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Optimizing Traditional and Marker Assisted Evaluation

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National Cattle Evaluation

- Genetic evaluation is conducted (inter)nationally on breed-specific basis
 - EPD are generally not comparable across breeds
 - For any breed, NCE systems contain both common and novel traits
- Methods for EPD prediction are mature
 - National cattle evaluation (NCE) systems have been in place for more than 2 decades
 - We have validated the correspondence between expected and realized progeny differences
 - Genetic trend shows pervasive industry and producer uptake of EPD technology
 - New traits for NCE follow the framework for economic relevance
- EPD are the "sum" of small, additive genetic effects
 - To some extent, EPD are a genetic "black box"

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Properties of NCE Traits

| Desirable property | Good examples | Poor examples |
|----------------------------------|----------------------------|----------------------------|
| Direct effect on revenue or cost | Feed intake, carcass yield | Birth weight, scrotal |
| Easily and cheaply measured | Weight | Feed intake, carcass merit |
| Stable genetic parameters | Weight rate | Fertility |
| High data density | Growth rate | Feed intake, carcass merit |
| Few genetic antagonisms | (few) | (most) |
| Measured early in life | Pre-yearling traits | Longevity, mature size |
| EPD are user friendly | Weight | Calving ease, stayability |
| High genetic variance | Growth rate | Carcass yield |
| Several indicators | Carcass merit, fertility | Longevity |

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Genetic Evaluation/NCE in the "-omics" Era

- There is tremendous interest in identifying *major genes* which explain EPD
 - Models are still developing, but most partition EPD into marker and polygenic effects
 - The "information package" should rely on industry familiarity with EPD/accuracy
- Marker assisted evaluation has large potential benefits for NCE accuracy
 - Young sires
 - Traits that are difficult and costly to measure
- Focus on the *optimal combination of marker and phenotypic data*
 - Recognize the importance of phenotypic data, and incorporate marker information
 - Methods to better allow for utilization of high-density SNP marker chips
 - Desirable approaches for animals with only phenotypic or only marker data

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"Traditional" NCE

$$y = Xb + Zu + e \implies \begin{bmatrix} X'X & X'Z \\ Z'X & Z'Z + \Lambda^{-1}\lambda \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \end{bmatrix}$$

Marker Assisted NCE (MA-BLUP?)

$$y = Xb + \{Zu + Wg\} + e \implies \begin{bmatrix} X'X & X'Z & X'W \\ Z'X & Z'Z + \Lambda^{-1}\lambda & Z'W \\ W'X & W'Z & W'W + M^{-1}\mu \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \\ \hat{g} \end{bmatrix} = \begin{bmatrix} X'y \\ Z'y \\ W'y \end{bmatrix}$$

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Data Density, Polygenic Heritability, and Accuracy

Deciding for Marker Assisted Evaluation

Phenomic cost/value decisions underlying marker assisted evaluation (MAE)

- **MAE will be beneficial for ERT where:**
 - Phenotypic data collection is costly and time-consuming, or is likely to never exist
 - Few or no indicator traits have been/ can be identified
 - Genetic variance attributable to "marker set" is at least *moderate*
 - Cost of genotyping is justifiable
- **Some candidates have been identified**
 - Feed intake and efficiency
 - Fertility
 - Disease resistance
 - Palatability and meat composition



Feed Intake as an Example

- **Feed intake is clearly a cost-side ERT**
 - Feed and supplementation account for >65% of non-fixed production costs
- **Intake and efficiency have complex intercorrelations with other ERT**
 - Growth rate, mature size, and body composition are all directly related to intake
 - Must be considered within the context of multiple trait selection
- **Traditional evaluation of feed utilization has progressed slowly**
 - Data collection cost exceeds \$150 per head
 - Very low data density at the population or breed level
 - Expression of intake/efficiency (e.g., RFI) forces few indicators
 - Polygenic architecture is well known and stable, but NCE are still prototypical

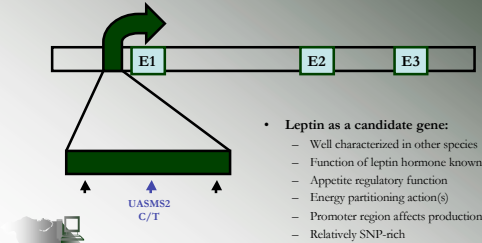


Feed Intake as an ERT

| Desirable property | Intake: | Comments: |
|----------------------------------|---------------|----------------------------------|
| Direct effect on revenue or cost | Yes | Major production cost |
| Easily and cheaply measured | No | ~\$150 per head |
| Stable genetic parameters | Yes | $h^2 = 0.40$ in most studies |
| High data density | No | Infrastructure is sparse |
| Few genetic antagonisms | Can be forced | Independent of anything as RFI |
| Measured early in life | Relatively | Near yearling ages is common |
| EPD are user friendly | Sort of... | Remember negative is better |
| High genetic variance | Yes | ± 3 lb DM per day is genetic |
| Several indicators | Yes, but... | Consider antagonisms |



Leptin: Intake/Efficiency Candidate Gene



- **Leptin as a candidate gene:**
 - Well characterized in other species
 - Function of leptin hormone known
 - Appetite regulatory function
 - Energy partitioning action(s)
 - Promoter region affects production
 - Relatively SNP-rich



UASMS2 in Angus and Charolais

1. Genotype and allele frequencies by breed

| Breed | n | CC | CT | TT | f(C) | f(T) | HWE |
|-----------|-----|-----|-----|----|-------|-------|-----|
| Angus | 451 | 234 | 182 | 35 | 0.721 | 0.279 | Yes |
| Charolais | 413 | 319 | 90 | 4 | 0.881 | 0.119 | Yes |

2. DM intake and RFI means by genotype and breed

| Breed | DM Intake | | | RFI | | |
|-----------|-----------|--------|--------|---------|----------|----------|
| | CC | CT | TT | CC | CT | TT |
| Angus | 7.15 | 7.20 | 7.50 | -0.015 | -0.006 | 0.094 |
| Charolais | 7.74 a | 7.58 b | 6.49 a | 0.052 a | -0.142 b | -0.983 c |



UASMS2 Marker Breeding Value (Charolais)

| Breed | DM Intake | | | RFI | | |
|-------------|-----------|--------|--------|-------|--------|--------|
| | CC | CT | TT | CC | CT | TT |
| Scaled Mean | 0.625 | 0.465 | -0.625 | 0.518 | 0.324 | -0.518 |
| MBV | 0.065 | -0.207 | -0.478 | 0.065 | -0.207 | -0.478 |

- Total additive genetic variance = $V(p)h^2 = (0.56)(0.40) = 0.224$
- Additive genetic variance attributable to UASMS2 = $2pq\alpha = 0.0154$
- UASMS2 accounts for <5% of the genetic variance in intake = d

Not enough alone!



Multiple Markers on SNP Panels

- Commercial SNP panels are now available for intake, RFI and other traits
 - Built from multiple validated SNP markers as a set
 - Marker breeding value (MBV) computed based on genotypes/haplotypes
 - Growing evidence that panels will be population (breed) specific to some degree
- High density SNP genotyping platforms are now in use
 - 10K SNP
 - 50K SNP
 - 300K SNP
- There are still issues with deriving MBV from high density "chips"
 - Information overload?
 - How much will be informative?



Genomic Breeding Value (GBV)

- Genomic breeding value (GBV) combines EPD and MBV
 - $GBV = I = b_1m + b_2u$ where $m = MBV$ and $u = polygenic BV$
- Optimal combination depends on:
 - Polygenic breeding value (EPD) accuracy (r^2)
 - Genetic variance attributable to the marker set (d)
- Gain in evaluation accuracy due to adding marker information:
 - Increases with increasing d
 - Decreases with increasing polygenic accuracy
 - Could be significant for animals with no phenotypic data: $GBV \approx m$
 - Will be essentially zero for old animals (founders?) with no marker data



MAE: Implementation and Adoption

- Increasing the contribution of markers to evaluation accuracy
 - Low polygenic accuracy ($r < 50\%$)
 - High predictive power of the marker set ($d > 10\%$)
- Industry adoption will largely depend on genotyping cost
 - For beef producers, threshold genotyping costs will likely be less than \$100
- Marker validation and calibration must be an ongoing exercise
 - Marker effects are likely to change under selection
- Information packaging is important
 - Independent selection for MBV (marker "score") and EPD can be antagonistic



GBV Information Packaging

Sire XYZ
Bull ABC ————
Dam ABC

Which is correct ?

| CED | BWT | WWT | YWT | MLK | TMAT | SCR | LMY | MARB |
|------|------|-------|-------|------|-------|------|-----|------|
| -3.5 | +6.8 | +35.2 | +96.5 | -4.5 | +13.1 | +0.9 | 0.0 | -1.3 |
| 76 | 82 | 77 | 80 | 63 | | 76 | 72 | 72 |
| 2 | 5 | 85 | 95 | 35 | | 55 | 50 | 18 |

PRO[®] Marbling : +5



GBV Information Packaging, 2

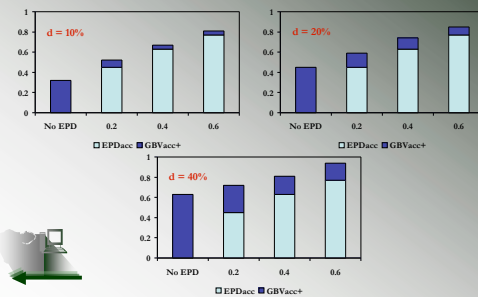
Sire KLM
Bull DEF ————
Dam DEF

| CED | BWT | WWT | YWT | MLK | TMAT | SCR | LMY | MARB |
|------|------|-------|-------|------|-------|------|------|------|
| +7.5 | -0.2 | +35.2 | +76.5 | +1.5 | +19.1 | +2.5 | +0.6 | +1.3 |
| 76 | 82 | 77 | 80 | 63 | | 76 | 72 | 72 |
| 82 | 85 | 85 | 75 | 50 | | 85 | 40 | 92 |

PRO[®] Marbling : 0



Increasing Accuracy with MAE



Some Final Thoughts

- **Marker assisted evaluation of ERT in beef cattle needs continued development**
 - Marker sets must be (re)validated
 - Marker panels will likely be specific (breeds, traits, etc.)
- **Evaluation using markers will impact some traits more than others**
 - Don't bother with growth
 - Time- and cost-intensive phenotypes have larger potential benefits with MAE
 - Traits for which no phenotypes will be available are good candidates for MAE
- **Cost versus benefit decisions must be made**
 - Investment in phenotyping
 - Cost of genotyping



Thanks.

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