

Mastering Mastitis:

How genetics can help & where we go from here

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Outline

- **The U.S. Evaluation System**
- **Current Considerations**
 - **The problem of trait definition**
 - Genetic versus genomic evaluations
 - Developing a mastitis resistance evaluation
 - Selection indexes and mastitis representation
 - **Marker validation and functional genetics**
- **Challenges and Opportunities**
 - Computational considerations
 - **Leveraging the microbiome**
 - **Phenomics and Big Data**

U.S. Evaluation System Process

1. Data inputs

DRPCs

Lactation, Reproduction, Health, Calving, Test-day, Yearly Average, Herd Info

Breed Associations

Pedigrees, Conformation, Holstein

Interbull Centre

International Pedigrees, GMACE results

NAAB

NAAB AI codes, Bull Controlling

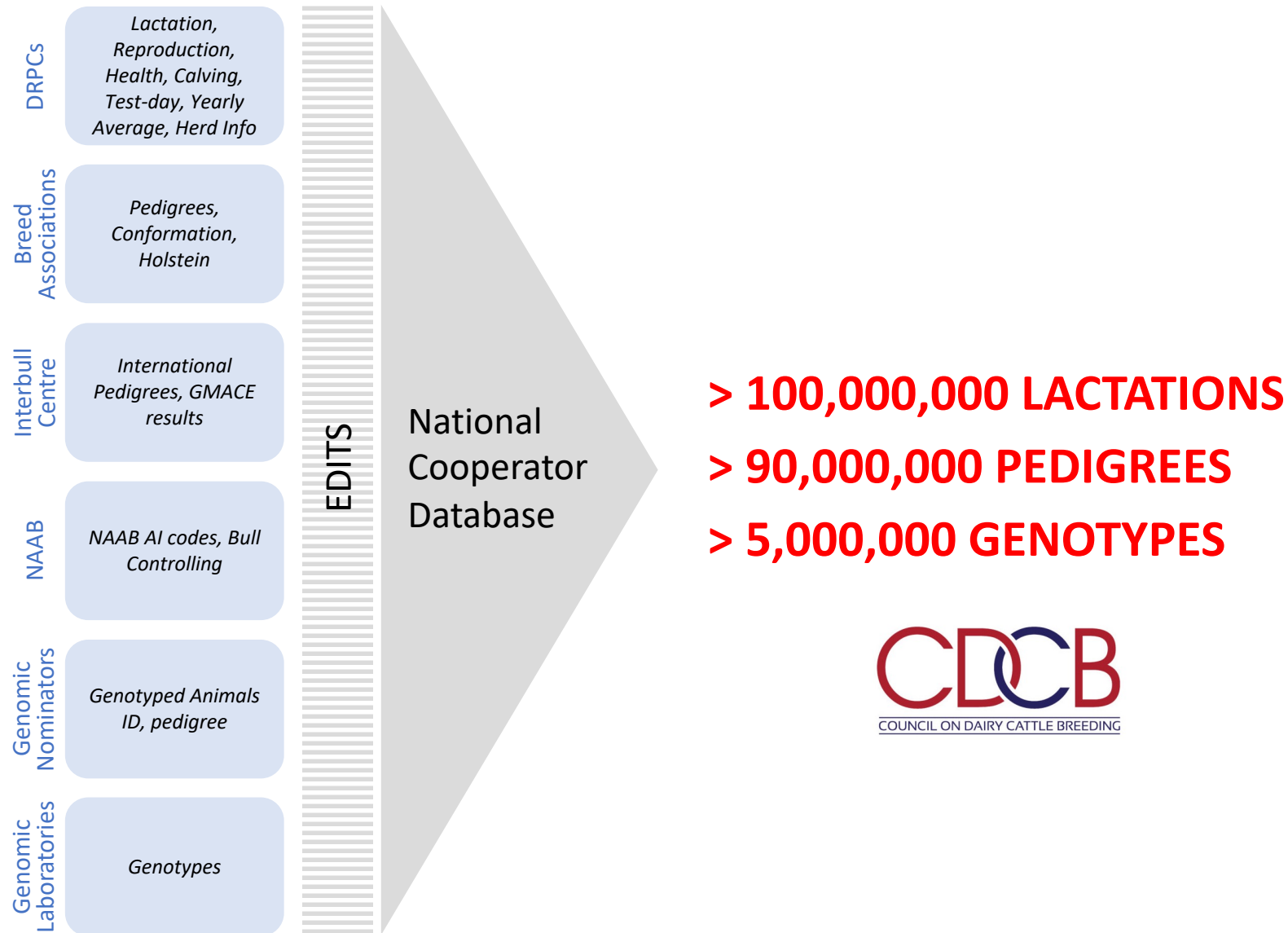
Genomic Nominators

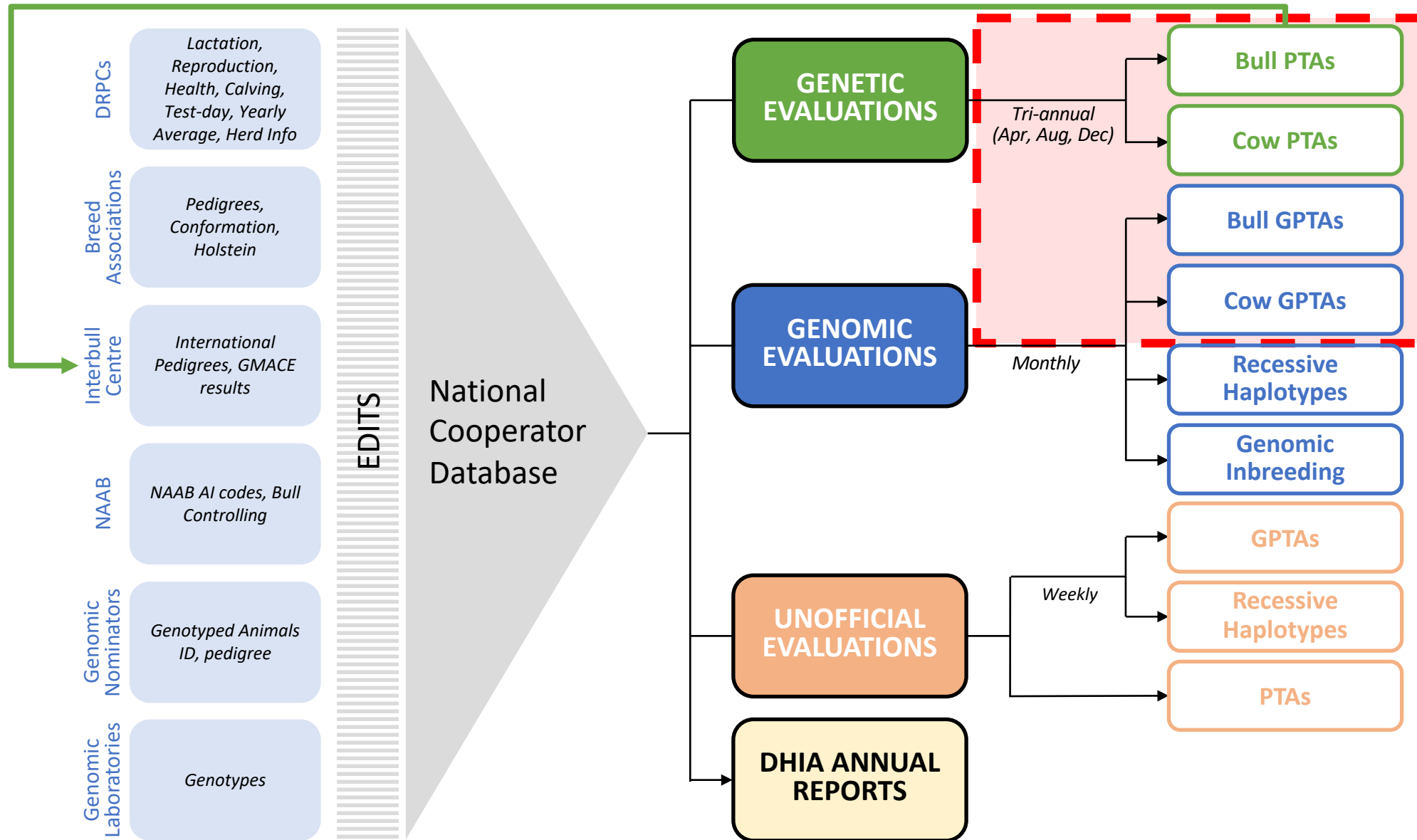
Genotyped Animals ID, Pedigree

Genomic Laboratories

Genotypes

PHENOTYPES
PEDIGREES
GENOTYPES





National evaluations for mastitis

1994: SCS

- 305d mean SCS

2018: Mastitis

- Case:Control

Cole et al., 2006; Parker Gaddis et al., 2012; CDCB, 2018; Parker Gaddis et al., 2020

National evaluations for mastitis

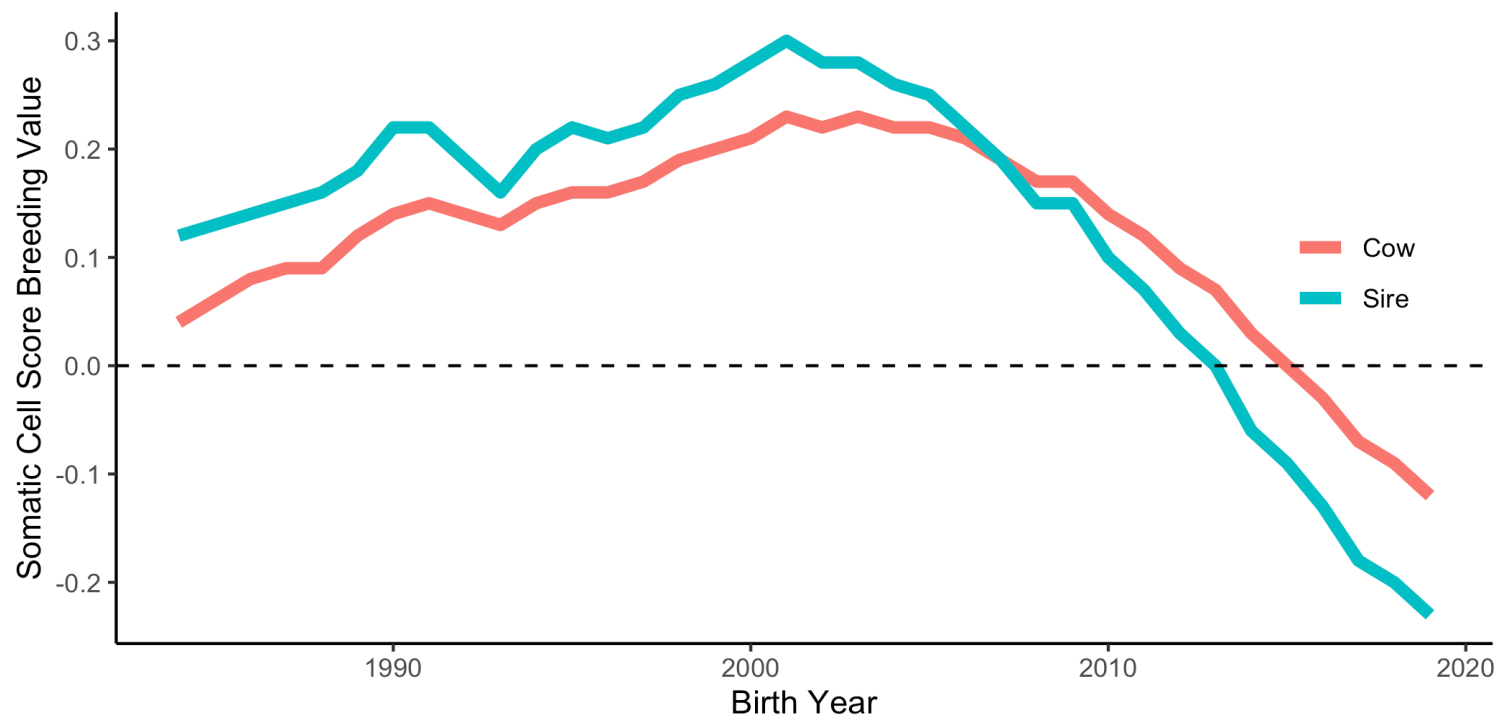
1994: SCS

- 305d mean SCS

Alternative SCS traits

- area under curve*
- recoverability*
- standard deviation*
- severity*

Genetic trends in SCS for Holstein or Red & White



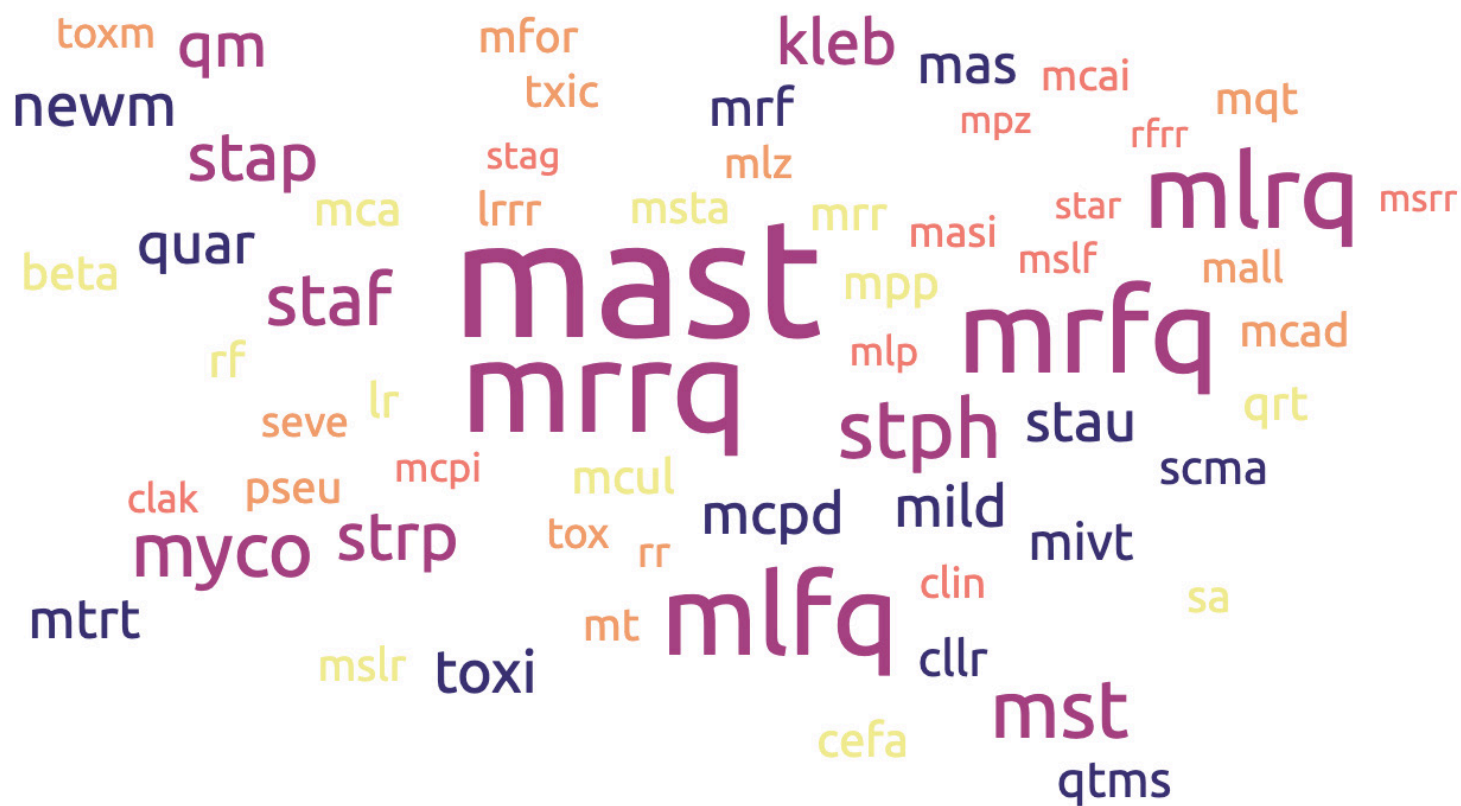
2018: Mastitis

- Case:Control

National evaluations for mastitis

1994: SCS

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2018: Mastitis

- Case:Control

National evaluations for mastitis

1994: SCS

- 305d mean SCS

**89.8% rate of MAST resistance
in US Holsteins**

mast

Alternative traits

- environmental v. contagious*
- gram (+) v. gram (-)*
- repeat diagnoses*

2018: Mastitis

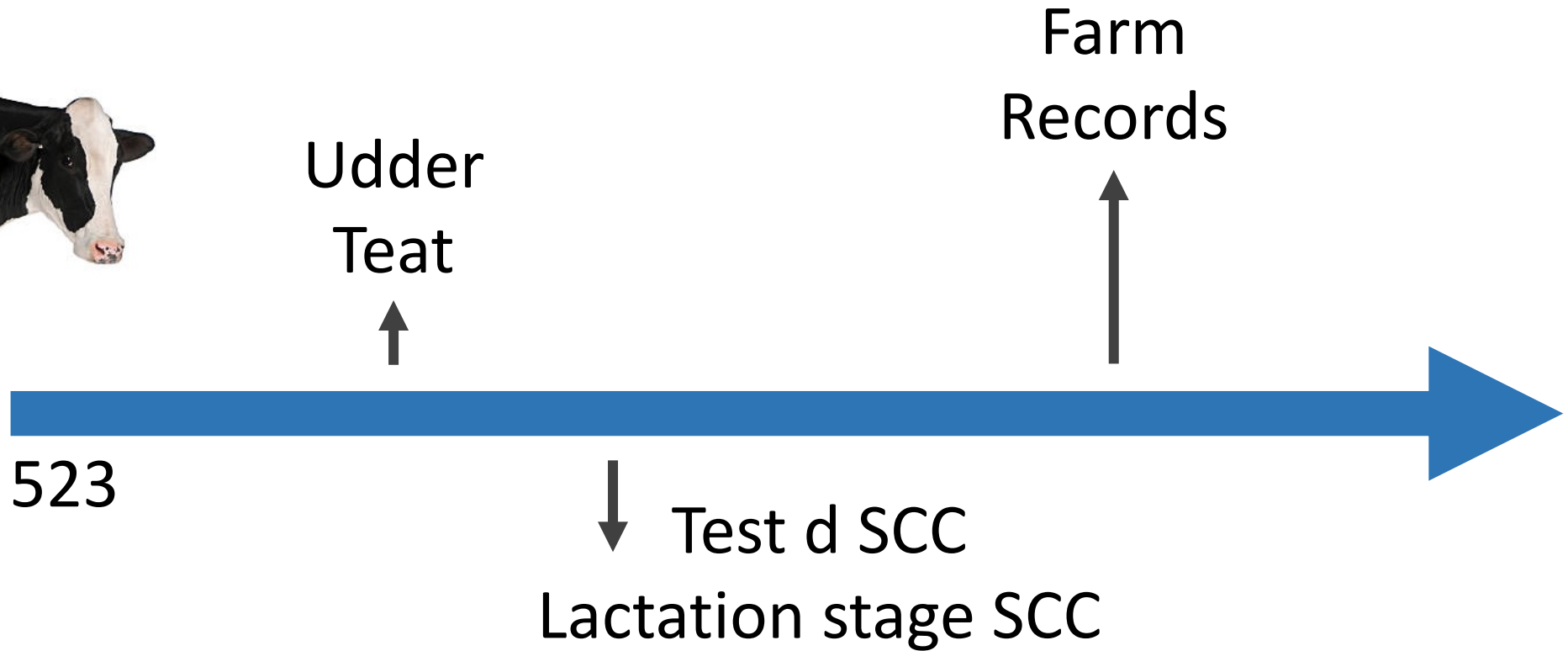
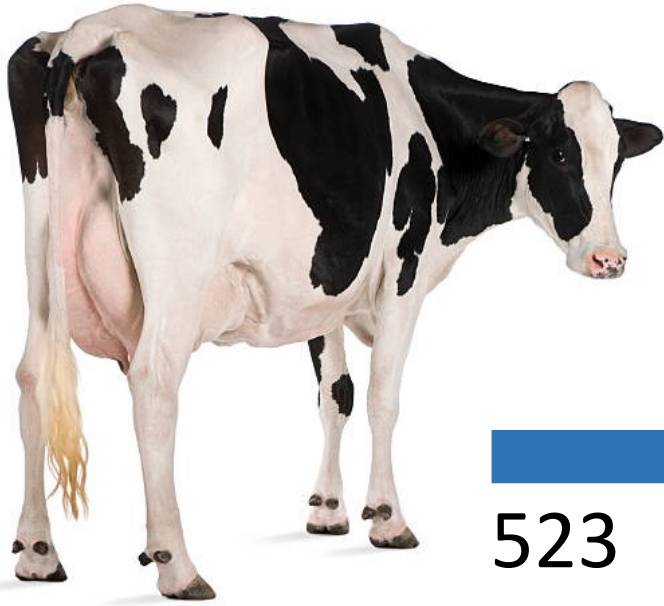
- Case:Control

The problem(?) of trait definition

Generalized phenotypes limit our ability to decipher the functional genetic mechanisms underlying mastitis

They work for animal breeding

An example



- A combination of genome-wide association and population genetic analyses **implicated 990 genes in mastitis resistance**

Redundancy is built into the immune system

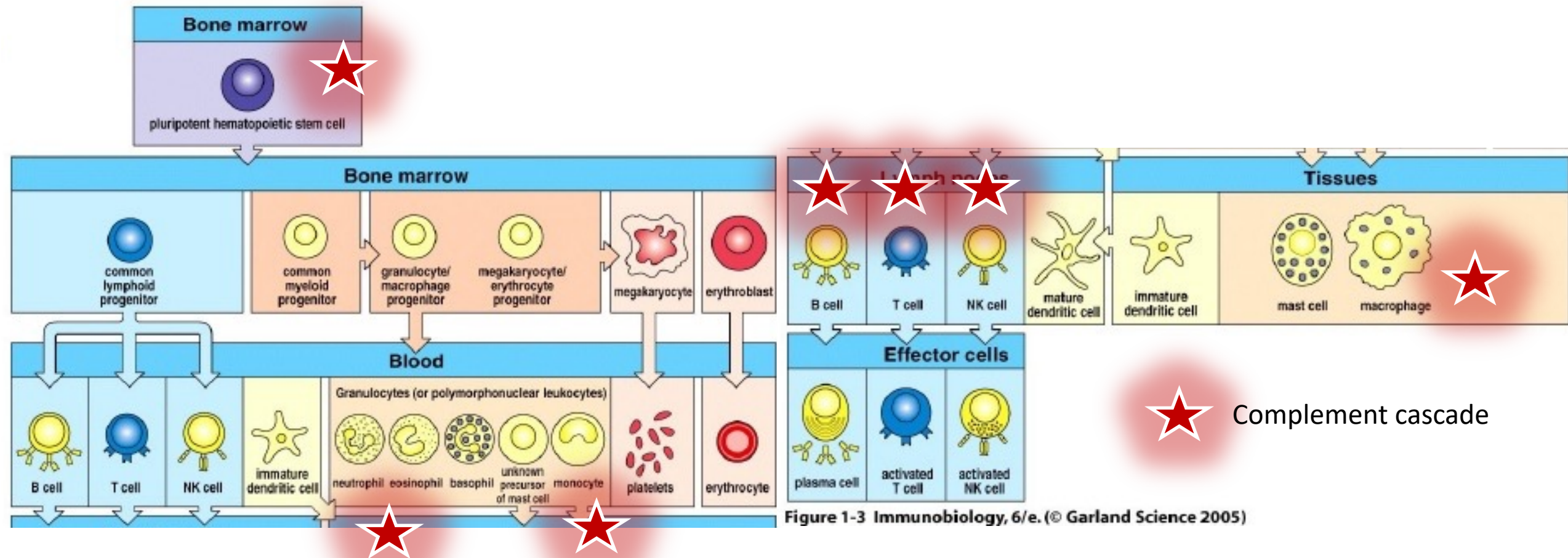


Figure 1-3 Immunobiology, 6/e. (© Garland Science 2005)

Mastitis is highly polygenic

- As of August 2021, there are **2,531 QTL** associated with MAST, SCC, SCS

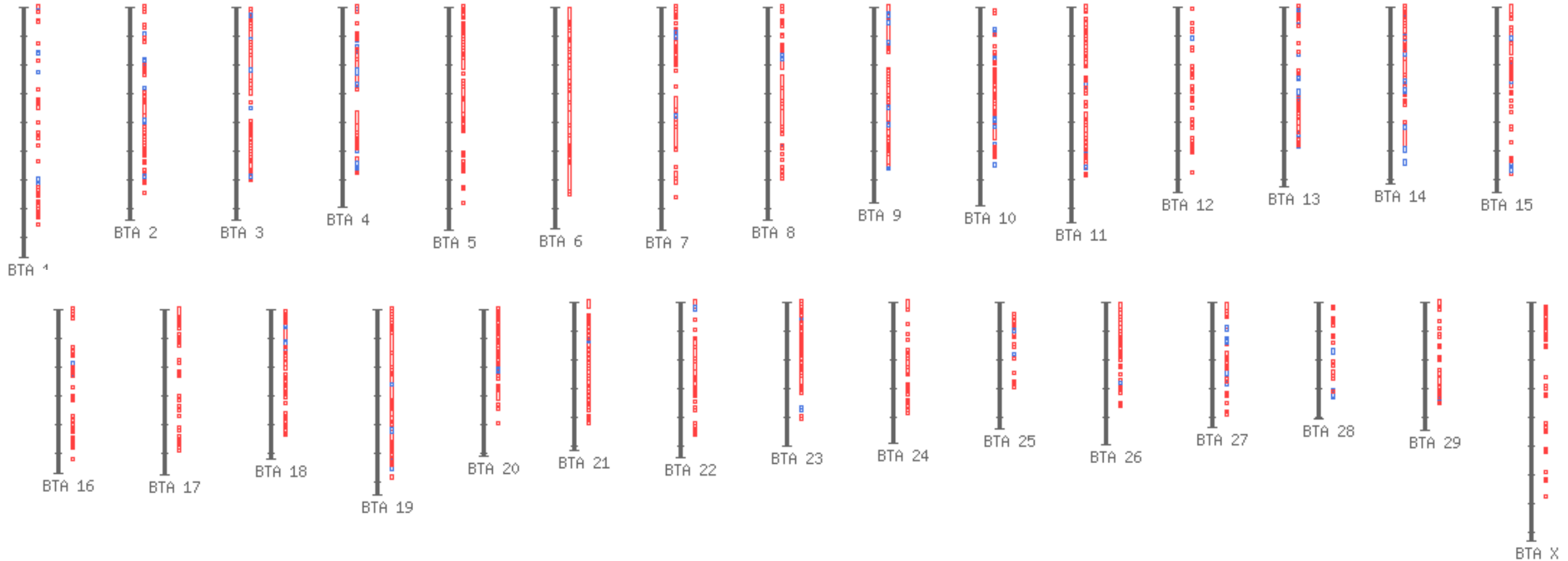
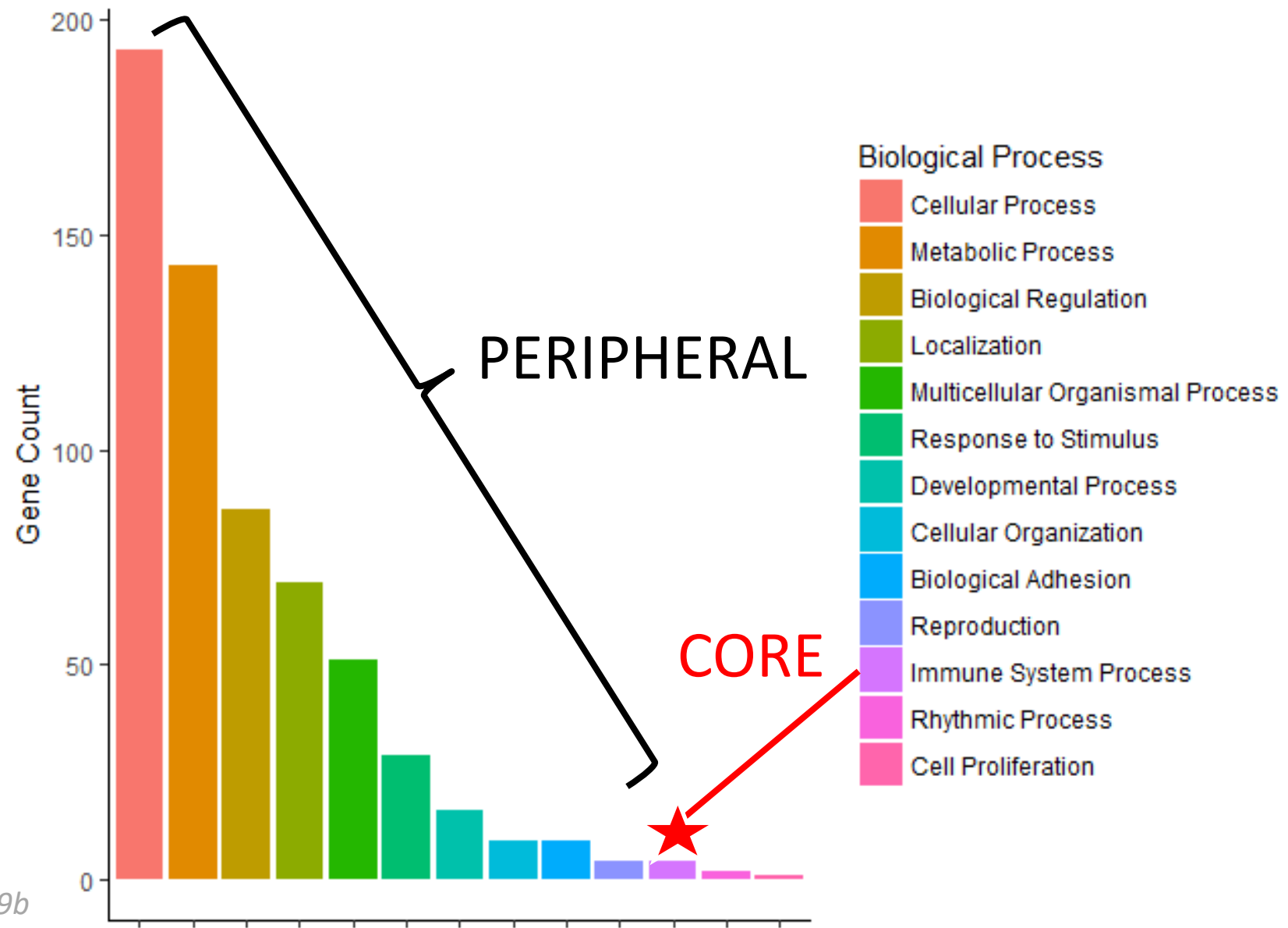


Figure adapted from: https://www.animalgenome.org/cqi-bin/QTLdb/BT/traitmap?trait_ID=1439;
Publication list (133 total): https://www.animalgenome.org/cqi-bin/QTLdb/BT/lstref?trait_ID=1439&traitnm=Mastitis

Mastitis may be omnigenic



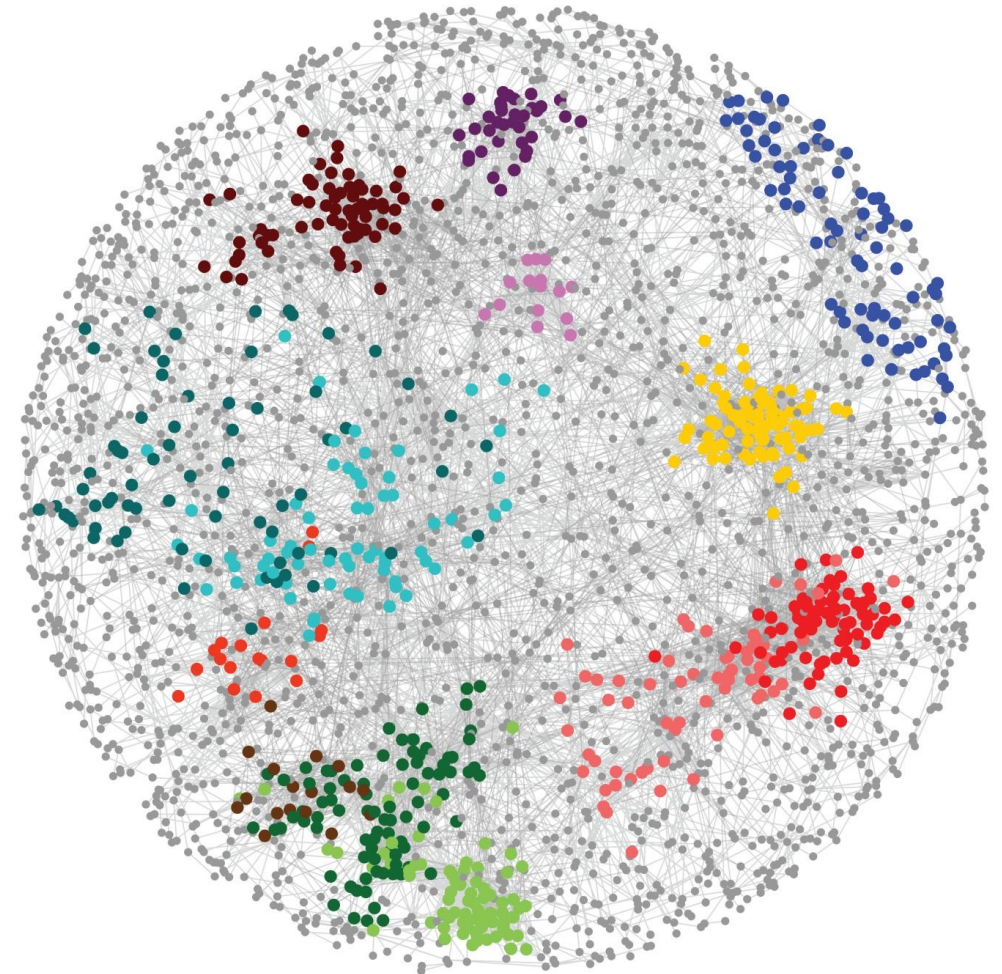
The “omnigenic” model

Boyle et al., 2017

Miles et al 2019b

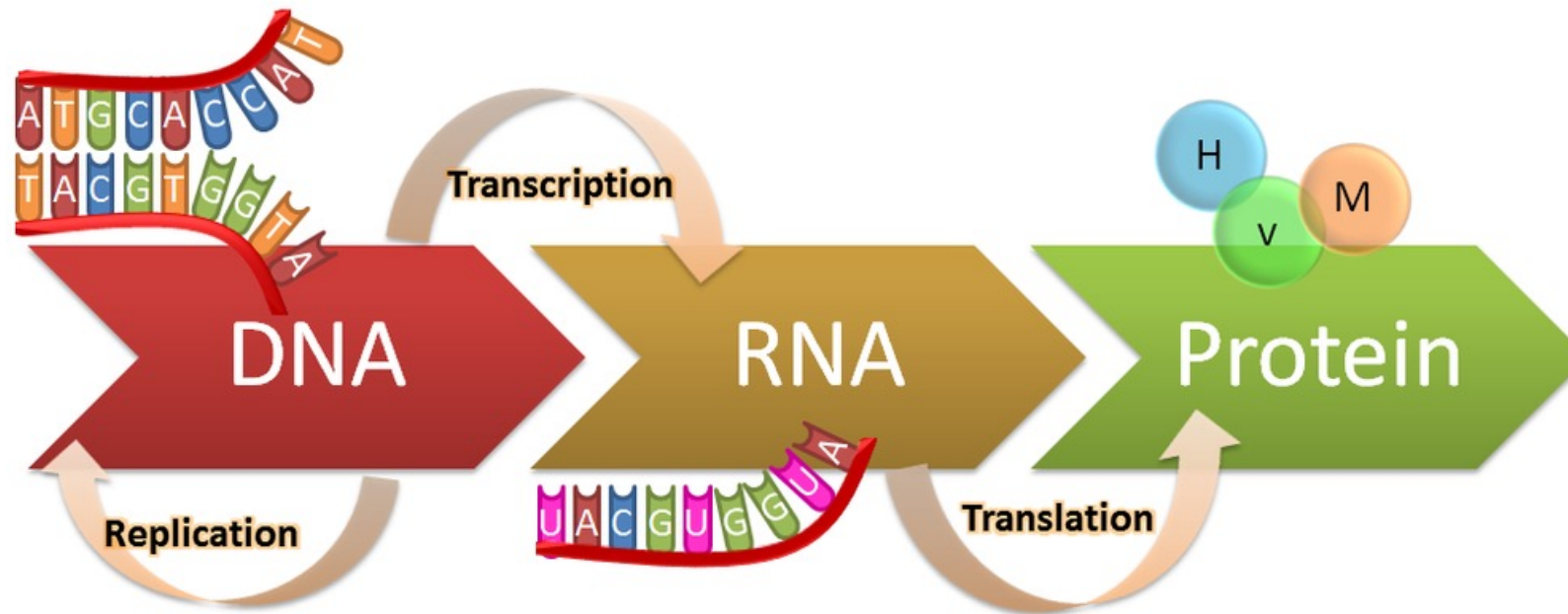
Mastitis may be omnigenic

- **We need a better understanding of cellular networks and regulatory function**
- **This may help prioritize SNP markers used in genomic selection based on biological insight and their downstream effects**



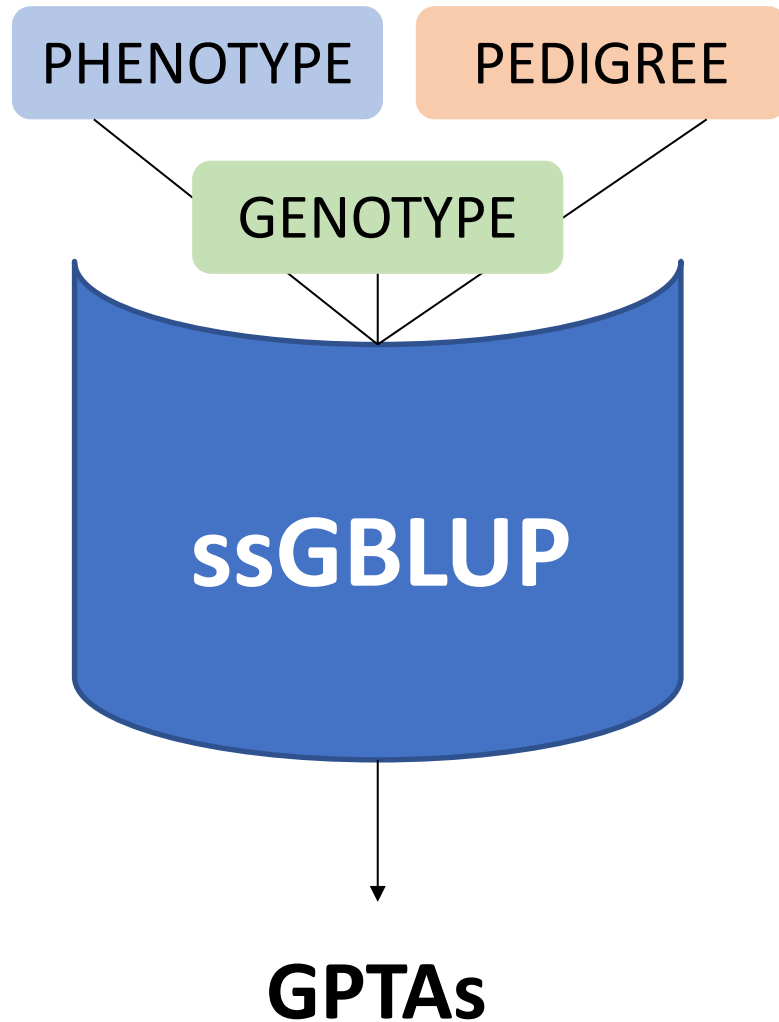
Mastitis may be omnigenic

- **Generating this information requires multi-omics approaches examining marker variants, gene expression, and protein function**



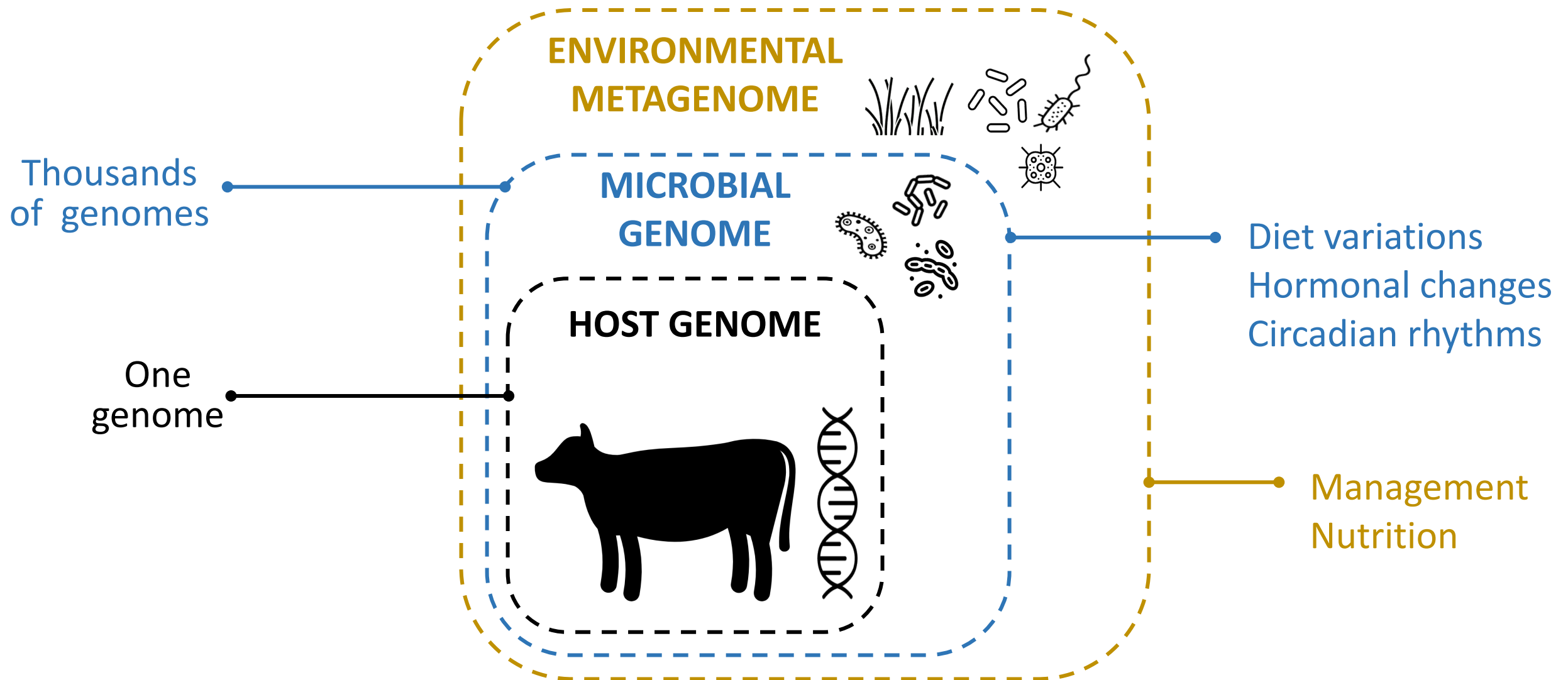
- **78,964 SNPs currently used in official U.S. evaluations; selected based on minor allele frequency, parent-progeny conflicts, and call rate**

Computational Considerations



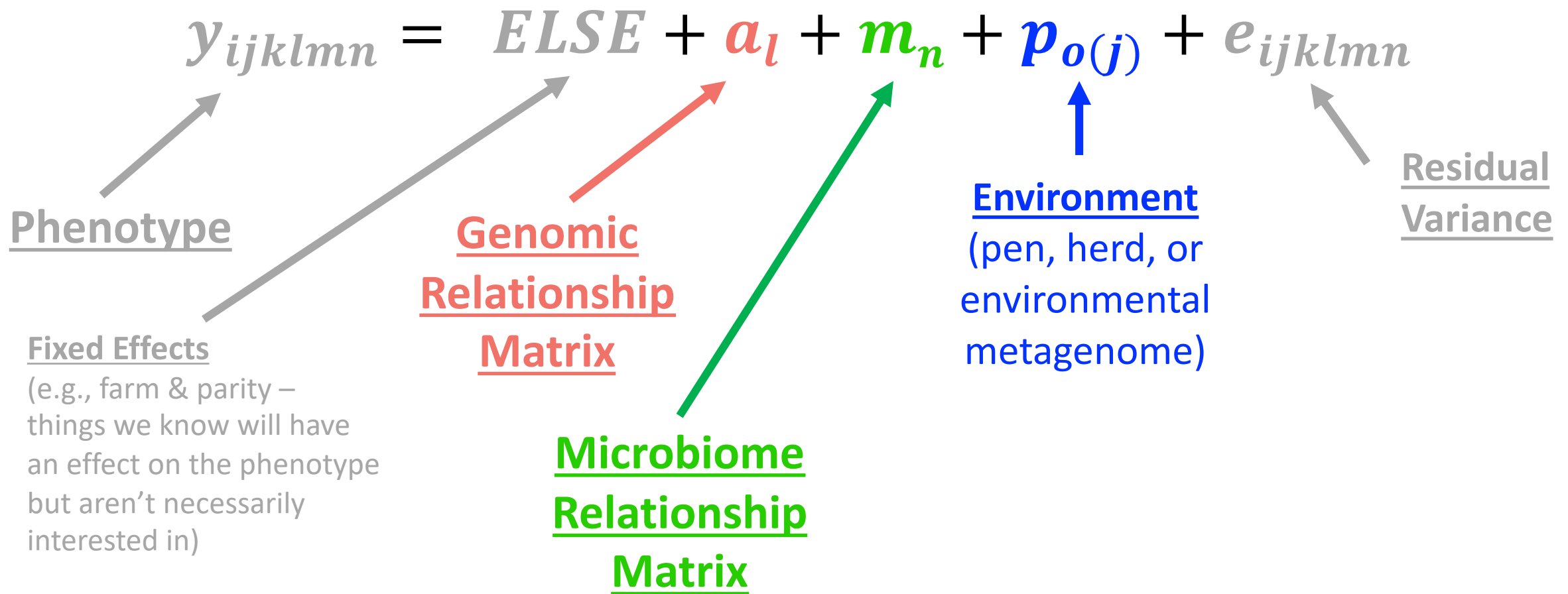
- Mitigate “pre-selection” biases with single-step Genomic Best Linear Unbiased Prediction
- Trait derivations:
 - Alternative SCS traits
 - Multiple categories of MAST
- Multi-trait models
 - SCS & MAST together

Leveraging the microbiome



Leveraging the microbiome

- Methods do exist to integrate host & microbial genetics into prediction models

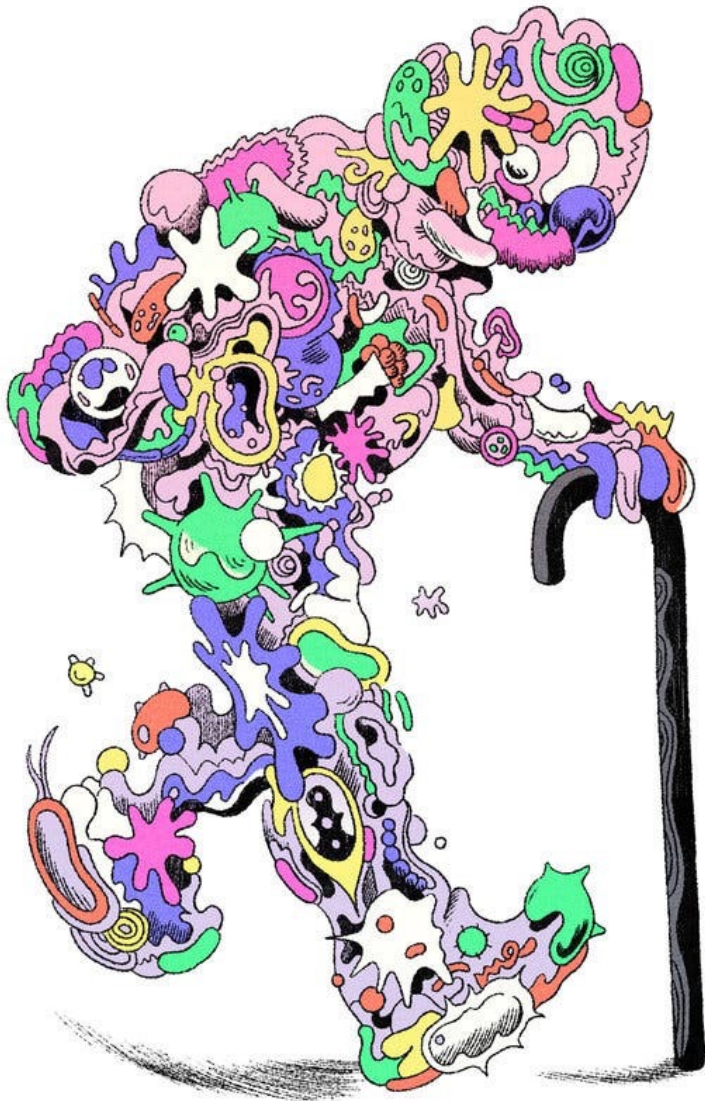


Leveraging the microbiome

BUT...

- **The goal of genomic selection is to maximize the amount of information that can be predicted at birth from the same, inexpensive DNA sample**
 - **Costs of mass-phenotyping microbiomes**
 - **Data standardization and flow**
- **Microbiome insights may be more practical for on-farm interventions than genomic selection**

“It’s the song, not the singer” (Doolittle & Booth, 2017)



Most existing literature has focused on microbiome composition, not overall functionality

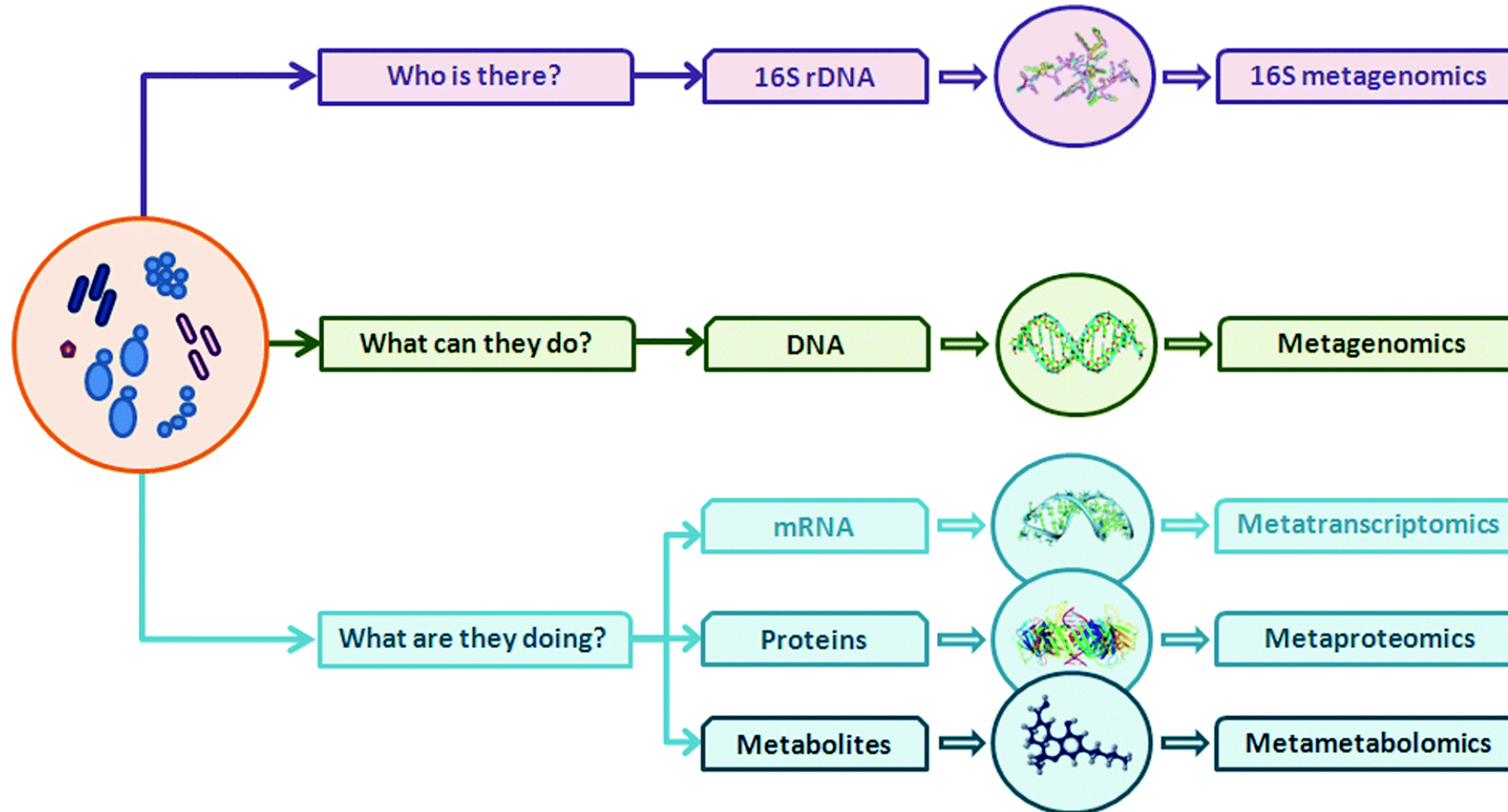
- Taxonomic composition varies over lifetime and by physiological state
- Multiple bugs can produce the same effect

Biochemical functions are more conserved

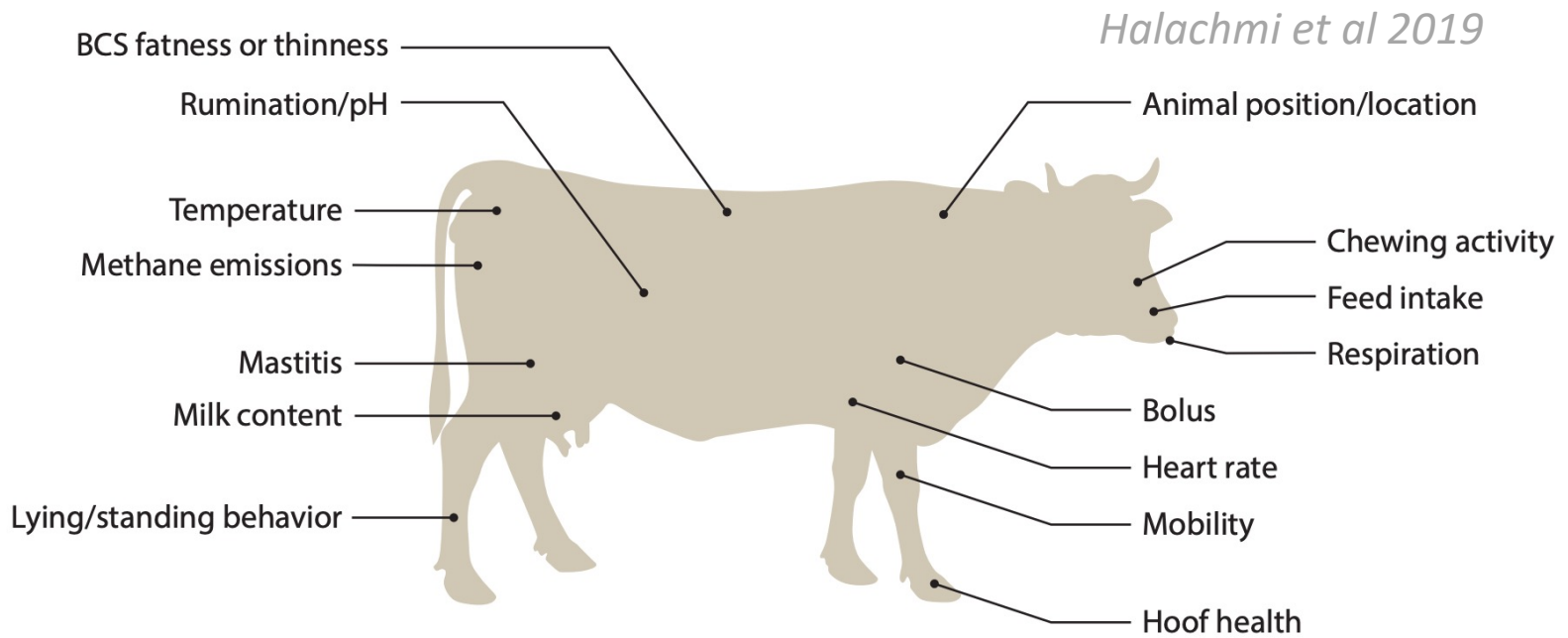
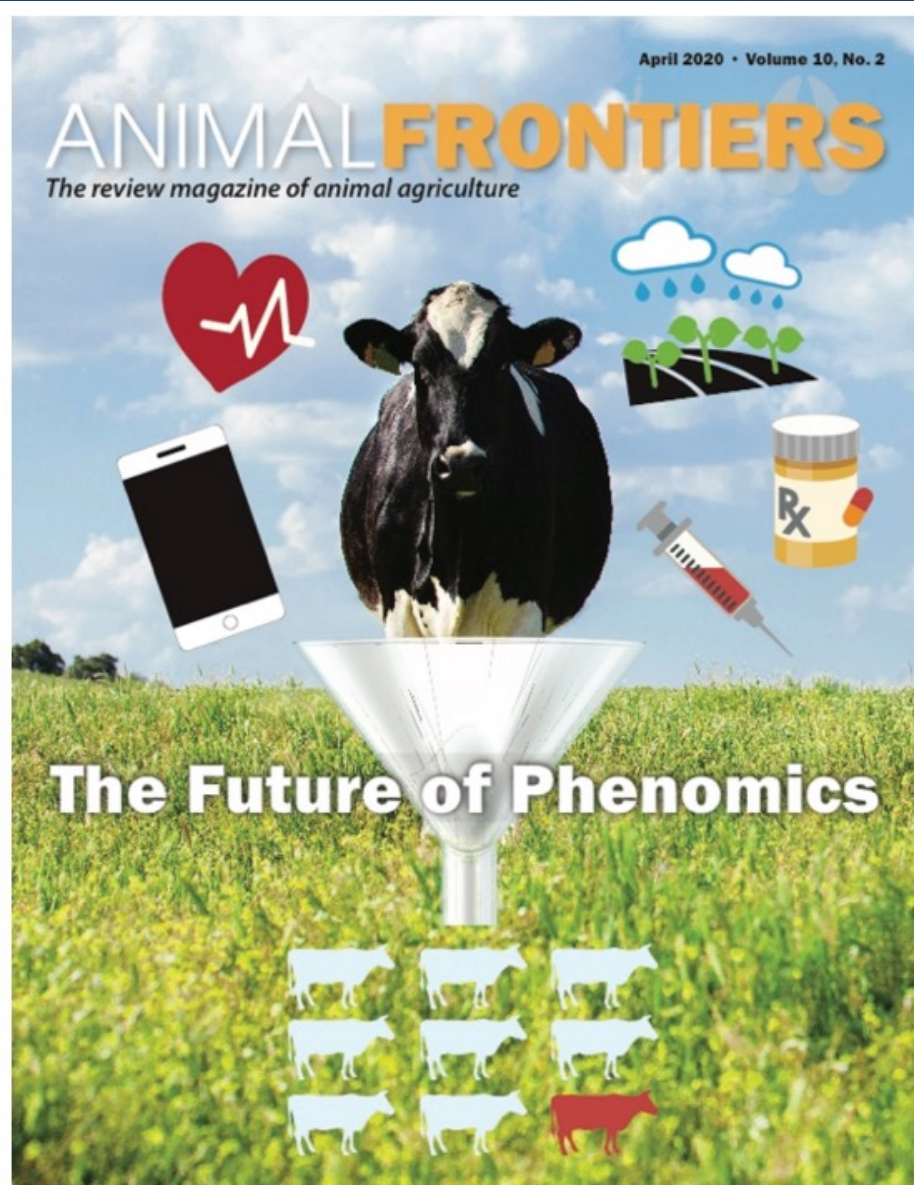
Image: NY Times (2021) “A Changing Gut Microbiome May Predict How Well You Age”

“It’s the song, not the singer” (Doolittle & Booth, 2017)

We should select on molecular signatures for greater impact

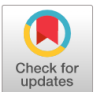


Big Data, Phenomics



EDITORIAL article

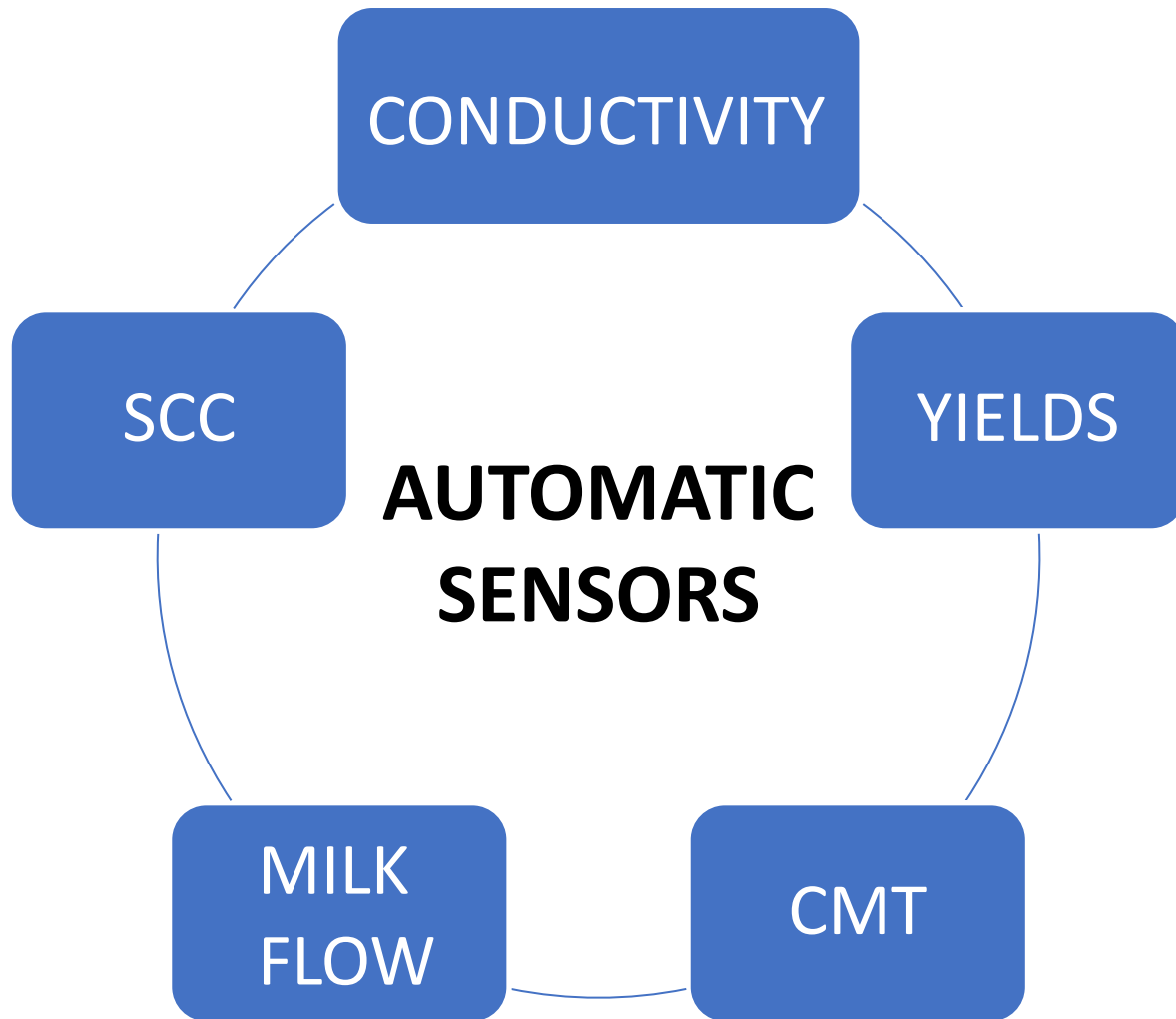
Front. Genet., 18 June 2021 | <https://doi.org/10.3389/fgene.2021.707343>



Editorial: High-Throughput Phenotyping in the Genomic Improvement of Livestock

Fabyano Fonseca Silva^{1*}, Gota Morota^{2,3} and Guilherme Jordão de Magalhães Rosa^{4,5}

Big Data, Phenomics



These are very useful for management decisions:

- **Monitoring subclinical mastitis**
- **Managing bulk tank SCC**
- **Culling**
- **Selective dry therapy**

Big Data, Phenomics

Translating these rapidly generated data into a form usable for genomic selection will be a new challenge

- **No standard data definitions or SOPs**
- **No standard validation, maintenance, or calibration protocols**
- **System bias and individual sensor bias**
- **Animal ID: phenotype mismatches**
- **Non-representative sampling**
- **Data storage, flow, quality control & assurance**

How can we standardize it....

... and who can use it?

- **No standards exist for sharing sensor-generated data**
- **Frequent software and technology updates could limit use and disrupt data flow**
- **Some companies plan to own sensor-generated data**
- **Currently, CDCB offers data stewardship but sole ownership and rights pertaining thereto remain with the producer**

Thank you.

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<https://www.ars.usda.gov/northeast-area/beltsville-md-barc/beltsville-agricultural-research-center/agil/>



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