Haplotypes impacting Fertility

Dr. Tom Lawlor, Holstein USA

2012 All Breeds Convention

January 21,2012

Syracuse, NY

In 2008, DNA sequence of the cow was first published.

And we keep learning more and more

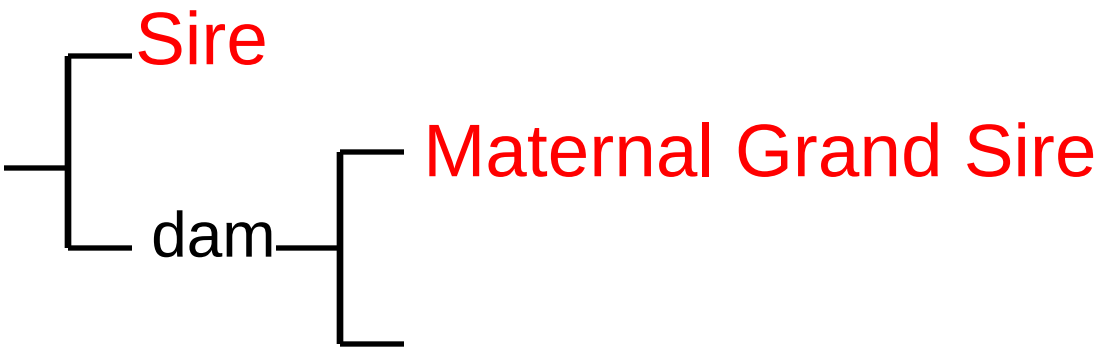
USDA research

Breed	Label	Frequency	Earliest Known Ancestors
Holstein	HH1	4.5%	Pawnee Farm Arlinda Chief
	HH2	4.6%	Willowholme Mark Anthony
	HH3	4.7%	Gray View Skyliner Glendell Arlinda Chief
Jersey	JH1	23.4%	Observer Chocolate Soldier
Brown Swiss	BH1	14.0%	West Lawn Stretch Improver

Evidence

- These haplotypes are **never observed** in a homozygous state in any live animals.

- **Decreased conception rate** was observed when a *carrier* sire was mated to a daughter of a *carrier* maternal grandsire



Every animal carries some undesirable genetic condition

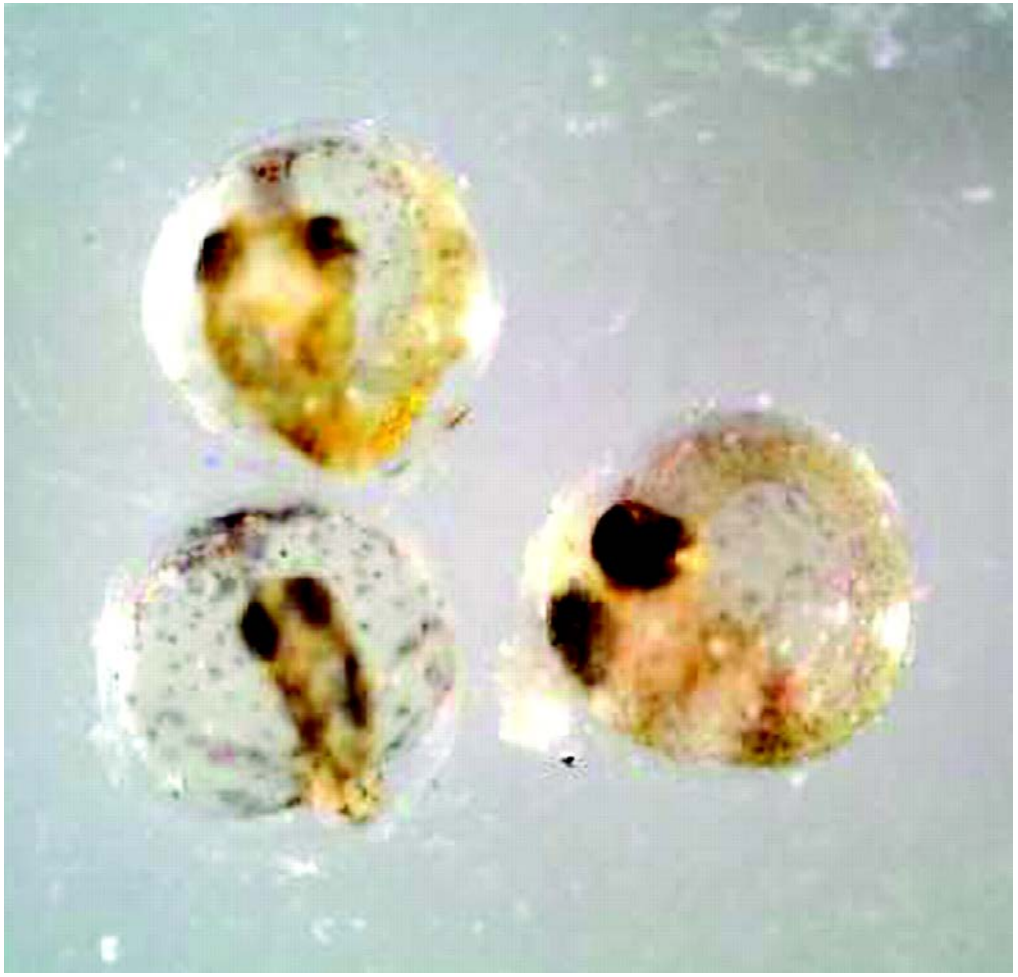
- It usually only comes to light if an animal is popular.
- We don’t want to punish only those animals from popular bloodlines.
- So ….. Don’t over-react.

It’s not surprising

- Birds do it…
- Bees do it…
- Fish do it…

➢ Produce unviable offspring

Basic biology tells us that ALL animals carry some lethal genes



Normal and mutant phenotypes for Zebra fish.

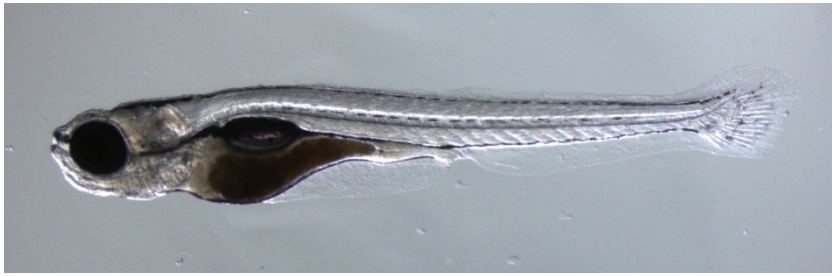
A R McCune et al. Science 2002;296:2398-2401

Science
AAAS

Zebra fish

Young fish are transparent, and their organs are fully formed after three days.

So it's easy to follow their embryonic development.

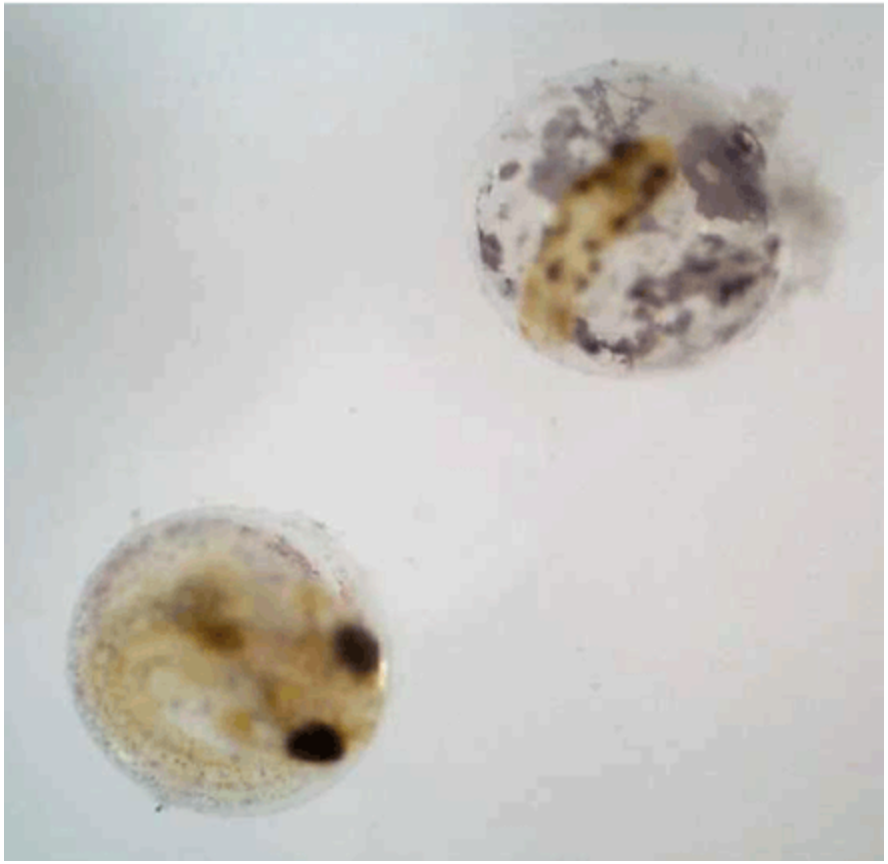


Example: Oxygen carrying defect

weissherbst (weh) mutation

Normal

Reduced hemoglobin



Twelve days post-fertilization.

Normal embryo

Defective embryo (small head)

The defective fry cannot eat.

The normal fry has a bolus of food in its gut.

Genetic Load

- The average number of unfavorable recessive gene mutations per individual in a population

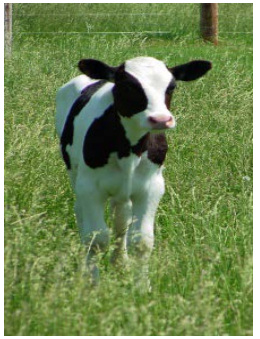
- Geneticists believe that most species carry a "**genetic load**" of 3-5 recessive lethal genes.

- It’s not a problem UNLESS your mate carries one of the same conditions.

What's a haplotype?

- A **haplotype** is a stretch of chromosome or DNA that is transmitted as a unit from one generation to the next.

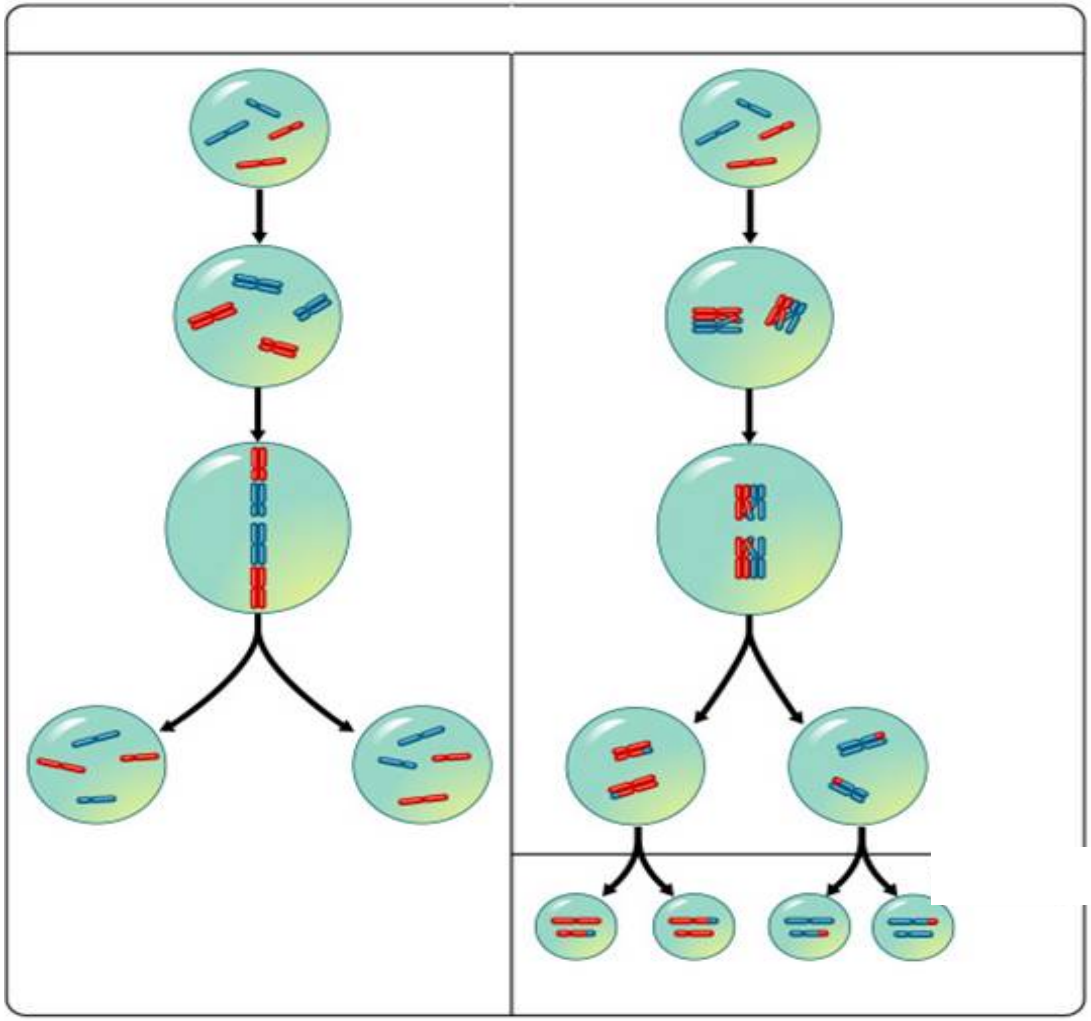
Haplotypes



- Where do they come from?
- How are haplotypes created?

Mitosis

Meiosis



Normal cell replication

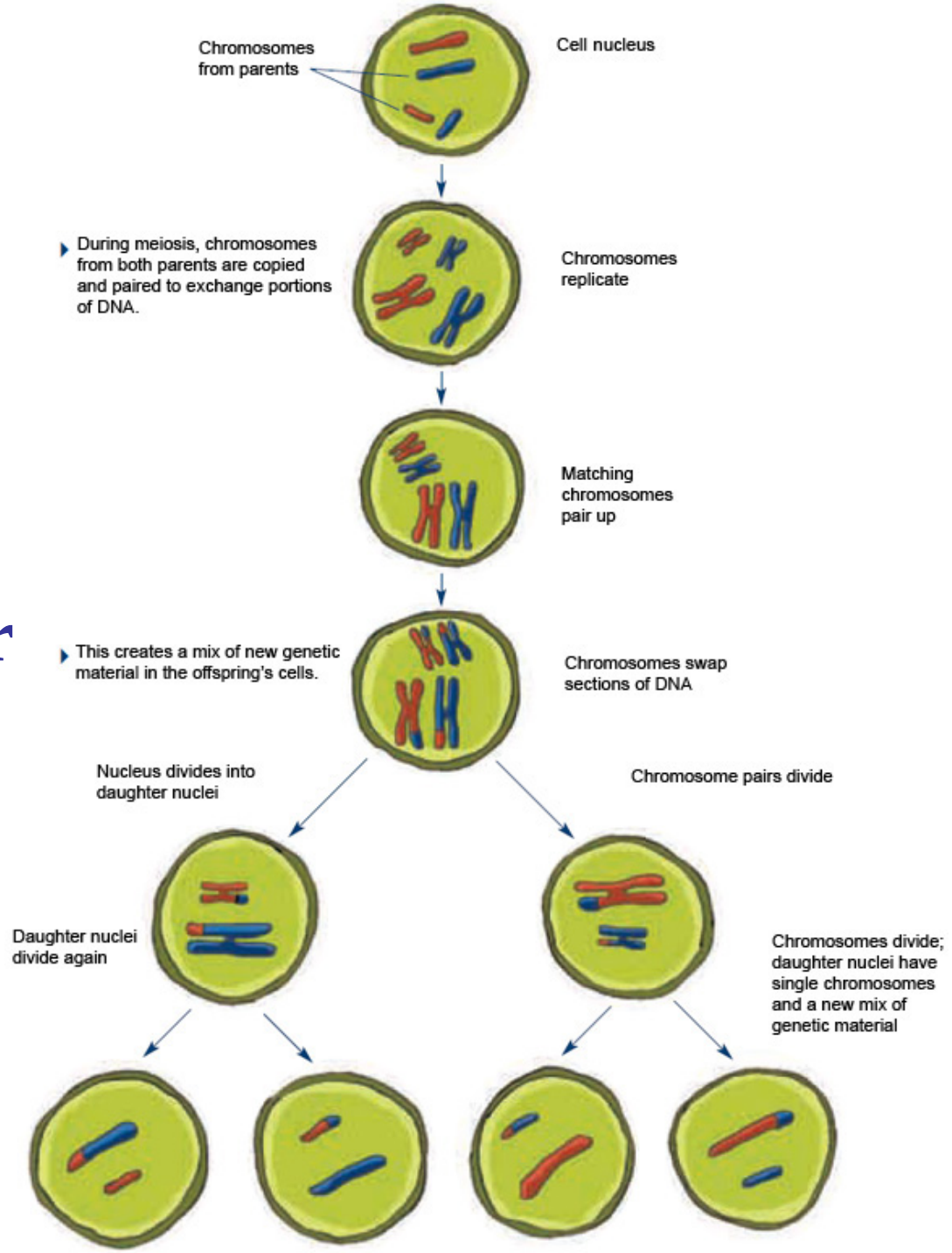
Sex cell replication

Meiosis

Duplicate

Crossing over occurs

Divide



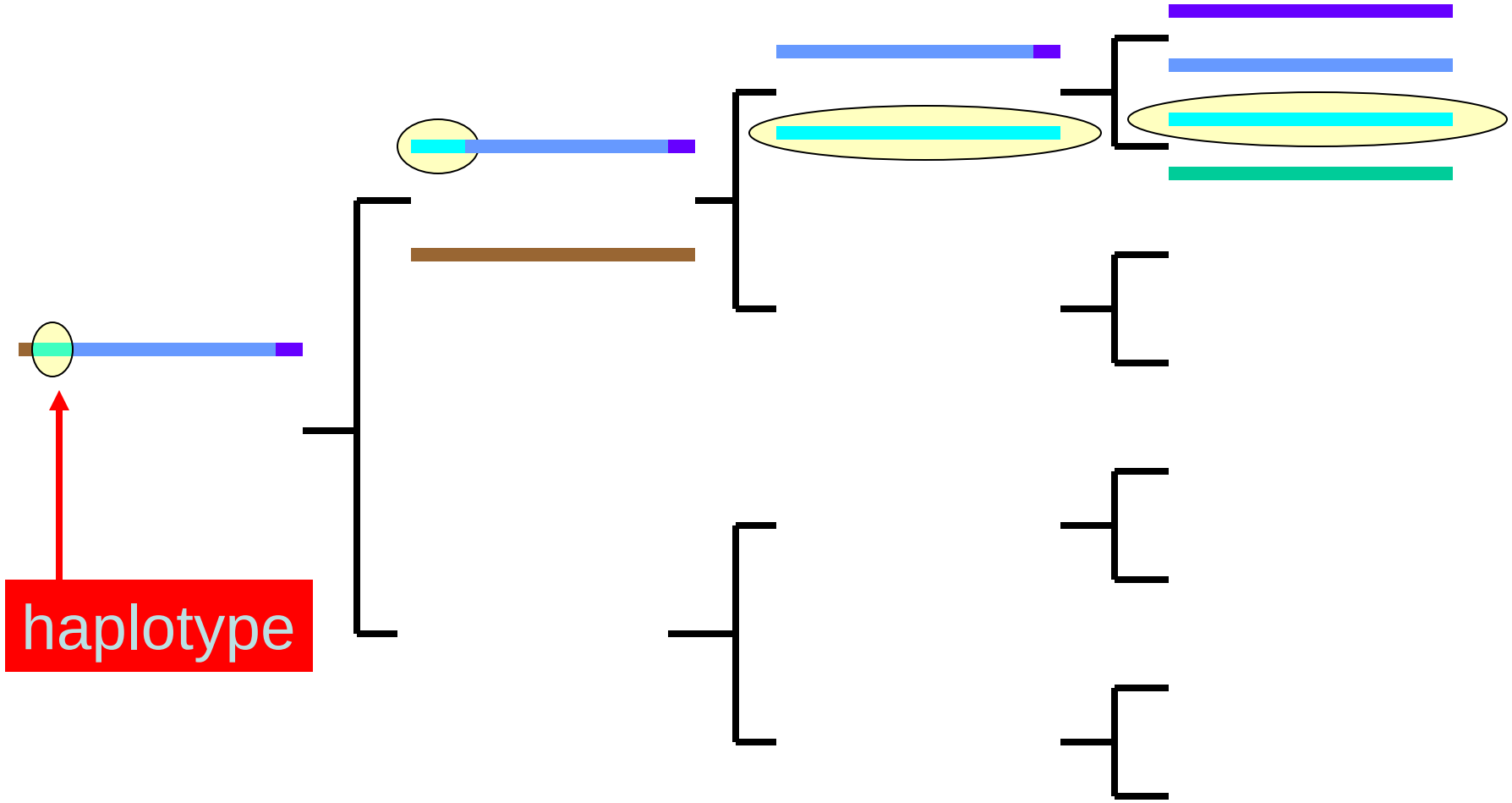
O-Style

know exactly where his DNA came from

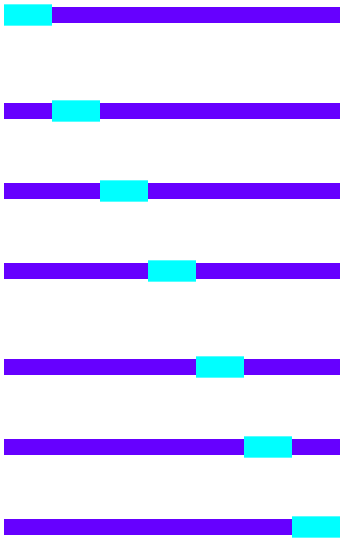
Chromosome 15

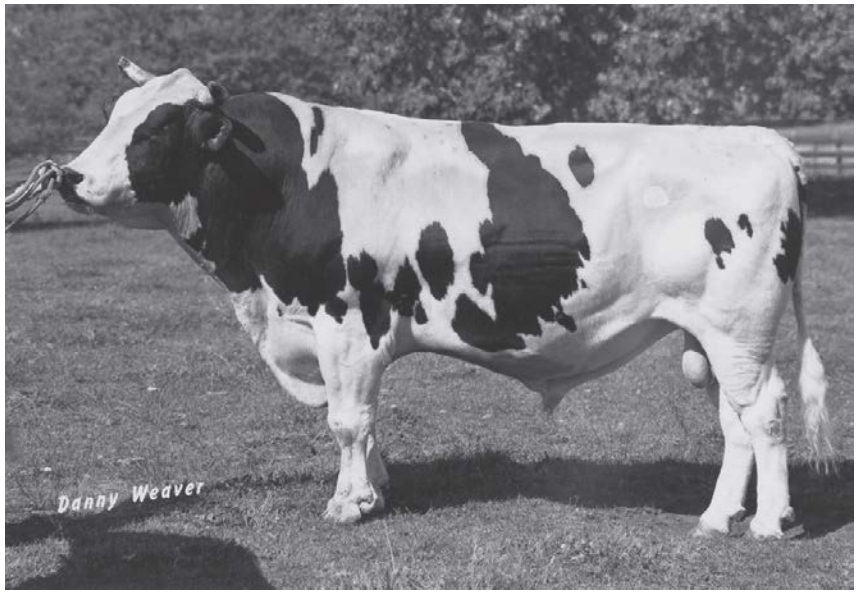
Haplotypes are created as the

original DNA sequence gets broken into smaller pieces



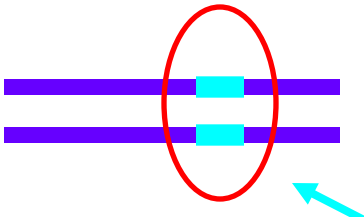
For a popular bull, we're able to find many small DNA segments (haplotypes) of his original chromosome amongst the current genotyped descendants

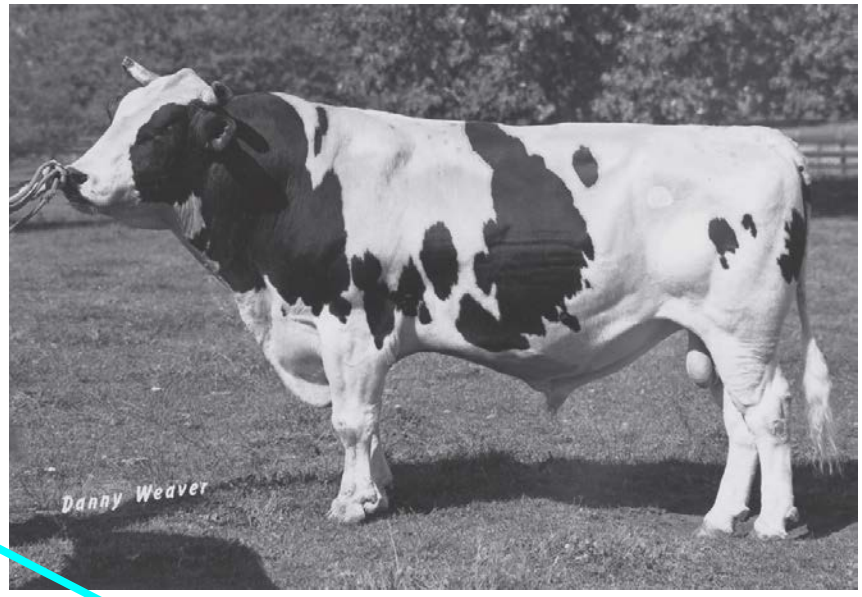




original chromosome

And we're usually able to find two identical (homozygous) copies of a haplotype.





original chromosome

Haplotypes impacting fertility

- Certain haplotypes never appear in a homozygous condition.

- For example, we never find an animal with the genotype

ATACTTAGGCTTATACCTAGGAGCTGACCTGAC
ATACTTAGGCTTATACCTAGGAGCTGACCTGAC

This stretch of DNA must contain a lethal condition

Bulls' status for haplotypes impacting fertility on the records of Holstein Association USA, Inc. as of 12/09/2011 (Blank=Tested-Free, C=Carrier)

Stud Code	Name	Registration	HH1	HH2	HH3
1HO09054	SCHULTZ FARM DC RAFE CRI-ET	USA 62398834	C		
	SCHULTZ-FARM-JE R B10211-ET	USA 66631680	C		
	SCHULTZ-FARM-JE R B10218-ET	USA 66631687	C		
	SCHULTZ-FARM-SHF ALTABAM-ET	USA 66631635	C		
	SCHUTTECREST AIR DENO-ET	USA 66076004	C		
	SCIPIOSPRING REESES	USA 66741932		C	
8HO02580	SCRUTON VINSON	USA 2100763	C		
7HO06166	SDA EMORY NICK PAT-ET	USA 17314808			C
	SEAGULL-BAY MADMAN-ET	USA 65751903			C
	SEAGULL-BAY MALVOY-ET	USA 65751907		C	C
	SEAGULL-BAY PLAYBOOK-ET	USA 66372145			C
11HO01855	SECOND-LOOK SEDUCER	USA 2004710			C
73HO02619	SEELBY CARNIVORE-ET	CAN 6167983	C		
14HO05664	SEITVIEW MARION MAXX-TW	USA 63443541	C		
1HO06402	SENECA-VALLEY SNAPPER	USA 121628772	C		

December 2011, Active AI 70% REL Bulls by JPI

REGISTRY STATUS CODES IN ANIMAL NAMES. Registry status codes PR and GR are an i for those animals recorded at the Provisional Register and Genetic Recovery levels, respe status code of HR is not included in the registration name. Refer to the inside back cover

Name of Bull	Registration Number	GT	JH1	NAAB Code
SUN VALLEY IMPULS JUPITER	USA 115870022	50K	F	29JE3615
TOLLENAARS IMPULS LOUIE 260-ET	USA 061929276	50K	C	14JE473
CAL-MART JACE STRUNK	USA 115685866	50K	F	29JE3616
PR OOMSDALE ROCKET GOOSE-ET	USA 067027311	50K	F	1JE672
D&E PAUL-ET	USA 115181456	50K	F	11JE944
TOLLENAARS IMPULS LEGAL 233-ET	USA 061929249	50K	C	29JE3506
ISDK Q IMPULS	DNK 000301592	50K	F	236JE3
ABBOTT OF D&E	USA 114756406	50K	F	11JE928
SF IMPULS 8916	USA 114635185	50K	C	1JE648
CAVE CREEK KANOO-ET	USA 114118219	50K	F	7JE1100
BW VENERABLE-ET	USA 114901730	50K	F	200JE986
CAVE CREEK VERMEER-ET	USA 114849531	50K	F	1JE666
TOLLENAARS ARTIST LYNDON-ET	USA 061929278	50K	F	29JE3508
PR OOMSDALE GRATITUDE LEXING LIAM	USA 067027366	50K	C	14JE509
VICTOR KIRK OF ALL LYNNS	USA 115255083	50K	C	11JE943
SR IMPULS STONE-ET	USA 114332783	50K	F	1JE634
FAIRWAY KLASSIC KILOWATT-ET	USA 114656667	50K	F	11JE921
DUTCH HOLLOW LEXICON	USA 115479865	50K	F	1JE700
RICHIES JACE TBONE A364	USA 113672851	50K	F	7JE1000
GABYS NATHAN PROTECTOR-ET	USA 115107063	50K	F	200JE343

Brown Swiss A.I. Sires Identified as BH1 Haplotype Carriers (*Tested using 50K chip)

BSUSA000000163153 1972 I 021BS00415 WEST LAWN STRETCH IMPROVER (M)
BSUSA000000176943 1980 I 029BS03687 JOHANN MR MAGIC ET
BSUSA000000179888 1982 I 029BS03700 JUST SO LUCRATIVE ET
BSUSA000000181329 1984 A 076BS09016 VICTORY ACRES JUBILAT EMORY*TM
BSUSA000000183095 1986 I 021BS00449 LONE OAK IMA DAZZLER ET
BSUSA000000183189 1986 I 029BS03712 JOHANN LUCIFER ET (M)
BSUSA000000184298 1987 I 014BS00215 SNOWBIRDS COMBUSTION ET
BSUSA000000184560 1988 I 151BS00015 SNOWBIRDS SIMONIZE
BSUSA000000186040 1989 A 076BS00900 VICTORY ACRES SIMON EVEN ET*TM
BSUSA000000186951 1990 I 029BS03721 ROUND HILL CONDUCTOR EXIDE ET
BSUSA000000187103 1990 I 001BS00480 LONE OAK IMA DOLLSON ET
BSUSA000000187361 1990 I 054BS00256 LYNDALE EMORY EMERALD ET
BSUSA000000187451 1990 I 009BS00071 R BAY EMORYS EARNEST T
BSUSA000000187362 1991 I 029BS03724 LYNDALE EMORY LEGACY ET
BSUSA000000187668 1991 I 001BS00493 BETTA VUE EMORY PRELUDE ET
BSUSA000000188212 1991 I 151BS00073 AMBER RAE EMORYS DUKE

Economic importance

- Economic loss is less when the loss is early.
- Economic loss is less when frequency is low.

Name	Haplotype frequency	Impact on Conception rate	Timing of Pregnancy Loss
HH1	4.5%	-0.35%	Throughout gestation
HH2	4.6%	-0.36%	Before day 100
HH3	4.7%	-0.36%	Before day 60
JH1	23.4%	-2.22%	Before day 60
BH1	14.0%	-0.98%	Before day 100

What should I do?

- **Continue to use animals of superior genetic merit.**

  Impact of reduced fertility is already partially taken into account in:

  Sire Conception Rate, Daughter Pregnancy Rate, NM$, TPI, JPI, and PPR.

- **Lower the risk of carrier-to-carrier matings.**

  Genotype your animals.

  Avoid certain sire-by-maternal grandsire matings.

Which families have which haplotypes?

Name	Key Sire Fathers
HH1	Chief, Mark, Lindy, Formation, Throne, Jordan-Red, Palermo
HH2	Outside, Boulet Charles, Colby, Million, Mr. Burns
HH3	Glendell, Rotate, Emory, O Man, Boss Iron, Snowman
JH1	Top Brass, Sooner, Berretta, Hallmark, Paramount, Jace, Louie
BH1	Stretch Improver, Emory, Prelude, Even, Earnest T Peerless, Vigor

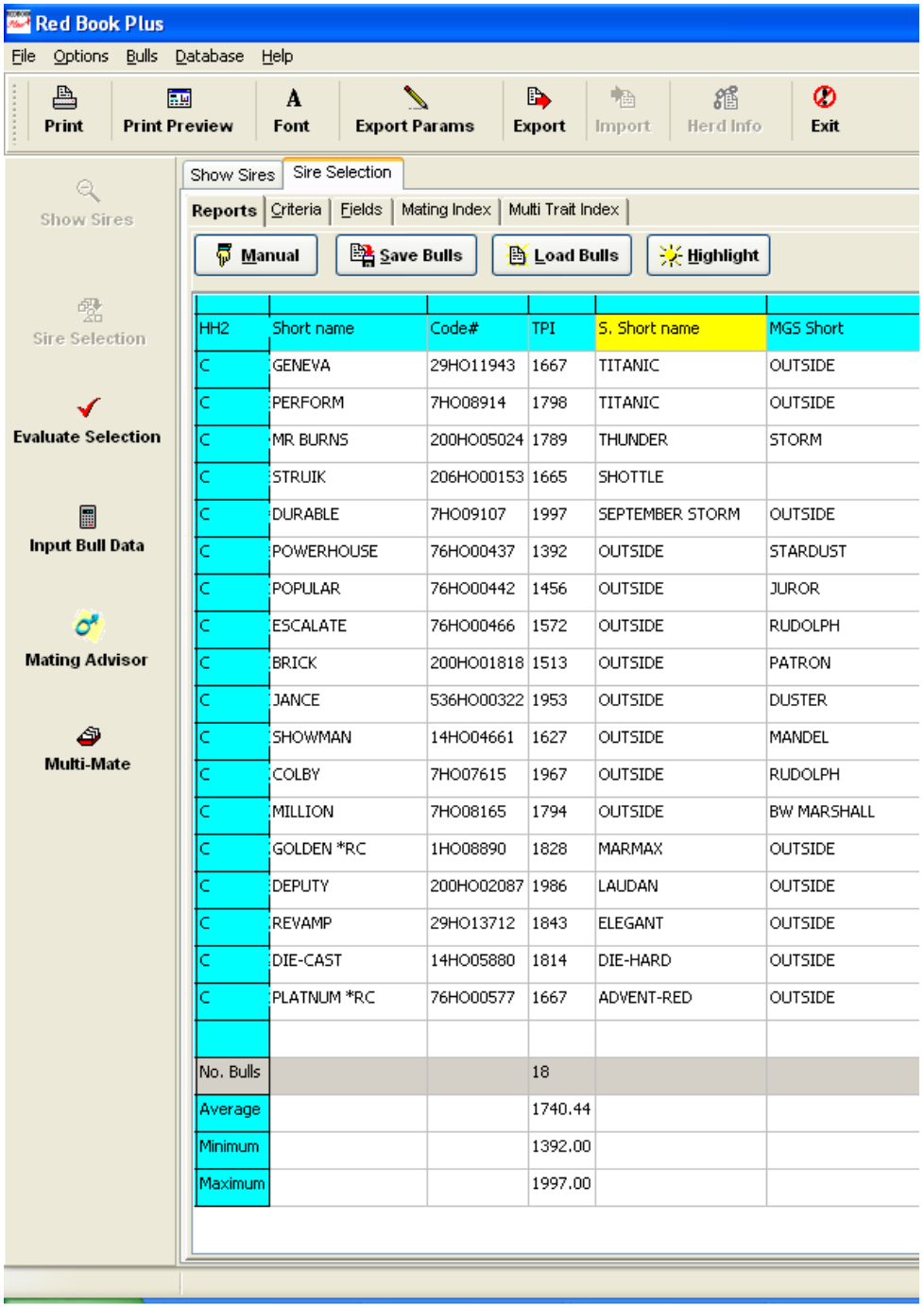
Which families have which haplotypes?

RED BOOK+ MultiMate Plus

1,017
Available Bulls

HH2

18 **C** bulls



HH2	Short name	Code#	TPI	S. Short name	MGS Short
C	GENEVA	29HO11943	1667	TITANIC	OUTSIDE
C	PERFORM	7HO08914	1798	TITANIC	OUTSIDE
C	MR BURNS	200HO05024	1789	THUNDER	STORM
C	STRUIK	206HO00153	1665	SHOTTLE	
C	DURABLE	7HO09107	1997	SEPTEMBER STORM	OUTSIDE
C	POWERHOUSE	76HO00437	1392	OUTSIDE	STARDUST
C	POPULAR	76HO00442	1456	OUTSIDE	JUROR
C	ESCALATE	76HO00466	1572	OUTSIDE	RUDOLPH
C	BRICK	200HO01818	1513	OUTSIDE	PATRON
C	JANCE	536HO00322	1953	OUTSIDE	DUSTER
C	SHOWMAN	14HO04661	1627	OUTSIDE	MANDEL
C	COLBY	7HO07615	1967	OUTSIDE	RUDOLPH
C	MILLION	7HO08165	1794	OUTSIDE	BW MARSHALL
C	GOLDEN *RC	1HO08890	1828	MARMAX	OUTSIDE
C	DEPUTY	200HO02087	1986	LAUDAN	OUTSIDE
C	REVAMP	29HO13712	1843	ELEGANT	OUTSIDE
C	DIE-CAST	14HO05880	1814	DIE-HARD	OUTSIDE
C	PLATNUM *RC	76HO00577	1667	ADVENT-RED	OUTSIDE
No. Bulls			18		
Average			1740.44		
Minimum			1392.00		
Maximum			1997.00		

RED BOOK+ MultiMate Plus

HH2C

Pedigrees

HH2	Short name	Code#	TPI	S. Short name	MGS Short
C	GENEVA	29HO11943	1667	TITANIC	OUTSIDE
C	PERFORM	7HO08914	1798	TITANIC	OUTSIDE
C	MR BURNS	200HO05024	1789	THUNDER	STORM
C	STRUIK	206HO00153	1665	SHOTTLE	
C	DURABLE	7HO09107	1997	SEPTEMBER STORM	OUTSIDE
C	POWERHOUSE	76HO00437	1392	OUTSIDE	STARDUST
C	POPULAR	76HO00442	1456	OUTSIDE	JUROR
C	ESCALATE	76HO00466	1572	OUTSIDE	RUDOLPH
C	BRICK	200HO01818	1513	OUTSIDE	PATRON
C	JANCE	536HO00322	1953	OUTSIDE	DUSTER
C	SHOWMAN	14HO04661	1627	OUTSIDE	MANDEL
C	COLBY	7HO07615	1967	OUTSIDE	RUDOLPH
C	MILLION	7HO08165	1794	OUTSIDE	BW MARSHALL
C	GOLDEN *RC	1HO08890	1828	MARMAX	OUTSIDE
C	DEPUTY	200HO02087	1986	LAUDAN	OUTSIDE
C	REVAMP	29HO13712	1843	ELEGANT	OUTSIDE
C	DIE-CAST	14HO05880	1814	DIE-HARD	OUTSIDE
C	PLATNUM *RC	76HO00577	1667	ADVENT-RED	OUTSIDE

Confirm Carrier status of ancestor

OUTSIDE

Bulls' status for haplotypes impacting fertility on the records of Holstein Association USA, Inc. as of 12/09/2011 (Blank=Tested-Free, C=Carrier)

Stud Code	Name	Registration	HH1	HH2	HH3
73HO01842	COMESTAR LOYDS-ET	CAN 5183344		C	
200HO05350	COMESTAR LS LOGICAL-ET	CAN 102482565		C	
39HO00767	COMESTAR MALIBU-ET	CAN 6581697	C		
200HO05312	COMESTAR MODEL FRANK-ET	CAN 101760604		C	
200HO05982	COMESTAR MOUNTAIN-ET	CAN 105331864		C	
200HO04618	COMESTAR NATIONAL-ET	CAN 9194914		C	
73HO02479	COMESTAR OUTSIDE-ET	CAN 6026421		C	
	COMESTAR PRIDE-ET	CAN 6571872	C		
	COMESTAR TEMPLAR	CAN 102482559		C	
	COMESTAR TRAVIS-ET	CAN 6334342	C		
11HO11126	COMYN-PBCD ALTASTAVELY-ET	USA 69932056			C
11HO09712	CON-RIVER ALTAKO-ET	USA 136868680	C		
7HO09532	CON-RIVER FBI AGENT-ET	USA 137915200	C		
9HO02253	CONANT-ACRES STAFFORD-ET	USA 2269283	C		
21HO01927	CONANT-ACRES-JY SAMUEL	USA 2080975			C

RED BOOK+ MultiMate Plus

HH3

41 **C** bulls

Male Carriers for Haplotypes Impacting Fertility on the Records of Holstein Association USA, Inc. as of 12/09/2011 (Blank=Tested-Free, C=Carrier, N=Not Tested)

Stud Code	Name	Registration	HH1	HH2	HH3
7HO06417	O-BEE MANFRED JUSTICE-ET	USA 122358313			C

RED BOOK+ MultiMate Plus

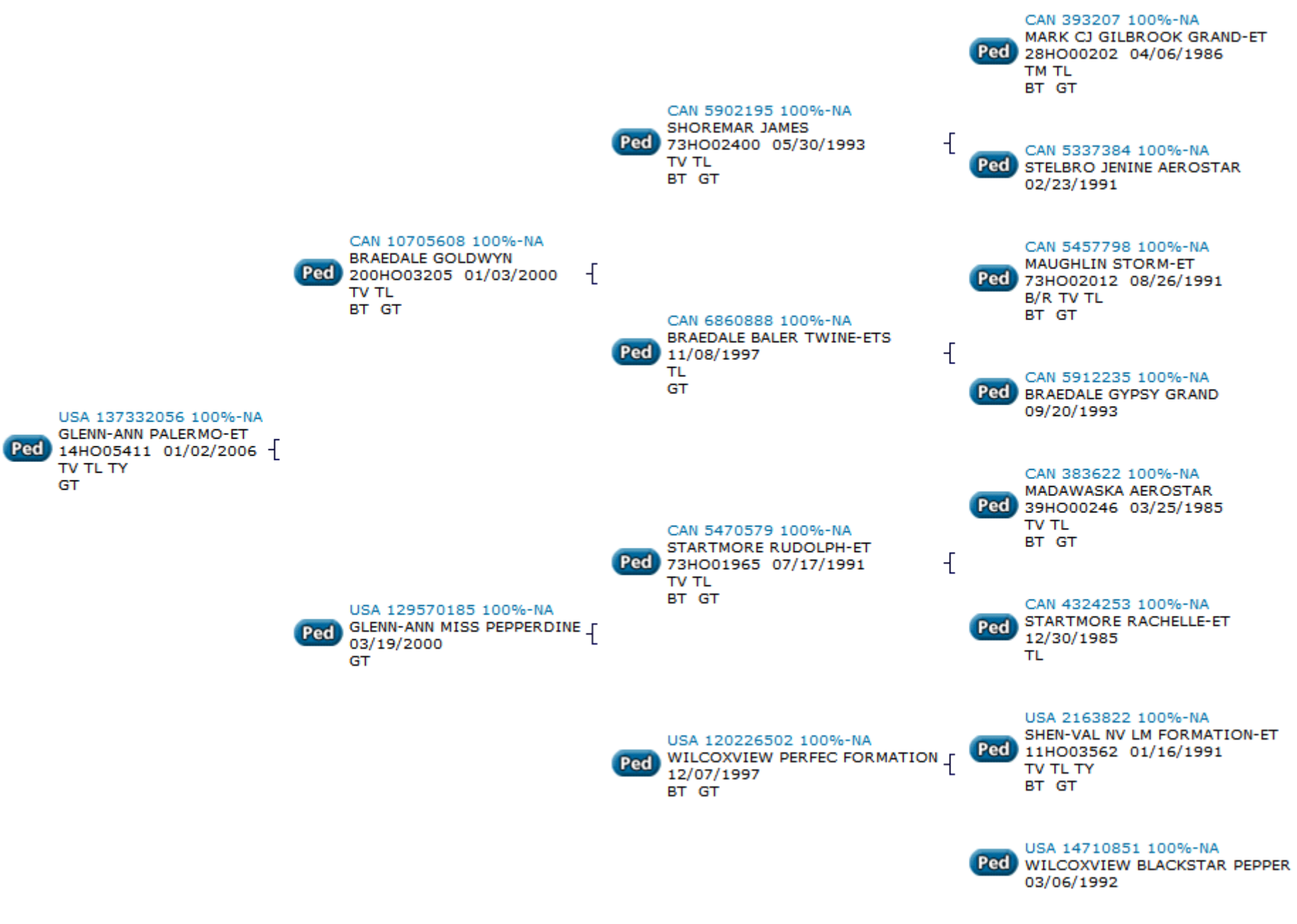
HH1

52 C bulls

Male Carriers for Haplotypes Impacting Fertility on the Records of Holstein Association USA, Inc. as of 12/09/2011 (Blank=Tested-Free, C=Carrier, N=Not Tested)

Stud Code	Name	Registration	HH1	HH2	HH3
14HO03831	VEAZLAND MARION-ET	USA 130153294	C		
11HO05570	OPSAL FINLEY-ET	USA 120780521	C		
11HO04400	DIXIE-LEE AARON-ET	USA 2265005	C		

14HO05411	GLENN-ANN PALERMO-ET	USA 137332056	C		



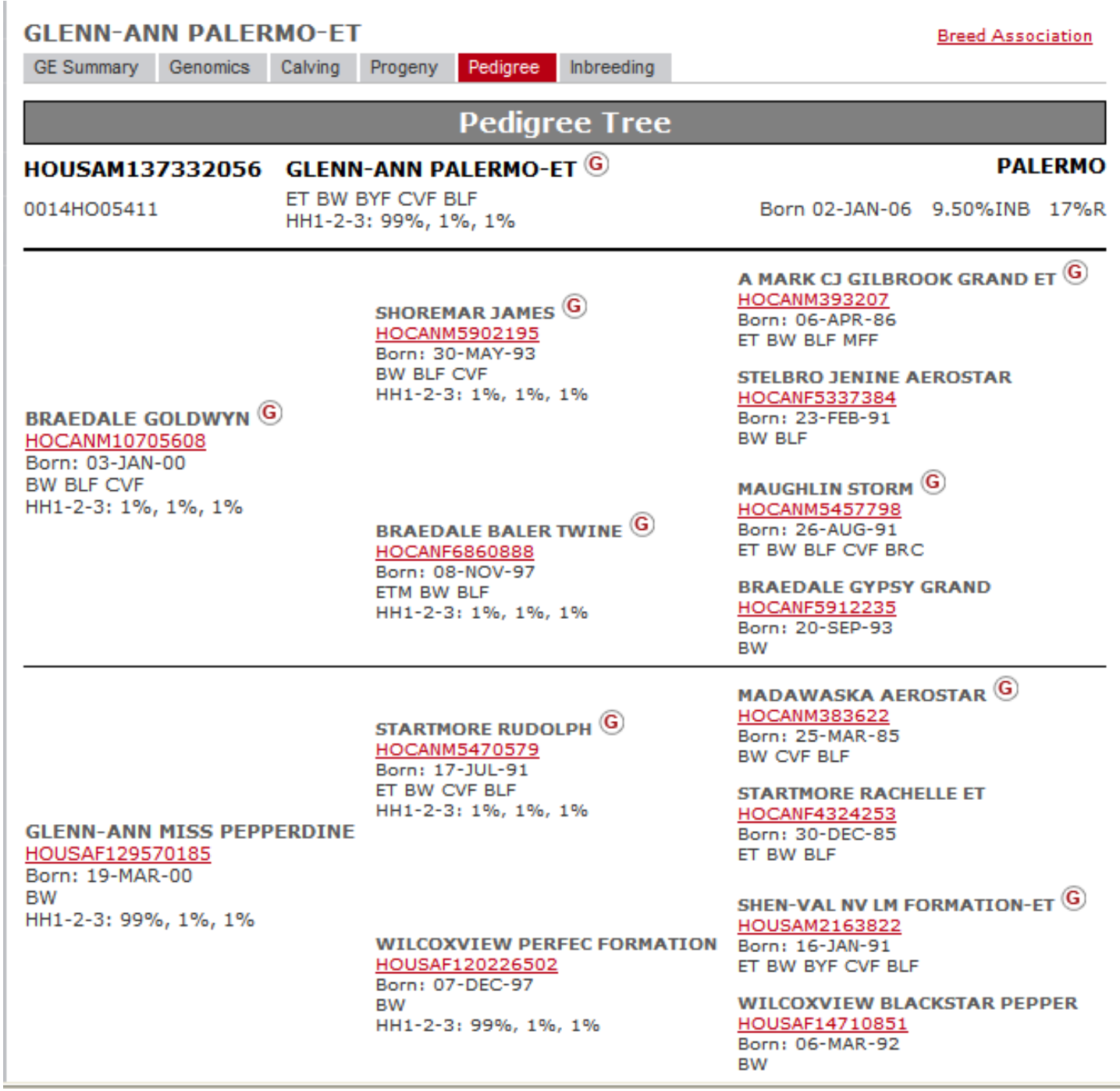
Goldwyn is NOT a carrier

Rudolph is NOT a carrier

Where is HH1 coming from ?

Probability of having a certain haplotype

www.cdn.ca



GLENN-ANN PALERMO-ET

Breed Association

GE Summary | Genomics | Calving | Progeny | Pedigree | Inbreeding

Pedigree Tree

HOUSAM137332056 **GLENN-ANN PALERMO-ET** Ⓖ **PALERMO**

0014HO05411

ET BW BYF CVF BLF
HH1-2-3: 99%, 1%, 1%

Born 02-JAN-06 9.50%INB 17%R

BRAEDALE GOLDWYN Ⓖ
HOCANM10705608
Born: 03-JAN-00
BW BLF CVF
HH1-2-3: 1%, 1%, 1%

SHOREMAR JAMES Ⓖ
HOCANM5902195
Born: 30-MAY-93
BW BLF CVF
HH1-2-3: 1%, 1%, 1%

A MARK CJ GILBROOK GRAND ET Ⓖ
HOCANM393207
Born: 06-APR-86
ET BW BLF MFF

STELBRO JENINE AEROSTAR
HOCANF5337384
Born: 23-FEB-91
BW BLF

BRAEDALE BALER TWINE Ⓖ
HOCANF6860888
Born: 08-NOV-97
ETM BW BLF
HH1-2-3: 1%, 1%, 1%

MAUGHLIN STORM Ⓖ
HOCANM5457798
Born: 26-AUG-91
ET BW BLF CVF BRC

BRAEDALE GYPSY GRAND
HOCANF5912235
Born: 20-SEP-93
BW

GLENN-ANN MISS PEPPERDINE
HOUSAF129570185
Born: 19-MAR-00
BW
HH1-2-3: 99%, 1%, 1%

STARTMORE RUDOLPH Ⓖ
HOCANM5470579
Born: 17-JUL-91
ET BW CVF BLF
HH1-2-3: 1%, 1%, 1%

MADAWASKA AEROSTAR Ⓖ
HOCANM383622
Born: 25-MAR-85
BW CVF BLF

STARTMORE RACHELLE ET
HOCANF4324253
Born: 30-DEC-85
ET BW BLF

WILCOXVIEW PERFEC FORMATION
HOUSAF120226502
Born: 07-DEC-97
BW
HH1-2-3: 99%, 1%, 1%

SHEN-VAL NV LM FORMATION-ET Ⓖ
HOUSAM2163822
Born: 16-JAN-91
ET BW BYF CVF BLF

WILCOXVIEW BLACKSTAR PEPPER
HOUSAF14710851
Born: 06-MAR-92
BW

SF IMPULS 8916

GE Summary | Genomics | Progeny | Pedigree | Inbreeding

Pedigree Tree

JEUSAM114635185 **SF IMPULS 8916** Ⓖ

0001JE00648

JH1: 99%

Born 19-MAY-05

JAS ARTIST Ⓖ
JEDNKM301607
Born: 11-OCT-98

JH1: 1%

SKAE IDE
JEDNKM49522
Born: 20-APR-92

JH1: 1%

MEADOW LAWN J IMPERIAL 50R ET Ⓖ
JECANM137656
Born: 04-JUL-83
ET

DANISH COW00394
JEDNKF4620600394
Born: 28-AUG-87

DANISHCOW00636
JEDNKF4004800636
Born: 21-OCT-95

JH1: 1%

FYN TANIC
JEDNKM47843
Born: 20-OCT-87

DANISHCOW00580
JEDNKF4004800580
Born: 15-DEC-93

SF LEMVIG 6900
JEUSAF111959583
Born: 30-NOV-00

JH1: 99%

ISDK FYN LEMVIG Ⓖ
JEDNKM300003

JH1: 1%

HIGHLAND DUNCAN LESTER Ⓖ
JEUSAM645454
Born: 11-OCT-85

DNK NO. 400650432
JEDNKF6500432
Born: 08-OCT-88

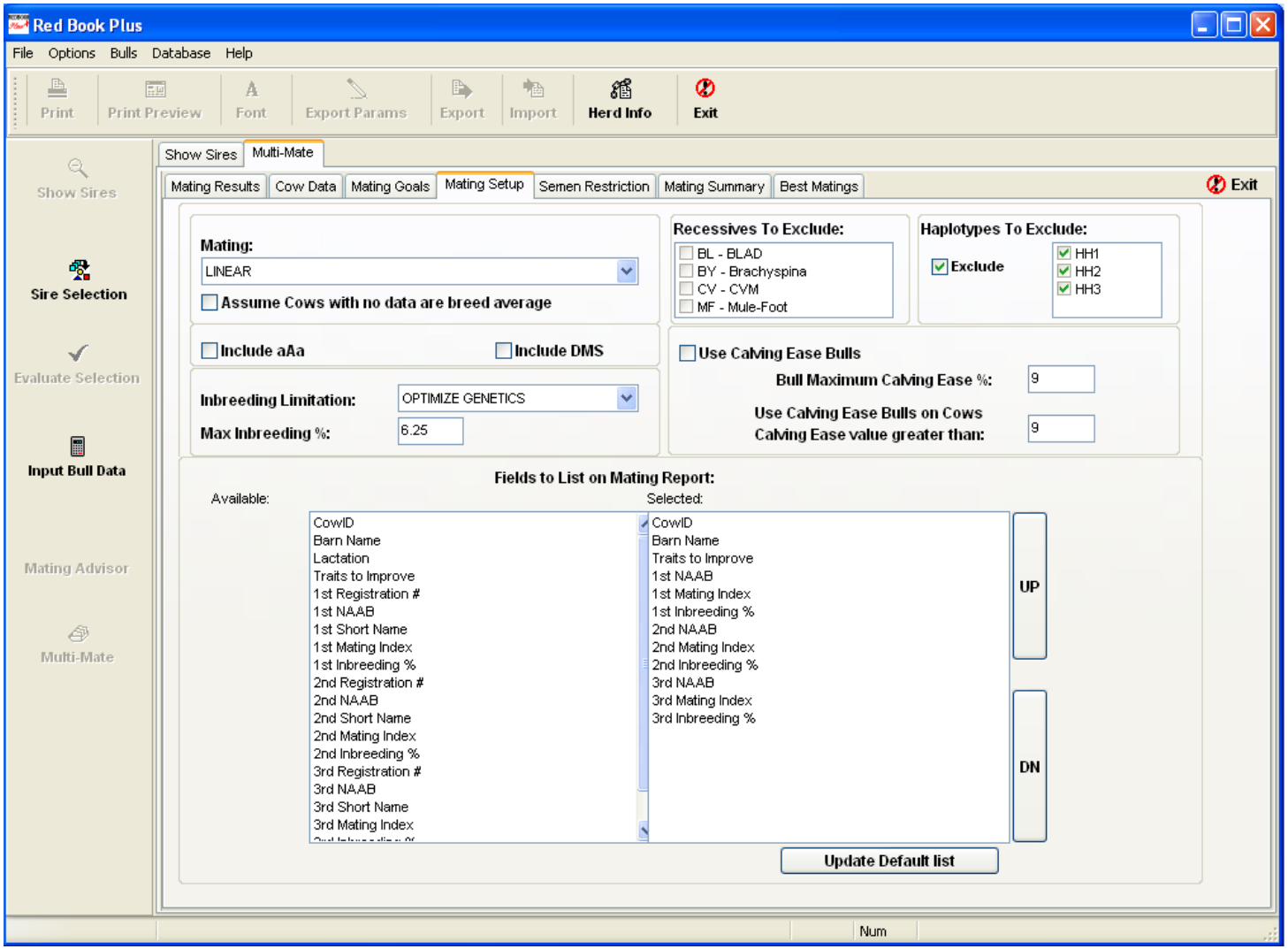
SF BERRETTA C3412
JEUSAF4015906
Born: 09-APR-96

JH1: 99%

MASON BOOMER SOONER BERRETTA Ⓖ
JEUSAM651835
Born: 18-MAR-89

SF SKY LINE B2861
JEUSAF379064943
Born: 23-JUL-93

Matings of HH1, HH2, and HH3 carrier females with carrier bulls can be excluded.



Exclude carrier to carrier matings

Recessives To Exclude:

- [ ] BL - BLAD
- [ ] BY - Brachyspina
- [ ] CV - CVM
- [ ] MF - Mule-Foot

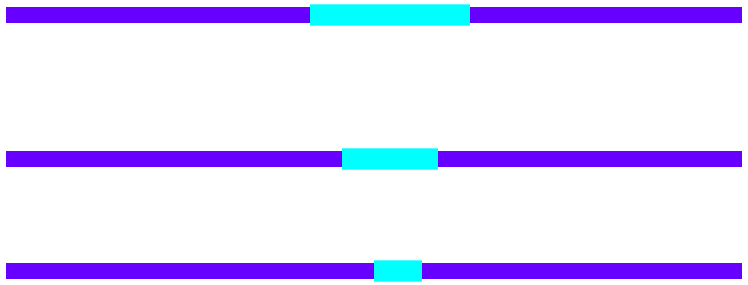
Haplotypes To Exclude:

- [x] **Exclude**

- [x] HH1
- [x] HH2
- [x] HH3

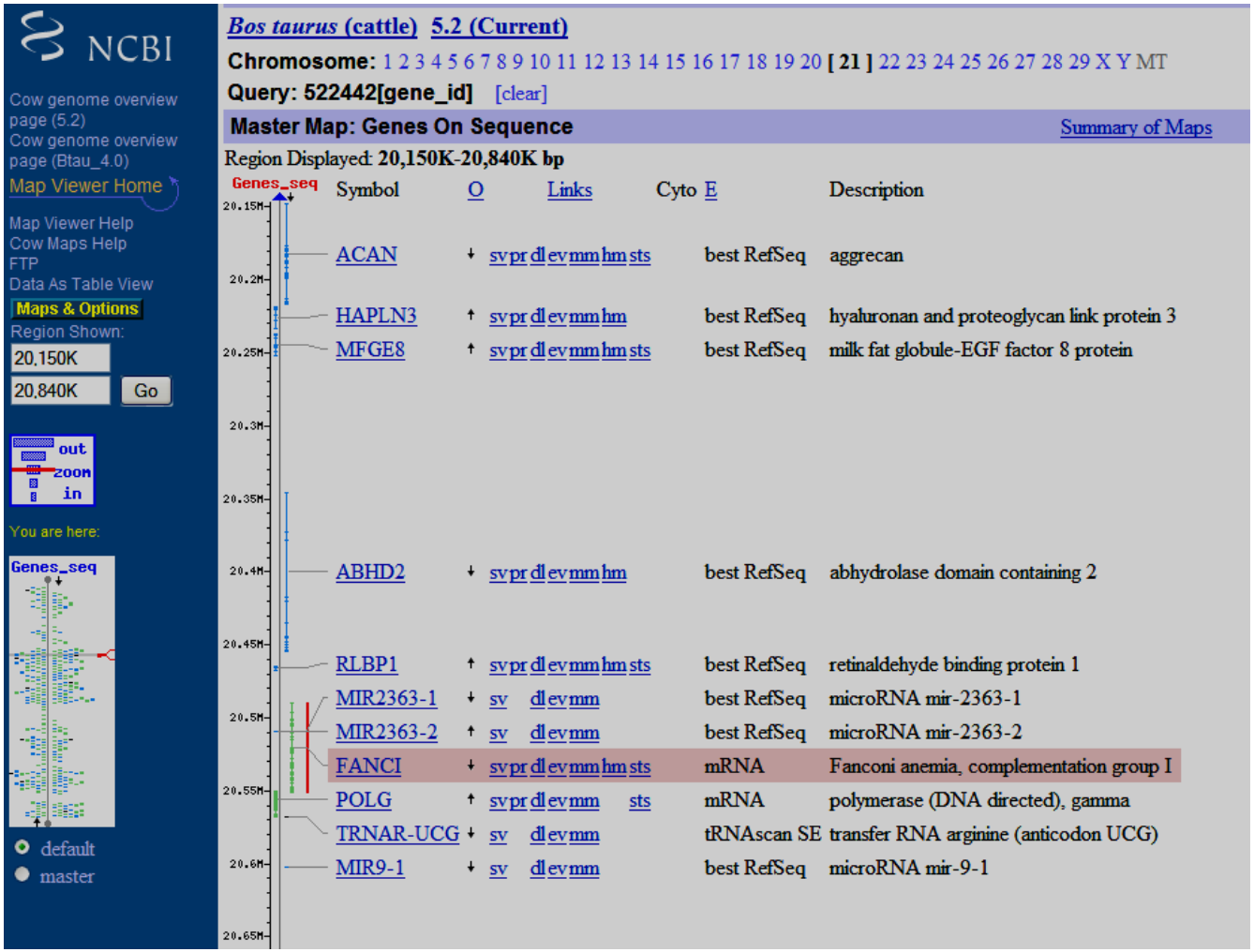
Will we ever find the cause of the genetic condition?

- Yes, as more animals are genotyped, new crossovers occur, which allows us to narrow down the affected DNA area segment.



- Example, we now have an exact gene test for Brachyspina.

Barachyspina is a deletion in a gene responsible for DNA repair.



HH1 -Haplotype

- Exact mutation found.

  CGA → arginine

  TGA → stop making this protein

- APAF1 gene is important for normal embryonic development *(apotosis).*

Will the haplotype status of an animal ever change?

- Home
- Bulls
- Cows & Heifers
- Archive
- Background Info
- Links

you are here:- Home

Official Genetic Evaluations for December, 2011

All reports are now available. See AIPL website for background information on updates in evaluation procedures for this run.

JH1 Status Changes for Bulls

The Animal Improvement Programs Laboratory (AIPL) has refined its procedures for detecting the presence of Jersey Haplotype 1 (JH1) in the DNA sequences of genotyped animals. AIPL research geneticists can now distinguish a smaller segment of the affected DNA that is responsible for the fertility issues. Most of the changes in JH1 status involve the detection of crossovers believed to carry the lethal segment.

This more sensitive analysis resulted in a change in carrier status for 12 Jersey bulls. Eleven (11) bulls are now designated as tested carriers of JH1, with the status code JH1C now recorded in the AJCA database and published on Official Performance Pedigrees and genetic evaluation reports. Listed in order from youngest to oldest, these bulls are:

GR Oomsdale Lou CC Charnesa-ET 7JE1134
BW Contador-ET 505JE116
GR TJF Gannon Robinhood 7JE1066
ISAU Riverside Automatic 200JE8155
Selects Mark of Tenngen-ET 7JE678
Osceola Aces Gypsy Traveler-ET 7JE516
Rock Maple Ace MacKenzie-ET 7JE484
Bridon Journey CAN139331
Sunset Canyon Roman-ET 1JE415
Schultz Duncan Shamrock 14JE185
CDF Top Brass Earl Bloss-ET 7JE189

The test status of one bull initially identified as a carrier of JH1 has been changed to tested free (JH1F):

Sunset Canyon Vegas-ET 29JE3558

The new normal.

- Due to modern genomic technology, undesirable genetic conditions are no longer considered rare.

- We expect to find them in some of our best genetic families.

- We should use the haplotype information to improve our breeds without causing undue economic hardship to the breeders of these animals.

Thank you – Any questions?