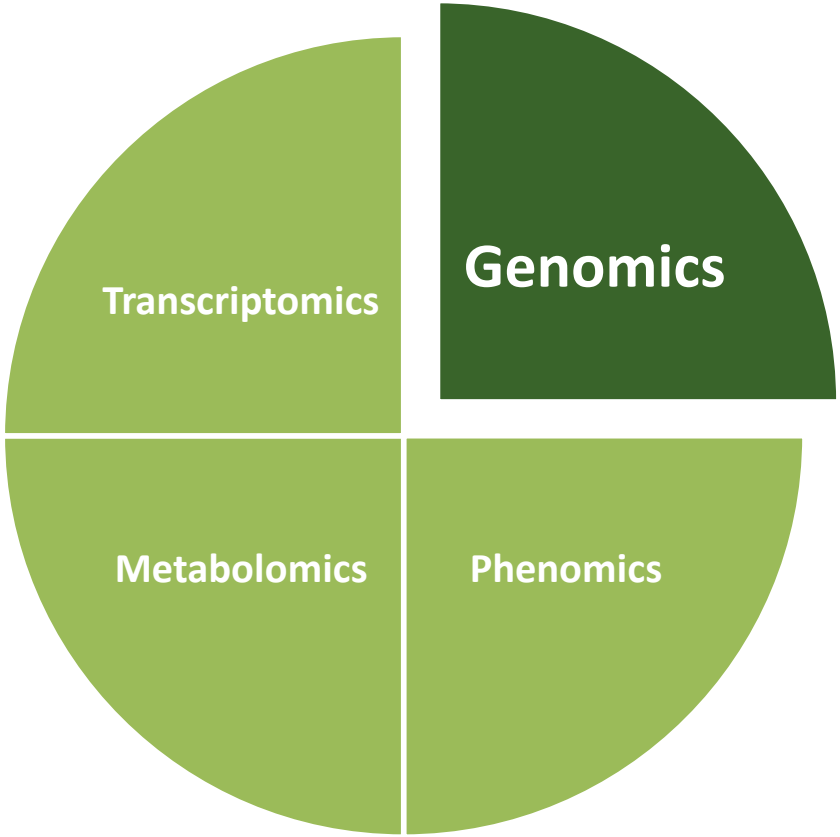
Genomic Prediction of Serum Biomarkers of Health in Early Lactation Dairy Cows

Tim Luke*, Thuy Nguyen, Simone Rochfort, Mary Abdelsayed
Caeli Richardson, Bill Wales & Jennie Pryce

AGRICULTURE VICTORIA

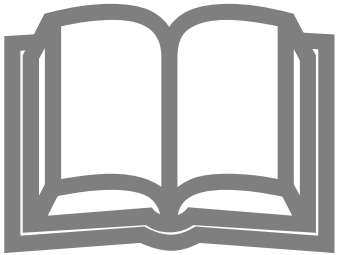
Systems Biology Approach



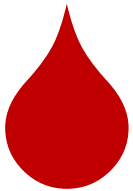
AGRICULTURE VICTORIA

Metabolic Health Phenotypes

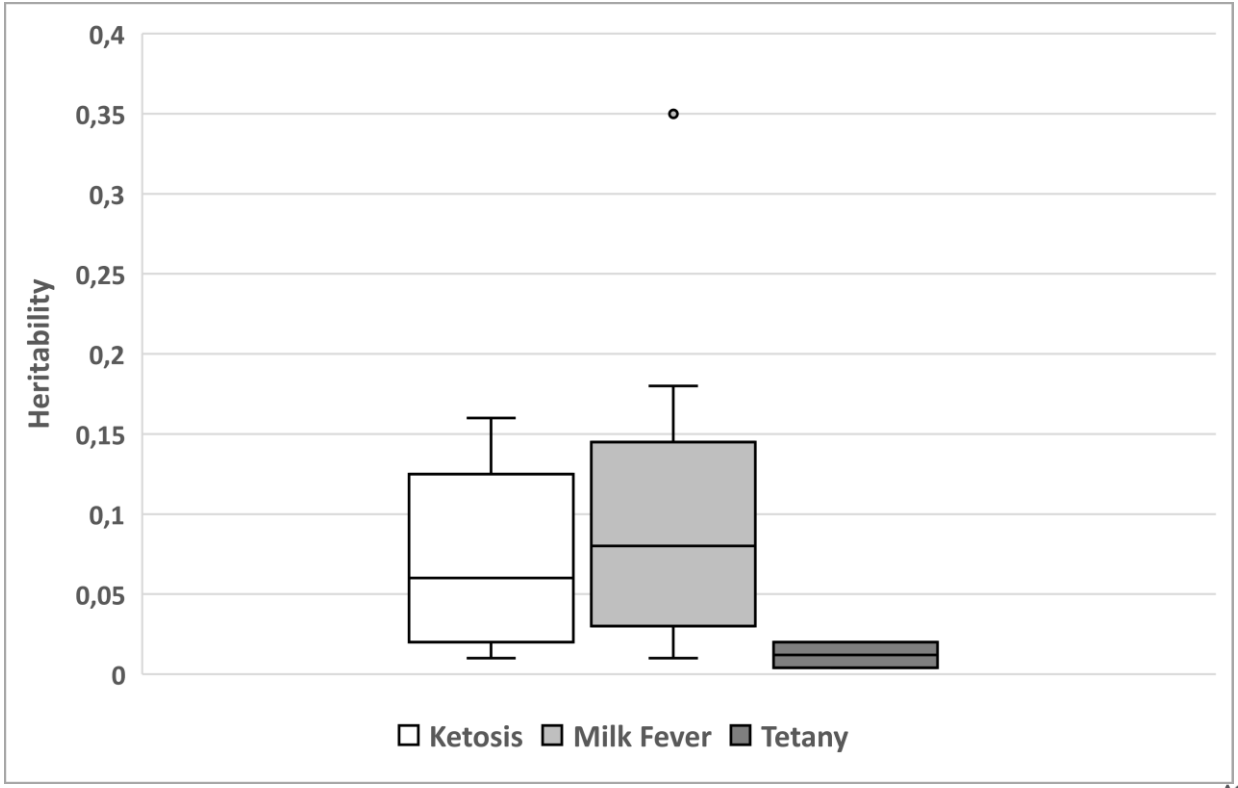
Producer/Veterinary Data



Biomarkers



Heritability of Metabolic Disease (1995-2015)



Pryce et al. 2016

AGRICULTURE VICTORIA

Serum Biomarkers of Health

ENERGY

BHBA

NEFA

PROTEIN

Albumin

Urea

IMMUNE

Albumin

Globulins

Albumin:Globulins

Haptoglobin

MINERAL

Calcium

Magnesium

AGRICULTURE VICTORIA

Serum Biomarkers of Health – Optimal Concentrations

Phenotype		Lower Threshold	Upper Threshold	Reference
BHBA		-	1.2 mmol/L	(Compton et al., 2014)
NEFA		-	0.7 mmol/L	(Ospina et al., 2010)
Globulin		-	50 g/L	(Whitaker, 2004)
Haptoglobin		-	1.4 g/L	(Pohl et al., 2015)
Ca		2.0 mmol/L	-	(Degaris and Lean, 2008)
Mg		0.62 mmol/L	-	(Anderson, 2009)
Urea		1.7 mmol/L	-	(Macrae et al., 2006)
Albumin		30 g/L	-	(Whitaker, 2004)
Albumin:Globulin		0.84	-	(Kaneko, 2008)

AGRICULTURE VICTORIA

Study Aims

1. Estimate the genetic parameters of serum biomarkers of health in early lactation dairy cows

2. Estimate the accuracy of genomic predictions of serum biomarker concentrations

3. Investigate correlations with existing health and production traits

Data Collection

1393 Holstein-Friesian Cows

0-30 DIM

14 herds

50k genotypes

Serum Metabolic Profiles

AGRICULTURE VICTORIA

Genetic Parameters

AGRICULTURE VICTORIA

Univariate Linear Mixed Animal Model in ASReml

$$y = \mu + herd_h + parity_i + date_j + b_1 DIM_{hij} + g_k + e_{hijk}$$

μ = mean

$herd_h$ = hth herd of origin (14 levels)

$parity_i$ = ith parity (4 levels: 1, 2, 3, 4+)

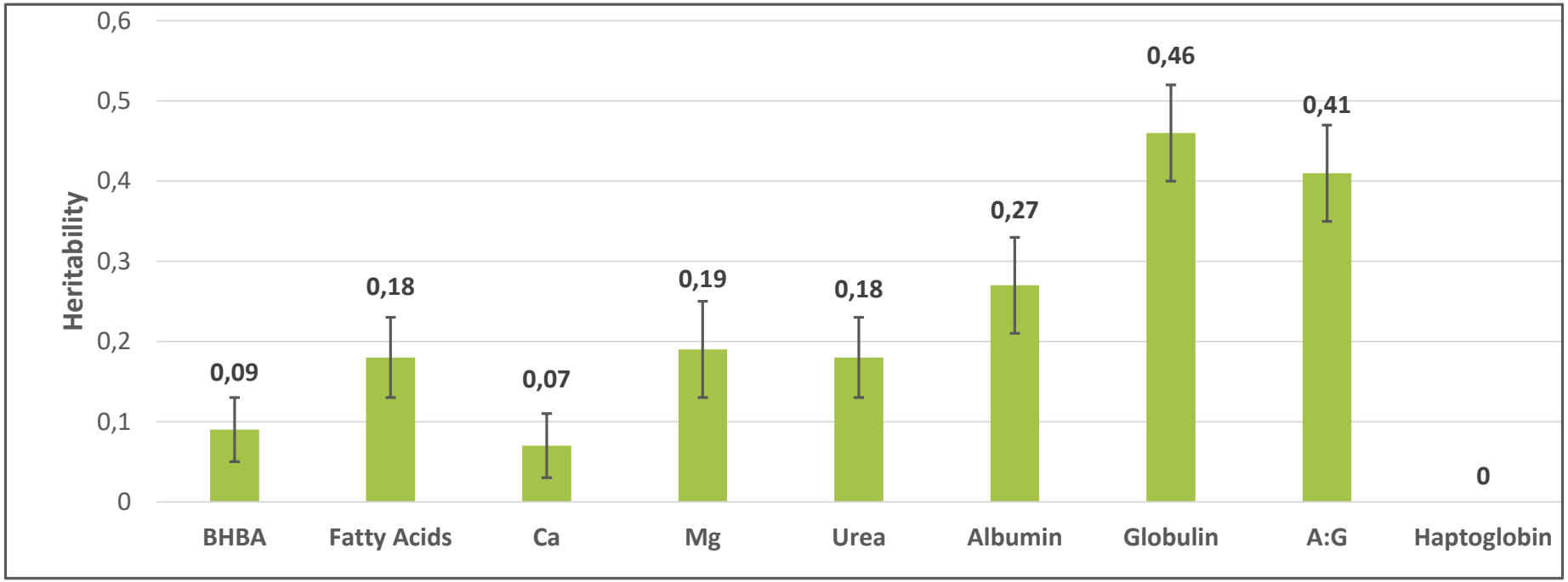
$date_j$ = jth sample collection date (20 levels)

b_1 = the regression coefficient on covariate of days in milk (0 to 30)

g_k = random additive genetic effect of the kth cow, captured from the GRM

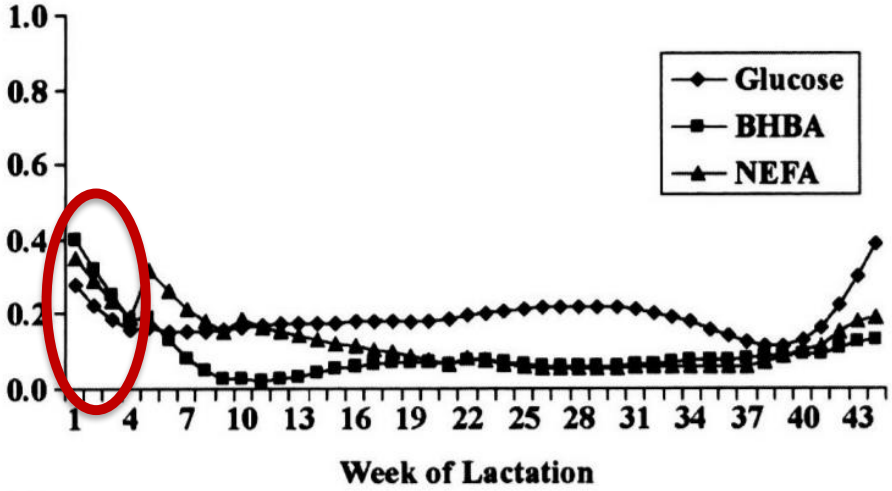
e_{hijk} = residual term

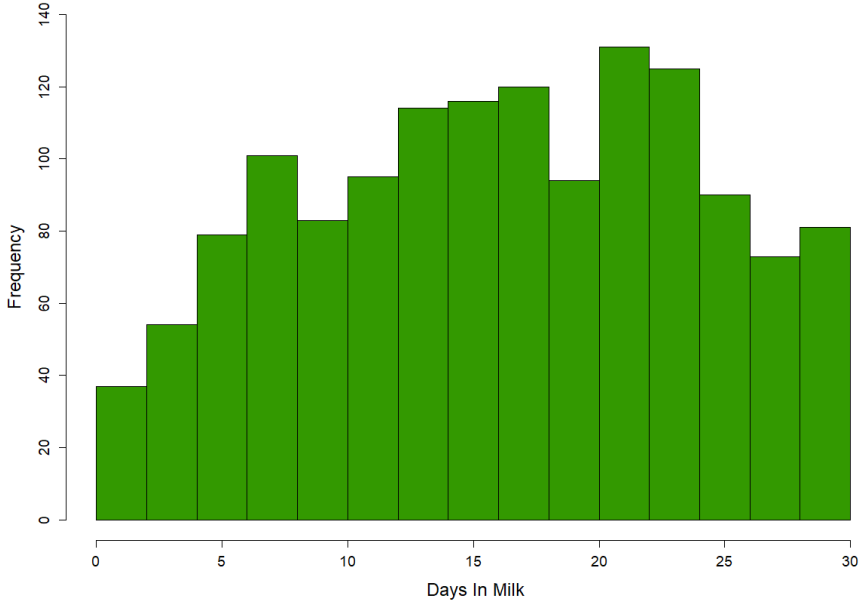
Estimated Genomic Heritabilities



AGRICULTURE VICTORIA

Discussion: Energy Metabolites

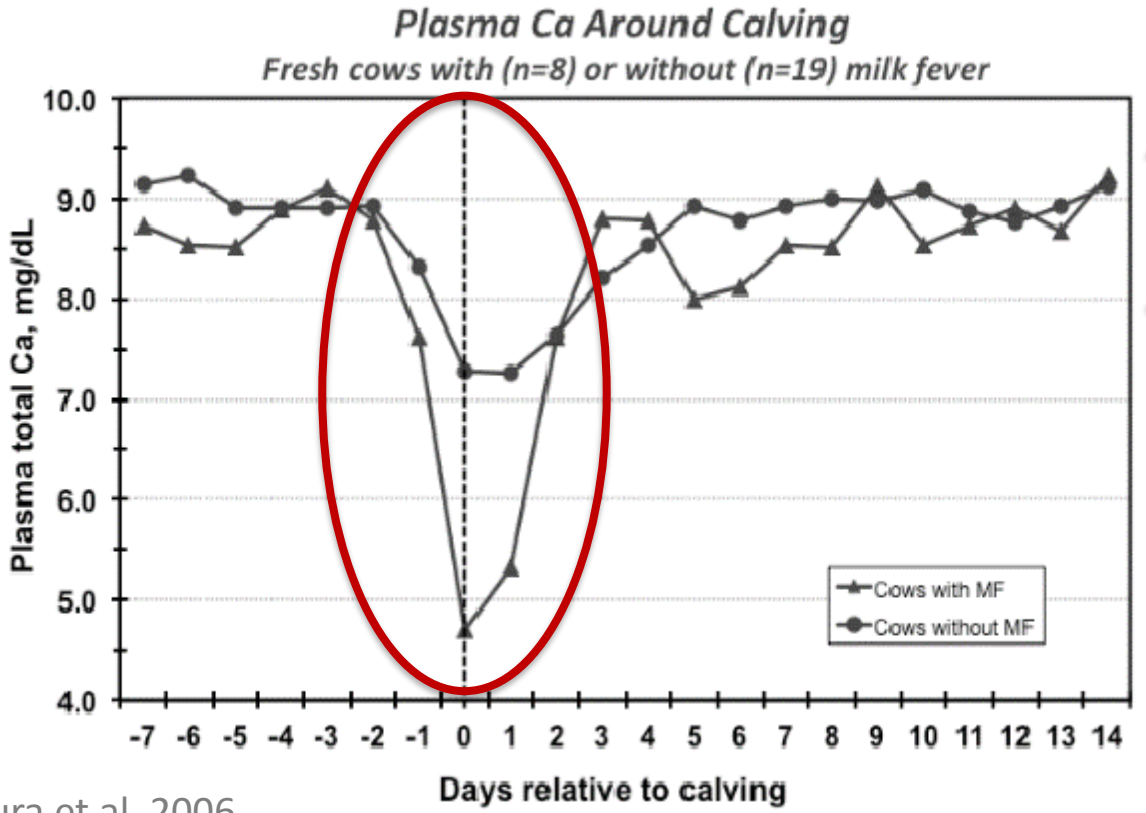




Oikonomou et al. 2008

AGRICULTURE VICTORIA

Discussion: Plasma Ca Concentration



Kimura et al. 2006

Ca Homeostasis

h^2 = 0.23 to 0.32

1, 2 & 8 DIM

Tsiamadis et al. (2016)

AGRICULTURE VICTORIA

Results: Genetic (above) and Phenotypic (below) Correlations

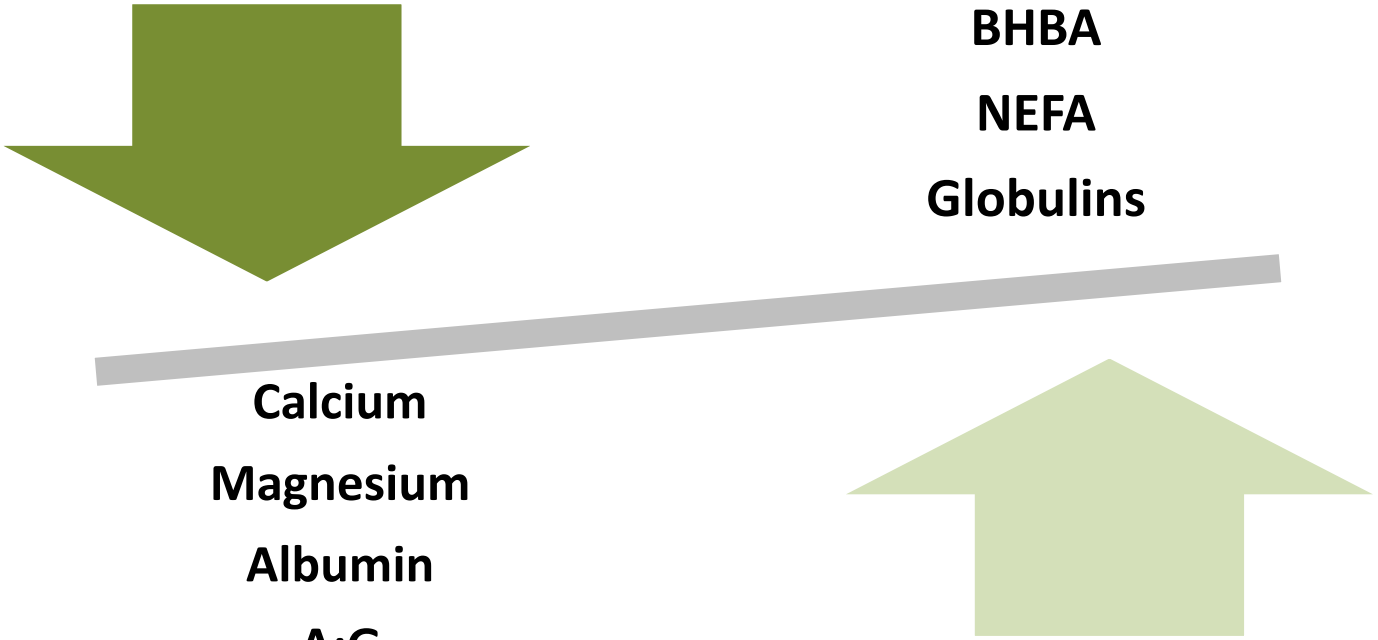
	$BHBA_{Log10}$	FA_{SQRT}	Ca	Mg	Urea	Albumin	Globulin	A:G
$BHBA_{Log10}$	**0.09 ± 0.04**	0.24 ± 0.26	-0.06 ± 0.42	0.38 ± 0.29	0.21 ± 0.28	0.11 ± 0.24	0.01 ± 0.22	-0.07 ± 0.23
FA_{SQRT}	0.20 ± 0.03	**0.18 ± 0.05**	-0.82 ± 0.44	-0.20 ± 0.21	-0.17 ± 0.21	-0.29 ± 0.18	-0.03 ± 0.16	-0.05 ± 0.16
Ca	-0.09 ± 0.03	-0.05 ± 0.03	**0.07 ± 0.04**	0.21 ± 0.33	0.48 ± 0.31	0.54 ± 0.22	-0.01 ± 0.25	0.12 ± 0.25
Mg	-0.02 ± 0.03	-0.01 ± 0.03	0.08 ± 0.03	**0.19 ± 0.06**	0.44 ± 0.22	0.29 ± 0.17	-0.21 ± 0.16	0.25 ± 0.16
Urea	0.16 ± 0.03	-0.06 ± 0.03	0.07 ± 0.03	0.06 ± 0.03	**0.18 ± 0.05**	0.79 ± 0.16	-0.16 ± 0.16	0.38 ± 0.16
Albumin	0.08 ± 0.03	0.10 ± 0.03	0.44 ± 0.02	0.34 ± 0.03	0.25 ± 0.03	**0.27 ± 0.06**	-0.50 ± 0.12	0.70 ± 0.08
Globulin	-0.14 ± 0.03	-0.05 ± 0.03	0.03 ± 0.03	-0.06 ± 0.03	-0.13 ± 0.03	-0.31 ± 0.03	**0.46 ± 0.06**	-0.96 ± 0.02
A:G	0.12 ± 0.03	0.07 ± 0.03	0.15 ± 0.03	0.18 ± 0.03	0.19 ± 0.03	0.63 ± 0.02	-0.87 ± 0.01	**0.41 ± 0.06**

Results: Genetic (above) and Phenotypic (below) Correlations

	$BHBA_{Log10}$	FA_{SQRT}	Ca	Mg	Urea	Albumin	Globulin	A:G
$BHBA_{Log10}$	**0.09 ± 0.04**	0.24 ± 0.26	-0.06 ± 0.42	0.38 ± 0.29	0.21 ± 0.28	0.11 ± 0.24	0.01 ± 0.22	-0.07 ± 0.23
FA_{SQRT}		**0.18 ± 0.05**	**-0.82 ± 0.44**	-0.20 ± 0.21	-0.17 ± 0.21	**-0.29 ± 0.18**	-0.03 ± 0.16	-0.05 ± 0.16
Ca			**0.07 ± 0.04**	0.21 ± 0.33	0.48 ± 0.31	**0.54 ± 0.22**	-0.01 ± 0.25	0.12 ± 0.25
Mg				**0.19 ± 0.06**	**0.44 ± 0.22**	**0.29 ± 0.17**	-0.21 ± 0.16	0.25 ± 0.16
Urea					**0.18 ± 0.05**	**0.79 ± 0.16**	-0.16 ± 0.16	**0.38 ± 0.16**
Albumin						**0.27 ± 0.06**	**-0.50 ± 0.12**	**0.70 ± 0.08**
Globulin							**0.46 ± 0.06**	**-0.96 ± 0.02**
A:G								**0.41 ± 0.06**

AGRICULTURE VICTORIA

Results: Genetic Correlation Trends



Accuracy of Genomic Predictions

AGRICULTURE VICTORIA

Accuracy of Genomic Prediction (1)

Iteration 1	**Test**	Train	Train	Train	Train
Iteration 2	Train	**Test**	Train	Train	Train
Iteration 3	Train	Train	**Test**	Train	Train
Iteration 4	Train	Train	Train	**Test**	Train
Iteration 5	Train	Train	Train	Train	**Test**

$$r = \frac{cor(GEBV, phenotype)}{h}$$

AGRICULTURE VICTORIA

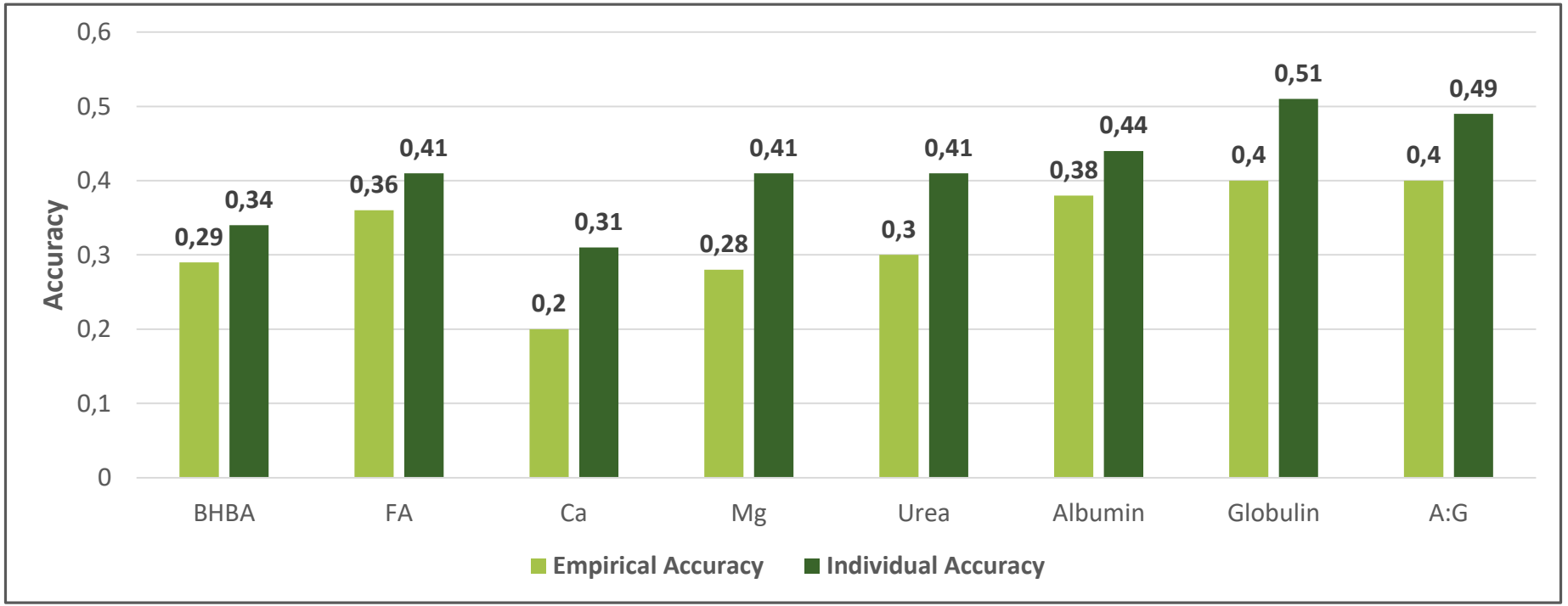
Accuracy of Genomic Prediction (2)

$$r_i = \sqrt{1 - \frac{SE_i^2}{\sigma_g GRM_{ii}}}$$

Results: Accuracy of Genomic Predictions

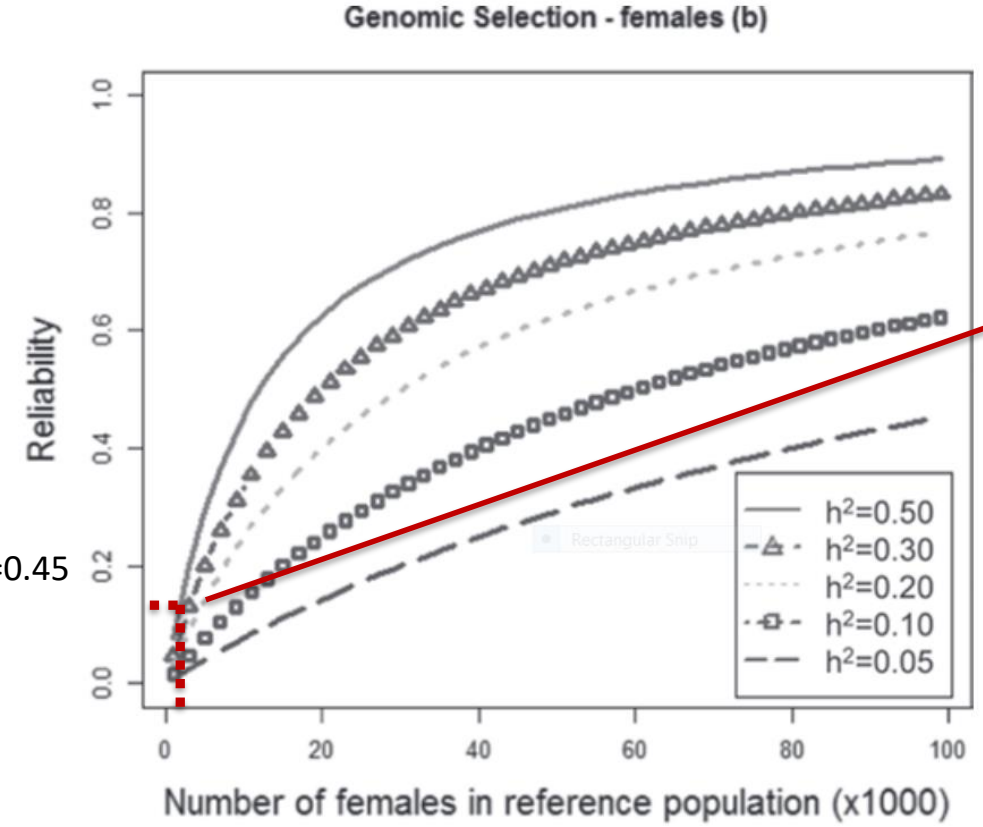
Trait	Cross-validation Fold					μ	$\frac{\mu}{h}$	r_i
	1	2	3	4	5			
$BHBA_{Log10}$	0.04	0.08	0.14	0.09	0.08	0.09	0.29	0.34
$NEFA_{SQRT}$	0.15	0.11	0.14	0.16	0.19	0.15	0.36	0.41
Calcium	0.02	0.09	0.12	-0.09	0.13	0.05	0.20	0.31
Magnesium	0.09	0.01	0.13	0.17	0.22	0.12	0.28	0.41
Urea	0.24	0.13	0.18	0.02	0.06	0.13	0.30	0.41
Albumin	0.18	0.26	0.25	0.15	0.14	0.20	0.38	0.44
Globulin	0.24	0.28	0.30	0.29	0.23	0.27	0.40	0.51
A:G	0.24	0.26	0.30	0.28	0.19	0.25	0.40	0.49

Accuracy of Genomic Prediction



AGRICULTURE VICTORIA

Accuracy of Genomic Prediction (Gonzalez-Recio et al. 2014)



r=0.45

Expected Accuracies:

0.0 – 0.40

Our Results:

0.2 – 0.40

Gonzalez-Recio et al. 2014

AGRICULTURE VICTORIA

Correlations with Existing Breeding Values for Health & Fertility

AGRICULTURE VICTORIA

Correlations with Existing EBV for Health & Fertility

$$r_i = cor\,(GEBV_j, EBV_k)$$

$\boldsymbol{GEBV_j}$ = Genomic Estimated Breeding Value for the j^{th} biomarker
$\boldsymbol{EBV_k}$ = Estimated Breeding Value for k^{th} existing trait

All GEBV with an individual reliability of < 0.1 were excluded

AGRICULTURE VICTORIA

Correlations between GEBV and Health & Production EBV

Trait	n	Survival	SCC	Daughter Fertility	Milk Yield	Protein Yield	Fat Yield
BHB	848	-0.15	-0.08	-0.11	-0.10	0.06	0.15
NEFA	1176	-0.27	-0.16	-0.20	-0.07	0.01	0.04
Ca	719	0.15	0.07	0.24	0.00	0.07	-0.10
Mg	1129	0.21	0.15	0.25	-0.06	-0.13	0.03
Alb	1228	0.45	0.32	0.37	0.11	0.03	0.07
Glob	1313	-0.25	-0.19	-0.20	-0.02	0.06	0.03
Urea	1161	0.38	0.23	0.26	0.10	0.05	0.10
A:G	1321	0.36	0.26	0.30	0.07	-0.01	0.01

Correlations between GEBV and Health & Production EBV

Trait	n	Survival	SCC	Daughter Fertility	Milk Yield	Protein Yield	Fat Yield
BHB	848	-0.15	-0.08	-0.11	-0.10	0.06	0.15
NEFA	1176	-0.27	-0.16	-0.20	-0.07	0.01	0.04
Ca	719	0.15	0.07	0.24	0.00	0.07	-0.10
Mg	1129	0.21	0.15	0.25	-0.06	-0.13	0.03
Alb	1228	0.45	0.32	0.37	0.11	0.03	0.07
Glob	1313	-0.25	-0.19	-0.20	-0.02	0.06	0.03
Urea	1161	0.38	0.23	0.26	0.10	0.05	0.10
A:G	1321	0.36	0.26	0.30	0.07	-0.01	0.01

Correlations between GEBV and Health & Production EBV

Trait	n	Survival	SCC	Daughter Fertility	Milk Yield	Protein Yield	Fat Yield
BHB	848	-0.15	-0.08	-0.11	-0.10	0.06	0.15
NEFA	1176	-0.27	-0.16	-0.20	-0.07	0.01	0.04
Ca	719	0.15	0.07	0.24	0.00	0.07	-0.10
Mg	1129	0.21	0.15	0.25	-0.06	-0.13	0.03
Alb	1228	0.45	0.32	0.37	0.11	0.03	0.07
Glob	1313	-0.25	-0.19	-0.20	-0.02	0.06	0.03
Urea	1161	0.38	0.23	0.26	0.10	0.05	0.10
A:G	1321	0.36	0.26	0.30	0.07	-0.01	0.01

Conclusions

- All traits studied were heritable except haptoglobin
- Trend in direction of genetic correlations was favourable
- Correlations with survival and fertility EBVs were small to moderate and favourable
- Correlations with production GEBV were small
- Promising biomarkers of early lactation health for genetic evaluation purposes
  1. NEFA
  2. Albumin
  3. Albumin:Globulin

Acknowledgments:

DJPR Ellinbank

Farmers

DataGene
Solutions for Herd Development

Dairy Australia

DairyBio

GARDINER FOUNDATION

AGRICULTURE VICTORIA