Genomic Selection for Novel Traits in Dairy Cattle

奶牛新性状的基因组选择

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Breeding Program
育种规划

- A pertinent and relevant breeding goal 相关且具有针对性的育种目标
- Appropriate breeding objectives 合适的育种目标
- High quality data from the relevant population 来自相关群体的高质量数据
- Accurate genetic/genomic evaluation system 准确的遗传/基因组评估体系
- Efficient and effective breeding scheme 高效和有效的育种方案
- A system to disseminate the elite germplasm to end users 一个将优秀遗传种质传递给终端用户的系统

Breeding Objectives
育种目标

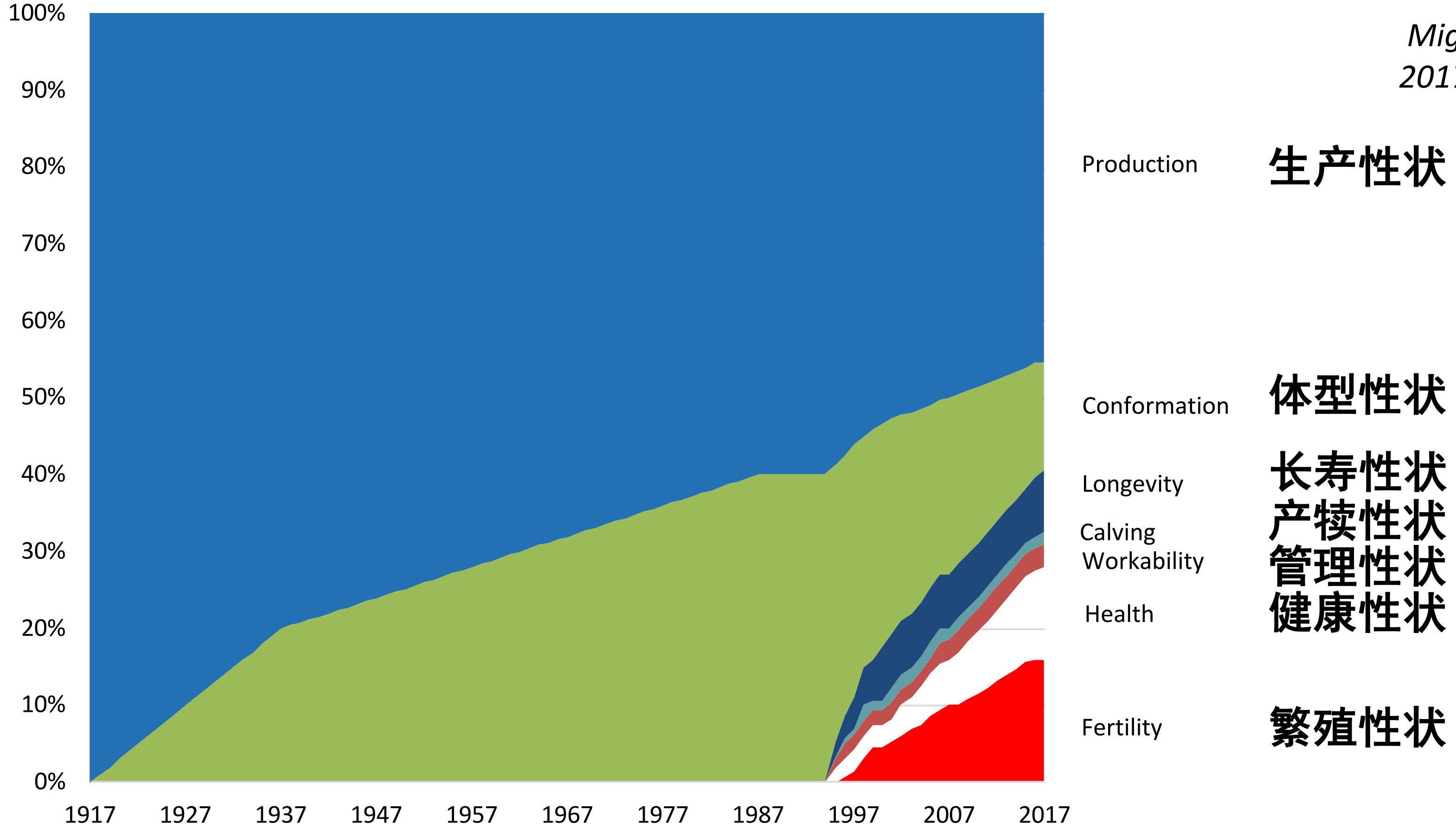
Historically & Currently

历史与现在

Internationally & in North America

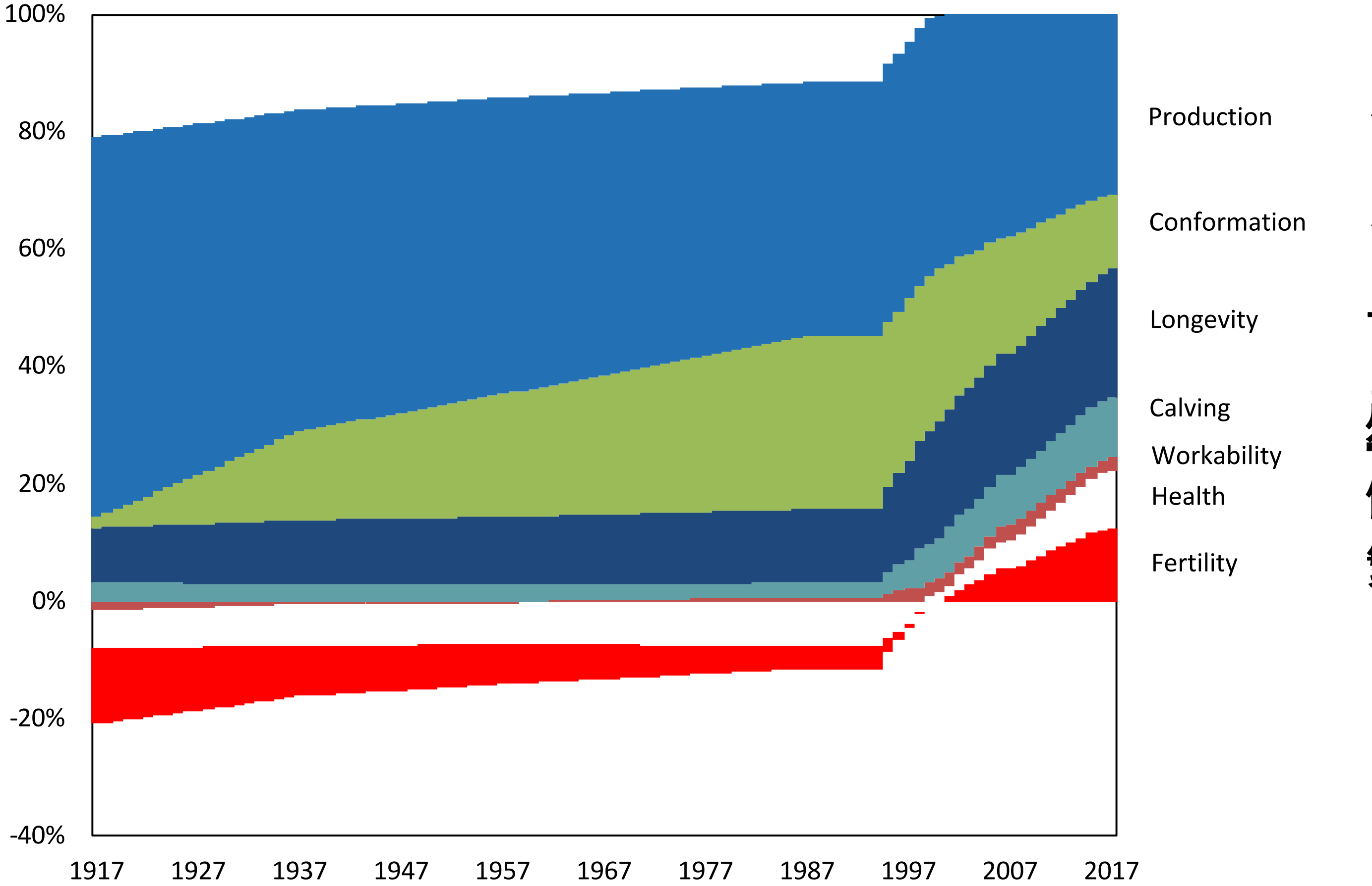
国际与北美

Selection goals over 100 years
100年以来的育种目标



Miglior et al. 2017, JDS 100

Selection response over 100 years
100年以来的选择进展



Miglior et al. 2017, JDS 100

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Range of Heritability
各性状遗传力的范围

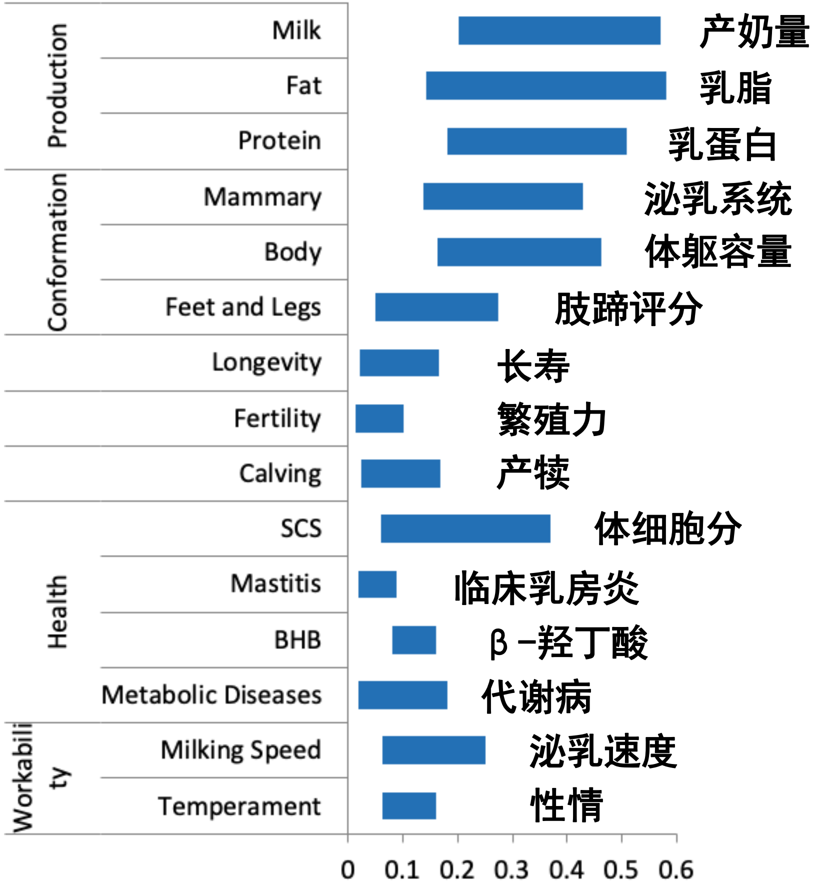
Miglior et al.
2017, JDS 100

生产性状

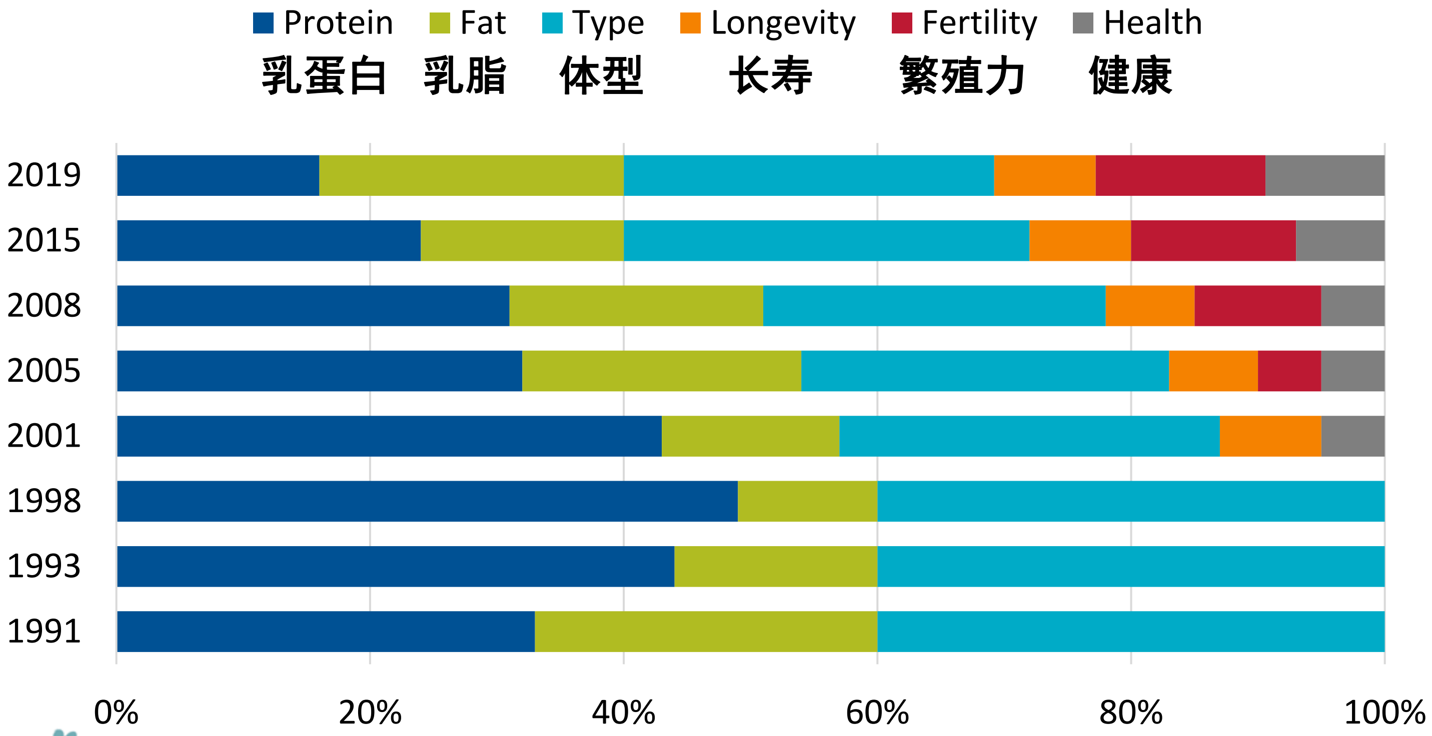
体型性状

健康性状

管理性状



Holstein LPI Relative Emphasis Over Time
不同时期荷斯坦牛终身效益指数（LPI）的组成



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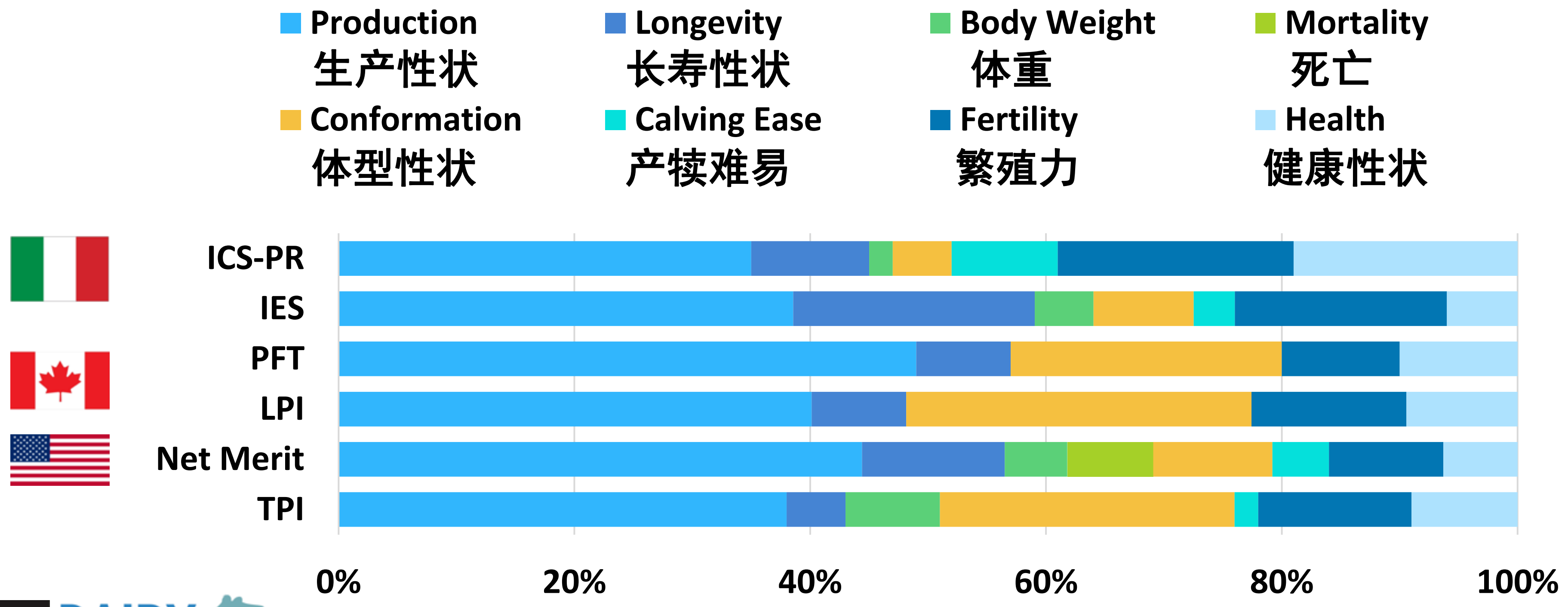
Comparison among US, Italy and Canada
美国、意大利和加拿大之间选择指数的差异



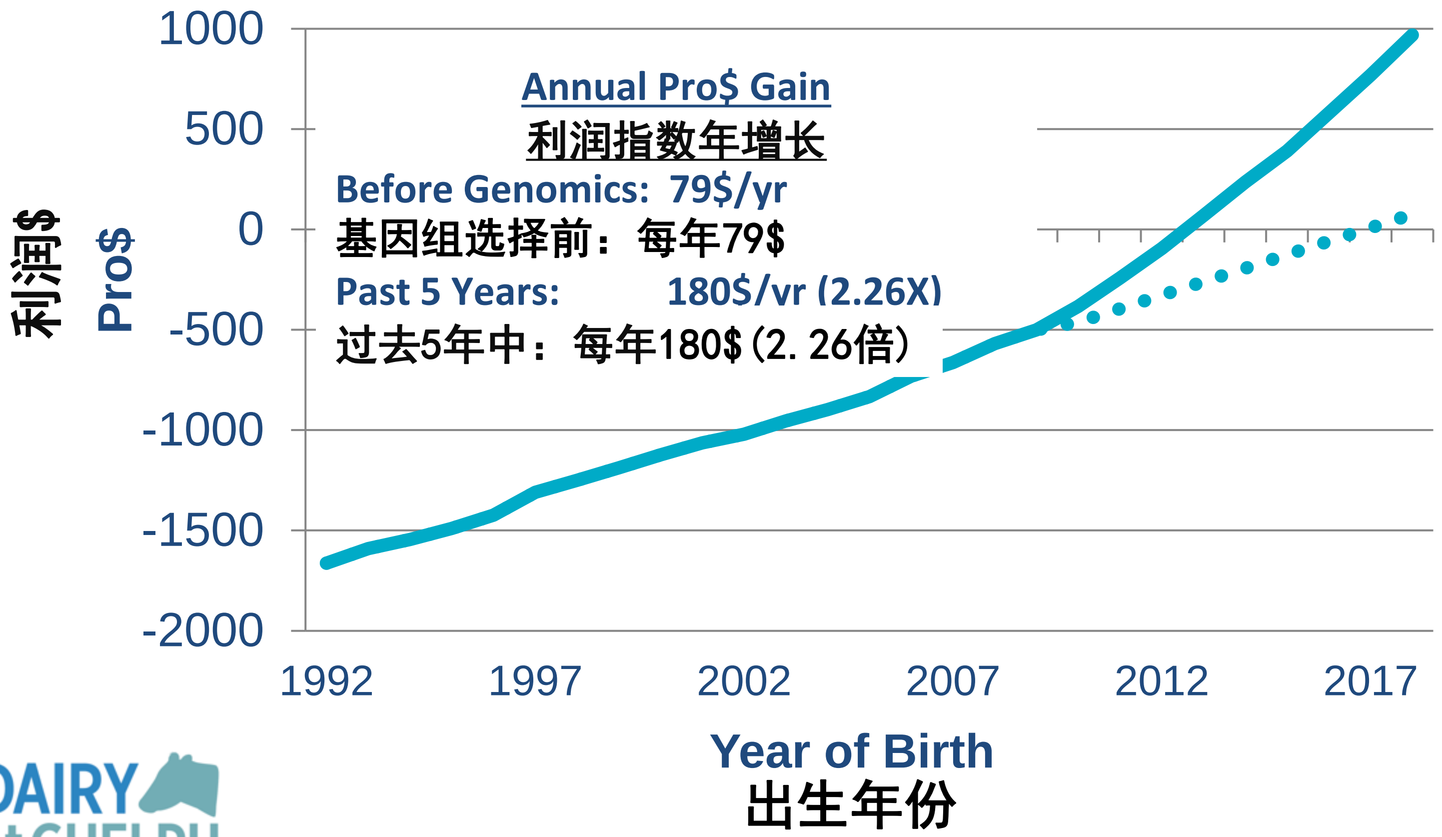
Which Health Traits are Evaluated
可评估的健康性状

	United States 美国	Canada 加拿大	Italy 意大利
Somatic Cells 体细胞数	√	√	√
Mastitis 乳房炎	√	√	
Ketosis 酮病	√	√	
Displaced Abomasum 真胃变位	√	√	
Subclinical Ketosis (BHB) 亚临床酮病（β-羟丁酸）		√	
Milk Fever 产乳热	√		
Metritis 子宫炎	√	√	
Retained Placenta 胎衣不下	√	√	
Cystic Ovaries 卵巢囊肿		√	
Hoof Lesions 肢蹄病		√	

Genomic Selection

基因组选择

Genetic Trends for CAN Holstein Females
加拿大荷斯坦母牛的遗传趋势



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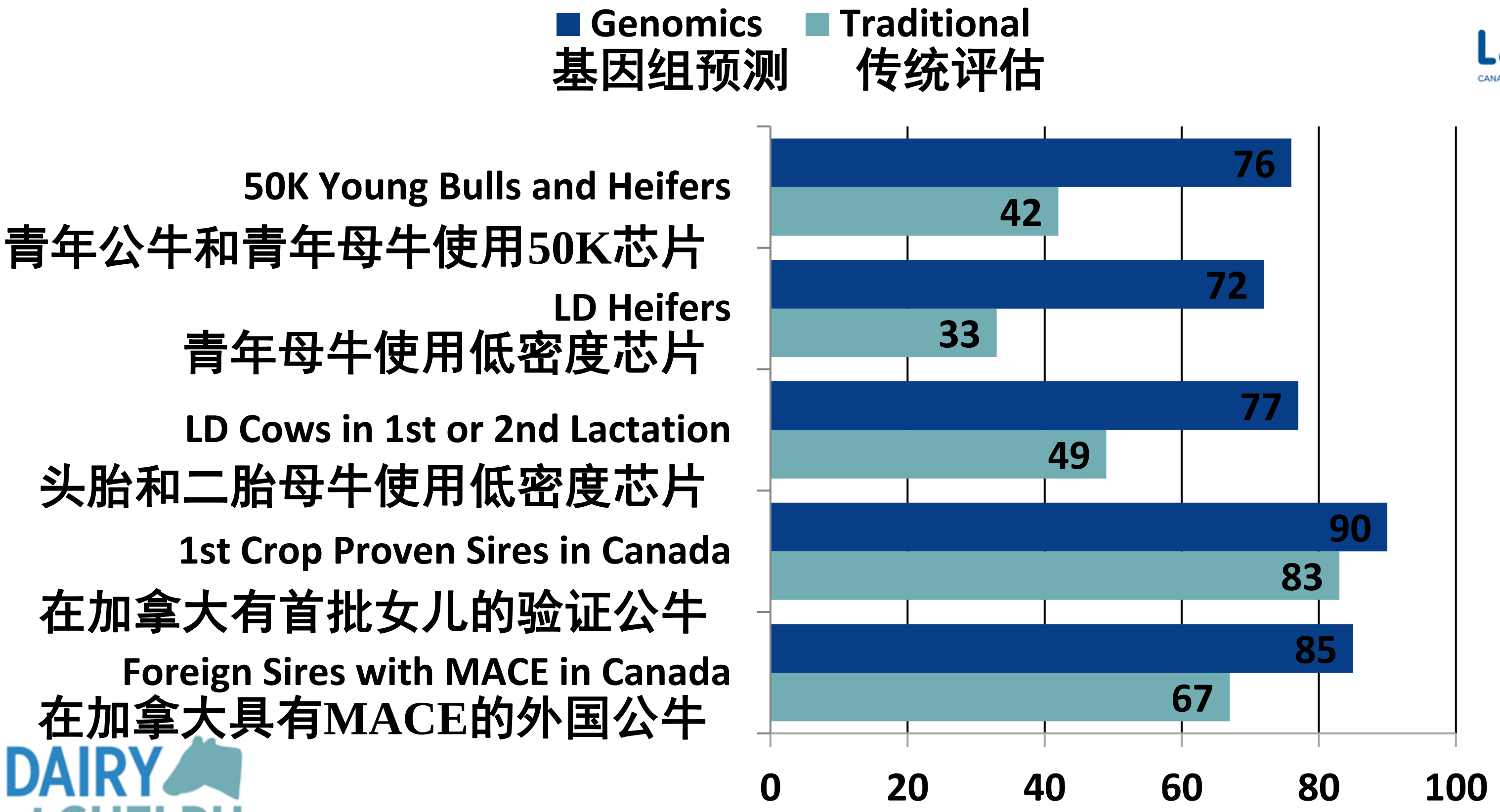
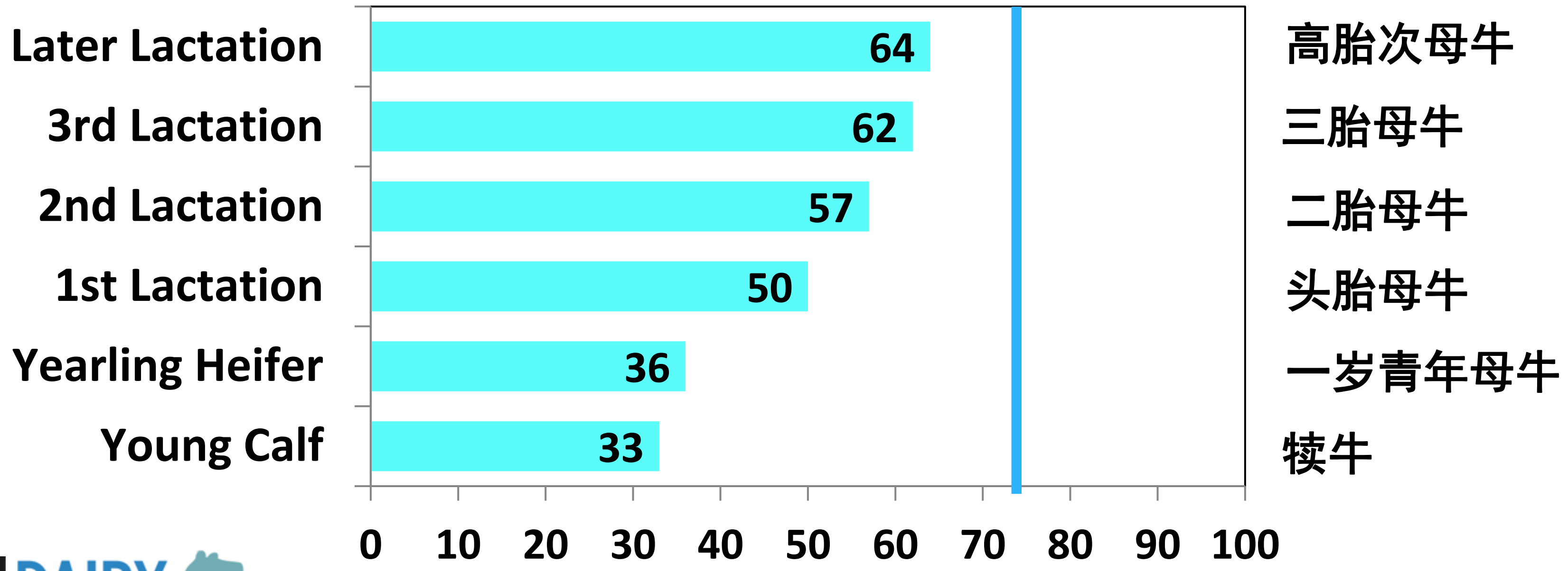
Gain in Reliability with Genomics
基因组提高预测可靠性



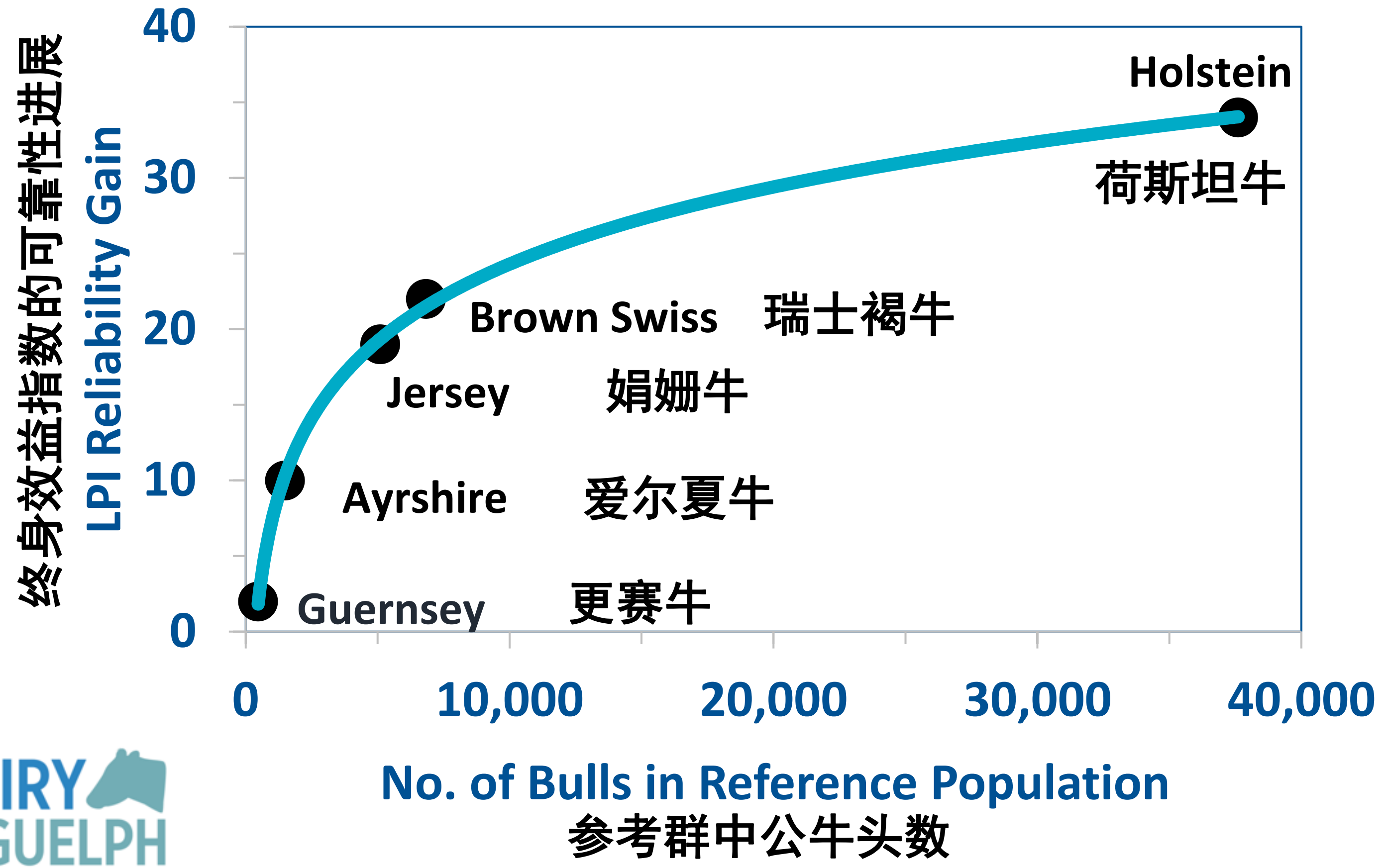
Gain in Reliability with Genomics
基因组信息提高预测可靠性

72-76% Reliability once genotyped

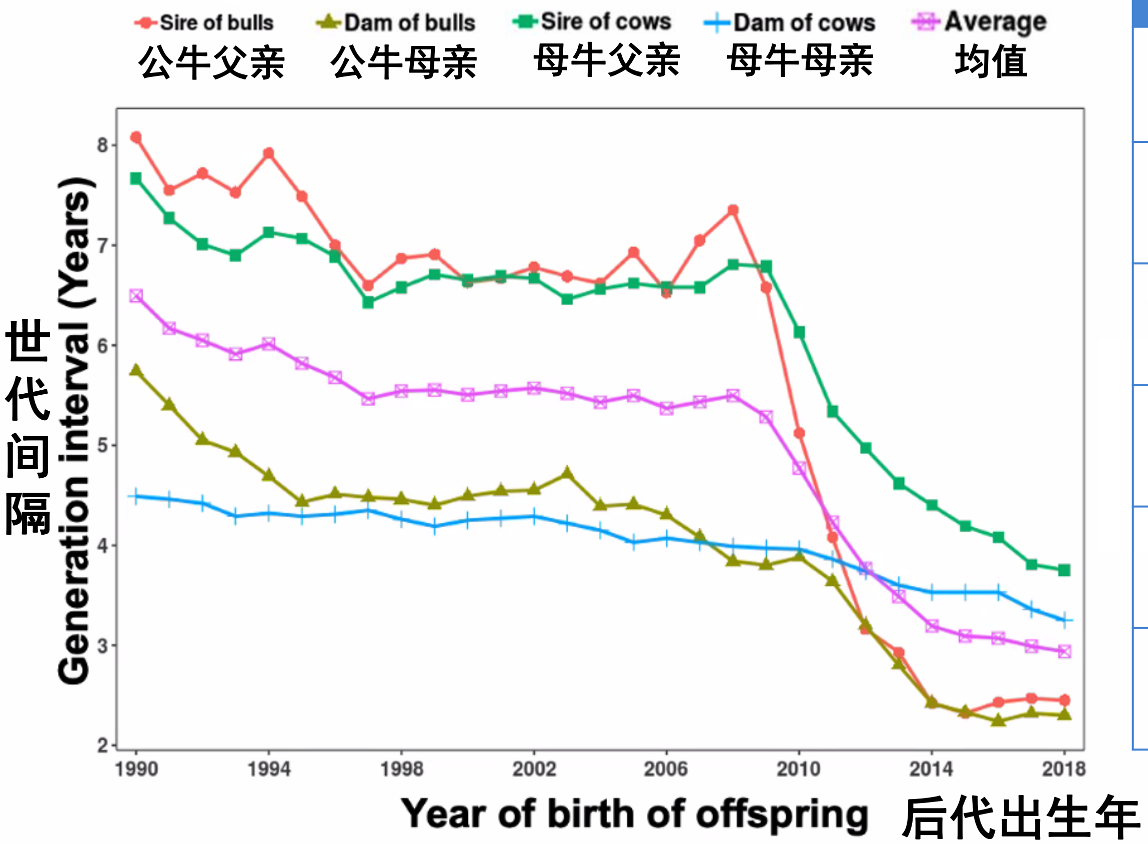
具有基因型信息后评估可靠性为72-76%



Reliability Gain by Reference Population
各品种参考群与其可靠性



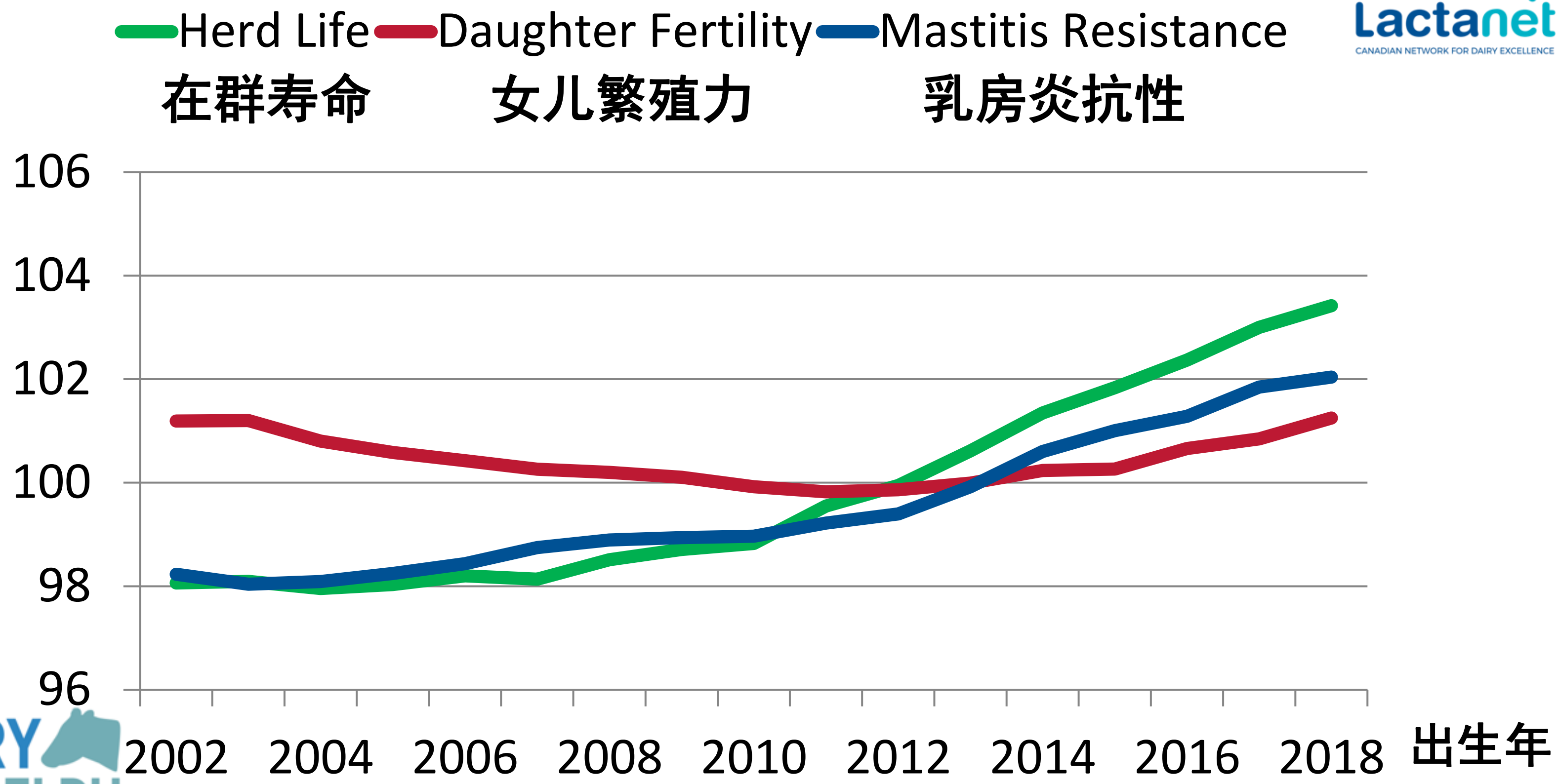
Generation interval 世代间隔



Makanjuola et al. 2020

	Number 数目
Pedigreed animals 具有系谱的奶牛	676,594
Founders 祖先	32,909
Generations traced 可追溯世代数	34
Genotyped bulls 具有基因型的公牛	55,735
Genotyped cows 具有基因型的母牛	158,831
SNP 单核苷酸多态性	43,801

Functional Traits Genetic Trends for Females
母牛功能性状的遗传趋势



Novel Traits

奶牛新性状

Arguably, the BIGGEST benefit of genomics is the opportunity to improve novel traits of importance

基因组预测的最大优势在于为选育提高重要新性状提供了契机

Traditional Selection
传统遗传选择

- Sophisticated statistical methods are used to predict the genetic merit of individuals **使用复杂统计方法预测个体遗传价值**
  - Information from daughters, parents and other relatives **需要其女儿、父母及其它亲属信息**
  - Genetic and environmental effects well separated**精细剖分遗传和环境效应**
- Their application has been very successful in dairy for the improvement of easily measured traits **在奶牛育种中使用传统评估技术改进那些易于测定性状已取得巨大成功**
  - Mainly due to the feasibility of recording traits from thousands of herds across the country **主要原因在于可以便利地获取全国数千牧场的性状记录**

New Phenotypes: Novel traits
新表型：新性状

- However, this strategy is not feasible for traits that are costly to measure 但传统选育策略不适用于测定成本高昂性状的遗传选择
- The advent of genomics provides an exceptional opportunity to genetically improve the national herd for those traits that are more costly to record 基因组预测技术的出现，为在遗传水平上选育测定成本高的性状提供了契机
- What is a novel trait? 什么是新性状？
  - An economically important trait that was not recorded or used in evaluation because too expensive 具有经济重要性，但因测定成本太高而从未被大规模记录或用于遗传评估的性状

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National Dairy Health Recording
全国奶牛健康性状数据

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- Starting in 2007, a national system for collecting health events in Canada

  2007年起，加拿大建立了系统收集全国奶牛健康事件的技术体系
  - Concentrates on eight key diseases 集中于8种主要疾病
- Producer-recorded on voluntary basis 农场主自愿参与记录
  - Herd participation ~40% of herds 约40%牧场参与
- Provides data for genetic evaluations for health traits 为奶牛健康性状的遗传评估提供数据
- Additionally some hoof trimmers are now sending their records in a standardized manner 此外部分修蹄技术人员用标准化的方式随时上报他们的修蹄数据

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Health Genetic Evaluations in Canada
加拿大奶牛健康性状的遗传评估

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2014

Mastitis Resistance
乳房炎抗性

- Clinical mastitis, SCS

临床乳房炎、体细胞分

2016

Metabolic Dis. Resistance
代谢病抗性

- Displaced abomasum, clinical, sub-clinical ketosis (milk BHB)

真胃变位、临床和亚临床酮病（牛奶β-羟丁酸）

2018

Hoof Health
蹄部健康

- 8 most prevalent hoof lesions

8种常见蹄病

2020

Fertility Disorders
繁殖紊乱

- Metritis, Retained Placenta, Cystic Ovaries

子宫炎、胎衣不下、卵巢囊肿

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Evaluation Enhancements
评估进展

健康性状收集

2007

Health traits

基因组预测

2009

Genomics

母牛参考群体

2017

Female reference population

一步法预测

2018

Single-Step model

Health Genetic Evaluations in Canada
加拿大奶牛健康性状遗传评估

2014

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2016

Two-Step genomic evaluation

两步法基因组评估

- traditional evaluation

  传统遗传评估

- SNP estimation

  SNP效应估计

Use of correlated predictor traits with high heritability

使用高遗传力的相关性状

- To increase reliability of EBV

  提高育种值估计可靠性

- To improve SNP estimation accuracy

  提高SNP效应值的估计准确性

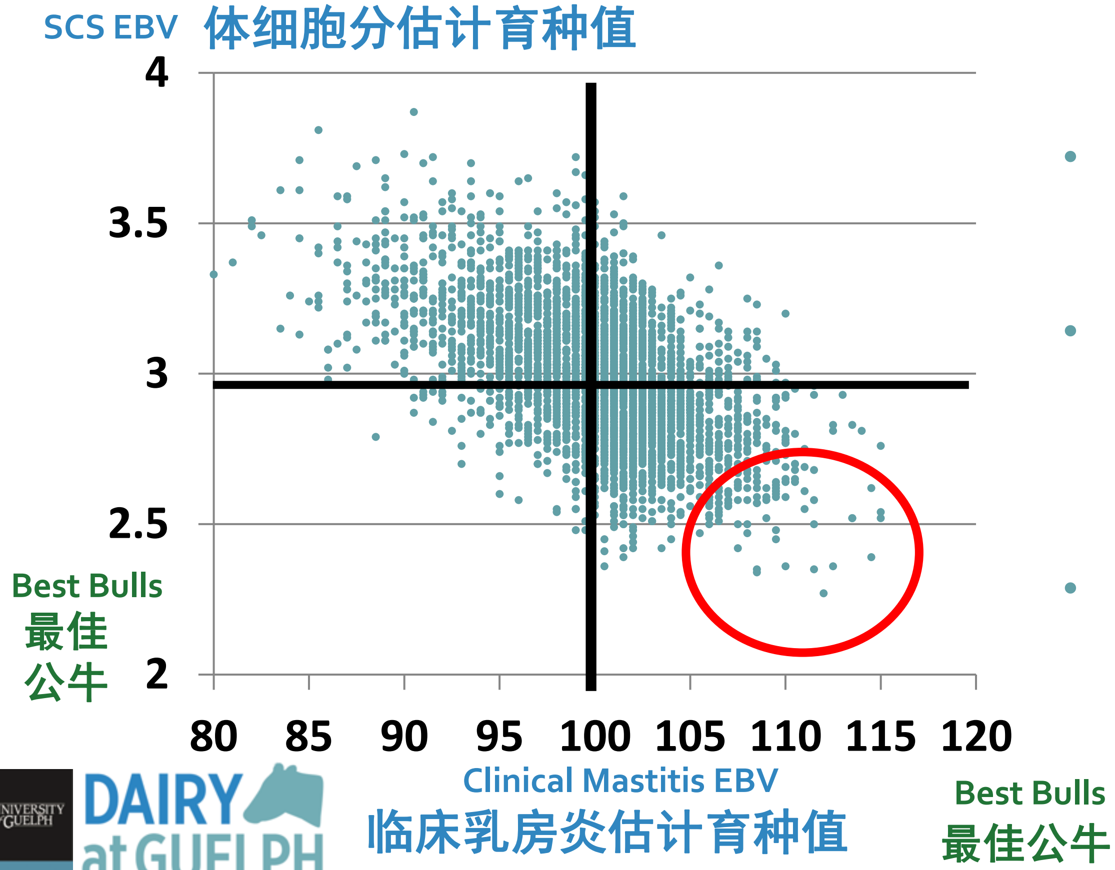
Index for Mastitis Resistance
奶牛乳房炎抗性指数

- Multiple-trait evaluation including mastitis and well correlated predictors with higher heritability多性状模型，包括乳房炎和具有高遗传力的强相关指标在内
  - Patterns of SCS, BCS, Udder Depth and Fore Udder 体细胞分、体况评分、乳房深度和前乳房附着
  - Increase of **+30 points in reliability of EBV** 育种值估计可靠性提升30个百分点
- Since Aug 2014, **Index for Mastitis Resistance** (MR) 2014年8月制定乳房炎抗性指数
  - $^{1}/_{3}$ CM-First + $^{1}/_{3}$ CM-Later + $^{1}/_{3}$ SCS
- Genomics 基因组预测
  - Holsteins: over 3,000 Canadian reference bulls 荷斯坦牛参考群体：>3000头加拿大公牛
  - **Increase in reliability of +16 points** for young bulls, and **+8** for proven bulls 青年公牛育种值估计可靠性提升16个百分点，验证公牛提升8个

Now we may use Interbull MACE to increase bull reference population

现可使用Interbull MACE扩大公牛参考群体

Why an Index with SCS and Mastitis?
为何制定包括体细胞分和乳房炎的综合指数



- Why not using just mastitis EBV? 为何不只用乳房炎估计育种值？
- Mastitis EBV are indicators of clinical mastitis 乳房炎估计育种值反映临床性乳房炎
- SCS EBV are indicators of subclinical mastitis 体细胞分估计育种值反映亚临床性乳房炎

Metabolic Diseases – Evaluation
代谢病—评估

First parity cows – 2nd Parity cows and later 头胎牛—经产牛

Metabolic disease traits (5-100 DIM) (h^2 = 0.02-0.06)

代谢性疾病性状 （产后5–100天）（遗传力：0.02-0.06）

- Clinical Ketosis (CK) and Displaced Abomasum (DA) 临床性酮病和真胃变位

Sub-clinical Ketosis (SCK) (5-45 DIM) 亚临床性酮病 （产后5-45天）

- Milk β-hydroxybutyrate (BHB) (h^2 = 0.08-0.15) 牛奶β-羟丁酸 （遗传力：0.08-0.15）

Milk recording predictor traits: (5-45 DIM) DHI记录中的指示性状 （产后5-45 天）

- Fat to Protein Ratio (F:P) (h^2 = 0.10-0.16) 脂蛋比 （遗传力：0.10-0.16）

First parity cows 头胎牛

Conformation indicator traits 体型性状中的指示性状

- Body Condition Score (BCS) (h^2 = 0.29) 体况评分 （遗传力：0.29）

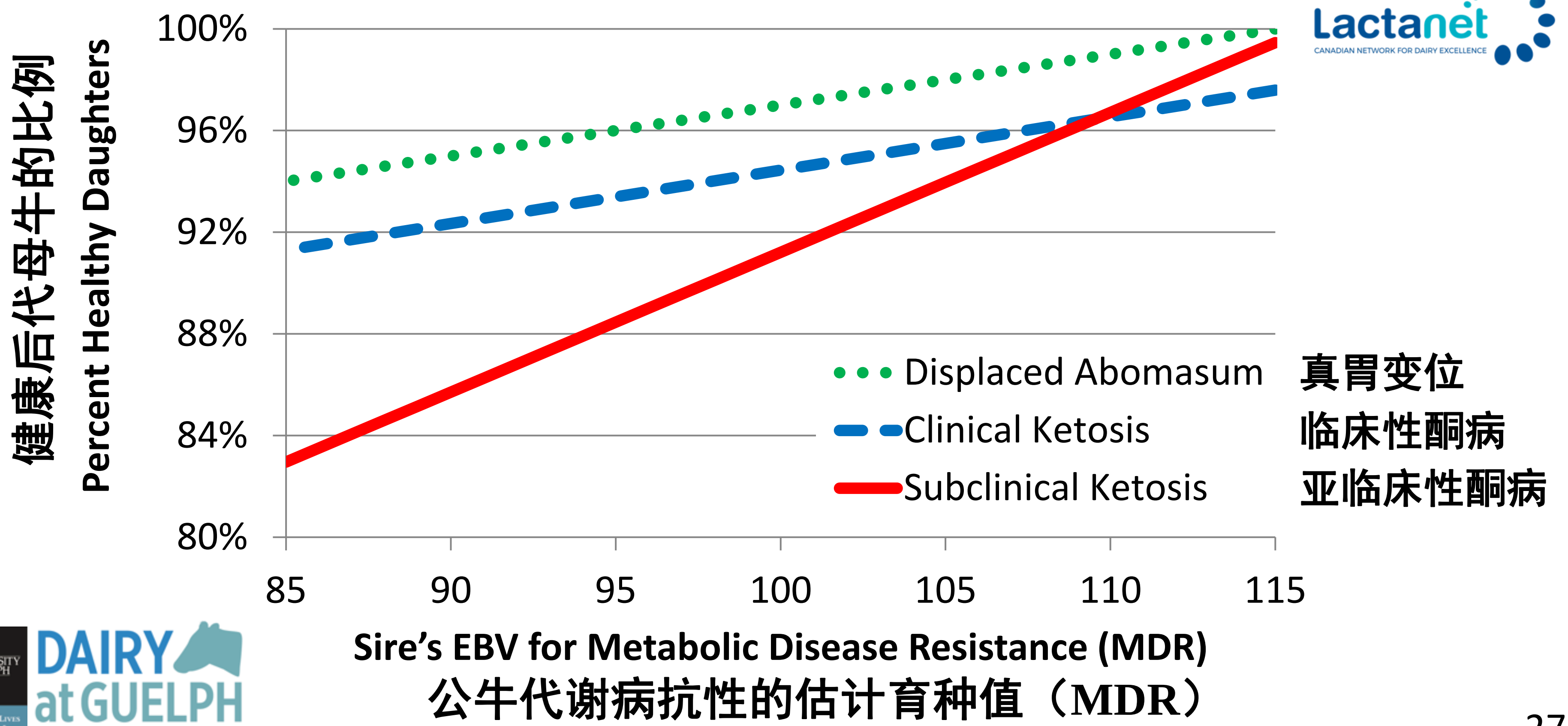
Index for Metabolic Diseases Resistance
代谢病抗性指数

MDR = 0.50 SCK + 0.25 CK + 0.25 DA （亚临床酮病+临床酮病+真胃变位）

- All components头胎与经产: $0.5^*EBV_1 + 0.5^*EBV_{2+}$
- Rational for weightings 合理的权重
  - Higher frequency and cost of CK compared to DA 临床性酮病的发病率和经济损失高于真胃变位
  - However, sub-clinical ketosis (SCK) more common than CK 然而，亚临床性酮病比临床性酮病发病率更高
  - Selection on SCK will induce a correlated response on CK and DA (genetic correlations) 直接选择亚临床性酮病抗性，临床性酮病及真胃变位的抗性将取得间接进展（遗传相关）
  - Higher heritability of SCK 亚临床性酮病遗传力较高
  - Quantity and quality of BHB records is superior to producer-recorder health data

β-羟丁酸记录的数量和质量优于场内健康记录

Expected Percentage of Healthy Daughters
健康后代母牛的预期比例



Health Genetic Evaluations in Canada
加拿大健康性状的遗传评估

Enlargement of female reference population **扩大母牛参考群**
- Over 20,000 genotyped cows

  >2万头具有基因型信息的母牛

Inclusion of hoof trimmers in animal improvement industry
将修蹄人员纳入奶牛健康提升项目
- Data pipeline for hoof lesions

  蹄病的数据记录标准化流程

Implementation of Single-Step genomic evaluation **实施一步法基因组评估**
- Increase of GEBV reliability

  提高基因组估计育种值的可靠性
- No need of correlated predictors

  无需相关的指示性状

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2018

Hoof Health **蹄部健康**
- 8 most prevalent hoof lesions **8种常见蹄病**

Fertility Disorders **繁殖障碍**
- Metritis, Retained Placenta, Cystic Ovaries **子宫炎、胎衣不下、卵巢囊肿**

2020

Hoof Lesions
蹄病

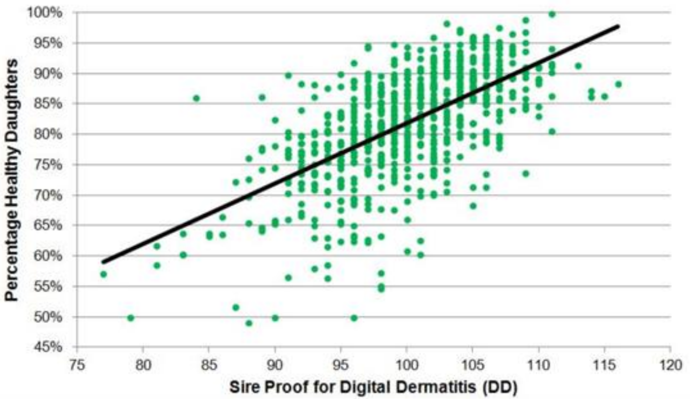
- In Canada, around 25-30% of cows have at least one hoof lesion 加拿大牛群中约25–30%的母牛至少患过一次蹄病
- Hoof lesions compromise the welfare of animals 蹄病不利于动物福利
- Economic loss, costs associated: 相关经济损失如下：
  - with treatment of lesions 蹄病的治疗费
  - with decreased cow performance (production and fertility) 奶牛性能下降（生产和繁殖）
- Low correlations between hoof lesions and feet and leg conformation traits 蹄病和肢蹄部位部位的体型评分之间的遗传相关低
- Solution: 解决办法
  - Use data collected by hoof trimmers 利用修蹄人员收集的数据

Large Differences among Sires
公牛间存在巨大差异

- From hoof trimmer tablets to DHI, and to CDN **修蹄人员将数据上传到DHI，再到CDN**
- Over 50 trimmers have been recruited**招募了50多位修蹄人员**
- 150,000 cows. Aim is 10-20% of milk recorded cows **15万头牛，目标是DHI参测群的10-20%**

Traits 性状		发病率 %	遗传力h^2
Digital Dermatitis	趾部皮炎	17.4	0.08
Heel Horn Erosion	蹄踵糜烂	2.4	0.08
Sole Hemorrhage	蹄底出血	7.2	0.03
Interdigital Dermatitis	趾间皮炎	2.6	0.05
Interdigital Hyperplasia	趾间增生	2.2	0.06
Toe Ulcer	趾尖溃疡	1.4	0.04
Sole Ulcer	蹄底溃疡	8.5	0.05
White Line	白线病	4.8	0.04

健康后代母牛占比



趾部皮炎的公牛育种值

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New Data Pipeline
新数据传输流程

修蹄人员

Herd inventory Interface

牛群数据管理系统

Lactanet

CDN

Hoof Lesions

蹄病

Trimming & HS Reports

修蹄&肢蹄健康报告

Dairy Producers

牧场

Management report

管理报告

Weekly GEBV for hoof health

蹄部健康每周估计基因组育种值

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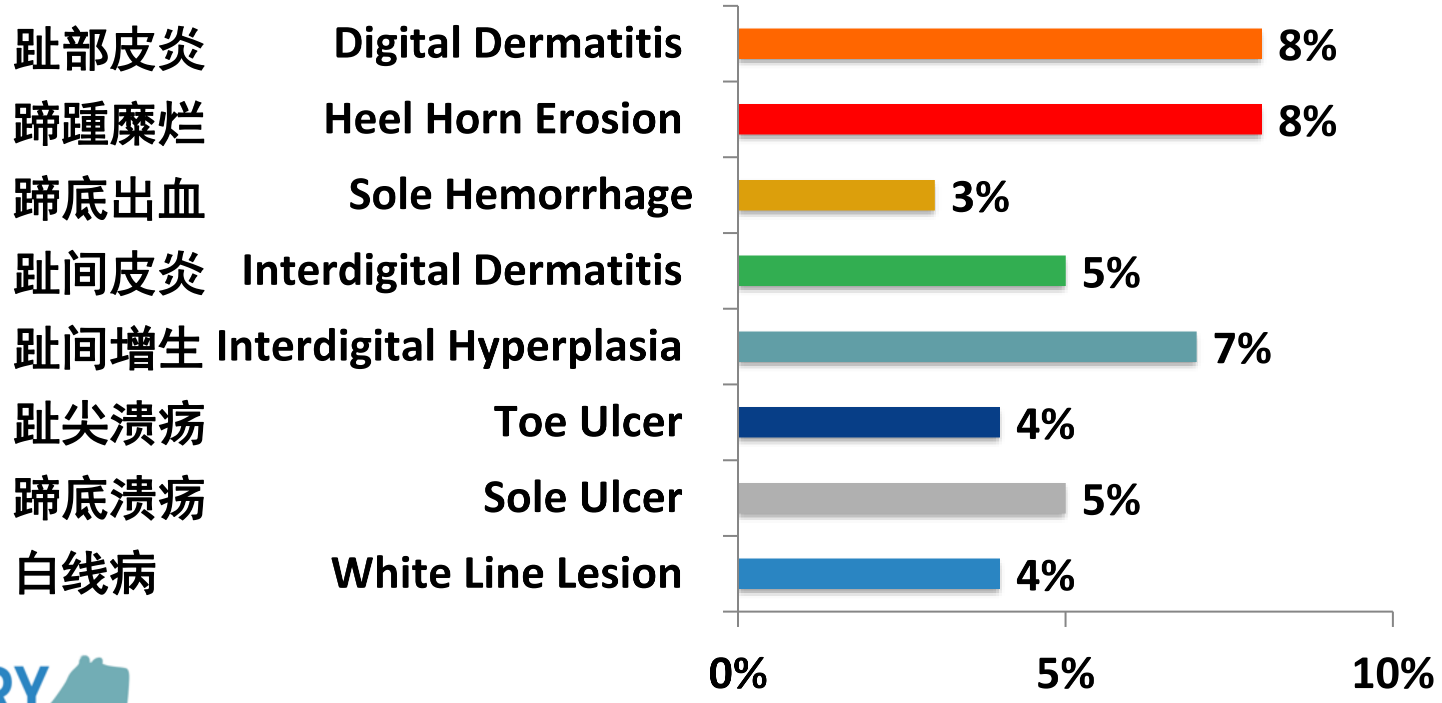
Heritability of Hoof Lesions
蹄病的遗传力



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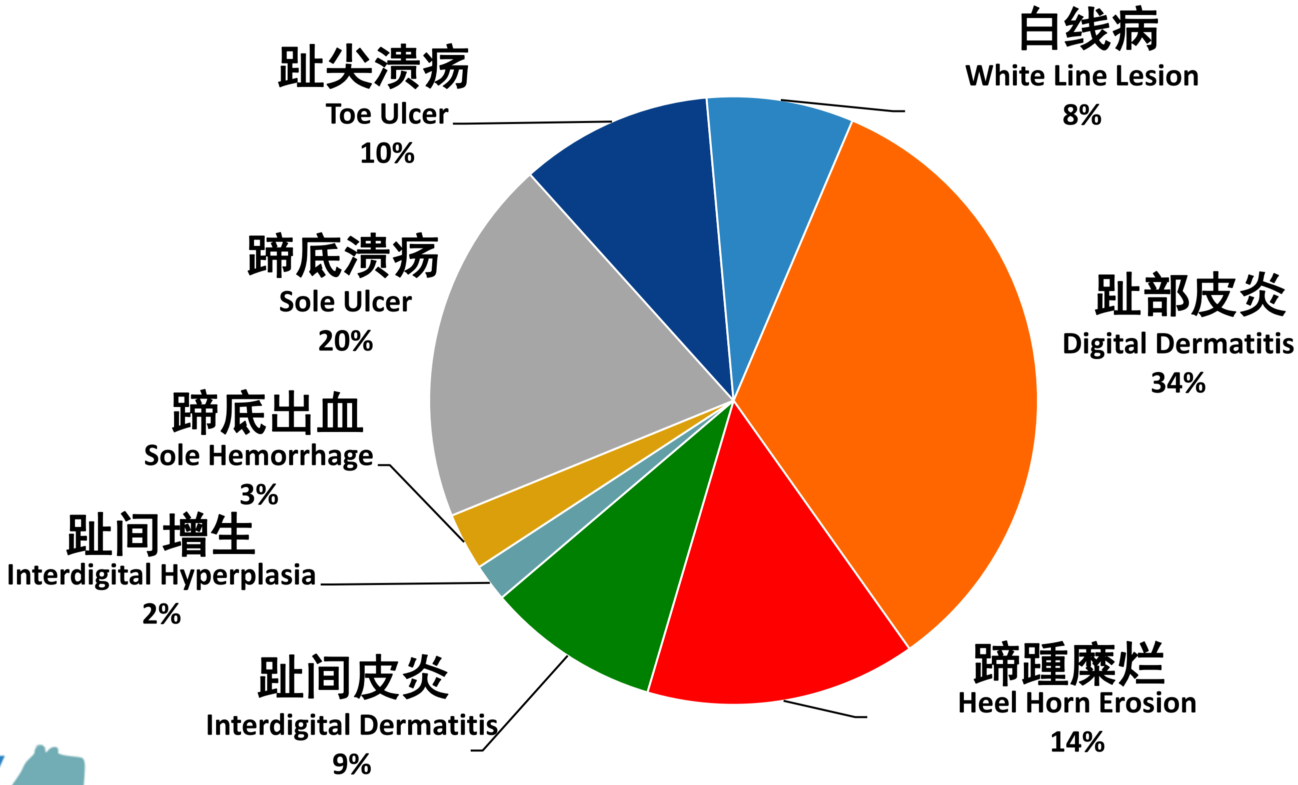
Single-step GBLUP
一步法基因组最佳线性无偏预测

- **Multiple-trait model** (8 lesions) **多性状模型 （8种蹄病）**
- **Animal linear model with repeated observations 线性动物模型，处理重复观察值**
- **Single-step GBLUP using Mix99 基于Mix99运算一步法GBLUP**
- **Environmental factors: 环境效应：**
  - Herd-Trimming Session **群体-修蹄期**
  - Trimmer **修蹄人员**
  - Days after calving **产犊后天数**
  - Parity **胎次**
  - Cow effect (PE) **母牛效应（永久环境效应）**

Trait Relative Emphasis for HH Index
HH指数的性状相对权重



Fertility Disorders – Phenotypes
繁殖障碍—表型

- Traits (0 = no case, 1 = at least one case):
  性状（0 = 未发生，1 = 至少发生一次）
  - Cystic Ovaries (**CO**): calving – 305 DIM
    卵巢囊肿：产犊–泌乳305天
  - Metritis (**MET**): calving – 150 DIM
    子宫炎：产犊–泌乳150天
  - Retained Placenta (**RP**): calving – 14 DIM
    胎衣不下：产犊–泌乳14天

Fertility Disorders – Model
繁殖障碍—模型

- Multiple-trait linear animal model 多性状线性动物模型

  H = (pedigree + genotypes) based relationships

  H =基于（系谱 + 基因型） 的亲缘关系矩阵

- No indicator traits in the model 模型中无相关的指示性状
- First and later lactations: different (correlated) traits 头胎及经产：不同（相关）性状
- Observations on lactations > 2 treated as repeated observations for lactation 2 2胎之后的观察值,视为经产牛的重复观察值
- 6 traits in total 总共6种性状

Fertility Disorders – Methods
繁殖障碍—方法

- Single-Step method (MiX99 software) “一步法”（MiX99软件）
- Reference population: all genotyped animals in the pedigree 参考群：系谱中所有具有基因型信息的个体
- Estimation of GEBV (phenotypes + pedigree + genotypes) GEBV估计值（表型+系谱+基因型）
- Calculation of DGV (reference) DGV计算（参考群）
- Estimation of SNP effects SNP效应估计值
- Calculation of DGV for other genotyped animals (not in Single-Step)计算其它具有基因型个体的DGV（不在“一步法”分析之内的）

Fertility Disorders – Genetic Parameters
繁殖障碍—遗传参数

- Single-Step method (MiX99 software) “一步法”（MiX99软件）
- Heritability: **0.02 – 0.03** (across all traits) 遗传力：0.02 - 0.03 （所有性状）
- Genetic correlation between first and later lactation traits: from **0.55** (CO) to **0.70** (MET) 头胎与经产牛该性状的遗传相关：0.55（卵巢囊肿）— 0.70（子宫炎）
- CO genetically uncorrelated with MET and RP 卵巢囊肿与子宫炎和胎衣不下无遗传相关
- Genetic correlations between MET and RP: 子宫炎和胎衣不下的遗传相关
    - **0.54** (first lactation) 头胎牛为0.54
    - **0.51** (later lactations) 经产牛为0.51

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Large Research Projects at CGIL
CGIL大型科研项目

2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023

Hoof Health 蹄部健康

Milk Spectral Data 牛奶光谱数据

Efficient Dairy Genome Project 高效奶牛基因组预测

Build Female Reference Population
建设母牛参考群

Breeding Strategies with Genomics
基因组育种策略

Resilient Dairy Genome Project
奶牛抗性的基因组预测

Large Research Projects at CGIL
CGIL大型科研项目

2014 2015 2016 2017 2018 2019 2020 2021 2022 2023

Hoof Health
蹄部健康

Hoof Health Evaluation & Herd Management Report
蹄部健康评估 & 牧场管理报告

Milk Spectral Data
牛奶光谱数据

Milk MIR pipeline and storage since 2013
自2013以来牛奶中红外光谱分析流程和数据储存

Efficient Dairy Genome Project
高效奶牛基因组预测

Feed Efficiency Evaluation
饲养效率评估

Build Female Reference Population 建立母牛参考群

Breeding Strategies with Genomics 基因组育种策略

奶牛抗性基因组预测 Resilient Dairy Genome Project

Fertility Disorders Evaluation
繁殖障碍评价

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Large Genomic Research Projects
大型基因组研究项目

THE Efficient Dairy GENOME PROJECT

高效奶牛基因组预测

- 2015-2020, $10.3M　**2015~2020, $1030万**
- Filippo Miglior & Flavio Schenkel (CGIL, Guelph), **圭尔夫大学**
  Paul Stothard (University of Alberta) **阿尔伯塔大学**

- Creation of international database for Feed Efficiency (FE) and Methane Emissions (ME)
  建立饲料效率和甲烷排放的国际数据库
- Australia, Canada, Denmark, Switzerland and USA
  澳大利亚、加拿大、丹麦、瑞士、美国
- **Single Step genomic evaluation for FE launched in April 2021 by Lactanet Canada**

加拿大Lactanet公司于2021.4启动了饲料效率的一步法基因组评估

- ***Milk MIR predictions for DMI & Methane Emissions***
  牛奶中红外光谱预测干物质采食量和甲烷排放：进行中
  (in Progress) -> Genetic evaluation for ME
  -> Herd monitoring for ME
  甲烷排放的遗传评估
  牧场甲烷排放的监测

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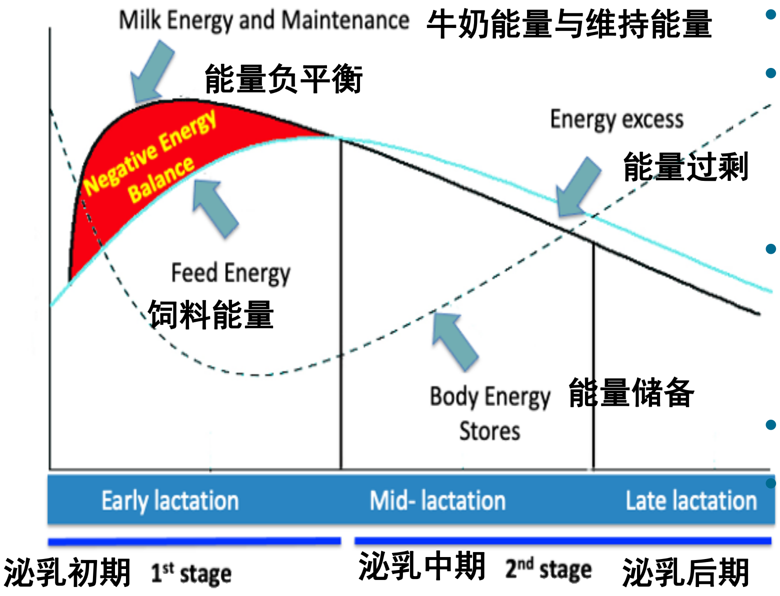
THE Resilient Dairy GENOME PROJECT

奶牛抗性基因组预测

- 2020-2024, $12.5M　**2020~2024, $1250万**
- Christine Baes (CGIL, Guelph), Marc-André Sirard (Laval), Ronaldo Cerri (UBC), Paul Stothard **圭尔夫大学，拉瓦尔大学，不列颠哥伦比亚大学，阿尔伯塔大学**

- Development of new health trait evaluations (Johne's, Leukosis, Respiratory Diseases, Calf Health) **开发新健康性状的评估（副结核病，白血病，呼吸道疾病，犊牛健康）**
- Closer-to-biology fertility traits **开发更具备生物学基础的繁殖性状**
- New evidence-based epigenomic data to complement the genetic selection strategy **新的表观基因组学数据以完善基因组选择策略**
- Further enhancement of Feed Efficiency, further analysis of Methane Emission data **进一步提高饲料效率，进一步分析甲烷排放数据**
- Same EDGP partners + Spain and Germany
  EDGP合作伙伴+西班牙和德国的
- **Development of Genomic Evaluations for Resiliency** **开发奶牛抗性能力的基因组预测体系**

Genomic Evaluation for Feed Efficiency
饲料效率的基因组预测



- **Single-Step** evaluation using Mix99 使用Mix99进行一步法评估
- Two lactation periods in first lactation 第一胎设置两个泌乳阶段
  - Up to 60 days in milk 产犊至泌乳60d产奶量上升阶段
  - **After 60 days in milk** 产犊60d后产奶量下降阶段
- **Three traits** (weekly averages) 三个性状（周平均）
  - Dry Matter Intake, Energy Corrected Milk, Metabolic Body Weight

  干物质采食量，校正奶量，代谢体重
- Feed Efficiency calculated as: 饲料效率的计算方法
- $EBV_{FE} = EBV_{DMI} - a*EBV_{ECM} - b*EBV_{MBW}$
  - Genetically **independent** of energy sinks 遗传上独立于能量消耗
  - **Equivalent to RFI** (Residual Feed Intake) 相当于剩余采食量
- Average Reliability of young bulls: **42%** 青年公牛平均可靠性：42%

Overall aim is to select for cows that use less feed at the same level of production and body size after peak of lactation

总体目标在于选择泌乳高峰后相同生产水平和体型下采食量较少的奶牛

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Cumulative FE and ME database by 2023
2023年饲料效率和甲烷排放[redacted]的累计数据规模

THE Resilient Dairy GENOME PROJECT

奶牛抗性基因组预测

Country 国家	No. of Cows with Feed Efficiency 具备饲料效率观察值奶牛头数	No. of Cows with Methane Emissions 具备甲烷排放量观察值的奶牛头数
Australia 澳大利亚	1,200	900
Canada 加拿大	3,000	900
Denmark 丹麦	1,400	450
Germany 德国	1,800	1,800
Spain 西班牙	250	3,000
Switzerland 瑞士	500	250
USA 美国	7,500	1,000
Total 总计	15,650	8,300

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Impact of Genomics
基因组预测的意义

- Many **GREAT** things have resulted from **GENOMICS**:

利用基因组预测已获得了许多有意义的结果

  - Accurate parentage verification and discovery

  更为准确的亲子关系鉴定和挖掘

  - Higher accuracy of selection for young animals

  幼畜选择准确性更高

  - Shorter generation interval between parents and the next generation of replacements**缩短世代间隔**
    - Both for heifers in a herd and for bulls in A.I. **牧场的小母牛和AI公牛**
  - Discovery & management of genetic recessives **发现和控制遗传缺陷**
  - FASTER rates of genetic progress are a **reality** **使加快遗传进展成为现实**
  - Improve new/novel traits of importance **选育提高重要的新性状**

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EDGP Funders & Participating Organizations
EDGP的资助方和参与组织

THE Efficient Dairy GENOME PROJECT

GenomeCanada

GenomeAlberta

Ontario Genomics

Alberta Agriculture and Forestry

Ontario MINISTRY OF RESEARCH & INNOVATION

Ontario Ministry of Agriculture, Food and Rural Affairs

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GrowSafe SYSTEMS®

ALBERTA milk

USDA

SRUC

QUALITAS

SEMEX® Genetics for Life®

AGRICULTURE VICTORIA

AARHUS UNIVERSITY

INRA SCIENCE & IMPACT

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