Gene editing technologies in cattle genetic improvement: Perspective from STgenetics

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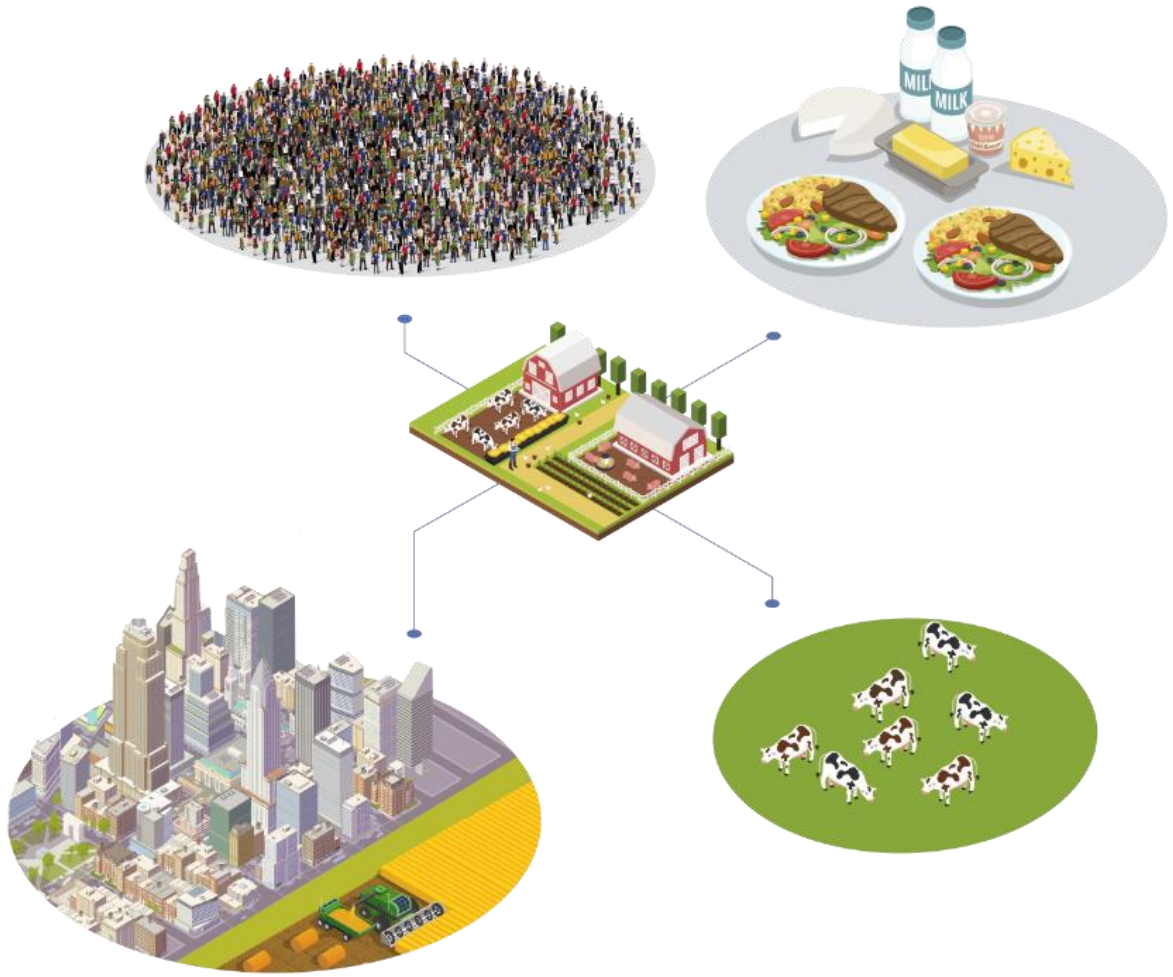
CSO STgenetics

Feeding the world population is a massive challenge

1.7 billion
additional people to feed by 2050 + a rapidly expanding emerging market middle class driving increased demand for protein



Food production **must double by 2050** to meet demand of world's growing population

The availability of **arable land** per capita has been reduced by nearly 60% since 1960

Livestock contributes ~14% of total human-induced **GHG[1] emissions**

Source: Population Reference Bureau, FAO, United Nations Environment Programme, World Resources Institute.
[1] GHG = Greenhouse Gases

STgenetics goal:

A sustainable future by utilizing Biotechnology, Bioinformatics and Biosensors to Improve Efficiencies in livestock production.

Proprietary end-to-end solutions and technology platforms

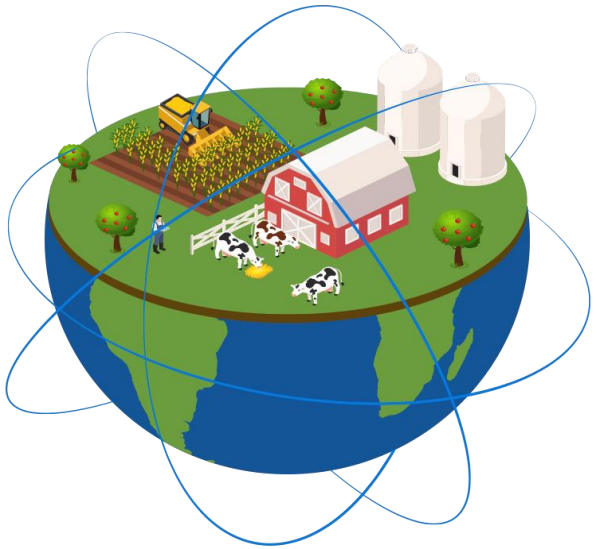
Our core technologies

Sperm Sex-Sorting Services

Optimize herd and accelerate genetic progress

Genomics and Reproduction

Identify genes influencing advantageous traits and accelerate dissemination and improvement



Premium Genetics

Improve genetics and output / yield

Bioinformatics and Biosensors

Monitoring, traceability and analysis of animal health and production efficiency

~20 years of innovation and leadership

1997
XY licenses sex-sorting technology from the USDA

2002
STgen licenses XY

2007
STgen acquires XY

2008
STgen acquires Monsanto's patents on sex-sorting technology

2009
Technology enhancements increase process efficiency and comparatibility with conventional sperm conception rate

cytonome-ST

2015
SexedULTRA product with 2.1M cells per straw and 90% purity launched

STgen launches STgenetics a proprietary bovine genetics business and acquires leading pig genetics company, Fastgenetics

2016
STgen acquires innovative genomic testing platform

GeneticVisions-ST™

2017
4M product with 4M cells per straw launched

STgen launches Ecofeed which ranks 500,000 heifers per year for our customers

STgen becomes majority shareholder[1] in UK's largest bull stud

cogent

2018
STgen launches innovative genomic mating software

Chromosomal Mating

2020
4M High Purity product with 95% or greater purity launched

2022
STgen acquires porcine genetics company

Acuity

Ultraplus product with 3% points higher fertility launched

Expected launch of Farmfits the next generation of health monitoring devices

2023
STgen acquires Ismene in Italy

INSEME

Launch of Acufast

AcuFast

2024
SUPERgen

Sperm sorter upgrade

STgen Inc.

Genetic Improvement

- Breeder's equation

$$\Delta G = \frac{i \times r_{TI} \times \sigma_A}{L}$$

Genomic technologies
Phenomics

Intentional Genetic Alterations
(e.g., gene editing)

Reproductive technologies

$$\text{Genetic Progress} = \frac{\text{selection accuracy x genetic variation x selection intensity}}{\text{generational interval}}$$

Genomic technologies + Reproductive technologies

Intentional Genetic Alterations
(e.g., gene editing)

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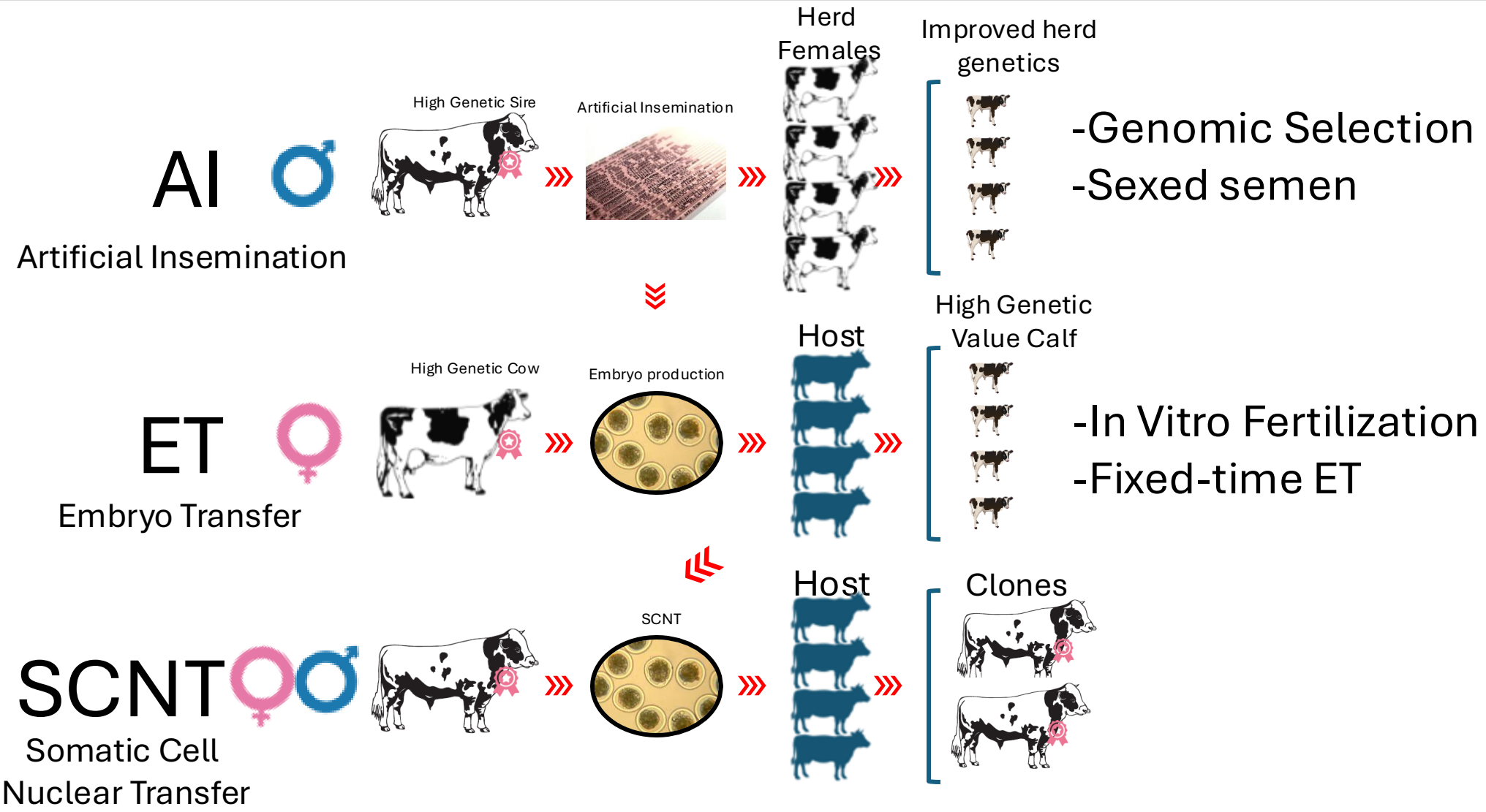
- ET and AI are robust technologies for genetic creation and delivery



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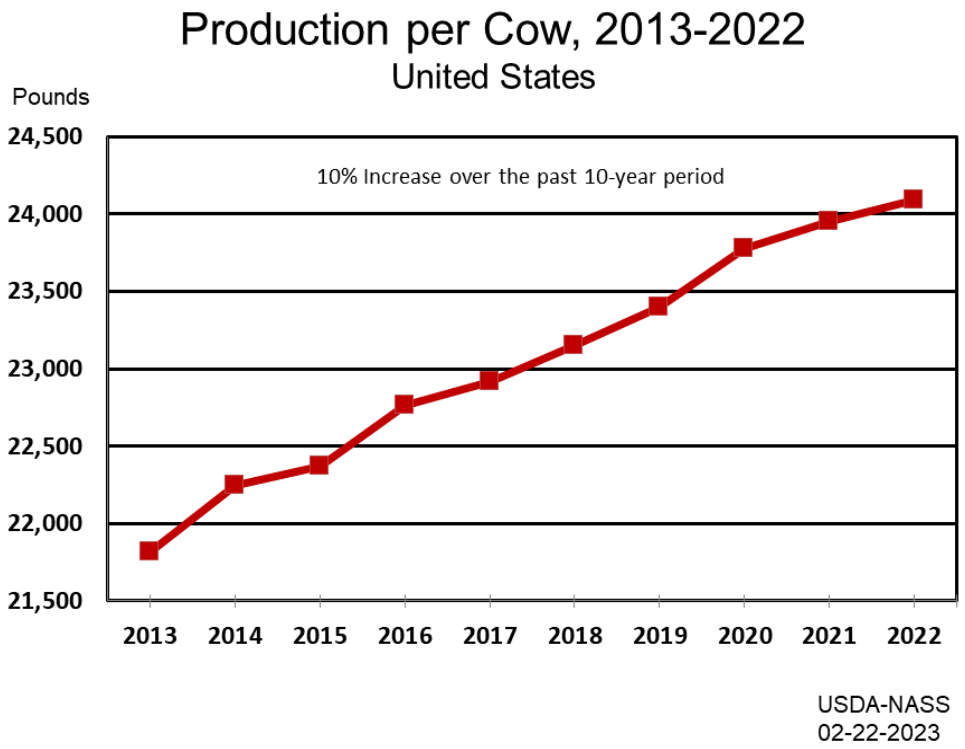
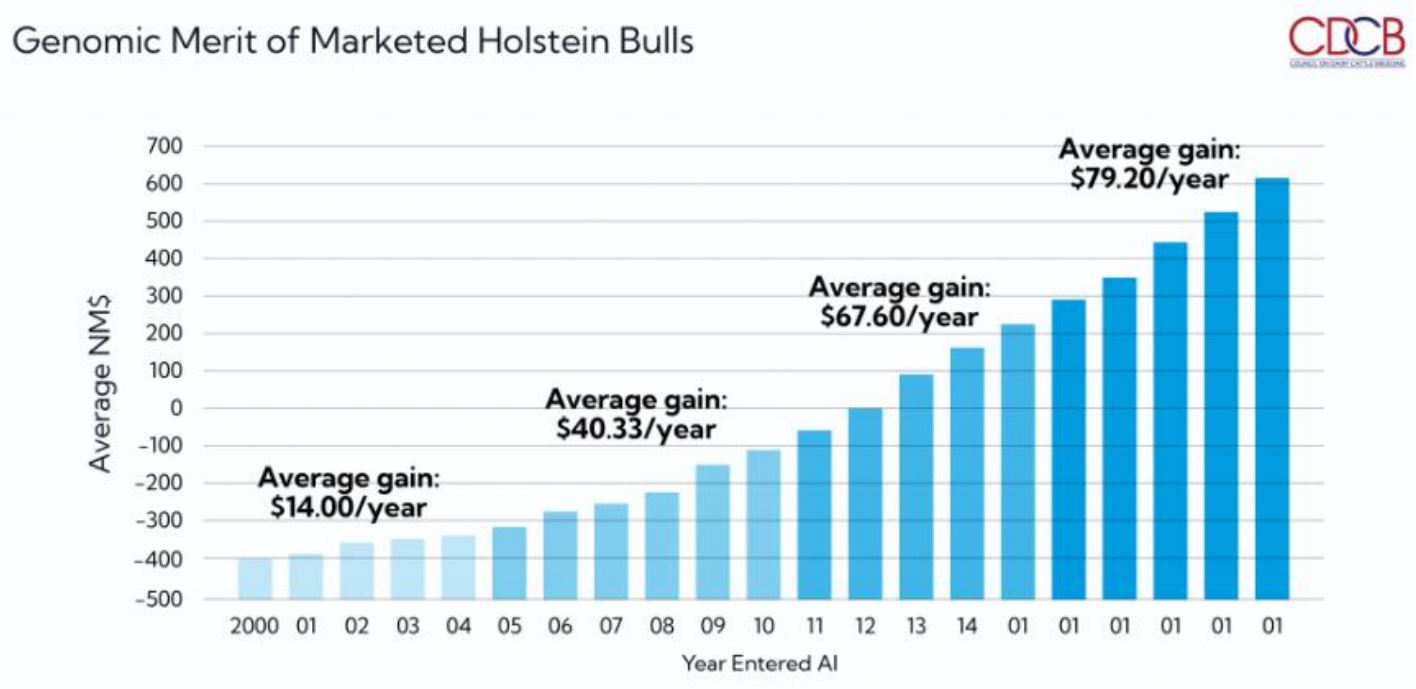
Genetic Progress = $\frac{\text{selection accuracy} \times \text{genetic variation} \times \text{selection intensity}}{\text{generational interval}}$

- Dairy genomic evaluations and genetic improvement is a global effort





- Extensive use of AI
- Strategic use of ET and IVF
- Extensive use of Genomics

Using:

- Top 1% of bulls (NM$1295 average) would result in 56% productivity/ profit improvement
- Top 10% of bulls (NM$1119 average) would result in 42% productivity/ profit improvement

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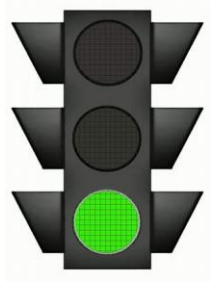
- Gene Editing



TECHNOLOGY

We can modify any sequence in the genome.

Efficient and precise.

Precise genome editing: CRISPR-Cas9, TALEN, ZFN, HR

- Remove allergens (e.g., beta lactoglobulin, alpha-galactosidase)
- Thermotolerance (e.g., slick, all white coat)
- Unwanted development (e.g., horns)
- Increase yield/quality (e.g., myostatin, SOCS2, omega-3)
- Disease resistance/tolerance (e.g., BVDV, TB)
- Sex ratio Skew (e.g., SRY knock-out for females, SRY knock-in for males)

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$$\text{Genetic Progress} = \frac{\text{selection accuracy} \times \text{genetic variation} \times \text{selection intensity}}{\text{generational interval}}$$

- Gene Editing

REGULATIONS

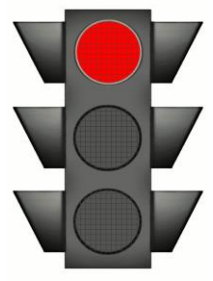
Regulatory system in place.

Cumbersome, time consuming, expensive.

Animals with IGA approved by the USA-FDA for human consumption:

- AquaBounty salmon: High growth fish (23 years and >$120 million)
- Alpha-gal KO pigs: Allergen removal from pork (byproduct of medical application)
- NANOS2 KO pig: Lack of male germ cells ($200,000 to approve five animals)
- Slick cattle: Increased thermotolerance (naturally occurring mutation, FDA ED)

- Gene Editing



MARKET ACCEPTANCE and COMPETITIVE ADVANTAGE

Likely to be controversial. Retailers push back is possible.

Edited genes so far only provide marginal value.

*The FDA has determined that there is no significant difference in milk from rbST treated cows and non-rbST treated cows

• MARKET ACCEPTANCE CONSIDERATIONS

- Benefit/risk to Genetic Companies, Producers, Processors, Retailers, and Consumers
- Traits that provide a direct benefit to consumers are more likely to achieve public acceptance (may be niche markets – e.g., α-gal knockout)
- Long generation intervals in cattle increase uncertainty of investment (especially for recessive traits)
- High value/cost of each animal requires significant investments
- Transparency in product labeling will require traceability and segregation, adding cost to novel products
- Trait will have to provide a significant value margin to justify risks
- Genetic changes cannot be reversed (different to rBST)
- Export/import markets and global genetic flow requires a coordinated global approach
- Genetic bottlenecks could limit widespread dissemination of novel traits

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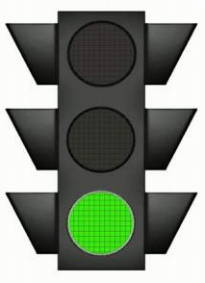
- STgenetics perspective on gene editing technologies applied to cattle



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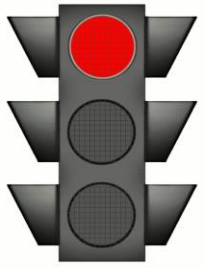

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