

National Program for Genetic Improvement of Feed Efficiency in Beef Cattle
 USDA-NIFA Award #2011-68004-30214

Beef Improvement Federation
 Manhattan, Kansas, June 15th 2016

www.BeefEfficiency.org

USDA
 United States Department of Agriculture
 National Institute of Food and Agriculture

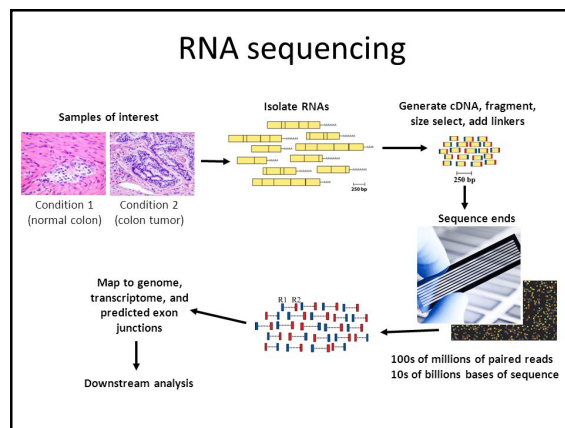
Animal Genomics @ MIZZOU **The Participants**

ILLINOIS UNIVERSITY OF ILLINOIS	VETERINARY MEDICINE & BIOMEDICAL SCIENCES MICHIGAN STATE UNIVERSITY	OWA STATE UNIVERSITY	K-STATE RESEARCH AND EXTENSION
Iowa State University Dr. Duran Garrick	University of Nebraska Dr. Matt Spangler	GeneSeek, A Neogen Company Dr. Elissa Marques	UNIVERSITY OF NEBRASKA LICKEL
Texas A&M University Dr. Chris Seabury	USDA-MARC Dr. Harvey Freenly	Washington State University Dr. Kris Johnson	GENESEEEK
University of Illinois Dr. Jan Beever	Dr. John Pollak	Dr. Holly Neibergs	USDA
University of Missouri Dr. Jerry Taylor, Project Director	Dr. Robert Schmalz	Dr. Robert Weaber	as
Dr. Monty Kerley	Dr. Jared Decker		
Dr. Robert Weaber			

17 investigators 9 institutions

Animal Genomics @ MIZZOU **Feed Efficiency Project Research Objectives**

- Assemble DNA samples, individual FI, growth and carcass data for 8,000 animals from 8 major beef breeds
- Genotype 2,400 animals from 6 breeds with BovineHD
 - 2,000 Angus and Simmental x Angus legacy animals already have been genotyped with the BovineSNP50 assay
- Analyze gene expression differences in 5 tissues from 18 low-efficiency and 18 high-efficiency animals
 - Skeletal muscle, liver, small intestine, anterior pituitary and hypothalamus
 - Angus (12), Simmental x Angus (12), Hereford (12)
- Provides data for:
 - Development of molecular estimated breeding values (MEBVs)
 - Genome Wide Association Analysis (QTLs)
 - GeneSet Enrichment Analysis (Pathway Analysis)
- Fine-map QTL regions using SNP detected from whole genome sequencing



Animal Genomics @ MIZZOU **RNA-Seq**

Animal Groups	Collection Year	Collection places	Animal Breed (number)	Total # of animals	RFI animals	Tissue list
1	2011	MU	Angus sired commercial steers	12	6 high steers	1. White Blood Cell (WBC)
					6 low steers	2. Shoulder Muscle (SM)
2	2013	UIUC	Charolais sired crossbred steers and heifers	12	3 high steers	3. Bone Marrow (BM)
					3 heifers	4. Liver (LVR)
3	2013	MU	Hereford sired steers	12	6 high steers	5. Heart (HRT)
					6 low steers	6. Lung (LNG)

7. Thymus (THY)
 8. Pancreas (PAN)
 9. Spleen (SPN)
 10. Small intestine (SI)
 11. Whole pituitary (WP)
 12. Hypothalamus (MEH)
 13. Adrenal gland (ADR)
 14. Kidney (KID)
 15. Abductor muscle (ABM)
 16. Plasma (PLAS)

Animal Genomics @ MIZZOU **RNA-Seq**

- RNA-Seq of 5 x 36 = 180 samples completed at MU
- Analysis completed by visiting postdoc Polyana Tizioto using TopHat v2.0.6:
 - 19,774 genes expressed in LVR - 6,278 were lowly expressed and could not be tested for DE
 - For MEH, SI, WP and SM we observed 19,734, 20,128, 20,302, and 19,128 expressed genes of which 4,486, 4,751, 5,012 and 5,770 were lowly expressed
 - Angus and Simmental x Angus animals had DE genes primarily related to immune function which may indicate that they were sub-clinically ill
 - In Herefords, DE genes involved in metabolic mechanisms such as pentose and glucuronate interconversions; starch and sucrose metabolism; steroid hormone biosynthesis; metabolism of xenobiotics by cytochrome P450; drug metabolism; androgen and estrogen metabolism; neuroactive ligand-receptor interaction; calcium signaling; and purine metabolism
 - DE genes analyzed in Ingenuity Pathway Analysis to identify the Driver Genes
 - Four DE driver genes are located in reported QTL regions (Saatchi et al. 2014; BMC Genomics 15:1004)
- Paper being written by Poly

Primary Breed	Secondary Breed	Sexes	HD	SNP	Total P & G	Phenotypes/DNA	Y2
Angus	X Angus	Chickadee	727	2071			
	X Angus	Edge Pass					
	X Angus	US	42				
	X Angus	US/Red Angus	44				
	X Angus	West Virginia	142				
	X Thruair	US	50	109		230	
	X Thruair	USMARC	112				59
	X Thruair	Red Ranch	22				
Charolais	X Charolais	Becher	12	867			
	X Simmental/Angus	USAC	804				
	X Thruair	USMARC	50				14
Garlbark	X Garlbark	Edge Pass	43				
	X Angus	Edge Pass	238				404
	X Red Angus	US	9				
	X Thruair	USMARC	96				13
Hereford	X Hereford	Olsen	502	774	1562		280
	X Hereford	West Virginia	15				
	X Hereford	Simplex	79				
	X Thruair	US	106				
	X Thruair	USMARC	16				8
Limousin	X Limousin	US	39	45	125		
	X Limousin	West Virginia	5				
	X Thruair	USMARC	86				38
Normande	X Normande	US/Red Angus	1				
Piedmontese	X Simmental/Angus	US/USACC	236		236		
Red Angus	X Red Angus	US/Red Angus	3	384			
	X Angus	USAC	158				
	X Hereford	US/Red Angus	44				
	X Red Angus	Becher	91				
	X Thruair	Red Ranch	38				
	X Thruair	USMARC					13
Simmental	X Angus	Edge Pass	9	1529			
	X Angus	US	128	1217			809
	X Thruair	Red Ranch	25				
	X Thruair	USMARC					40
Thruair	X Thruair	Red Ranch	88	68			
Wagyu	X Wagyu	Becher	27	27			
Total			1121	5979	7686		909

Phenotypes & Genotypes

Animals genotyped with the 50K or 800K assays

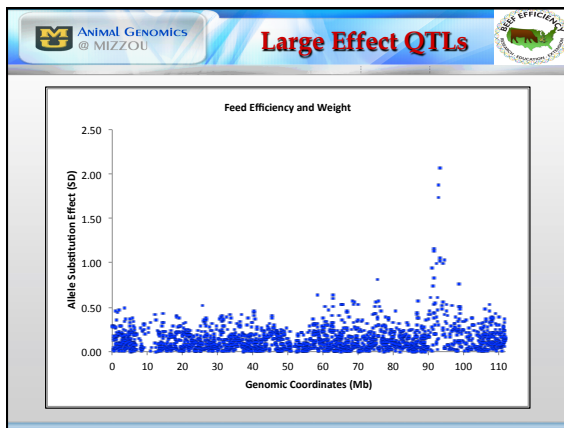
NB: Most cattle are crossbreds and we need to estimate breed composition



Study	DMI	ADG	MBW	RFI
Hereford	0.41	0.27	0.50	0.45
USMARC	0.35	0.30	0.47	0.49
Simmental	0.27	0.23	0.38	0.32
Angus	0.35	0.19	0.49	0.21



Heritabilities



Brd	#SNP	%Var	chr	Mb	Mid-test Metab Wt	SNP	%Var	chr	Mb	Gain on Test	SNP	%Var	chr	Mb	ResidFeed Intake	SNP	%Var	chr	Mb
AAN	261	10.39	7	23	261	14.24	7	23	304	1.05	9	93	304	2.21	6	50			
AAN	219	2.78	7	0	219	3.99	7	0	292	0.78	7	251	292	1.60	18	2			
AAN	277	1.75	21	13	277	1.97	21	13	184	0.41	3	82	184	0.85	18	6			
AAN	210	1.64	1	107	265	1.94	1	98	233	0.38	4	69	267	1.01	22	48			
AAN	638	1.16	30	145	340	0.71	10	44	280	0.34	15	79	638	0.72	30	145			
AAN	304	0.81	6	50	246	0.65	8	83	253	0.32	4	2	306	0.68	21	5			
AAN	453	0.80	18	6	250	0.45	5	70	324	0.31	14	34	298	0.51	2	104			
AAN	321	0.58	26	42	239	0.41	17	64	268	0.31	1	34	302	0.49	6	73			
HER	195	4.33	3	70	299	3.78	20	4	193	0.16	7	93	299	1.57	20	4			
HER	214	1.95	31	115	183	2.55	7	93	312	3.13	5	106	353	1.45	19	54			
HER	223	0.98	22	51	225	1.76	18	63	287	2.60	8	0	319	0.91	25	23			
HER	316	0.97	19	57	195	1.25	3	70	182	1.26	11	34	195	0.68	3	70			
HER	360	0.87	19	55	336	1.09	7	111	370	1.00	14	5	323	0.66	13	21			
HER	212	0.87	2	2	247	0.78	17	25	211	0.98	8	2	345	0.62	5	107			
HER	283	0.78	3	73	274	0.70	8	3	267	0.67	8	1	436	0.57	12	77			
HER	287	0.69	8	0	211	0.66	8	7	394	0.46	16	74	253	0.54	21	27			
SIM	302	0.86	15	52	192	3.14	14	24	295	1.23	2	11	380	2.40	15	82			
SIM	345	0.78	18	33	288	2.58	20	6	197	0.82	4	58	201	1.75	14	41			
SIM	360	0.69	28	53	321	1.72	15	73	211	0.79	7	92	230	1.58	10	85			
SIM	297	0.61	15	55	109	1.71	21	71	205	0.54	4	25	289	1.45	25	7			
SIM	340	0.51	17	41	218	1.40	18	50	288	0.50	16	38	241	1.35	18	37			
SIM	196	0.45	2	49	288	0.67	19	59	243	0.47	14	29	316	1.14	25	8			
SIM	282	0.44	18	40	193	0.66	14	25	223	0.39	15	83	321	0.64	28	5			
SIM	278	0.39	14	46	344	0.64	3	115	312	0.37	6	94	196	0.63	7	49			
CPT	23	0.99	8	52	21	3.49	6	38	25	2.42	20	8	12	1.95	14	43			
CPT	22	0.94	13	40	25	2.08	6	39	21	1.43	6	30	23	1.19	5	113			
CPT	13	0.76	2	44	16	1.41	14	24	25	1.27	12	54	24	0.88	8	9			
CPT	21	0.74	10	14	13	1.23	6	35	23	0.98	2	16	20	0.80	14	25			
CPT	13	0.57	6	35	23	0.84	7	27	18	0.67	11	33	22	0.73	19	37			
CPT	15	0.51	27	4	26	0.82	12	45	32	0.58	14	10	18	0.72	17	93			
CPT	25	0.41	24	38	25	0.81	20	4	20	0.57	2	14	27	0.71	15	65			
CPT	20	0.35	13	41	8	0.72	12	37	19	0.55	13	69	19	0.62	2	22			
CPT	25	0.35	3	85	24	0.70	1	42	10	0.55	7	93	23	0.60	3	4			

Breed	QTL	Trait	Breed	QTL	Trait
Hereford	1_72	RFI	SimAngus	13_43	RFI
Angus	1_98	MMWTV	SimAngus	13_53	ADG
Angus	1_105	DMI	Hereford	14_6	MMWTV
Angus	1_108	MMWTV	SimAngus	14_7	ADG
Angus	1_111	MMWTV	SimAngus	14_17	DMI
Hereford	1_144	ADG	SimAngus	16_20	MMWTV
Angus	2_29	RFI	Angus	14_27	RFI
Angus	2_63	DMI	Hereford	15_44	MMWTV
SimAngus	3_22	ADG	SimAngus	15_57	DMI
SimAngus	3_22	ADG	Angus	15_79	ADG
Hereford	3_73	DMI	SimAngus	15_82	RFI
Hereford	3_75	ADG	SimAngus	17_18	MMWTV
Angus	3_82	ADG	Angus	17_57	DMI
SimAngus	4_10	MMWTV	Hereford	18_18	MMWTV
Angus	4_59	ADG	Hereford	18_34	RFI
Hereford	5_106	ADG	SimAngus	18_54	ADG
Angus	6_16	ADG	Hereford	19_53	DMI
SimAngus	6_39	MMWTV	Hereford	20_56	MMWTV
SimAngus	6_90	DMI	Hereford	20_5	MMWTV
Hereford	6_113	RFI	Hereford	20_5	MMWTV
Angus	7_0	MMWTV	Angus	20_78	ADG
Angus	7_24	MMWTV	Angus	20_72	ADG
Angus	7_26	ADG	Angus	20_72	MMWTV
SimAngus	7_26	ADG	Angus	21_11	MMWTV
Angus	7_29	DMI	SimAngus	22_18	DMI
Hereford	7_93	ADG	SimAngus	22_57	RFI
Hereford	8_2	ADG	Hereford	24_41	DMI
Hereford	8_4	MMWTV	SimAngus	26_14	DMI
Angus	8_13	RFI	SimAngus	27_22	MMWTV
SimAngus	8_57	RFI	SimAngus	27_28	ADG
Angus	8_106	DMI	SimAngus	28_1	MMWTV
Angus	9_50	DMI	SimAngus	28_20	RFI
Angus	9_59	ADG	Hereford	X_23	MMWTV
Hereford	10_46	DMI	Hereford	X_105	MMWTV
Angus	11_6	DMI	Hereford	X_113	MMWTV
Angus	11_80	RFI	SimAngus	X_148	MMWTV
Angus	11_97	DMI			
Angus	12_91	RFI			
SimAngus	13_16	MMWTV			

Are QTLs Really Different Between Breeds?

The more you include smaller effect QTLs and allow 3-4 Mb separating QTL, the more evidence you find for pleiotropic and common QTL among breeds



New Genotyping Assay

- **New \$500K USDA grant to Taylor, Seabury and Neibergs**
- Develop a custom genotyping assay (GCP-F250) with ~185K "functional variants" and ~35K to impute the 50K set to aid imputation and accuracy of genotyping of potential causal variants
- Will genotype 4,500 feed efficiency animals

Chip Design: Data Sources

Breed	No. Animals	No. Unique Reads	Total Bases	Av. Raw Coverage
Angus	109	82,263,951,806	8,137,666,488,753	25.74
Hereford	18	15,603,339,064	1,501,290,942,627	28.76
Limousin	12	3,704,169,818	357,264,463,240	10.27
Charolais	14	8,560,329,604	858,471,719,367	21.14
Simmental	11	8,902,705,282	885,698,817,042	27.76
Gelbvieh	8	6,366,906,096	633,479,558,830	27.31
Maine Anjou	5	4,061,220,172	403,867,224,031	27.85
Romagnola	4	901,544,762	89,666,842,589	7.73
Shorthorn	2	1,446,405,682	143,863,277,001	24.80
Red Angus	14	4,430,950,144	441,846,880,499	10.88
Holstein	55	13,650,662,246	1,358,163,462,700	8.52
Jersey	9	1,399,450,902	139,150,036,295	5.33
N'Dama	1	739,233,320	73,483,493,461	25.34
Brahman	11	1,871,667,422	167,772,161,118	5.26
Nelore	8	1,668,006,036	165,728,918,125	7.14
Gir	6	1,583,737,248	157,449,065,756	9.05
Beefmaster	10	8,351,392,646	830,865,082,100	28.65
Canisdi	132	96,911,894,312	8,634,051,009,336	22.55

Whole Genome Sequence for 262 taurines


Whole Genome Sequence for 35 indicines/composites

Chip Design: Data Sources

RNA-Seq Data for 153 animals including BRD challenge experiment

Breed	No. Animals	No. Unique Reads	Total bases	Total Raw Coverage	Av. Raw Coverage
Angus	93	27,406,410,110	1,547,182,582,741	45,072.99	484.66
Hereford	11	3,815,784,459	302,094,954,473	8,800.72	800.07
Holstein	37	1,983,658,906	98,024,059,808	2,855.67	77.18
Crossbred	12	2,307,589,296	113,800,430,204	3,315.27	276.27
Total	153	35,513,442,771	2,061,102,027,226	15,011.16	409.55

Chip Design: Data Sources



- Run 4 of the 1000 Bulls Genome Project
 - 35,431,202 variants called in 1,147 animals
 - 1121 males, 24 females, 2 unknown
 - 24 breeds and composites
- dbSNP Build 146
 - 99,453,756 variants
- UMD3.1 annotation

Chip Development

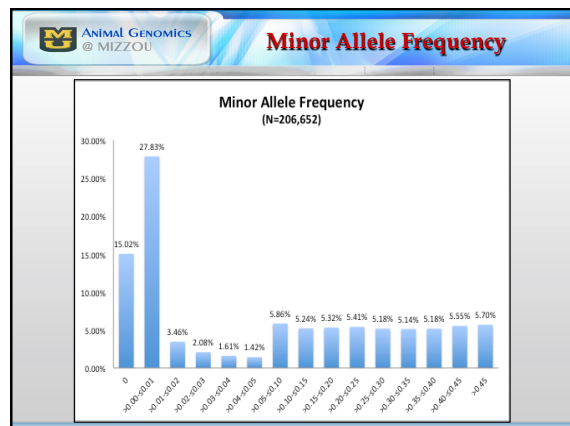
Classification	Number of Validation Sources ¹						TOTAL
	4	3	2	1	Chip	0	
AA Genomic	6485	25455	24545	17732	60	965	75242
AA RNA	0	168	3018	12106	11	19736	30461
AA 1KBulls	0	76	2037	8449	18	102	10642
UTR Genomic	8019	8299	1684	645	0	0	18647
UTR RNA	0	59	792	378	5	0	1234
UTR 1KBulls	0	0	429	2931	8	0	3368
Promoter ²	28	67	0	0	0	0	95
Splice Genomic	945	3643	4227	2509	0	0	11334
Splice RNA	0	5	205	4102	3	0	4315
Splice 1KBulls	0	0	835	2743	9	8	3595
snRNA Genomic	94	539	592	267	0	0	1492
snRNA RNA	0	3	20	16	0	0	39
Conserved Non-Coding Elements ³	311	1771	1207	61	0	0	3350
Multi-allelic ⁴	105	311	191	237	0	0	844
No Homozygotes Genomic	4	36	48	56	0	0	144
No Homozygotes RNA	0	14	42	8	0	0	64
No Homozygotes 1KBulls	0	0	13	53	1	0	67
BRD/FE QTL regions ⁵	3734	12303	5370	2134	0	0	23541
Imputation	0	0	0	0	31729	0	31729
TOTAL	19725	52749	46155	54427	33884	20333	227233

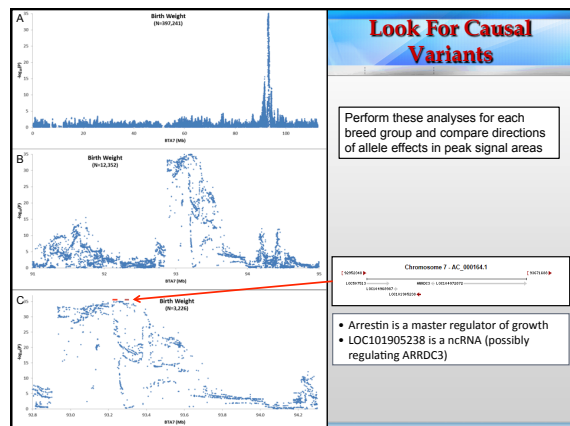
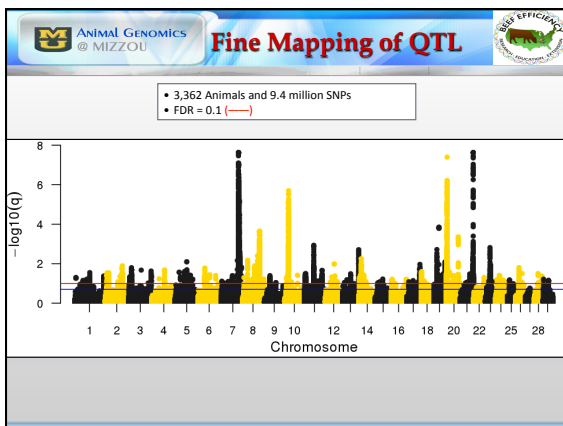
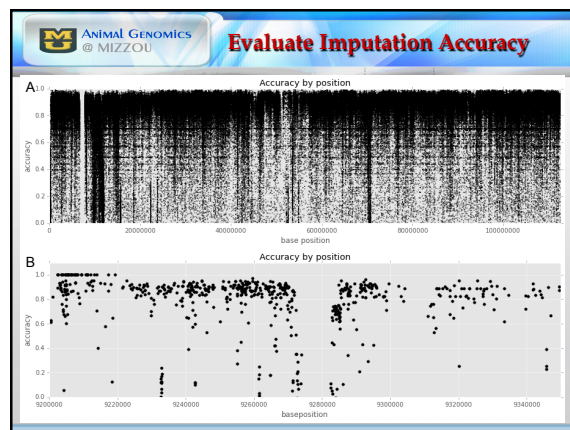
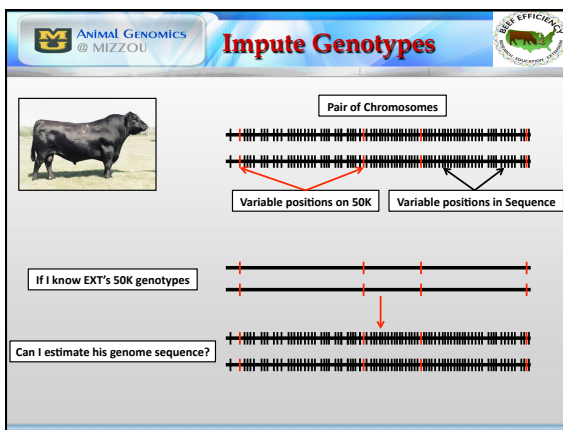
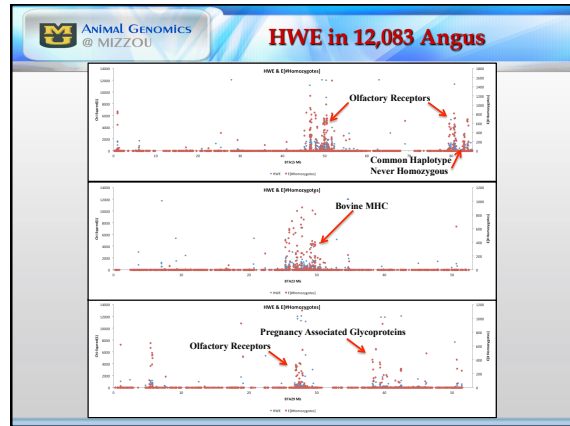
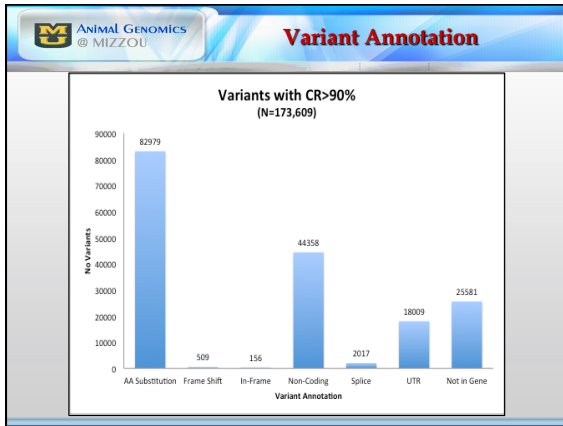
¹Indicine WGS, RNA-Seq, 1K Bulls and dbSNP
²100 bp upstream of gene annotation start (5' UTR or start codon)
³Sequence conserved in 9 ruminant genomes. SNPs have PhastCons conservation scores >0.5 and CNE length >10bp
⁴Coding variants but one sequenced animal had a 3rd allele (possible false positive)
⁵Highest MAF variant within each 5 kb bin across QTL regions


Genotyping Status

BREED	NO. GENOTYPED	% GENOTYPED
AIN	12083	66.13
AFD	945	5.17
LM	219	1.20
CHA	20	0.11
SIM	274	1.50
BRVH	7	0.04
GEL	307	1.68
PIED	9	0.05
RMG	8	0.04
ANR	1255	6.87
CIC	4	0.02
HO	1994	10.91
JER	9	0.05
GNS	7	0.04
NDAM	8	0.04
BR	14	0.08
NEL	8	0.04
GIR	11	0.06
CROS	1073	5.87
BEFM	3	0.02
SGT	11	0.06
SHK	2	0.01
18271/22 Breeds		

PROJECT	NO. GENOTYPED	% GENOTYPED
Heifer Fertility	11,506	62.97%
Feed Efficiency	4609	25.23%
Bovine Respiratory Disease	1971	10.79%
HapMap/History of Cows	185	1.01%
	18,271	










ANIMAL GENOMICS
@ MIZZOU

Conclusions



- **FE project has collected a resource population of ~10,000 genotyped and phenotyped animals representing the major US beef breeds**
- **Shown that greenhouse gas production does not differ between high and low efficiency animals per lb of DMI – but it does per lb of beef produced**
- **Developed a new genotyping assay for the beef industry**
- **Shown that FE and component traits are highly heritable**
- **Shown that there are large effect QTL for all traits**
 - Many are pleiotropic and shared among breeds
- **Last phase of current project is to use new GGP-F250 data to try and identify causal variants**
 - Include these on Zoetis and GeneSeek chips
- **Industry must continue to collect intake and growth phenotypes and collect DNA samples!**






National Program for Genetic Improvement of Feed Efficiency

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Number of Visits



The Project

- Agronomy
- Animal Care
- Breeding
- Data Management
- Diagnostics
- Development
- Genotyping
- Intake
- Phenotyping
- Production
- Research
- Statistics
- Training
- Veterinary

Multiple breeds to help them:

- Understand genetic marker set
- Implement genetic marker set within their selection goals
- Utilize marker tests for selection of feed intake in their selection strategies

15,883 unique page views from 98 countries

The Research

- Gene expression analysis of various tissues in animals with differences in feed efficiency

Updated RFI Calculator

RFI Project Calendar			
Month	Year	Event	Status
Jan	2012	Project Start	Completed
Feb	2012	Genotyping	In Progress
Mar	2012	Phenotyping	In Progress
Apr	2012	Analysis	In Progress
May	2012	Reporting	In Progress
Jun	2012	Project Review	Completed
Jul	2012	Project Review	Completed
Aug	2012	Project Review	Completed
Sep	2012	Project Review	Completed
Oct	2012	Project Review	Completed
Nov	2012	Project Review	Completed
Dec	2012	Project Review	Completed
Jan	2013	Project Review	Completed
Feb	2013	Project Review	Completed
Mar	2013	Project Review	Completed
Apr	2013	Project Review	Completed
May	2013	Project Review	Completed
Jun	2013	Project Review	Completed
Jul	2013	Project Review	Completed
Aug	2013	Project Review	Completed
Sep	2013	Project Review	Completed
Oct	2013	Project Review	Completed
Nov	2013	Project Review	Completed
Dec	2013	Project Review	Completed
Jan	2014	Project Review	Completed
Feb	2014	Project Review	Completed