ImmuneDEX: Measuring and Selecting for Immune Competence in Angus

Presented by: Brad Hine (CSIRO) and Christian Duff (Angus Australia)

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In this Presentation we will cover:

1. What is immune competence and why is it important?
2. How are immune competence phenotypes assessed?
3. What phenotypes are available and what analyses has been undertaken?
4. What is ImmuneDEX?
5. What does the future hold?

Which sire has the best immune system to handle disease challenges?

- Consumer awareness and concern regarding the use of antibiotics in all food-producing animals is increasing

  Why?

- Perceived contribution of agriculture to the ever increasing problem of antimicrobial resistance

Productivity

Resistance to Disease

Productivity ≠ Disease Resistance

The Perfect Storm is Brewing

- Selection for productivity alone is inadvertently

  ⬆ increasing disease susceptibility

- Restrictions on use of antibiotics in food producing animals is

  ⬇ reducing our ability to treat disease

What can we do as an Industry?

Genetics x Environment x Management (GxExM)

E: Develop strategies to reduce environmental pathogen load.

M: Develop alternatives to antibiotics.

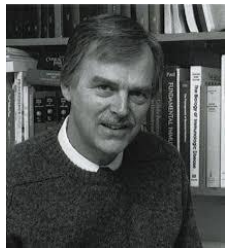
G: Develop genetic strategies to improve disease resistance (eg. ImmuneDEX).

Be proactive rather than reactive

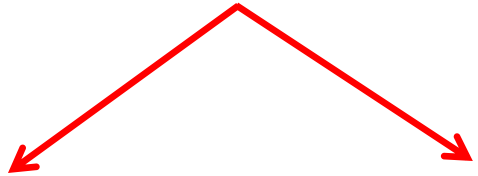
Genetic strategies to improve disease resistance

- Immune responses in cattle are heritable
- Breeding for resistance to specific diseases has been very successful
- Breeding for general disease resistance

Immunity+™
Disease Resistant Genetics



Adaptive Immune Responses



Type I

Intracellular Pathogens
eg. viruses
(largely cell-mediated)

Type II

Extracellular Pathogens
eg. worms
(largely antibody-mediated)

Combine measures of cell-mediated and antibody-mediated immune responses

Breeding for General Disease Resistance

Selection for resistance to one disease can inadvertently increase susceptibility to other diseases

Good strategy to combat –

- Complex diseases caused by multiple agents eg. BRD
- Emerging diseases

Assessing immune competence in Australian Angus

- Ensure testing does not restrict future sale of animals by using **commercial vaccine** to induce measurable responses

- Predict the ability of an animal to mount an immune response when **under Stress**

The “best” immune system is not the strongest one, but rather, the one that “maximises fitness in light of constraints” (Martin and Coon, 2010)

Assessing immune competence

Induce immune responses (vaccination) on day of weaning

↓

Measure immune responses

↓

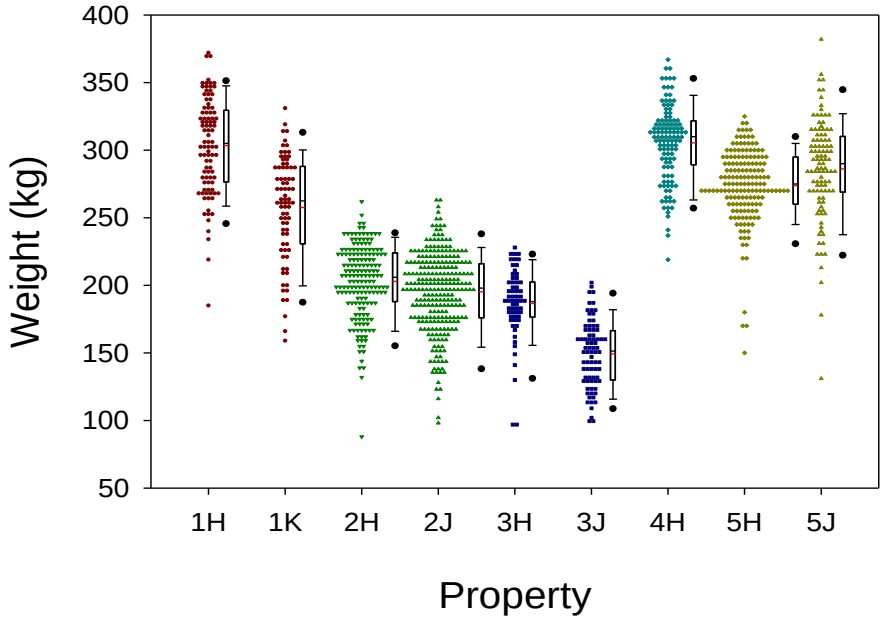
Combine measures of antibody and cell-mediated immunity to rank animals

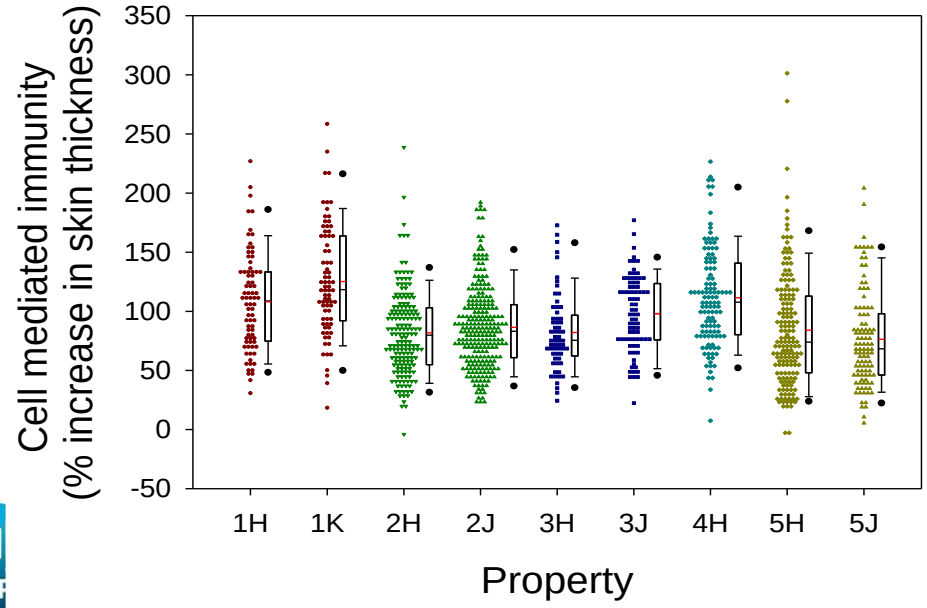
↓

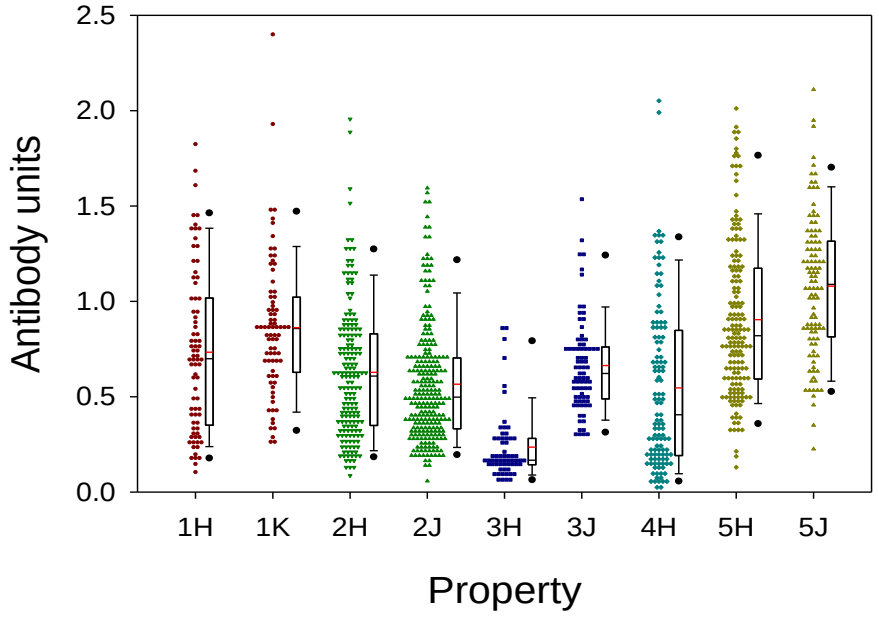
Angus ImmuneDEX

ImmuneDEX

- An **Index** which:-
  - Predicts the ability of an animal to mount an **Immune Response** to a disease challenge when **Under Stress**
  - Is expected to reflect **Broad-based Disease Resistance**
  - Will provide a tool for Australian Angus producers to place **Selection** emphasis on **Health** for the first time


Weight (kg)
400
350
300
250
200
150
100
50
1H
1K
2H
2J
3H
3J
4H
5H
5J
Property


Cell mediated immunity
(% increase in skin thickness)
350
300
250
200
150
100
50
0
-50
1H
1K
2H
2J
3H
3J
4H
5H
5J
Property


Antibody units
2.5
2.0
1.5
1.0
0.5
0.0
1H
1K
2H
2J
3H
3J
4H
5H
5J
Property

Health costs at the feedlot

- Lost production days = Days on feed when an animal died (based on $4.88/hd/day)
- Lost capital investment = Actual purchase cost of animal which died
- Disease treatment costs

Immune competence group	Cost / hd*
High	$3.53
Average	$28.24
Low	$103.36

11.7% of animals (low immune competence) contribute to 35% total health associated costs incurred at feedlot

*Excludes labour costs, opportunity cost, disease risk costs
Requires validation in an industry standard disease risk environment

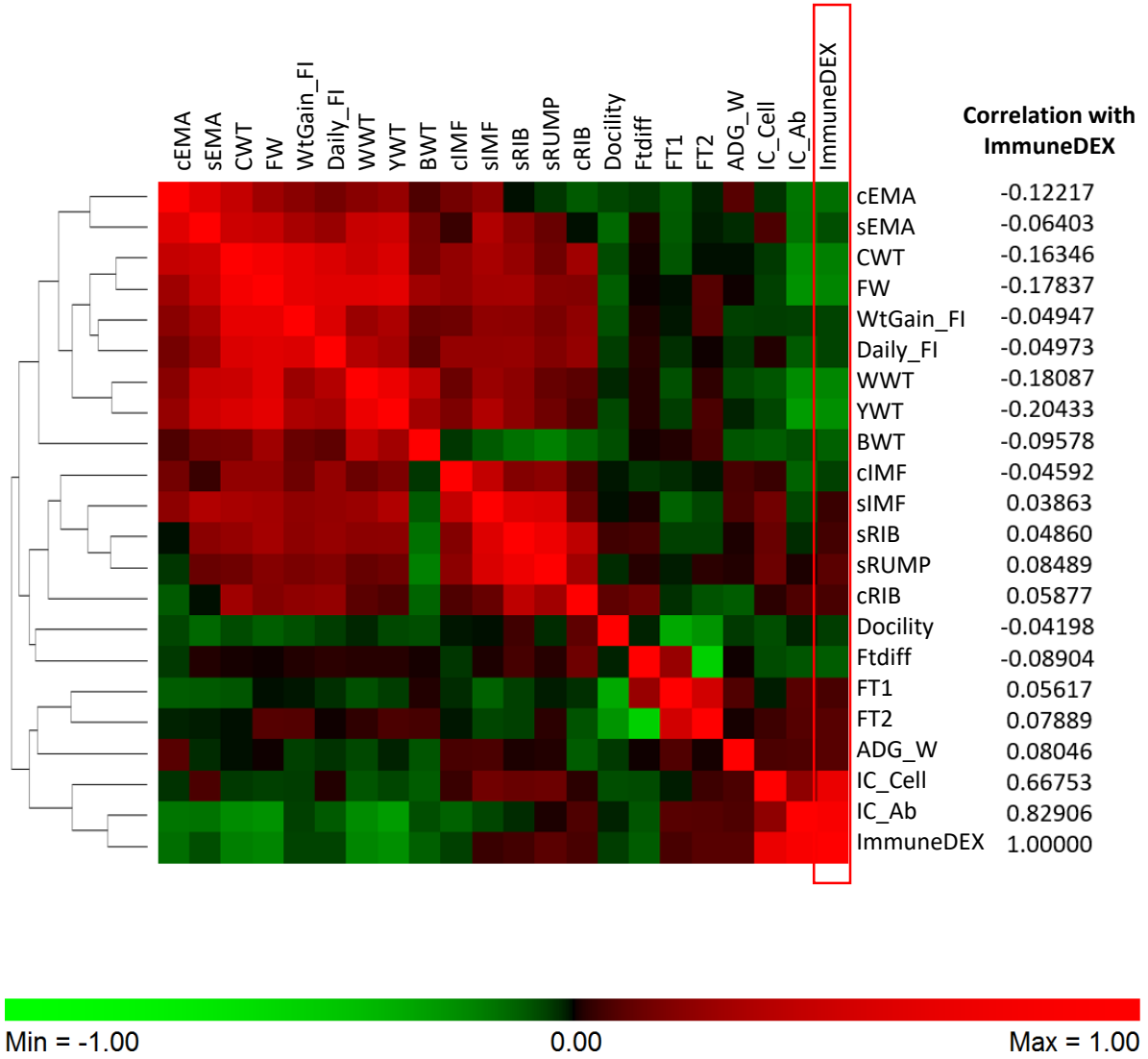
Phenotypes Recorded and Analysed

- Phenotypes for immune competence have been gathered and analysed on ~3000 steer and heifer progeny from the Angus Sire Benchmarking Program (ASBP).
- Representing 165 sires (ASBP Cohorts 2,3,6,7)
- These phenotypes have been used to calculate Research Breeding Values (RBVs)
- Sire list released in May 2019.

ID	Name	ASBP Cohort	ImmuneDEX RBV	ImmuneDEX Acc	ImmuneDEX Prog	Mid May 2019 Angus BREEDPLAN EBVs ABI	CED	200	400	600	MCW	Milk	SS	DOC	Cwt	EMA	Rib	Rump	RBY	IMF
HKFK146	PARINGA RED PILBARA K146	6	+70	92%	20	+115	+1.5	+30	+59	+56	+16	+7	+1.7	+0	+37	+4.1	+0.8	+3.6	-2.8	+4.9
WDCK314	COONAMBLE KEVIN K314	7	+50	88%	14	+129	+0.7	+50	+92	+122	+106	+19	+4.0	+12	+69	+4.7	+1.1	+2.0	-0.3	+1.6
NFWL039	GLENAVON REVENUE L039	7	+49	85%	11	+118	-2.5	+52	+98	+125	+103	+25	+0.9	-7	+79	+8.0	-1.7	-3.2	+1.6	+1.7
DKKJ516	HARDHAT GM AGRONOMIST Y21 J516	6	+48	93%	23	+96	-4.0	+45	+83	+99	+73	+15	+1.3	-10	+56	+8.7	-0.3	-0.8	+1.2	+2.1
HBUK267	ANVIL KOKODA K267	7	+44	92%	21	+139	+1.1	+53	+96	+124	+101	+23	+2.4	+6	+74	+4.7	-1.4	-1.6	+0.0	+3.2
NZEB11	WAITAWHETA B11	3	+44	88%	14	+50	+2.9	+22	+55	+66	+40	+15	+0.8	+6	+25	-3.2	+2.6	+1.2	-2.1	+0.1
EDUJ41	DENHOLM GLEN G10 BARTEL J41	6	+43	96%	39	+135	+5.2	+43	+82	+97	+57	+25	+2.5	+15	+42	+9.3	-1.8	+0.0	+1.9	+2.1
SMPK22	PATHFINDER KOMPLETE K22	7	+42	93%	24	+109	+5.8	+38	+76	+89	+67	+25	+2.2	+4	+66	+7.5	+4.2	+2.6	-0.5	+1.6
HKFE27	PARINGA IRON ORE E27	2	+41	86%	12	+122	+3.4	+39	+73	+97	+103	+16	+2.3	+28	+75	+7.4	+0.2	+0.1	+0.0	+1.9
NZE16932009490	TE MANIA QUANTUM 09 490	2	+40	80%	8	+121	-3.4	+53	+89	+117	+123	+0	+2.7	+17	+70	+2.6	-0.6	+2.8	-1.2	+2.7
NXTD154	TWYNAM D154	2	+40	67%	5	+126	-4.6	+50	+93	+120	+113	+14	+2.3	+8	+72	+13.0	+1.7	-1.8	+2.2	+1.3
NZE14738009934	MERCHISTON EXPEDITION 934	2	+40	67%	5	+100	-6.5	+59	+113	+158	+153	+13	+4.3	+9	+71	+0.6	-3.8	-2.0	+1.3	-0.1
NGXE617	BONGONGO E617	2	+39	88%	14	+105	-0.6	+42	+84	+104	+97	+16	+1.2	+16	+67	+2.0	+1.6	-1.7	-0.9	+2.2
NBHF318	CLUNIE RANGE FERRARI F318	2	+39	90%	17	+131	-1.3	+56	+99	+131	+114	+16	+2.0	-2	+97	+4.1	-2.8	-2.1	+0.8	+2.0
ECMK63	BANNABY REALITY K63	7	+39	90%	17	+105	+3.2	+44	+78	+105	+107	+12	+2.0	+17	+59	+3.9	-0.4	-0.7	-0.3	+2.1
NXOE91	AJC E91	6	+38	90%	17	+146	+4.6	+47	+76	+111	+95	+18	+1.9	-12	+58	+4.5	+0.6	+0.0	-1.8	+5.2
NZE1036	KAKAHU MISSION 1036	3	+38	79%	8	+133	-1.7	+47	+85	+120	+105	+14	+2.1	-2	+62	+10.6	+1.6	-0.1	+1.1	+1.8
DKKK15	HARDHAT GM GRASS KING Y21 K15	7	+38	90%	17	+96	-4.1	+46	+83	+98	+68	+13	+0.6	-6	+59	+10.0	+0.2	-0.2	+2.0	+1.2
USA17328461	G A R SURE FIRE	7	+38	92%	22	+158	+3.4	+50	+91	+109	+86	+17	+4.0	+8	+69	+8.6	+0.0	-0.2	+1.7	+2.7
NZE17683004790	KAHARAU CLASS 790	2	+37	66%	5	+90	-4.4	+45	+81	+110	+108	+5	+1.5	+10	+43	+7.0	-0.7	-1.9	+1.6	-0.1
QFCF23	GK 26 FEDERER F23	6	+37	93%	23	+66	-8.4	+53	+87	+108	+89	+7	+0.9	+25	+50	+1.9	-0.1	-1.1	+1.1	-0.8
NHZJ140	HAZELDEAN JAIPUR J140	7	+37	91%	20	+123	+5.0	+38	+77	+110	+94	+29	+2.9	+35	+73	+4.9	-0.6	-1.4	+1.2	+1.6
AMQH64	BROOKLANA HI TOWER H64	6	+37	92%	20	+125	-3.8	+50	+97	+136	+130	+17	+2.1	+15	+73	+5.8	+2.0	+0.0	-0.6	+2.7
GMJF20	THE GLEN CAVALIER F020 F20	2	+37	85%	11	+111	+2.2	+43	+76	+104	+89	+20	+1.9	+16	+57	+8.6	-2.4	-6.3	+4.6	-1.1
HIOL21	AYRVALE LEGACY L21	7	+36	85%	11	+143	-2.2	+58	+108	+147	+127	+21	+0.5	+14	+91	+9.7	-2.7	-1.9	+1.5	+2.5
WGMF195	MORDALLUP TIMELINE F195	3	+36	86%	12	+84	-10.2	+48	+78	+107	+109	-4	+1.8	+9	+56	+4.5	-2.5	-1.0	+2.0	+0.4
NORK522	RENNYLEA KODAK K522	7	+36	89%	16	+151	+5.0	+45	+86	+103	+105	+13	+4.3	-8	+66	+3.1	+3.3	+1.2	-1.0	+3.9
NBBC126	BALD BLAIR HIGHLANDER C126	2	+36	79%	8	+62	-0.4	+45	+76	+105	+106	+16	+1.4	-5	+64	+3.3	-1.9	-1.3	+0.8	+1.0
NXOK41	AJC K41	7	+35	86%	12	+142	-5.5	+62	+106	+143	+121	+16	+1.8	-3	+86	+9.1	-2.2	-3.6	+2.4	+2.4
NORF857	RENNYLEA AMBASSADOR F857	3	+35	91%	19	+137	-6.8	+44	+91	+116	+106	+16	+1.7	+2	+84	+2.0	+1.9	+0.8	-1.4	+5.0
DKKJ518	HARDHAT GM GRASS RANGE Y21 J518	6	+35	89%	15	+102	-1.6	+45	+77	+101	+82	+15	+1.4	-1	+61	+14.1	-2.0	-1.7	+3.2	+0.9
NZE18954008D213	WAITANGI D213	2	+35	86%	12	+103	+4.7	+46	+84	+100	+104	+1	+3.3	+9	+58	+6.1	-0.1	+0.1	+2.2	-0.4
NRZH028	CLEA H028	6	+34	93%	23	+140	+3.9	+38	+78	+96	+74	+23	+0.9	+10	+58	+12.5	+1.3	-0.6	+0.8	+4.2
NGCL154	DULVERTON LARRY L154	7	+34	91%	19	+111	-2.1	+51	+92	+131	+106	+17	+1.7	-21	+75	+2.2	-0.5	-0.5	+0.1	+1.8
NWMH162	MUNDOO HOT STUFF H162	5	+34	77%	7	+66	+0.3	+42	+75	+89	+86	+14	+0.0	+22	+44	+6.4	-3.7	-2.7	+2.8	-1.2
QRFJ347	RAFF HINGAIA J347	6	+34	94%	27	+116	+0.9	+50	+91	+131	+129	+19	+1.5	+17	+81	+14.6	-0.8	-2.0	+3.0	-0.1
USA16396573	S A V CAMARO 9272	3	+34	87%	13	+117	+3.4	+47	+77	+93	+74	+9	+1.9	-5	+47	+1.3	+0.8	-1.0	+0.9	+1.6
AMQH29	BROOKLANA DREAM H29	6	+34	92%	21	+113	-1.0	+44	+77	+102	+87	+14	+1.3	+12	+53	+9.7	-3.3	-2.3	+3.3	+0.9
SJVG10	GLENTANNER KODIAK G10	3	+34	87%	13	+70	-0.9	+44	+73	+94	+93	+11	+1.3	+21	+44	-3.2	-1.3	-0.6	-0.1	+0.3
NORH708	RENNYLEA H708	5	+34	90%	16	+172	-3.6	+45	+100	+128	+109	+13	+2.5	+12	+71	+10.5	-2.6	-4.2	+1.8	+5.7

Genetic Parameters

- Moderately heritable (h^2)
  - Antibody Mediated– 0.23
  - Cell Mediated – 0.28
- Correlation suggesting
  - Weak, negatively correlated with some of the production traits (e.g. carcase weight and eye muscle area),
  - Weak, favourably correlated with the stress and temperament related traits.


cEMA
sEMA
CWT
FW
WtGain_FI
Daily_FI
WWT
YWT
BWT
cIMF
sIMF
sRIB
sRUMP
cRIB
Docility
Ftdiff
FT1
FT2
ADG_W
IC_Cell
IC_Ab
ImmuneDEX
Correlation with ImmuneDEX
cEMA -0.12217
sEMA -0.06403
CWT -0.16346
FW -0.17837
WtGain_FI -0.04947
Daily_FI -0.04973
WWT -0.18087
YWT -0.20433
BWT -0.09578
cIMF -0.04592
sIMF 0.03863
sRIB 0.04860
sRUMP 0.08489
cRIB 0.05877
Docility -0.04198
Ftdiff -0.08904
FT1 0.05617
FT2 0.07889
ADG_W 0.08046
IC_Cell 0.66753
IC_Ab 0.82906
ImmuneDEX 1.00000
Min = -1.00
0.00
Max = 1.00

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Immune competence traits assessed during the stress of weaning are heritable and favorably genetically correlated with temperament traits in Angus cattle

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Abstract

Selection for production traits with little or no emphasis on health-related traits has the potential to increase susceptibility to disease in food-producing animals. A possible genetic strategy to mitigate such effects is to include both production and health traits in the breeding objective when selecting animals. For this to occur, reliable methodologies are required to assess beneficial health traits, such as the immune capacity of animals. We describe here a methodology to assess the immune competence of beef cattle which is both practical to apply on farm and does not restrict the future sale of tested animals. The methodology also accommodates variation in prior vaccination history of cohorts of animals being tested. In the present study, the immune competence

Angus AUSTRALIA CSIRO mla MEAT & LIVESTOCK AUSTRALIA

ImmuneDEX

- Genomic breeding value
- Selection Index optimally combining antibody and cell mediated components.
- Provides an estimate of the genetic differences between animals for overall immune competence, a key component of resilience.
- **Higher** ImmuneDEX values indicate an animal is expected to produce a **higher proportion of progeny** with an enhanced ability to resist disease challenges and therefore have a **lower disease incidence**.

AAABG

Association for the Advancement of Animal Breeding and Genetics

http://www.aaabg.org/aaabghome/proceedings23.php

A METHOD FOR DEVELOPING A BREEDING OBJECTIVE TRAIT FROM MULTIPLE COMPONENTS USING THE EXAMPLE OF IMMUNE COMPETENCE IN AUSTRALIAN ANGUS CATTLE

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SUMMARY

Traits that are being recorded in livestock improvement programs might not be suitable breeding objective traits themselves, which is an important aspect for the consideration of novel traits in breeding programs. Here we demonstrate, using the example of immune competence in cattle, how multiple novel traits can be reduced to a single breeding objective trait. It was demonstrated that it is possible to achieve a high heritability for the novel single breeding objective trait and maximise the genetic correlation with one of the major production traits, here final weight. An approach as described here would maximise the genetic gain in the novel trait.

INTRODUCTION

In order to respond to future livestock industry needs, novel traits are being developed to promote sustainable livestock production. One such desirable attribute of the animal is immune competence (IC) (Wilkie *et al.* 1999), which has demonstrated health benefits in dairy cattle (Thompson-Crispi *et al.* 2012; Aleri *et al.* 2019). A protocol for measuring IC has been developed in Australian Angus Cattle (Hine *et al.* 2019). Immune competence has two components: cell-mediated (Cell-IR) and antibody-mediated immune responses (Ab-IR). These represent two aspects of adaptive immune responses that help control infectious disease. However, in a breeding objective context, it would be easier to use immune competence, as a combination of Ab-IR and Cell-IR, as a single breeding objective trait. The aim of this study was to combine the two immune response traits into a single breeding objective trait, here IC, so that the heritability for IC is high and the correlation of IC with final weight (FW), one of the key profit drivers, is maximised to allow for the highest possible genetic gain in the novel trait through direct and correlated response.

MATERIALS AND METHODS

Data. A protocol has been developed to measure Cell-IR and Ab-IR in commercial beef herds (Hine *et al.* 2019). Immune response phenotypes were recorded on 1,149 Angus cattle from the Angus Sire Benchmarking Program. Animals originated from five different herds and were born across three years. Link sires were used to provide connections between herds and birth cohorts. Not all animals within a herd could be tested in one day, and up to 7 test cohorts exist within a herd.

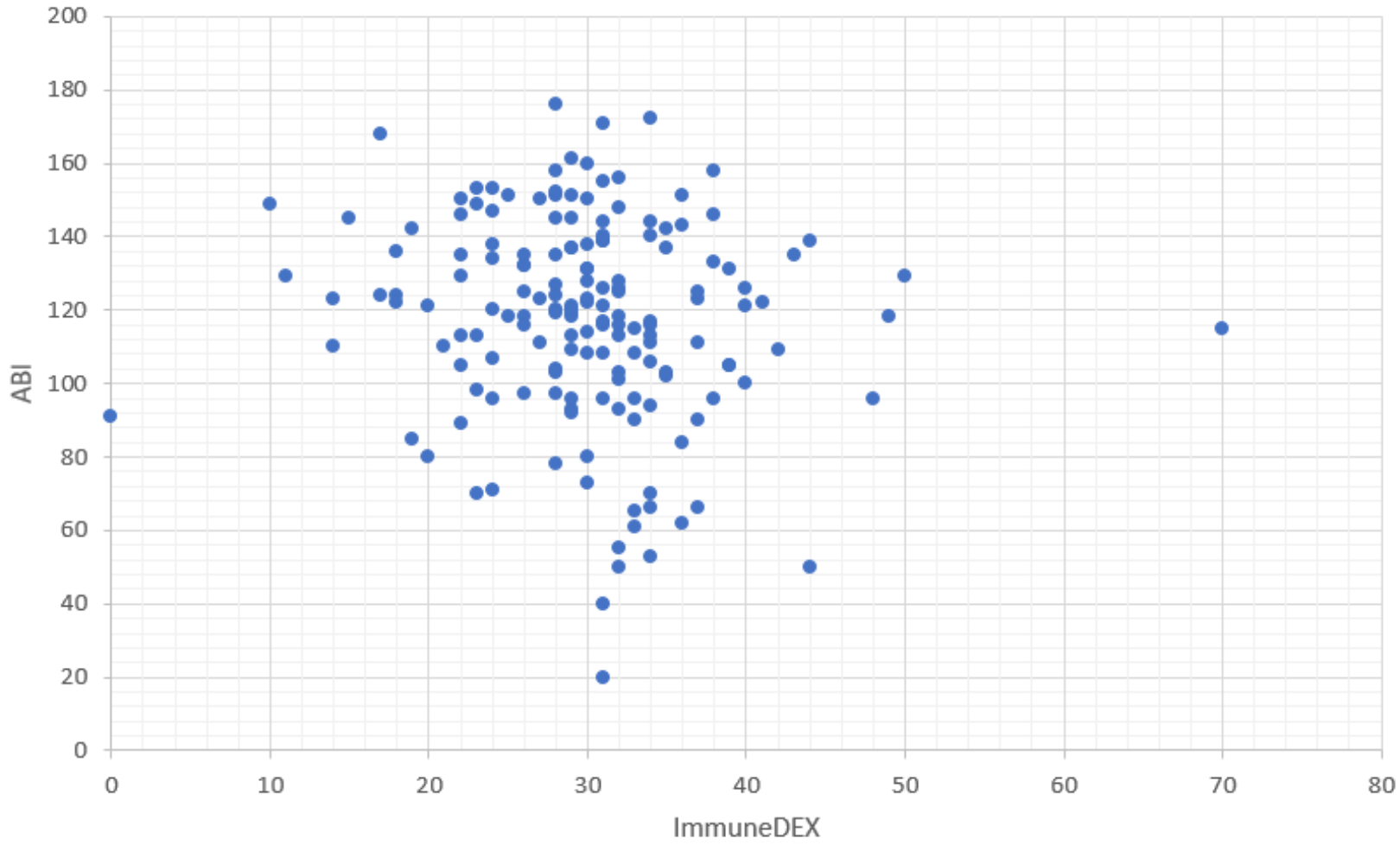
What the RBVs are saying

ID	Name	ASBP Cohort	ImmuneDEX RBV	Acc	Prog
HKFK146	PARINGA RED PILBARA K146	6	+70	92%	20
WDCK314	COONAMBLE KEVIN K314	7	+50	88%	14
NFWL039	GLENAVON REVENUE L039	7	+49	85%	11
DKKJ516	HARDHAT GM AGRONOMIST Y21 J516	6	+48	93%	23
HBUK267	ANVIL KOKODA K267	7	+44	92%	21
NZEB11	WAITAWHETA B11	3	+44	88%	14
EDUJ41	DENHOLM GLEN G10 BARTEL J41	6	+43	96%	39
SMPK22	PATHFINDER KOMPLETE K22	7	+42	93%	24
HKFE27	PARINGA IRON ORE E27	2	+41	86%	12
NZE16932009490	TE MANIA QUANTUM 09 490	2	+40	80%	8
NXTD154	TWYNAM D154	2	+40	67%	5
NZE14738009934	MERCHISTON EXPEDITION 934	2	+40	67%	5
NGXE617	BONGONGO E617	2	+39	88%	14
NBHF318	CLUNIE RANGE FERRARI F318	2	+39	90%	17
ECMK63	BANNABY REALITY K63	7	+39	90%	17
NXOE91	AJC E91	6	+38	90%	17
NZE1036	KAKAHU MISSION 1036	3	+38	79%	8
DKKK15	HARDHAT GM GRASS KING Y21 K15	7	+38	90%	17
USA17328461	G A R SURE FIRE	7	+38	92%	22
NZE17683004790	KAHARAU CLASS 790	2	+37	66%	5

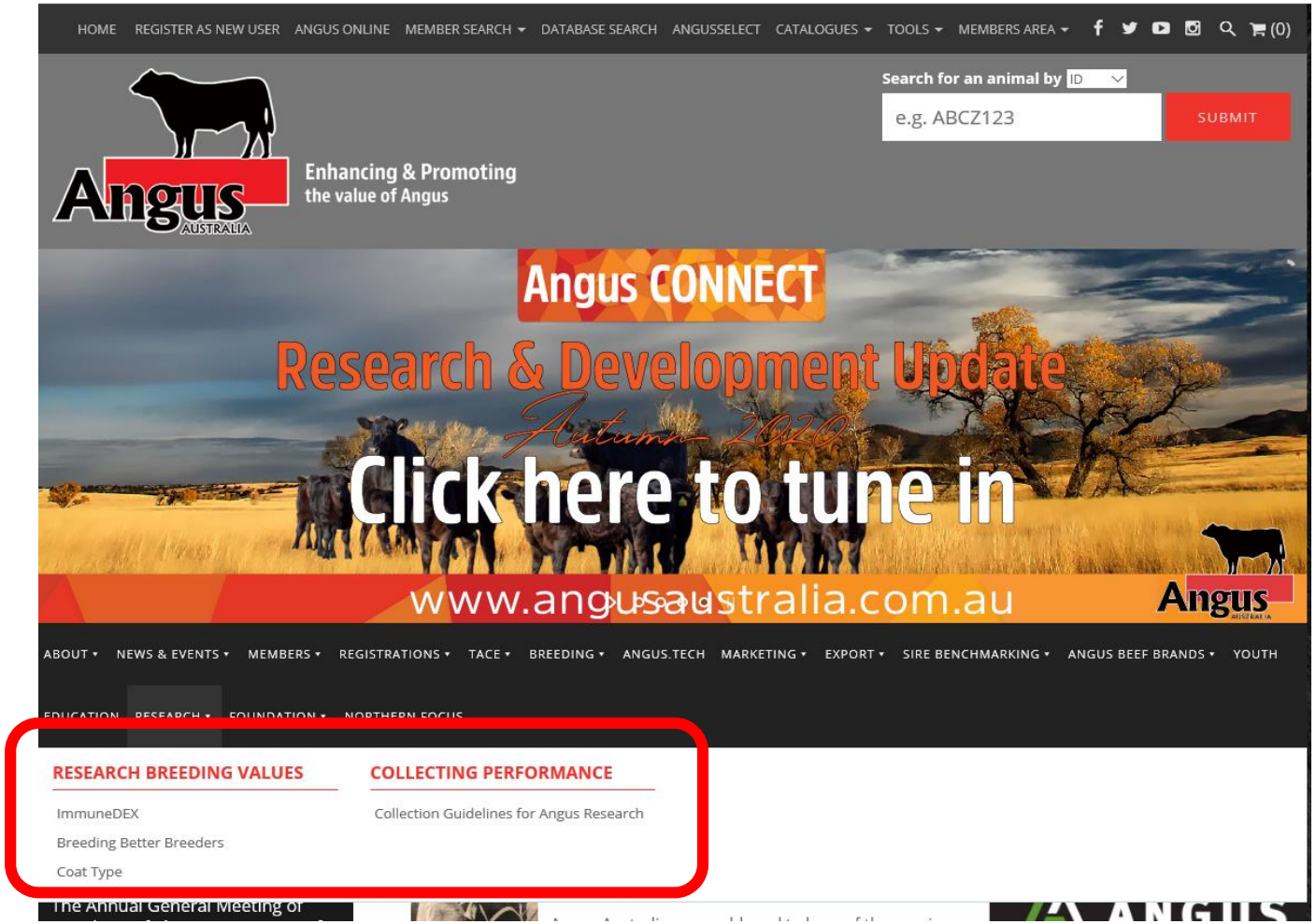
Advice to breeders on using ImmuneDEX

- There is significant variation in the ImmuneDex value across the bulls
  - Ranging from +70 to +0
- Incorporating into breeding program
  - Appropriate pressure aligning with your breeding objective
  - Use as a screen/filter on potential sires.
- Research Breeding Values so may change as more data is analysed and models enhanced.
- Limited at this stage to the Angus Sire Benchmarking Program sires

Significant variation within Angus



Where to find the ImmuneDEX RBVs



Future of ImmuneDEX

- Continue to collect phenotypes as part of the Angus Sire Benchmarking Program to develop RBVs for more bulls and improve accuracy
  - Aim → 5000 Angus animals with Genotypes and IC Phenotypes by mid 2021.
- Update ImmuneDEX RBVs including Cohort 8 and 9 sires expected second half of 2020
- Further validate the benefits in the field
  - Separate CSIRO-MLA project examining the benefit of selecting for immune competence in standard commercial feedlot environments
- Development a pipeline for all animals genomically tested (>5000 SNPs) through Angus Australia to receive ImmuneDEX predictions.

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