**  
Raccolta di fenotipi di molti animali parenti per stimare il **valore dell'intero genoma di un toro o di una vacca**



= EBV

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**Selezione genomica:**  
Raccolta di fenotipi di molti animali per stimare parentela e il **valore di marcatori e aplotipi nell'intera popolazione**



G. Mendel

## Prediction of Total Genetic Value Using Genome-Wide Dense Marker Maps

T. H. E. Meuwissen,\* B. J. Hayes<sup>†</sup> and M. E. Goddard<sup>†,‡</sup>

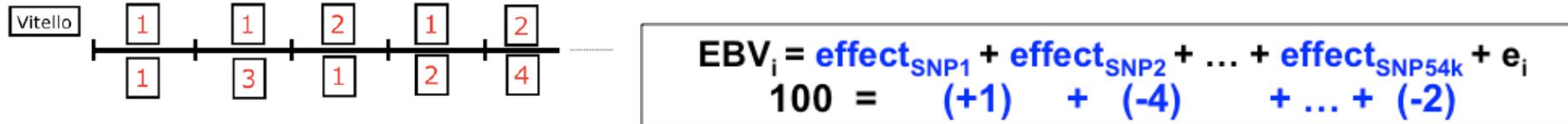
\*Research Institute of Animal Science and Health, 8200 AB Lelystad, The Netherlands, <sup>†</sup>Victorian Institute of Animal Science, Atwood 3049, Victoria, Australia and <sup>‡</sup>Institute of Land and Food Resources, University of Melbourne, Parkville 3052, Victoria, Australia

Manuscript received August 17, 2000 Accepted for publication January 17, 2001

### ABSTRACT

Recent advances in molecular genetic techniques will make dense marker maps available and genotyping many individuals for these markers feasible. Here we attempted to estimate the effects of ~50,000 marker haplotypes simultaneously from a limited number of phenotypic records. A genome of 1000 cM was simulated with a marker spacing of 1 cM. The markers surrounding every 1-cM region were combined into marker haplotypes. Due to finite population size ( $N_e = 100$ ), the marker haplotypes were in linkage disequilibrium with the QTL located between the markers. Using least squares, all haplotype effects could not be estimated simultaneously. When only the biggest effects were included, they were overestimated and the accuracy of predicting genetic values of the offspring of the recorded animals was only 0.32. Best linear unbiased prediction of haplotype effects assumed equal variances associated to each 1-cM chromosomal segment, which yielded an accuracy of 0.73, although this assumption was far from true. Bayesian methods that assumed a prior distribution of the variance associated with each chromosome segment increased this accuracy to 0.85, even when the prior was not correct. It was concluded that selection on genetic values predicted from markers could substantially increase the rate of genetic gain in animals and plants, especially if combined with reproductive techniques to shorten the generation interval.

# La Selezione Genomica in azione



$$DGV_i = g_{SNP1} * effect_{SNP1} + g_{SNP2} * effect_{SNP2} + \dots + g_{SNP54k} * effect_{SNP54k} + e_i$$

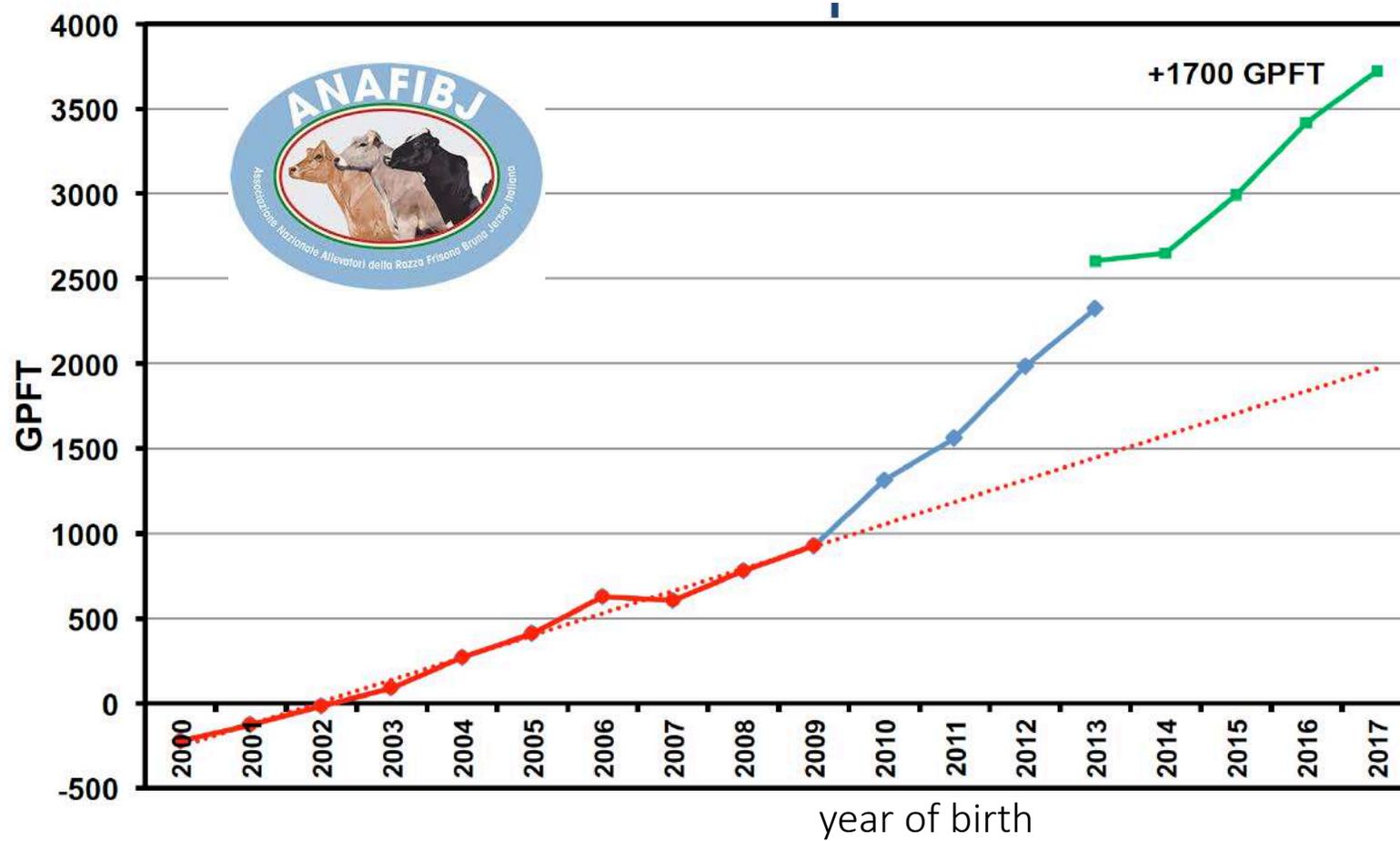
$$DGV_i = 0 * (+1) + 2 * (-4) + \dots + 1 * (-2)$$

DGV



G-EBV

# Selezione Genomica



Great impact in (dairy cattle) breedin



Raffaella  
Finocchiaro



Jan-Thijs  
Van Kaam

# Produttività negli ultimi 100 anni

8 Kg/d



**1930**

1.5 t/ha



40 Kg/d

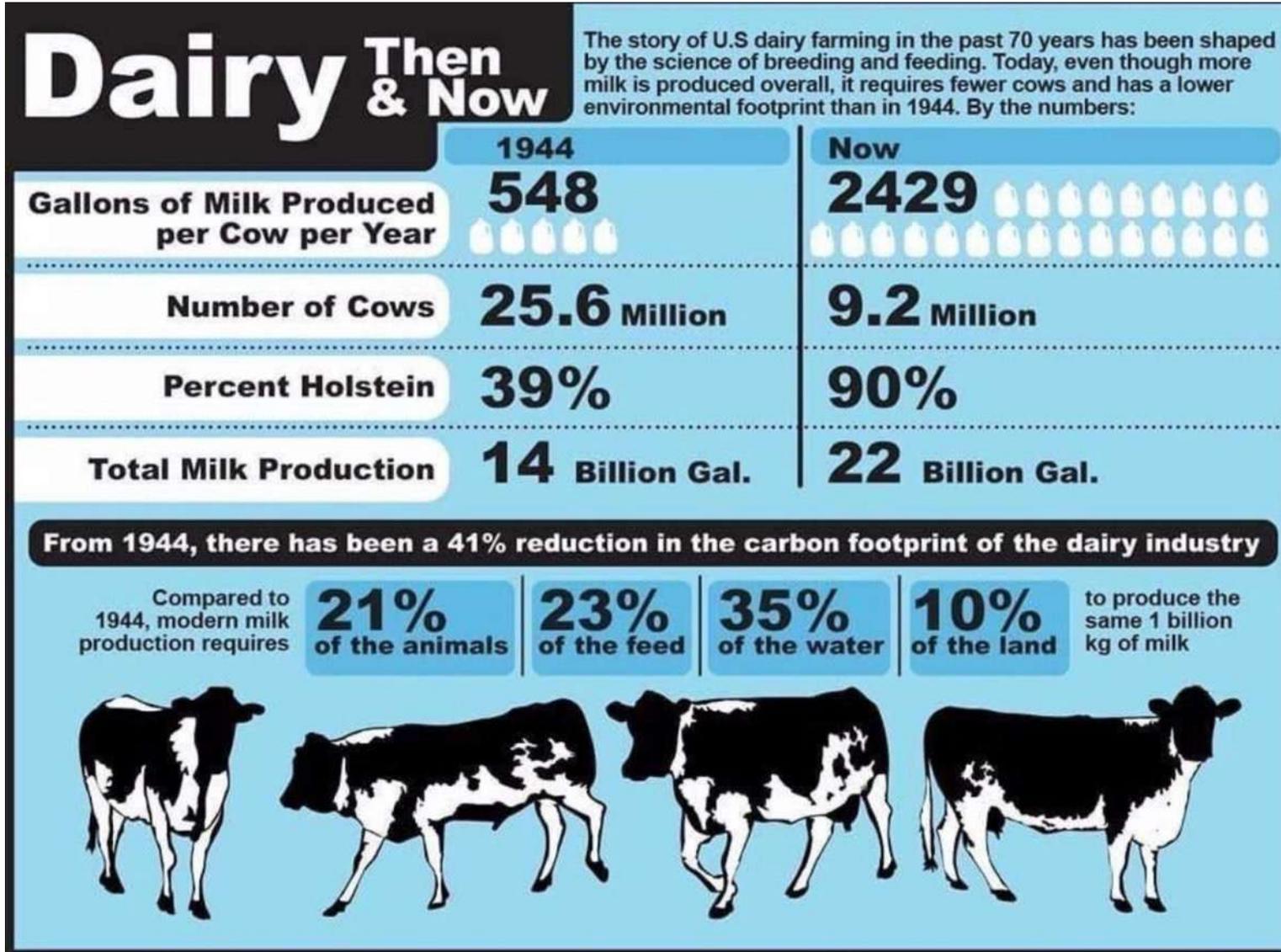


**2024**

15 t/ha

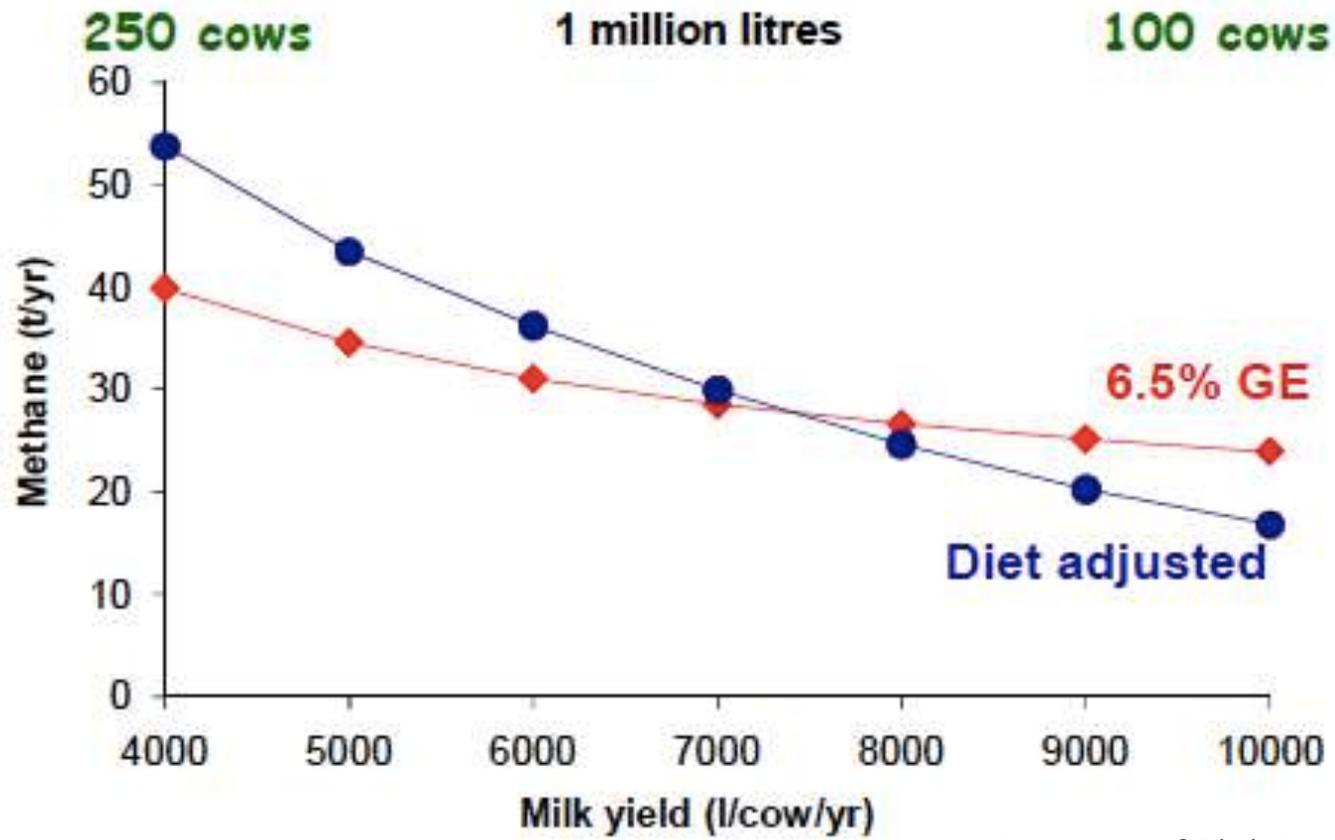


# Produttività negli ultimi 100 anni



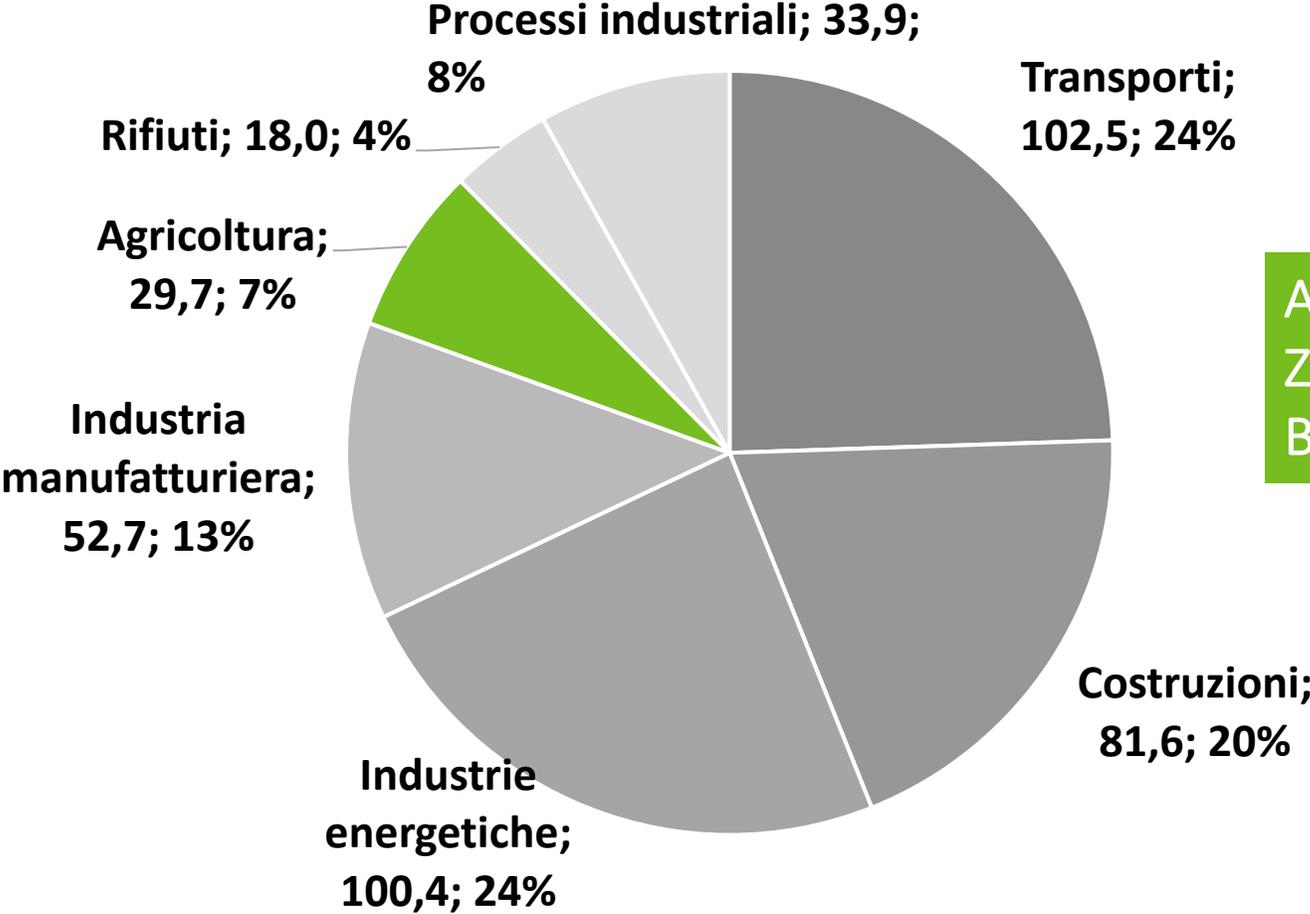
# Efficienza e impatto

Produzione di latte ed emissioni di metano



Courtesy of Phil Garnsworthy

# Dati ISPRA



Agricoltura: 29.7 Mt CO<sub>2</sub>-eq  
Zootecnia: 23.7 Mt CO<sub>2</sub>-eq  
Bovino da Latte: 12.5 Mt CO<sub>2</sub>-eq

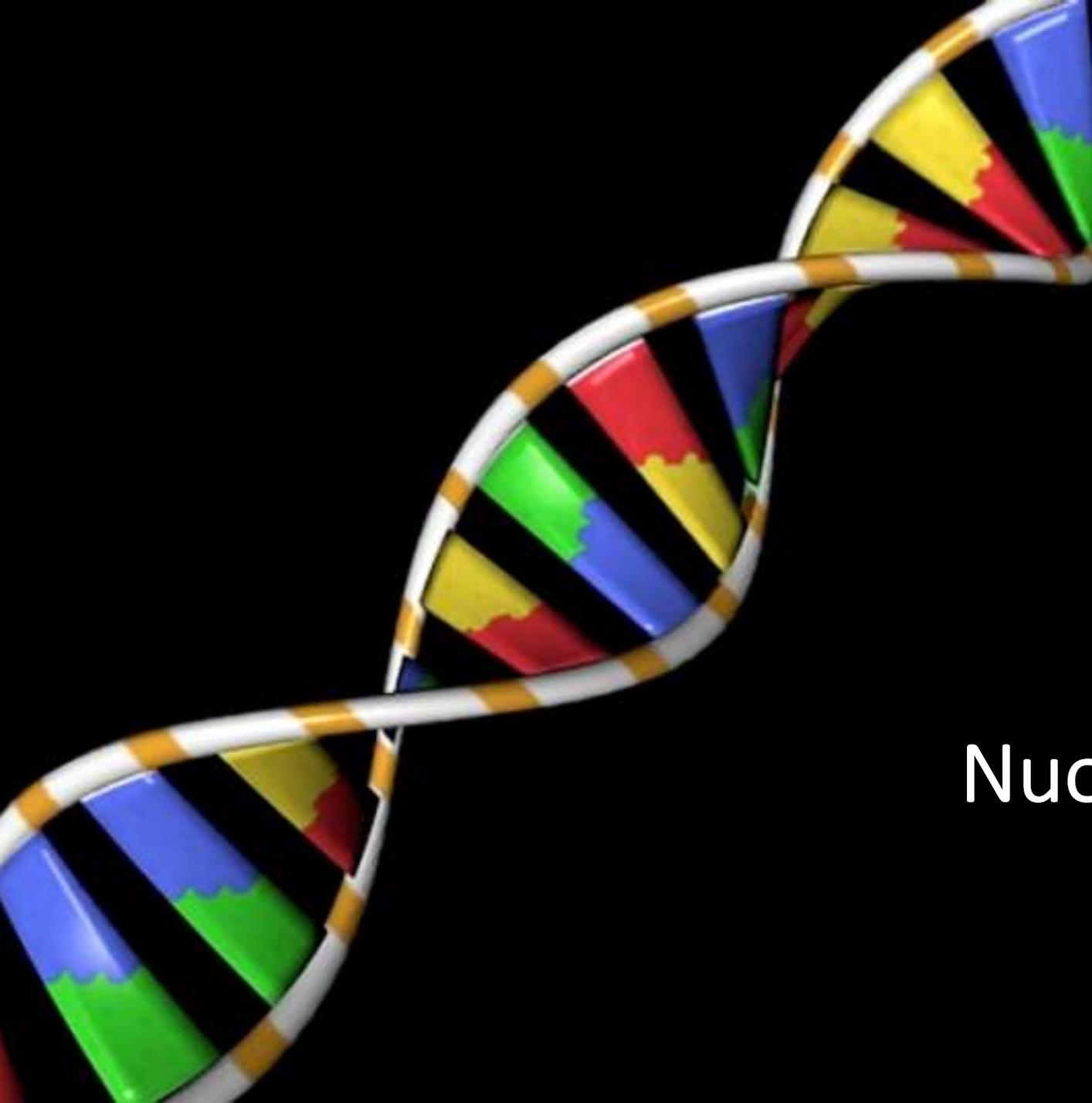


4.2%

nLCA

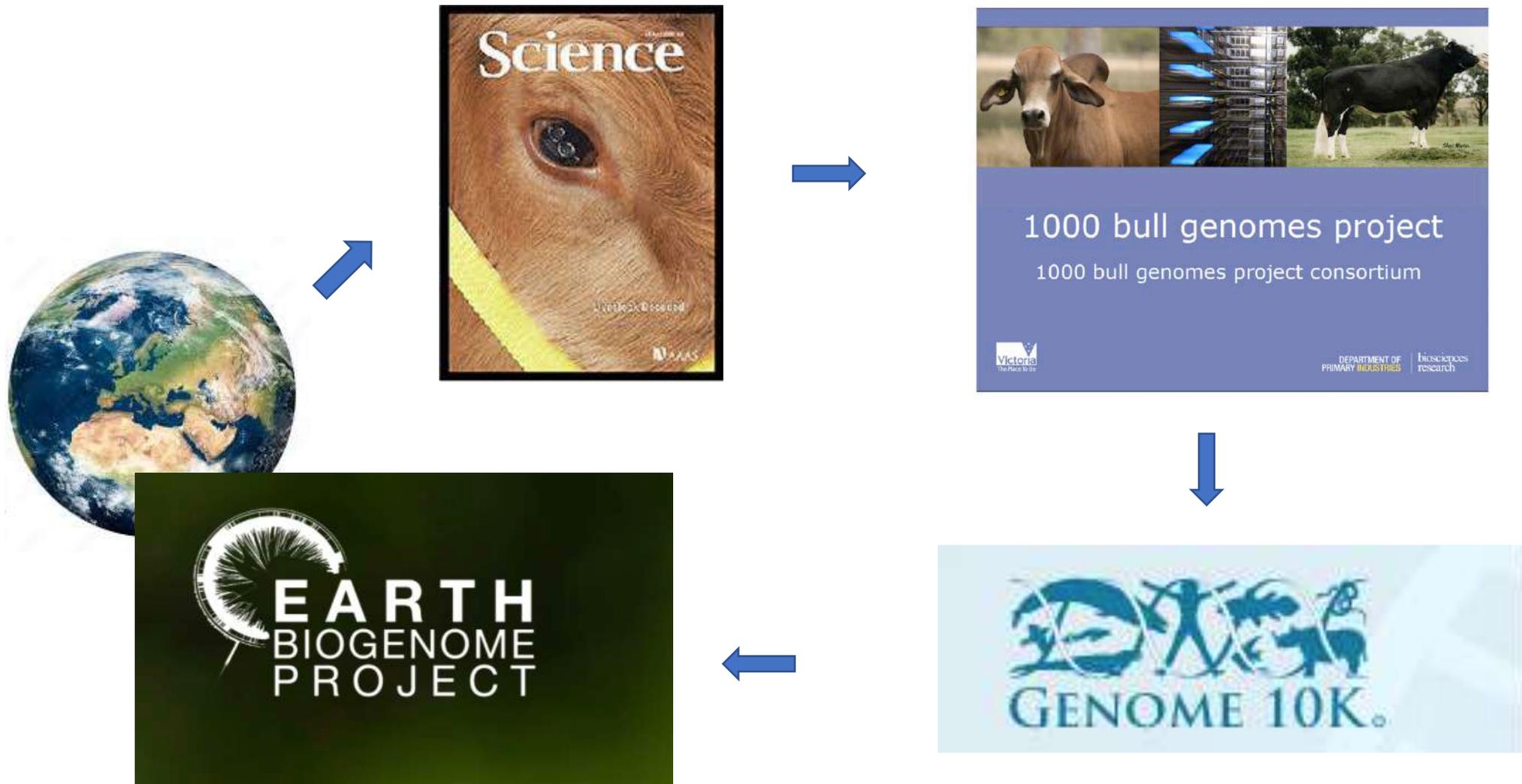


Dove stiamo andando

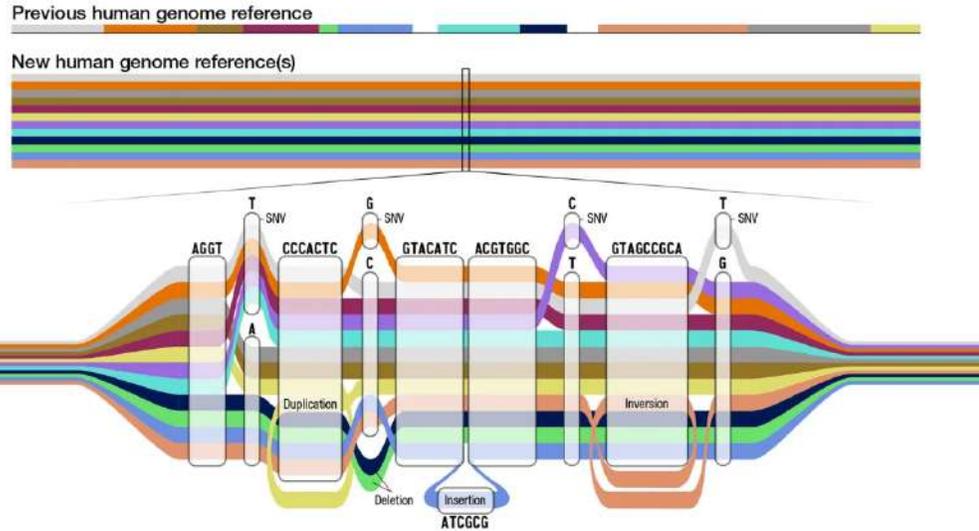


# Nuova genomica

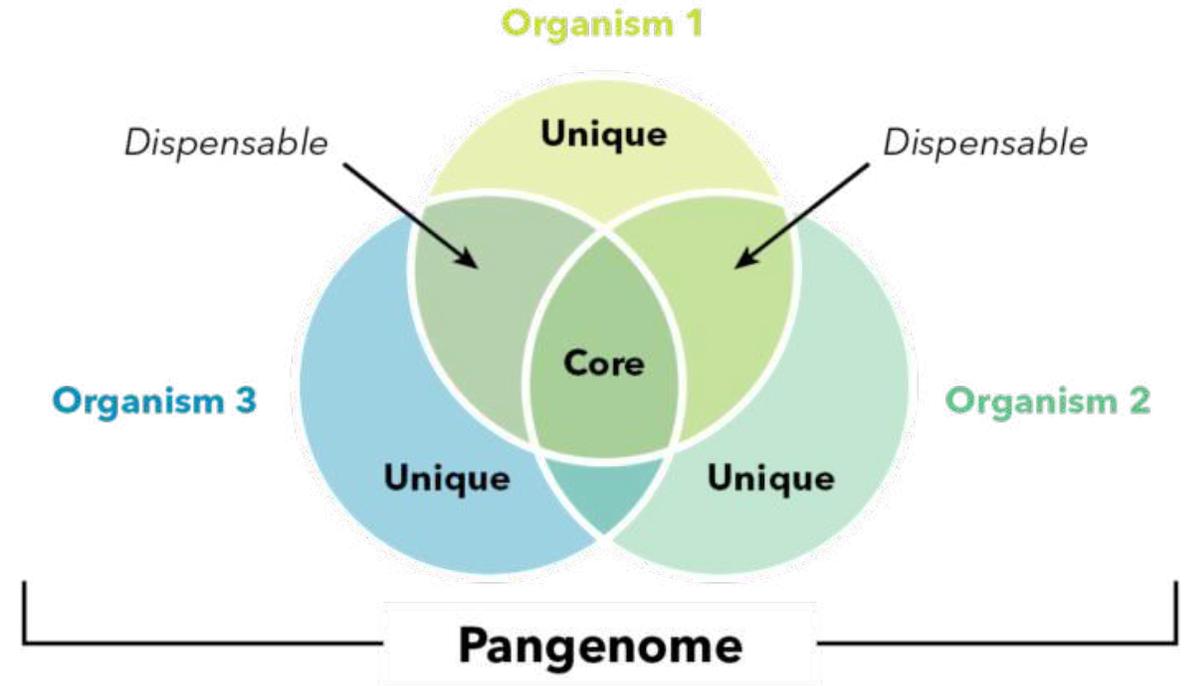
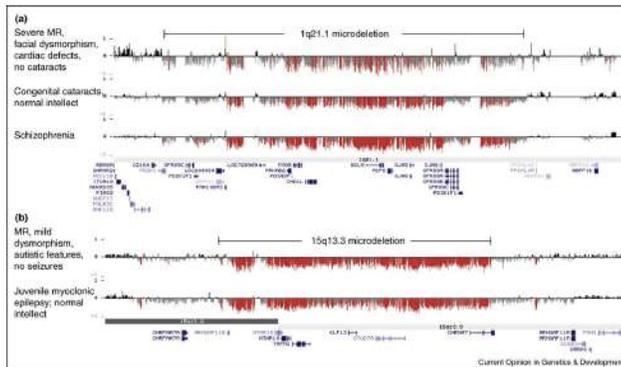
# Dal singolo animale al pianeta intero



# Dal genoma al Pangenoma



## Copy Number Variations (CNVs)



Gene editing

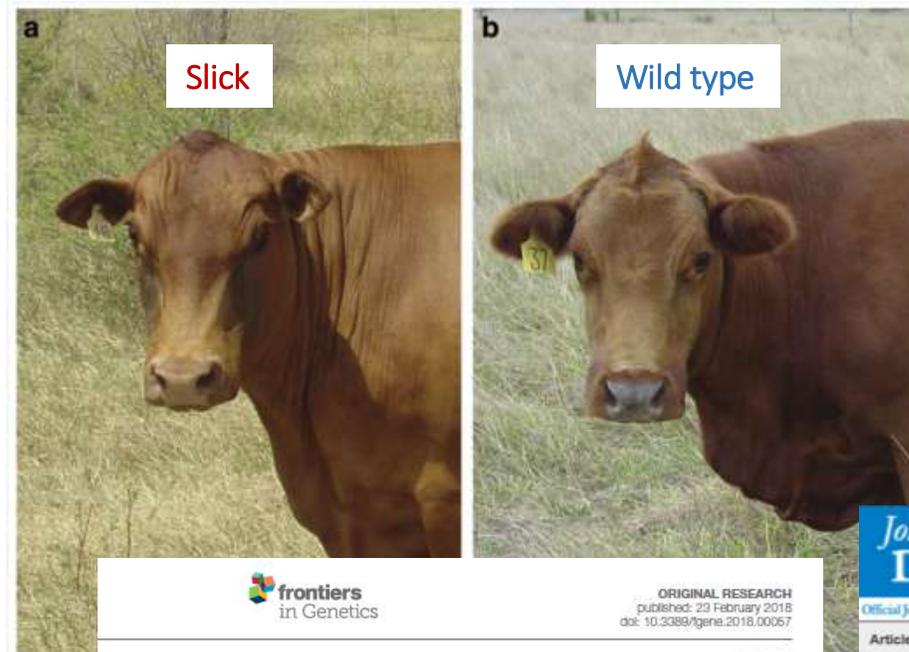
# Making the cut

CRISPR genome-editing technology shows its power



And Science's 2015 Breakthrough of the Year is...

# La mutazione SLICK



La mutazione SLICK è insorta naturalmente in bovini di razza Senepol del Sud America.

SLICK induce un cambiamento nel gene del recettore per la prolattina che conferisce un'aumentata tolleranza alle temperature elevate.

## Convergent Evolution of Slick Coat in Cattle through Truncation Mutations in the Prolactin Receptor

Laercio R. Porto-Neto<sup>1</sup>, Derek M. Bickhart<sup>2</sup>, Antonio J. Landaeta-Hernandez<sup>3</sup>, Yuri T. Utsunomiya<sup>4,5</sup>, Melvin Pagan<sup>6</sup>, Esbal Jimenez<sup>6</sup>, Peter J. Hansen<sup>7</sup>, Serdal Dikmen<sup>8</sup>, Steven G. Schroeder<sup>9</sup>, Eui-Soo Kim<sup>10</sup>, Jiajie Sun<sup>11</sup>, Edward Crespo<sup>3</sup>, Norman Amati<sup>3</sup>, John B. Cole<sup>3</sup>, Daniel J. Nisler<sup>1</sup>, Jose F. Garcia<sup>4,5,12</sup>, Antonio Reverter<sup>1</sup>, William Barendse<sup>1</sup> and Tad S. Sonstegard<sup>10\*</sup>



Journal of Dairy Science<sup>®</sup>  
Official Journal of the American Dairy Science Association<sup>®</sup>

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Article in Press

### The *SLICK* hair locus derived from Senepol cattle confers thermotolerance to intensively managed lactating Holstein cows

S. Dikmen, F.A. Khan<sup>1</sup>, H.J. Huson<sup>2</sup>, I.S. Sonstegard, J.L. Moss, G.E. Dahl, P.J. Hansen

<sup>1</sup> Present address: Department of Population Medicine, Ontario Veterinary College, University of Guelph, Guelph, ON, N1G 2W1, Canada  
<sup>2</sup> Present address: Department of Animal Science, Cornell University, Ithaca, NY 14853

Received: February 27, 2014; Accepted: May 20, 2014; Published Online: July 01, 2014

# Morfologia e fisiologia

## ✓ Heat Tolerance

- Gene: *PRLR*
  - Target: SLICK1, SLICK2, SLICK3, SLICK4, SLICK5

## ✓ Milk Production

- Gene: *GHR*
- Gene: *DGAT*
  - Target: High Milk Allele

## ✓ Size/ Fertility

- Gene: *PLAG1*
  - Target: Small stature / High Fertility

## ✓ Trypanosoma Tolerance

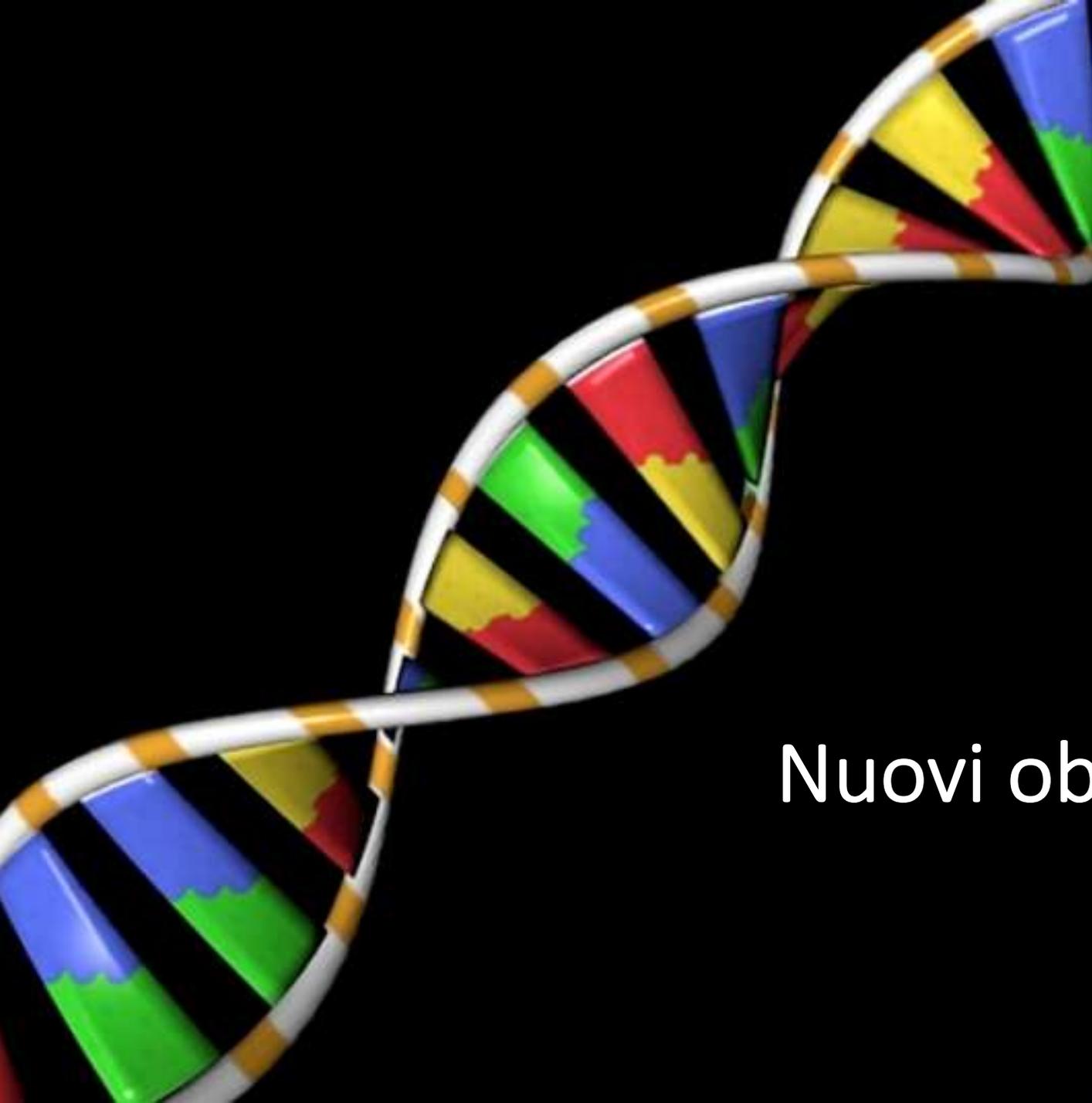
- Gene: *DHRS4*
- Gene: *FDX2*
  - Target: Tryps Tolerance

## ✓ Tuberculosis Resistance

- Gene: *IFI16*
  - Target: Zebu Allele
- Gene: *IL1A*
  - Target: Zebu Allele
- Gene: *IRF3*
  - Target: Taurus, Zebu Allele, Recombinant Allele
- Gene: *NOD2*
  - Target: Taurus, Zebu Allele, Recombinant Allele
- Gene: *MARCO*
  - Target: Taurus Allele, Deleterious Allele
- Gene: *NLRP3*
  - Target: Zebu Allele

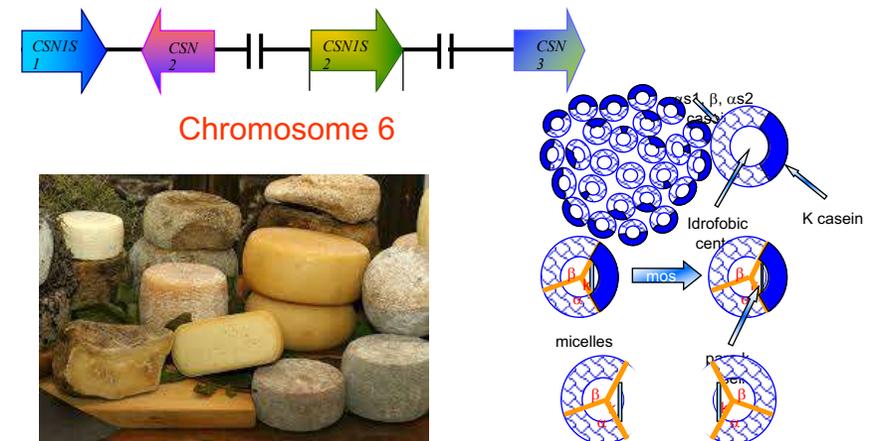
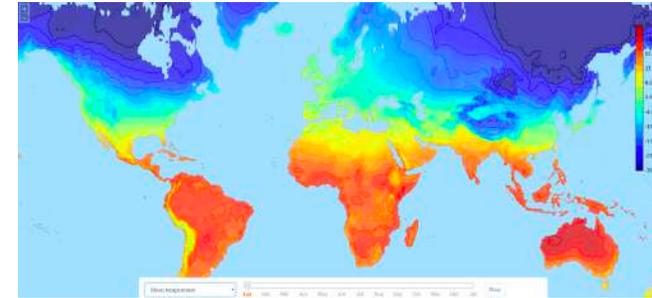
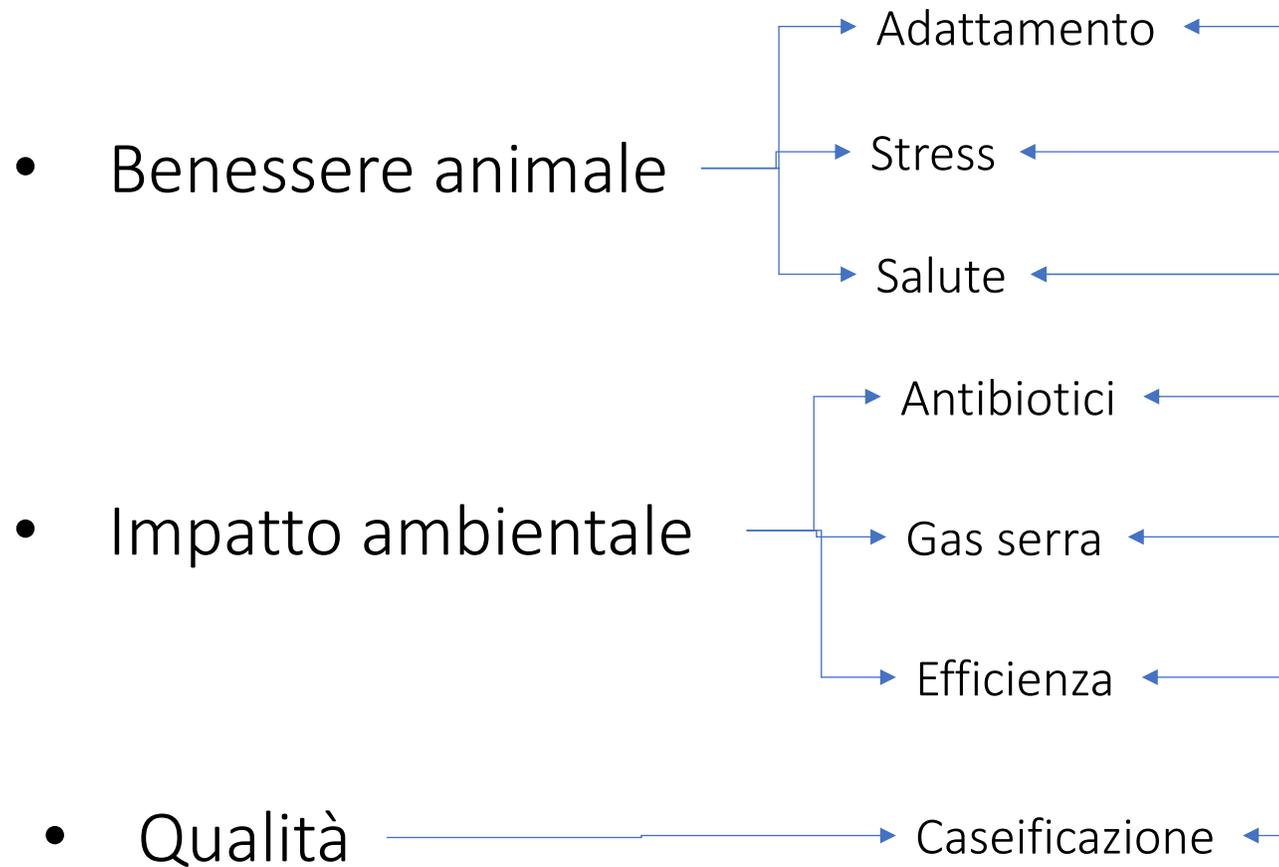
Tad Sonstegard





Nuovi obiettivi di selezione

# Obiettivi vecchi e nuovi





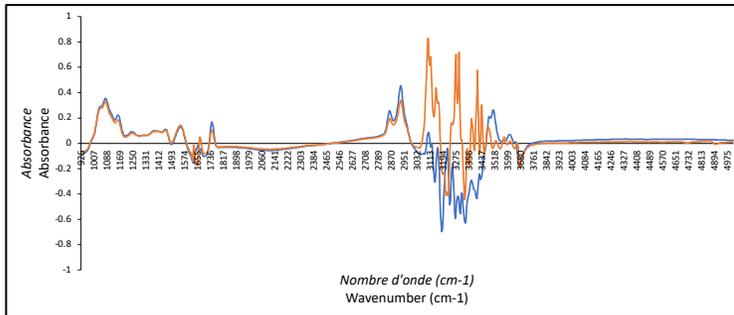
Nuovi fenotipi

# Nuovi fenotipi



Livestock Environment Opendata

50 milioni di spettri



**J. Dairy Sci.** 102:11751–11765  
<https://doi.org/10.3168/jds.2019-16804>  
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**Persistence of differences between dairy cows categorized as low or high methane emitters, as estimated from mid-infrared spectra and measured by GreenFeed**

**J. Dairy Sci.** 100:2433–2453  
<https://doi.org/10.3168/jds.2016-12030>  
© 2017, THE AUTHORS. Published by FASS and Elsevier Inc. on behalf of the American Dairy Science Association®. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

**Invited review: Large-scale indirect measurements for enteric methane emissions in dairy cattle: A review of proxies and their potential for use in management and breeding decisions**

**J. Dairy Sci.** 98:5740–5747  
<http://dx.doi.org/10.3168/jds.2014-8436>  
© American Dairy Science Association®, 2015.

**Hot topic: Innovative lactation-stage-dependent prediction of methane emissions from milk mid-infrared spectra**

**animal**  
AN INTERNATIONAL JOURNAL OF ANIMAL BIOSCIENCE  
Cambridge University Press

**Potential use of milk mid-infrared spectra to predict individual methane emission of dairy cows**

Published online by Cambridge University Press: 28 February 2012

F. Dehareng, C. Delfosse, E. Froidmont, H. Soyeurt, C. Martin, N. Gengler, A. Vanlierde and P. Dardenne

Show author details

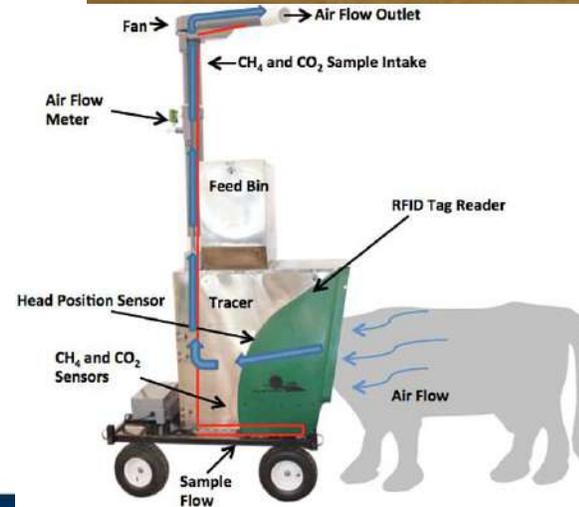
Article Metrics

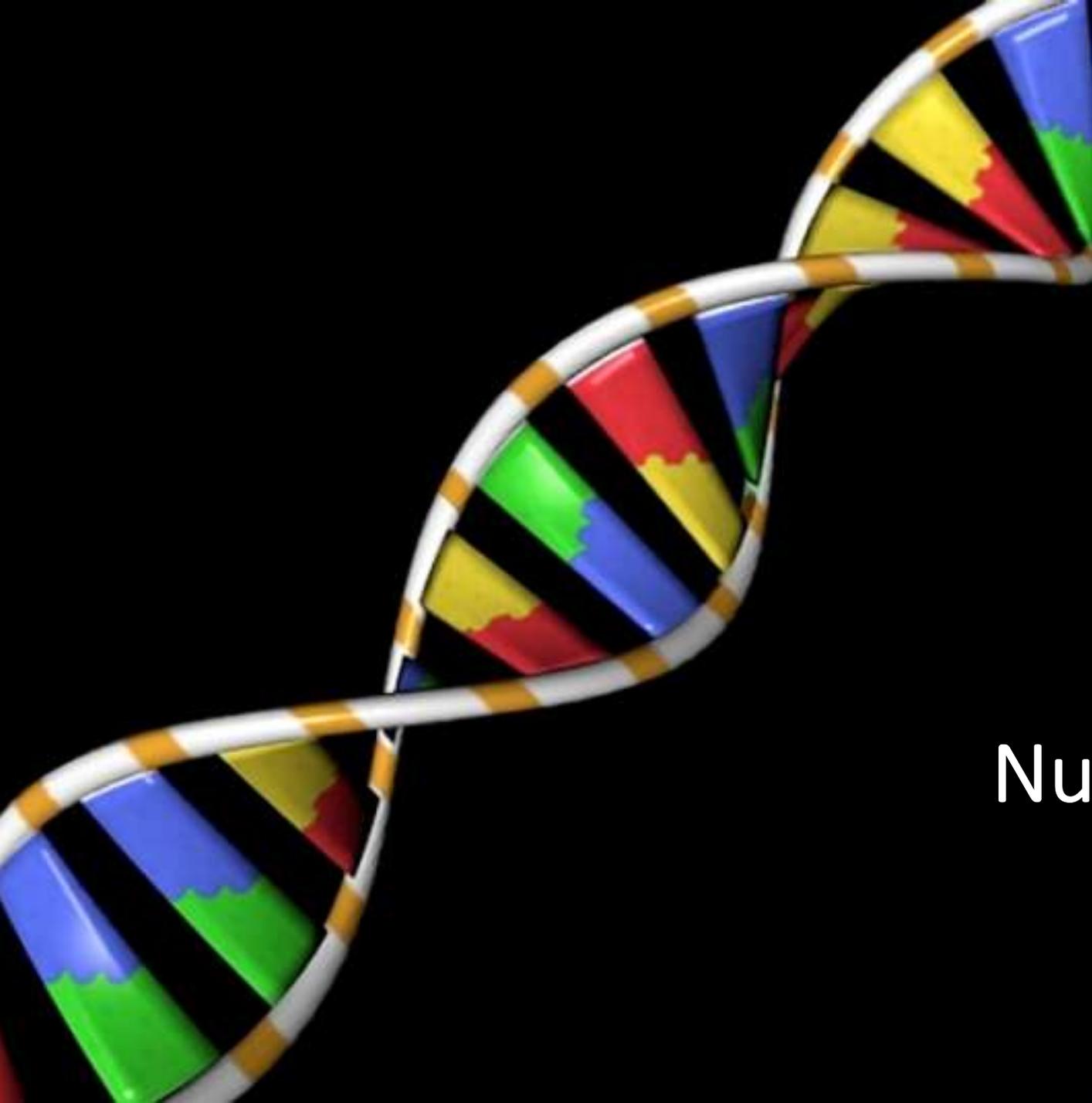
Acidi grassi, Lattoferrina, Dimensione globuli di grasso, emissioni di metano, ingestione di sostanza secca

# Nuovi fenotipi



Sensori  
Podometri  
Ruminometri  
Telecamere

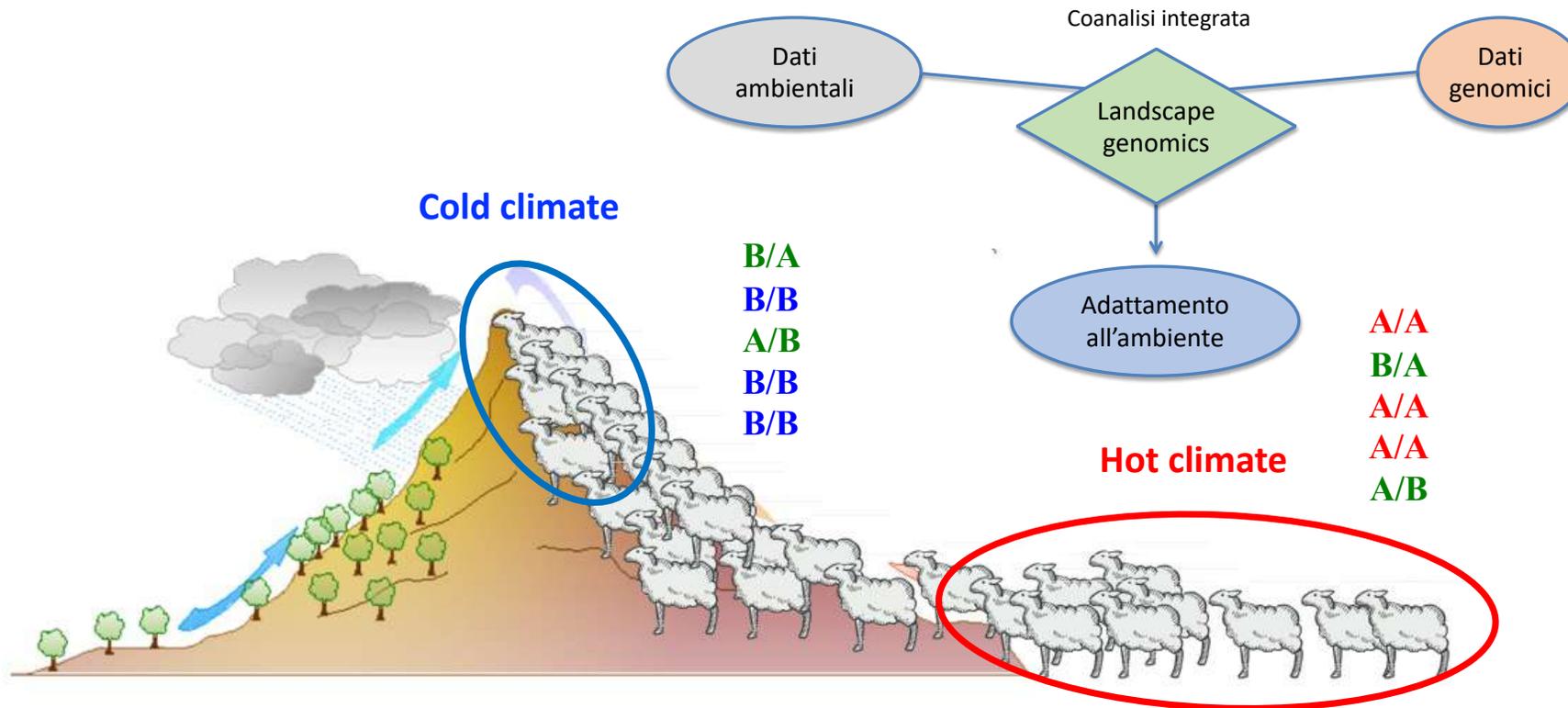




Nuovi approcci

# Landscape genomics

Comprendere i **meccanismi molecolari** che sottendono l'**adattamento degli animali domestici alle variazioni ambientali** è un fattore chiave per lo sviluppo di un'agricoltura **“climate-smart”**.



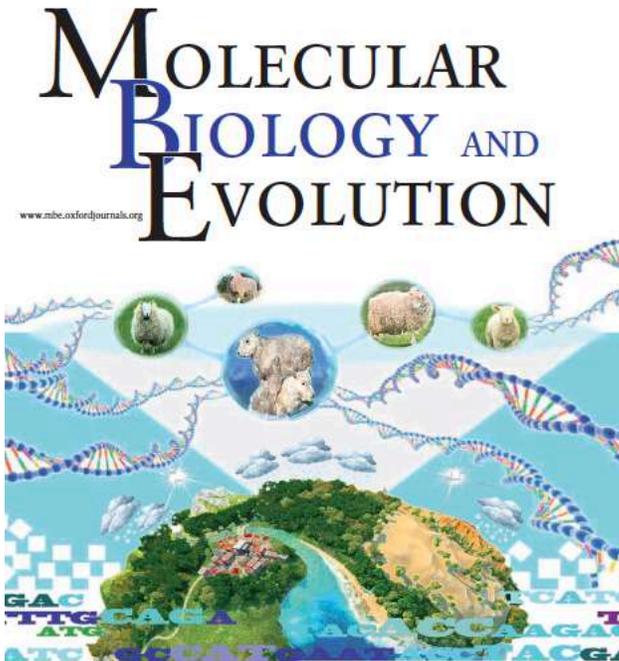
La **“Landscape genomics”** cerca di spiegare il pattern spaziale di distribuzione della variabilità genetica in relazione all'**adattamento locale** all'ambiente (Joost et al., 2003).

# Landscape genomics

## Adaptations to Climate-Mediated Selective Pressures in Sheep

Feng-Hua Lv,<sup>1</sup> Saif Agha,<sup>2,3</sup> Juha Kantanen,<sup>4,5</sup> Licia Colli,<sup>6,7</sup> Sylvie Stucki,<sup>2</sup> James W. Kijas,<sup>8</sup> Stéphane Joost,<sup>2</sup> Meng-Hua Li,<sup>\*1</sup> and Paolo Ajmone Marsan<sup>6,7</sup>

Volume 31 • Number 12 • December 2014



● Standing variation as source of adaptive changes

8 geni coinvolti nella  
regolazione endocrina e  
del sistema immunitario.

9 geni coinvolti nel  
metabolismo energetico.

Chr.	Gene	Position (bp)	Gene Size (kb)	SNP	$F_{ST}^a$	z  Score <sup>b</sup>	Max Wald <sup>c</sup>
1	<i>EVI5</i>	68957918–69191464	233.50	OAR1_73673800 <sup>d</sup>	0.55**	5.35	15.81
2	<i>FBXO8</i>	105386295–105423924	37.63	OAR2_113355547	0.37*	9.74	17.59
2	<i>CHN1</i>	134023000–134022999	70.92	OAR2_142314137	0.29**	5.42	14.37
				OAR2_143195752	0.46**	5.48	15.62
2	<i>ACVR2A</i>	160457581–160549550	91.97	OAR2_170004218	0.35**	6.99	15.06
2	<i>NMUR1</i>	232366028–232483197	117.20	s74305	0.51**	11.20	16.41
				OAR2_245260141	0.32*	8.71	17.33
				OAR2_245638268	0.39*	8.35	14.93
				OAR2_245680195	0.42*	10.37	14.57
5	<i>IL12RB1</i>	4854306–4869950	15.64	s33778 <sup>d</sup>	0.35**	5.40	15.87
5	<i>ARHGEF18</i>	13935201–14021434	86.23	s48780 <sup>d</sup>	0.38**	8.02	14.88
10	<i>ALOX5AP</i>	30365435–30388526	23.09	s18834	0.84**	8.79	17.66
				s68983	0.67**	8.61	18.85
				s12004	0.54**	7.06	14.67
				OAR10_30746533	0.70**	7.24	17.37
10	<i>EDNRB</i>	53508345–53534498	26.15	OAR10_53694894	0.23*	6.83	19.21
				OAR10_54710595	0.33**	5.46	17.06
15	<i>THY1</i>	29450455–29452173	1.72	s13895	0.36*	6.74	16.08
				s02747	0.38*	6.38	15.70
15	<i>ARAP1</i>	50442784–50529042	86.26	OAR15_55184101 <sup>d</sup>	0.63**	7.54	15.70
19	<i>XCR1</i>	53235736–53236748	1.01	s18532	0.61**	8.60	18.16
				OAR19_56419475	0.27*	5.25	16.21
19	<i>CXCR6</i>	53290059–53291081	1.02	s18532	0.61**	8.60	18.16
				OAR19_56419475	0.27*	5.25	16.21
19	<i>CCR9</i>	53333188–53340782	7.60	s18532	0.61**	8.60	18.16
				OAR19_56419475	0.27*	5.25	16.21
20	<i>PRL</i>	34258080–34266415	8.34	OAR20_37437726	0.57**	9.54	19.18
				s39515	0.62**	9.90	19.15
22	<i>PLCE1</i>	15009437–15337740	328.30	OAR22_18841208_X <sup>d</sup>	0.46**	8.24	14.55
				OAR22_18876523	0.53**	7.75	16.38
				OAR22_18929579	0.47**	5.90	15.00
				OAR22_19052408	0.44**	5.89	16.91
22	<i>TBC1D12</i>	15398171–15490853	92.68	OAR22_18841208_X	0.46**	8.24	14.55
				OAR22_18876523	0.53**	7.75	16.38
				OAR22_18929579 <sup>d</sup>	0.47**	5.90	15.00
				OAR22_19052408	0.44**	5.89	16.91

<sup>a</sup>Based on the  $F_{ST}$ -based selection test between the 2 groups of 11 populations (see Materials and Methods).

<sup>b</sup>Based on the LFMM test (Frichot et al. 2013).

<sup>c</sup>Based on the spatial analysis method (Joost et al. 2007).

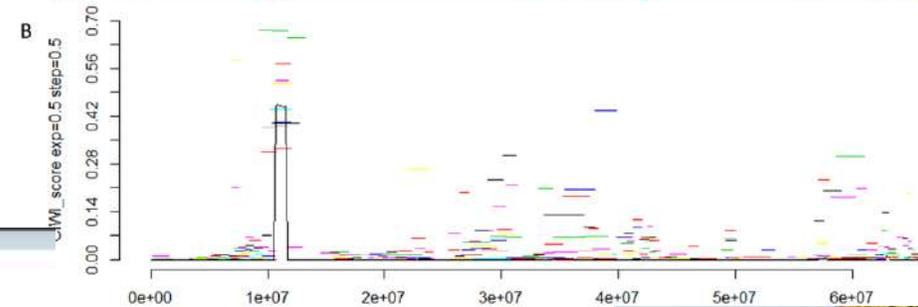
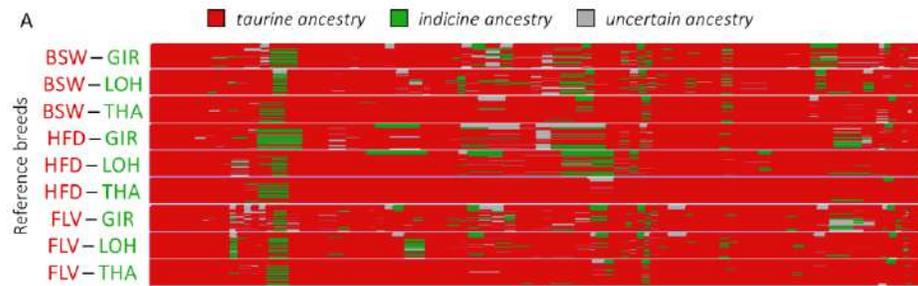
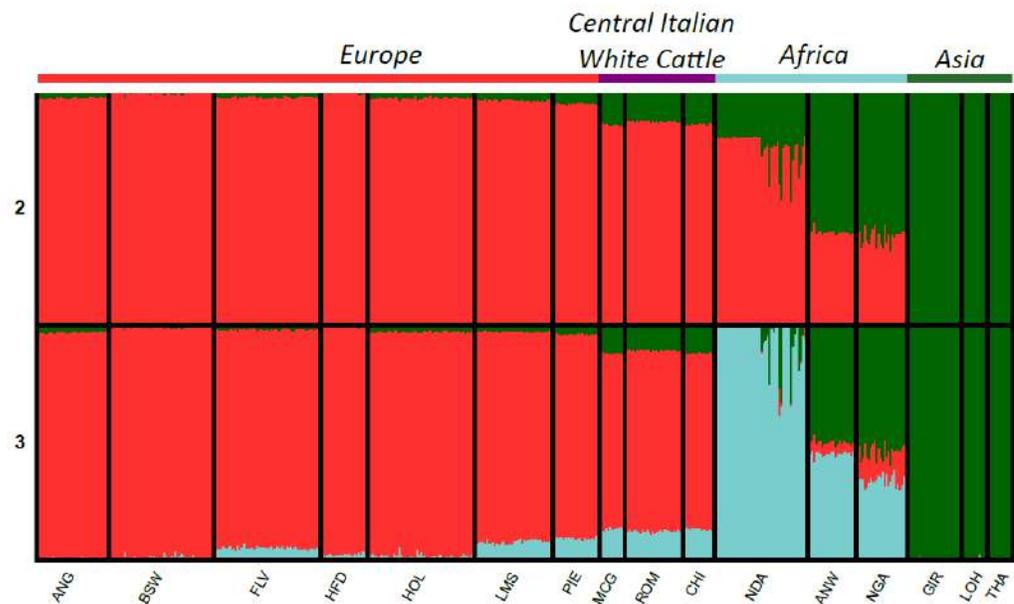
<sup>d</sup>SNPs within genes.

Significant at the level of \* $P < 0.05$  and \*\* $P < 0.01$ .

# Introgressione adattativa



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Mario Barbato  
(UNICATT)

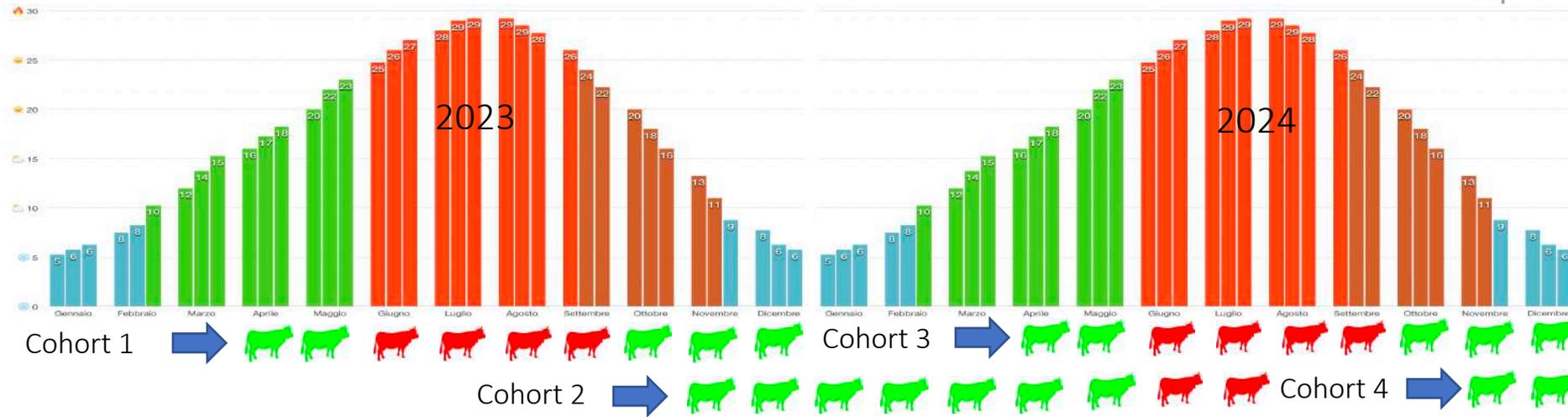
OPEN

## Adaptive introgression from indicine cattle into white cattle breeds from Central Italy

Mario Barbato<sup>1\*</sup>, Frank Hailer<sup>2</sup>, Maulik Upadhyay<sup>3,4</sup>, Marcello Del Corvo<sup>1</sup>, Licia Colli<sup>1</sup>, Riccardo Negrini<sup>2</sup>, Eui-Soo Kim<sup>3</sup>, Richard P. M. A. Crooijmans<sup>3</sup>, Tad Sonstegard<sup>5</sup> & Paolo Ajmone-Marsan<sup>1\*</sup>

Quattro geni candidati  
*KLHL36* → funzione ignota  
*USP10* → gluconeogenesi  
*KIAA0513* e *FAM92B* → efficienza alimentare

# Biologia dei sistemi



- Primipare e secondipare
- Stesso stadio di lattazione (30-60 DIM) all'inizio dell'esperimento
- Stessa dieta
- Collezione sistematica di dati sugli animali (sensori, greenfeed etc.)
- Collezione sistematica di dati ambientali in stalla
- Sangue, latte, liquido ruminali e feci raccolte ogni 2 settimane e durante picchi di temperatura

## CREI

FONDAZIONE  
INVERNIZZI

Centro di ricerca Romeo ed Enrica Invernizzi  
per le produzioni lattiero-casearie sostenibili



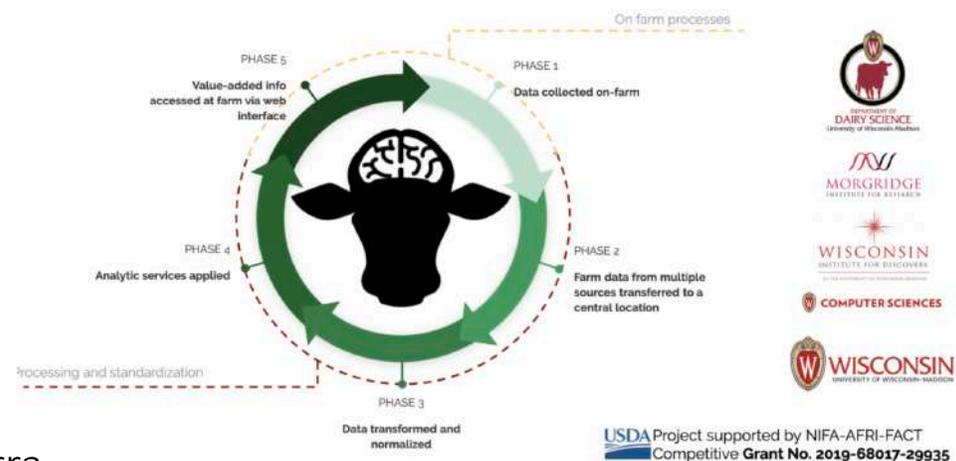
Nuovi modelli

# Nuovi modelli

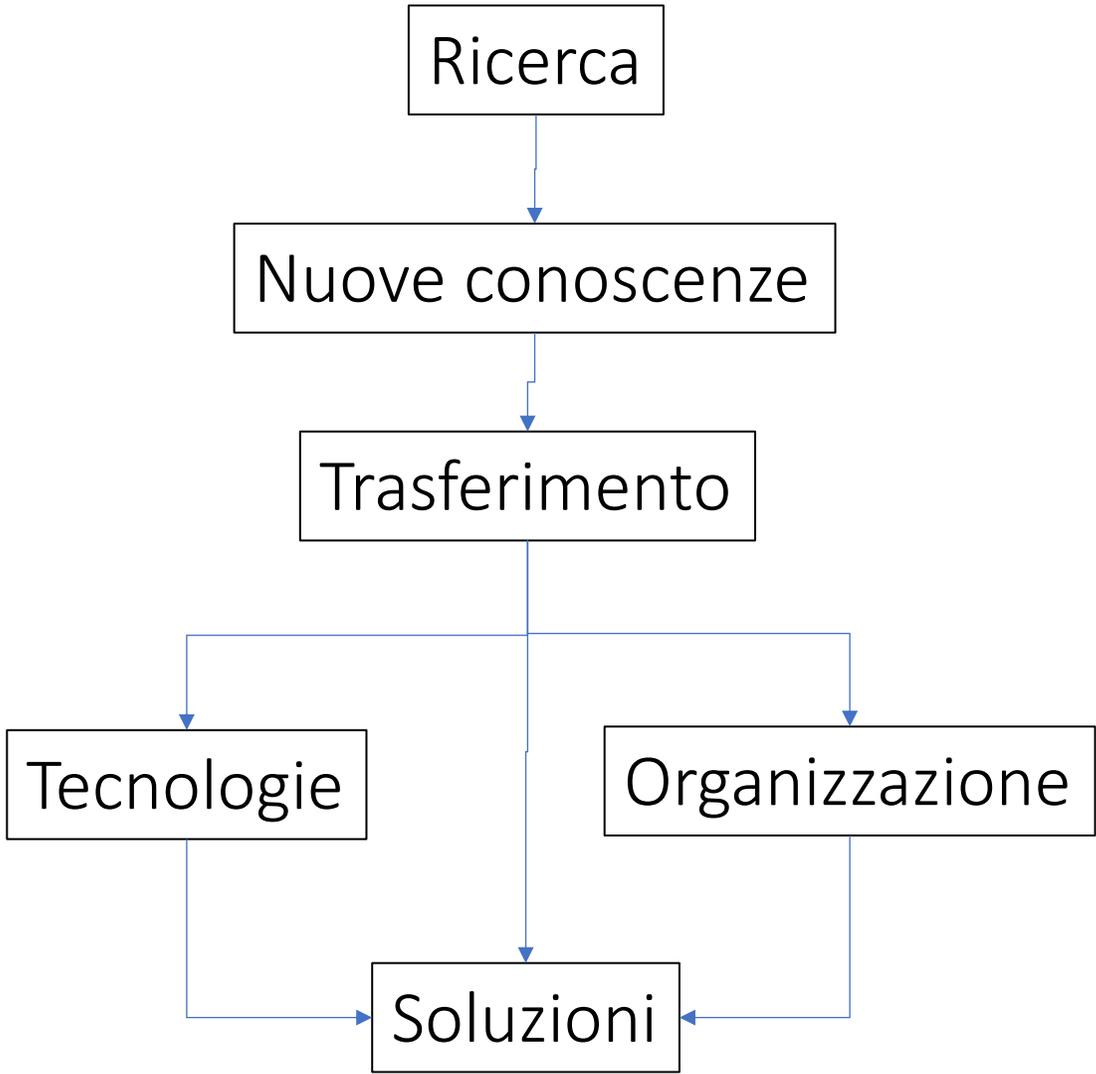


- Dieta di precisione
- Monitoraggio del benessere
- Prevenzione malattie
- Riduzione sprechi
- Riduzione produzione di gas serra
- Management delle deiezioni

## Dairy Brain - a continuous decision making engine



# La ricerca, concausa e risoluzione dei problemi



Piacenza



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Grazie per  
l'attenzione

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Cremona