

Recent Advances in Sheep Genomics

Noelle E. Cockett
Utah State University

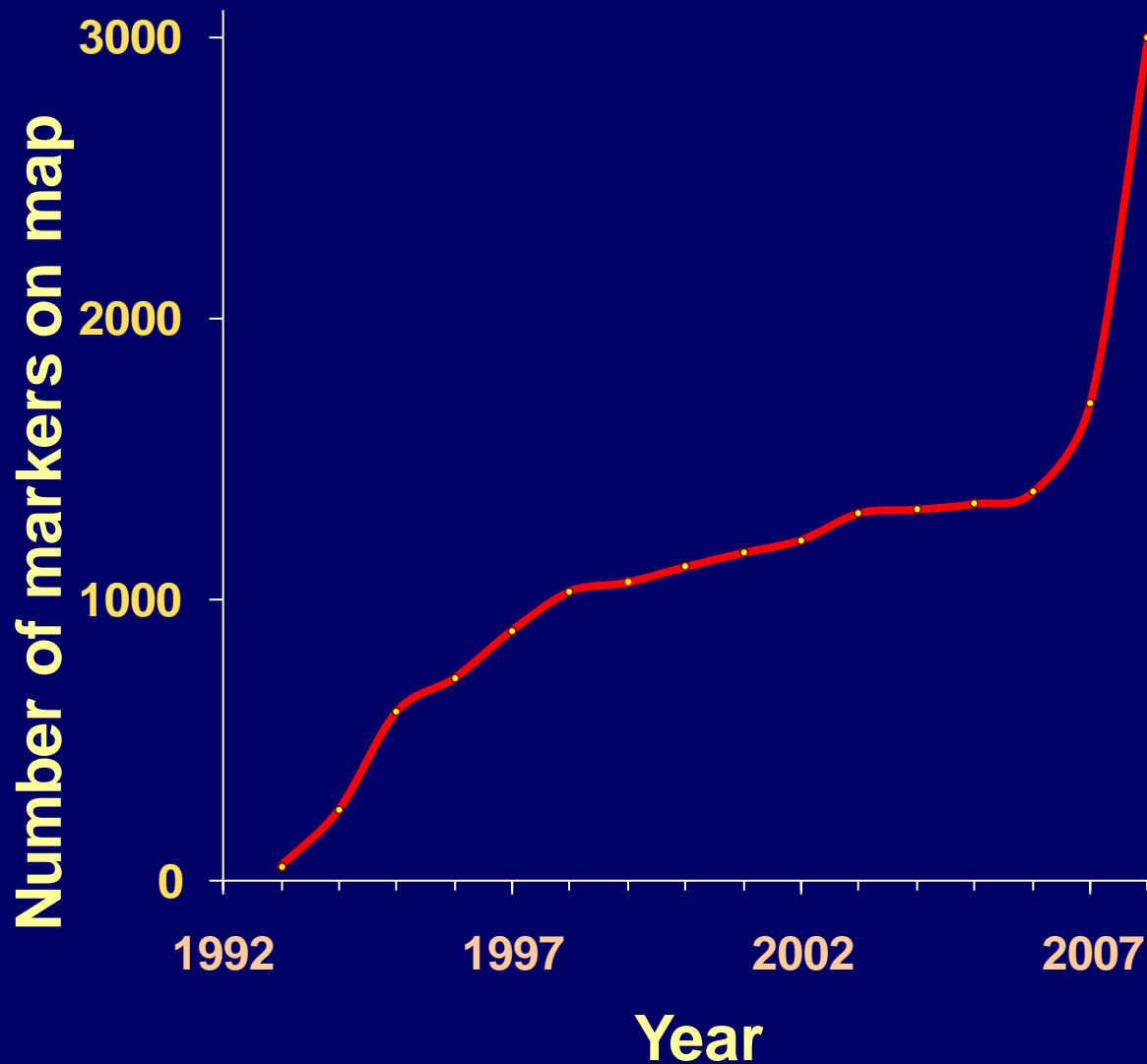


International Sheep Genome Consortium

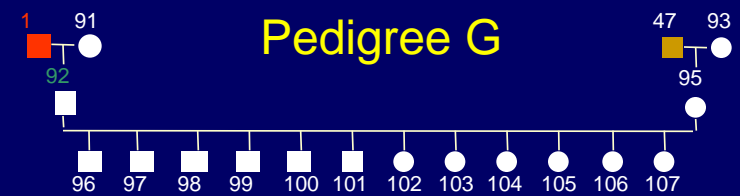
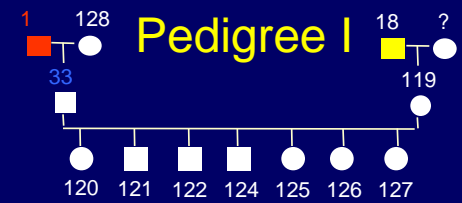
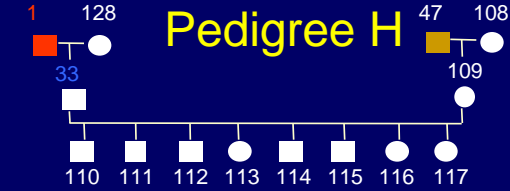
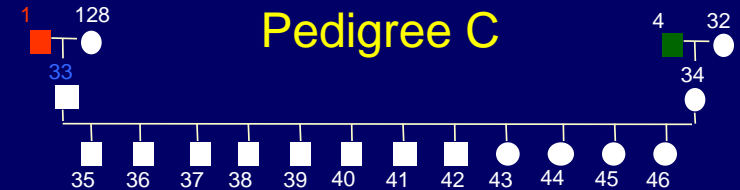
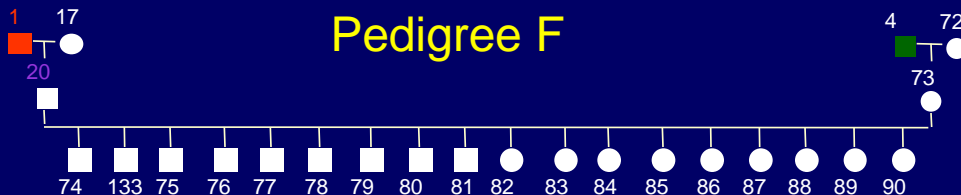
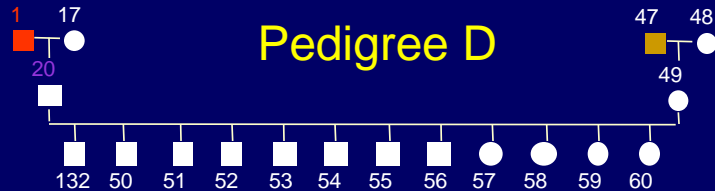
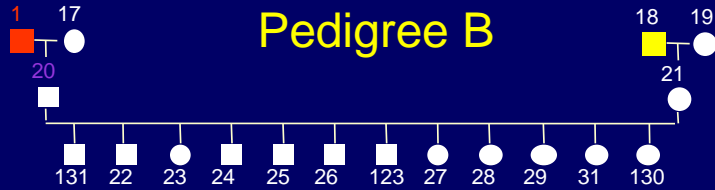
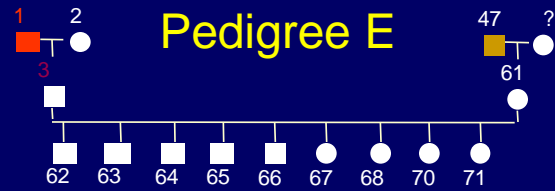
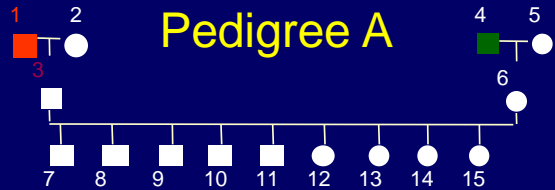


- Alan Archibald, Roslin Institute
- Steve Bishop, Roslin Institute
- Noelle Cockett, Utah State University
- Brian Dalrymple, CSIRO
- Clare Gill, Texas A&M University
- Olivier Hanotte, ILRI
- Ben Hayes, Vic DPI
- James Kijas, CSIRO
- Terry Longhurst, Meat and Livestock Australia
- Jill Maddox, University of Melbourne
- John McEwan, AgResearch
- Sean McWilliam, CSIRO
- Frank Nicholas, University of Sydney
- Hutton Oddy, University of New England
- Herman Raadsma, University of Sydney
- Laurant Schibler, INRA
- Ross Tellam, CSIRO
- Chris Warkup, Genesis Faraday Partnership

Growth of the Sheep Linkage Map



International Mapping Flock



Produced by AgResearch
(New Zealand)

Sheep Linkage Map Version 5 (SM5)

2,528 markers, ~3,800 cM

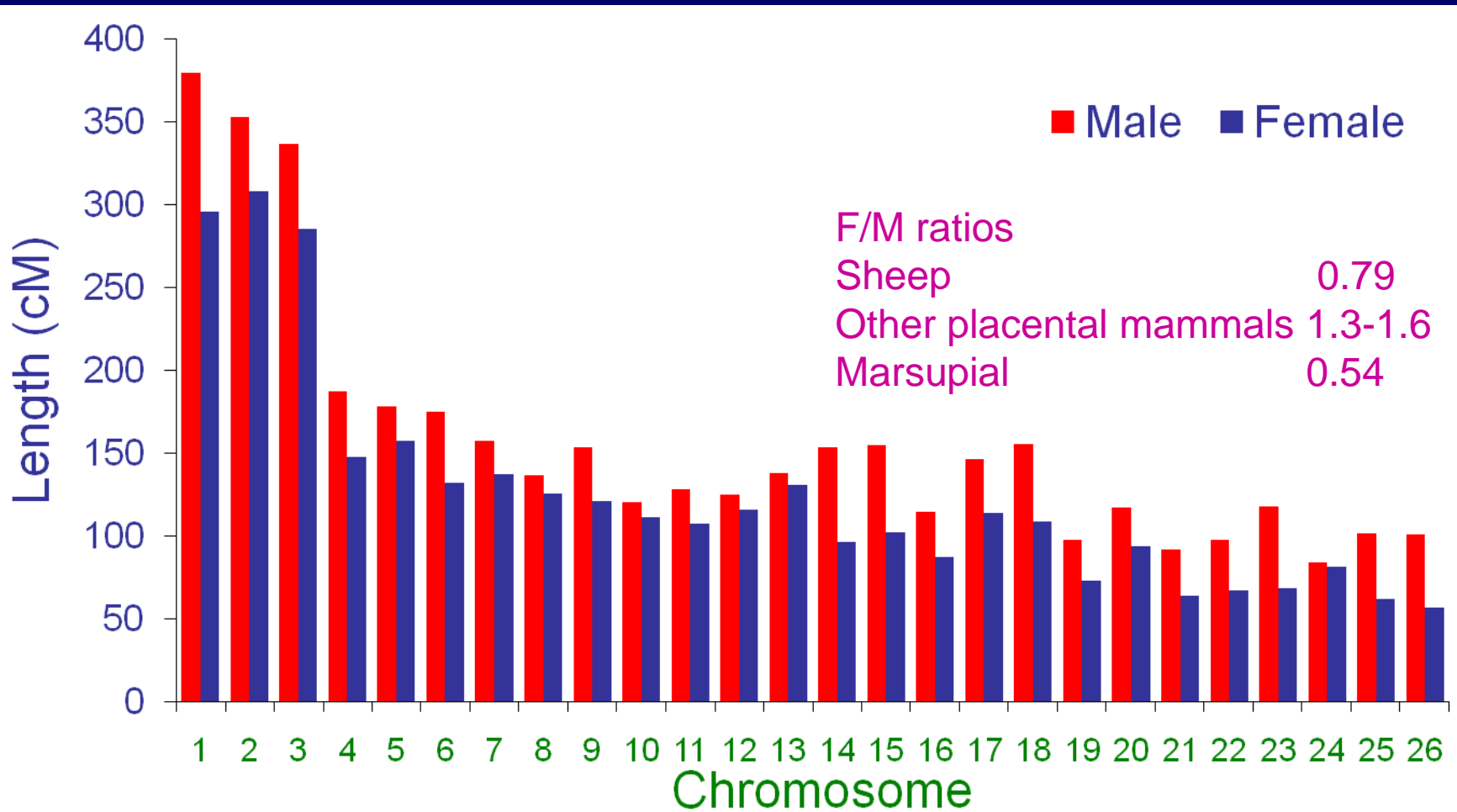
- 2,383 on autosomals, 145 on X chromosome
- 1,111 SNPs from 1.5K array, rest mainly microsatellites
- 1,420 unique positions, 2.5 cM average spacing between positions

Autosomal map expanded by 220 cM (6%)

- 168 cM (4.8%) at ends of chromosomes and 54 cM (1.2%) map inflation
- Some previously identified double recombinants disappeared with extra markers

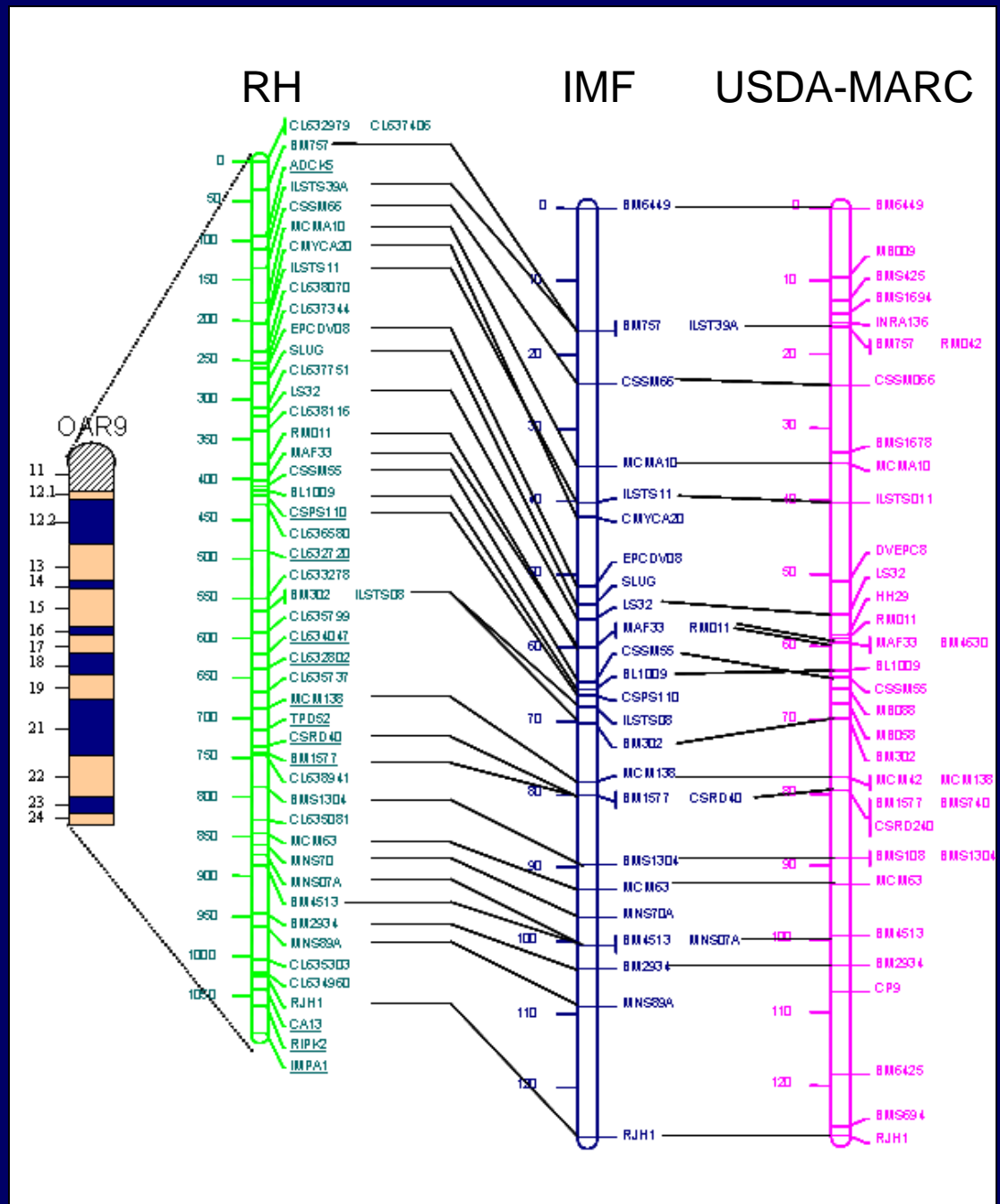
<http://rubens.its.unimelb.edu.au/~jillm/jill.htm>

Comparison of Male and Female Chromosome Lengths (SM5)



Ovine Radiation Hybrid Map

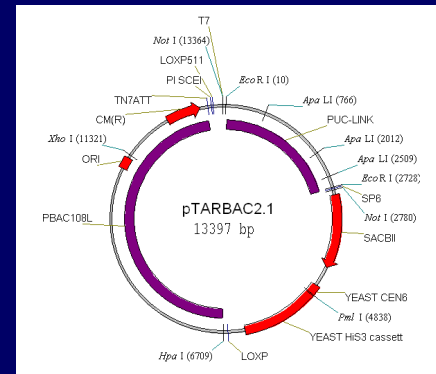
- 5,000 rad panel (USUoRH5000)
- Distributed to five international labs
- 3567 loci typed on panel
- High density maps for all but OARY
- 2754 loci on maps



CHORI-243

Ovine BAC Library

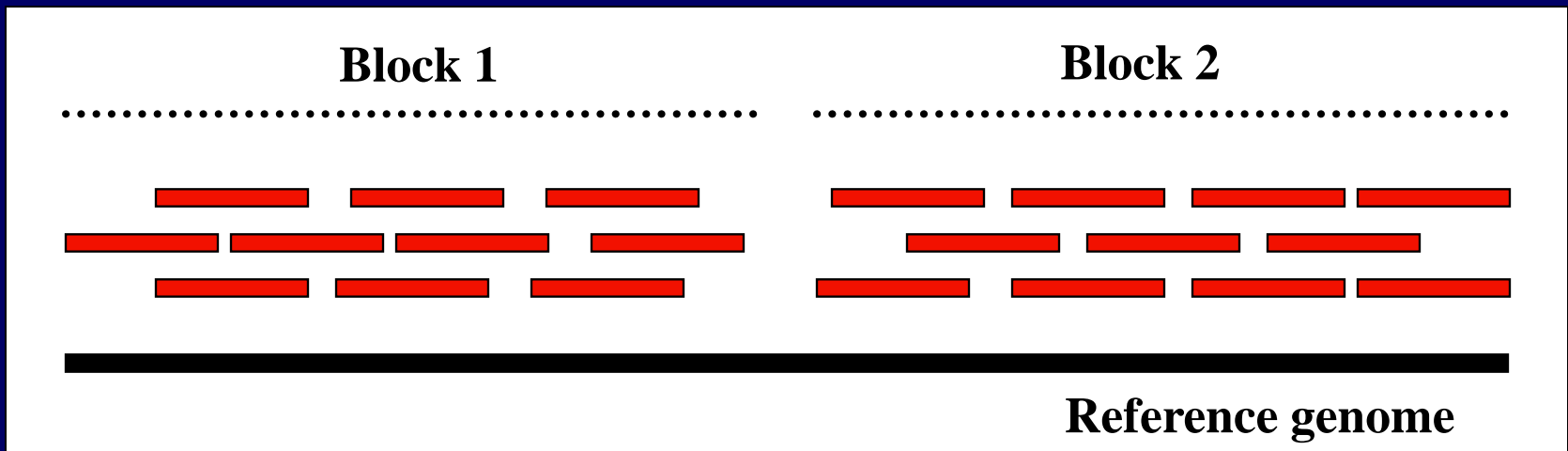
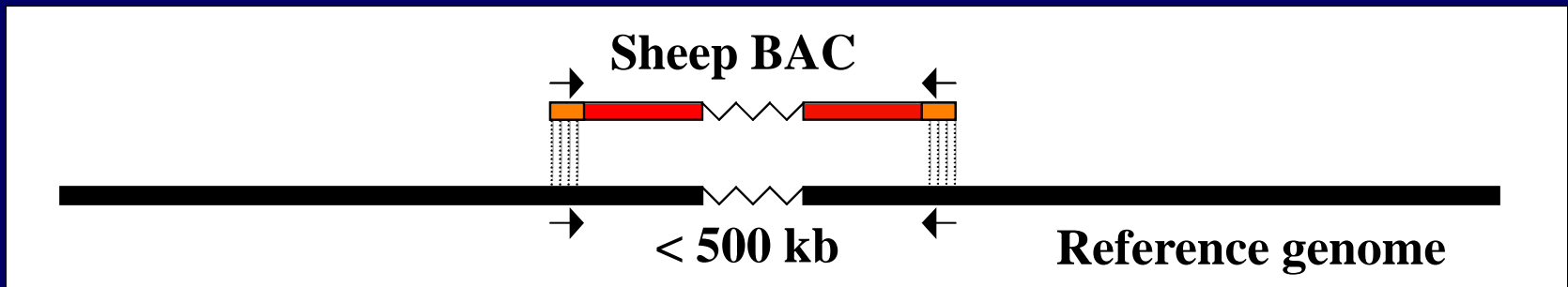
- 202,752 clones with 184 Kb average insert
- 376,493 sequences from 193,073 clones
- 258,650,691 bp of sequence (6% of the genome)



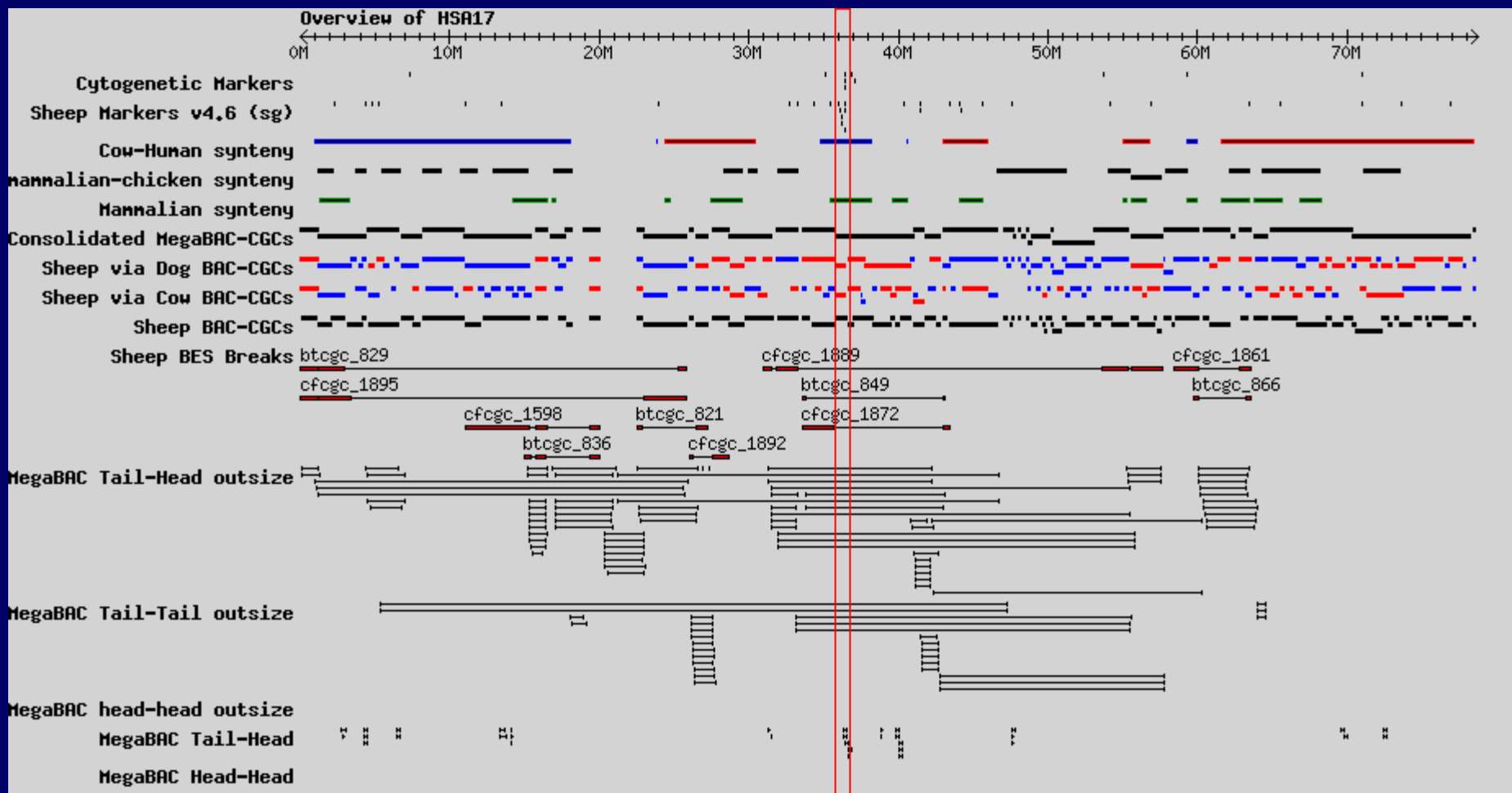
<http://www.ncbi.nlm.nih.gov/genome/guide/sheep>

Ovine Whole Genome Physical Map

Arrange ovine BACs into overlapping contigs using reference genome

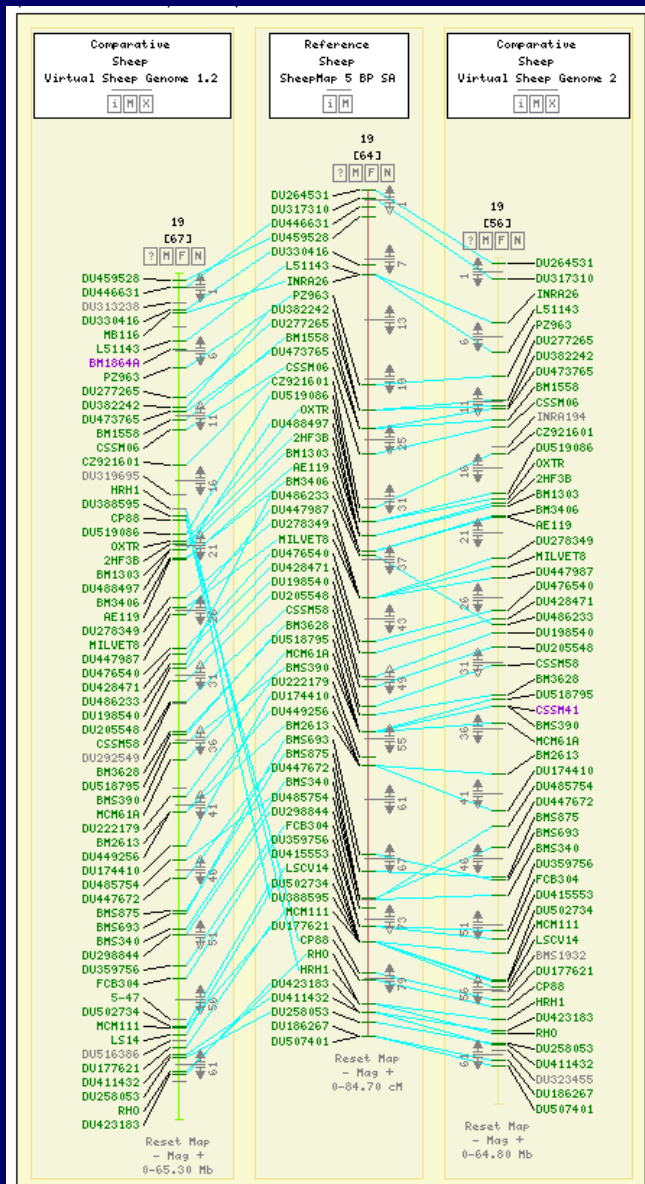


Virtual Sheep Genome

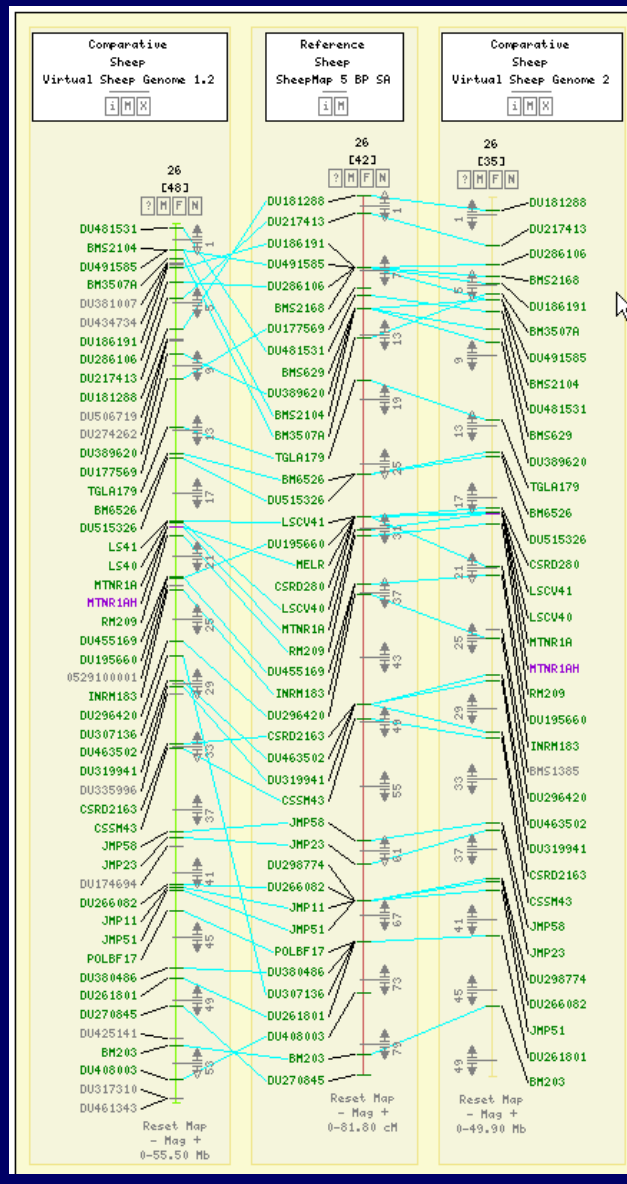


www.livestock.genomics.csiro.au/SheepGenomics/

VSG1.2 vs Linkage Map (SM5) vs VSG2

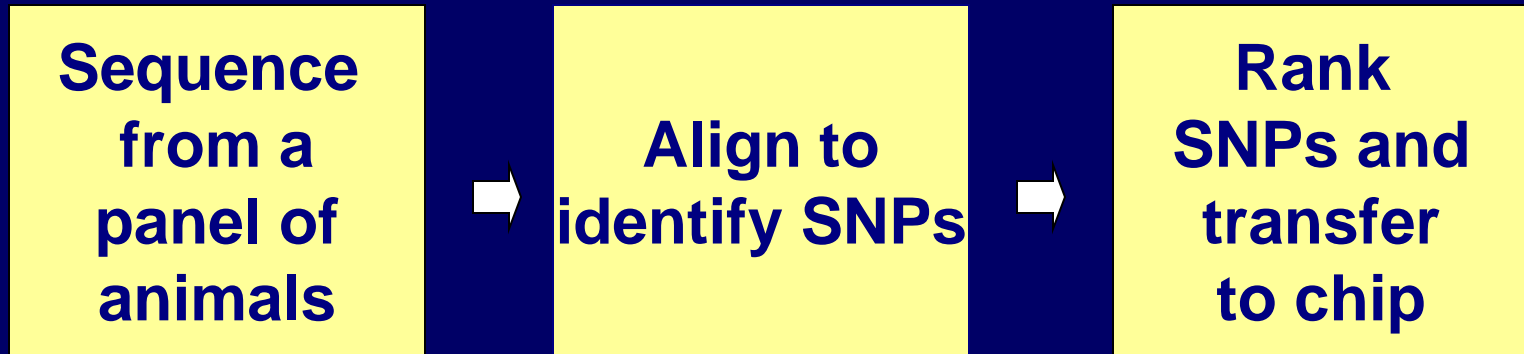


OAR19



OAR26

Ovine SNP Markers



Diversity panel:



Texel
AgResearch



Red Masai
ILRI



Romney
AgResearch



Poll Dorset
SheepGenomics



Awassi
Uni. Sydney



Merino
SheepGenomics



Lacaune
INRA



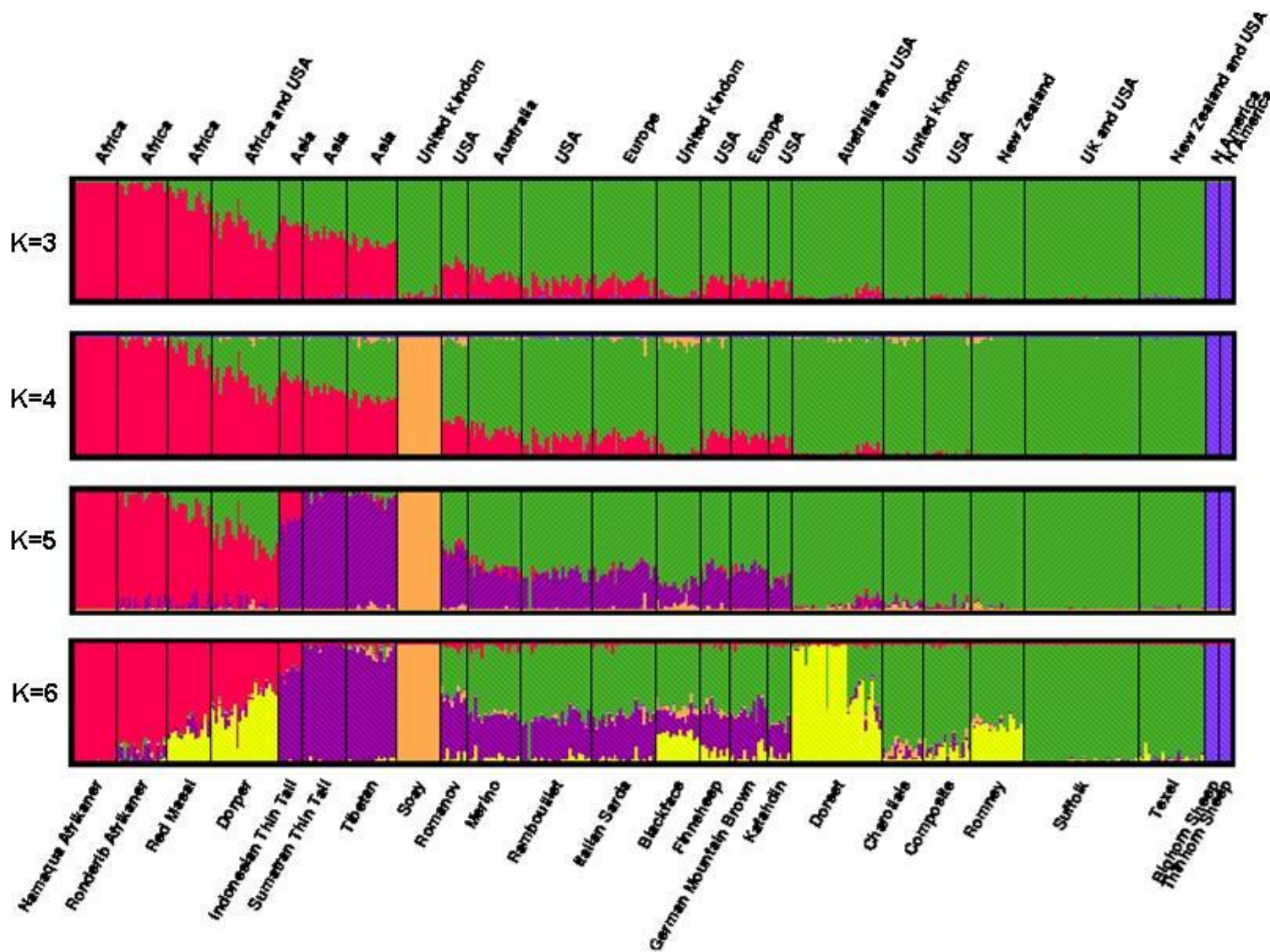
Katahdin
USU



Gulf Coast Native
USU

Illumina Ovine 1536 SNP Array

- **Integration of SNPs into linkage map**
(Jill Maddox, University of Melbourne)
- **Integration of SNPs into RH map**
(Noelle Cockett and Chunhua Wu, Utah State University; Brian Dalrymple, CSIRO)
- **Genetic diversity, variation and phylogenetics**
(James Kijas, CSIRO, Australia)
- **SNP panels for parentage assignment**
(Mike Heaton, USDA/ARS MARC)



Illumina Ovine SNP50 BeadChip

Source 1: 6 sheep (Romney, Texel, Merino, Dorset, Rambouillet and Suffolk) using Roche 454 FLX at BCM-HGSC to 0.5X coverage each (3X coverage total)

9.7 Gbp of sequence generated

Source 2: Pool of 60 sheep using reduced representation and Solexa GA at Illumina

3 Gbp of sequence generated

llumina Ovine SNP50 BeadChip

A subset of 59,454 SNPs selected from 354,448 total SNPs

BeadChip commercially released January, 2009

Using a test panel of 92 animals from 10 breeds:

- 54,200 loci displayed assay signal
- 49,000 SNP passing QC
- 99% displayed polymorphism
- Average MAF = .25

Sheep Linkage Map (SM6) Ovine SNP50 Chip

Total number of SNPs on chip	59,454
Number of SNPs reported on	54,241 [#]
Number of SNPs passing QC	~49,000
Number of SNPs localized to a chromosome using IMF	44,146
Number of SNPs localized to a chromosome using Falkiner*	49,220
Number of ChrUn SNPs localized to a chromosome	312
Number of chromosome discrepancies between SM6 linkage map and VSG/Btau4	137

Illumina, GeneSeek reported 54,977 loci but 650 dropped

* 2,325 Falkinder male progeny only, still need to add in 1,733 female progeny

More families wanted for 50K SNP linkage map!

- Half-sibling families with at least 20 offspring per sire
 - Can establish phase by genotyping sire's parents
- Full-sibling families with both parents and grandparents available

Contact Jill Maddox:

(jillian.maddox@alumni.unimelb.edu.au)

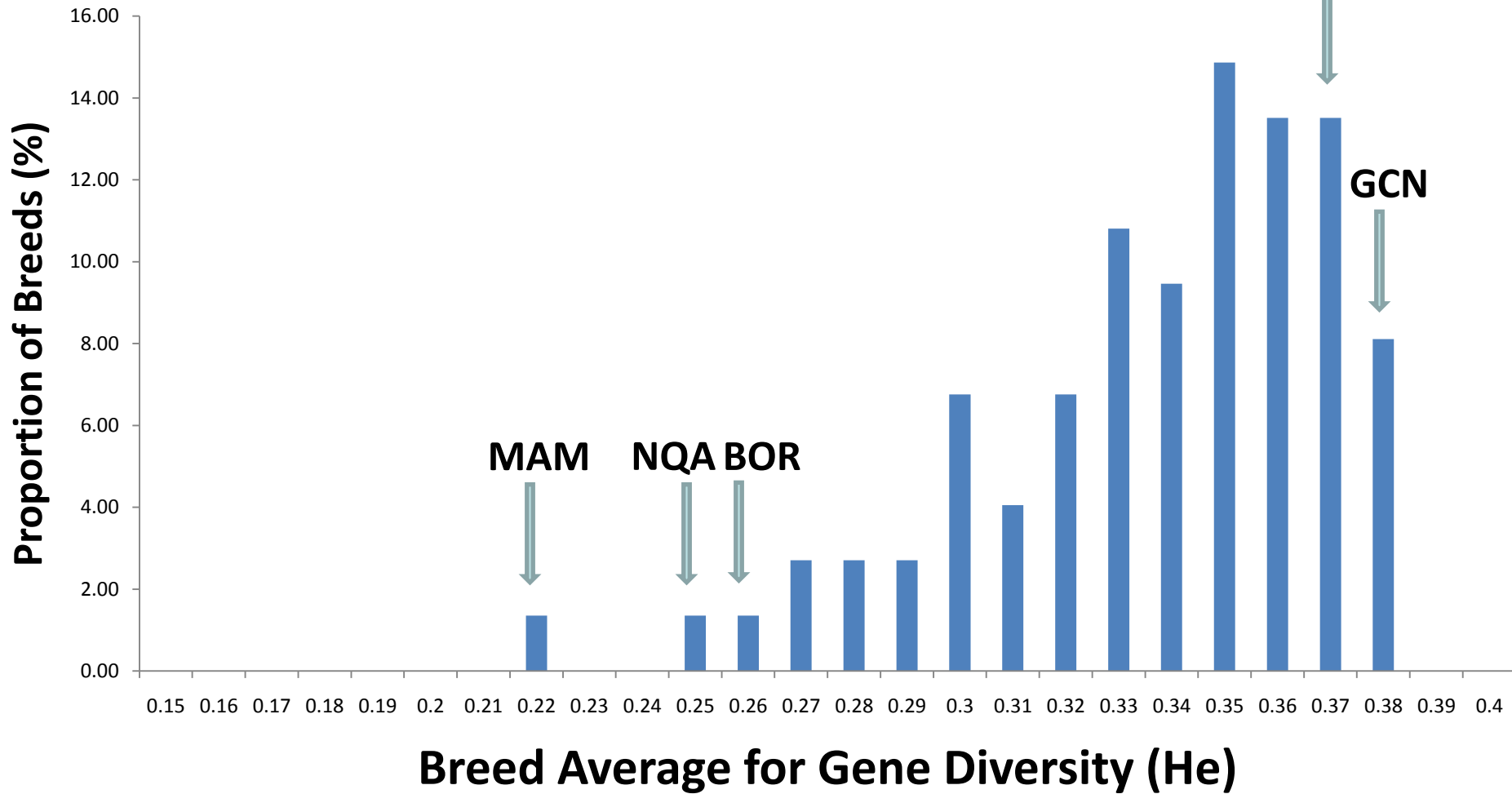
The Sheep HapMap and Breed Diversity Experiment

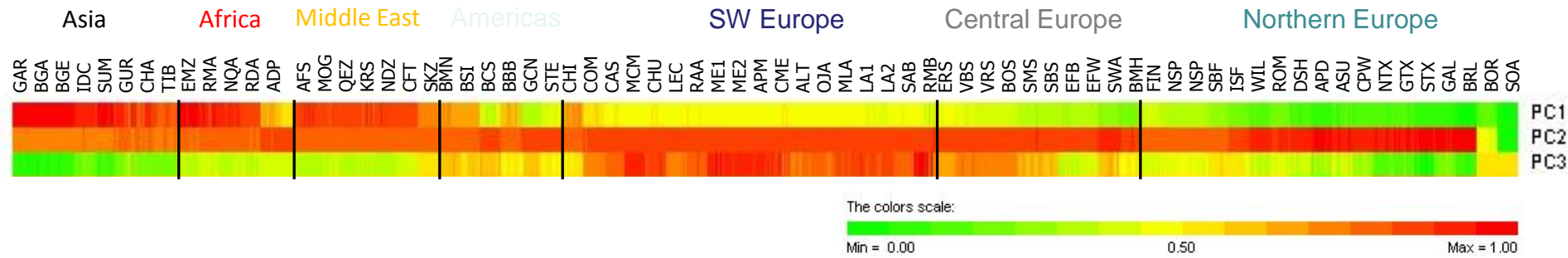


Total of 3400 animals from 74 breeds genotyped using the SNP50 BeadChip

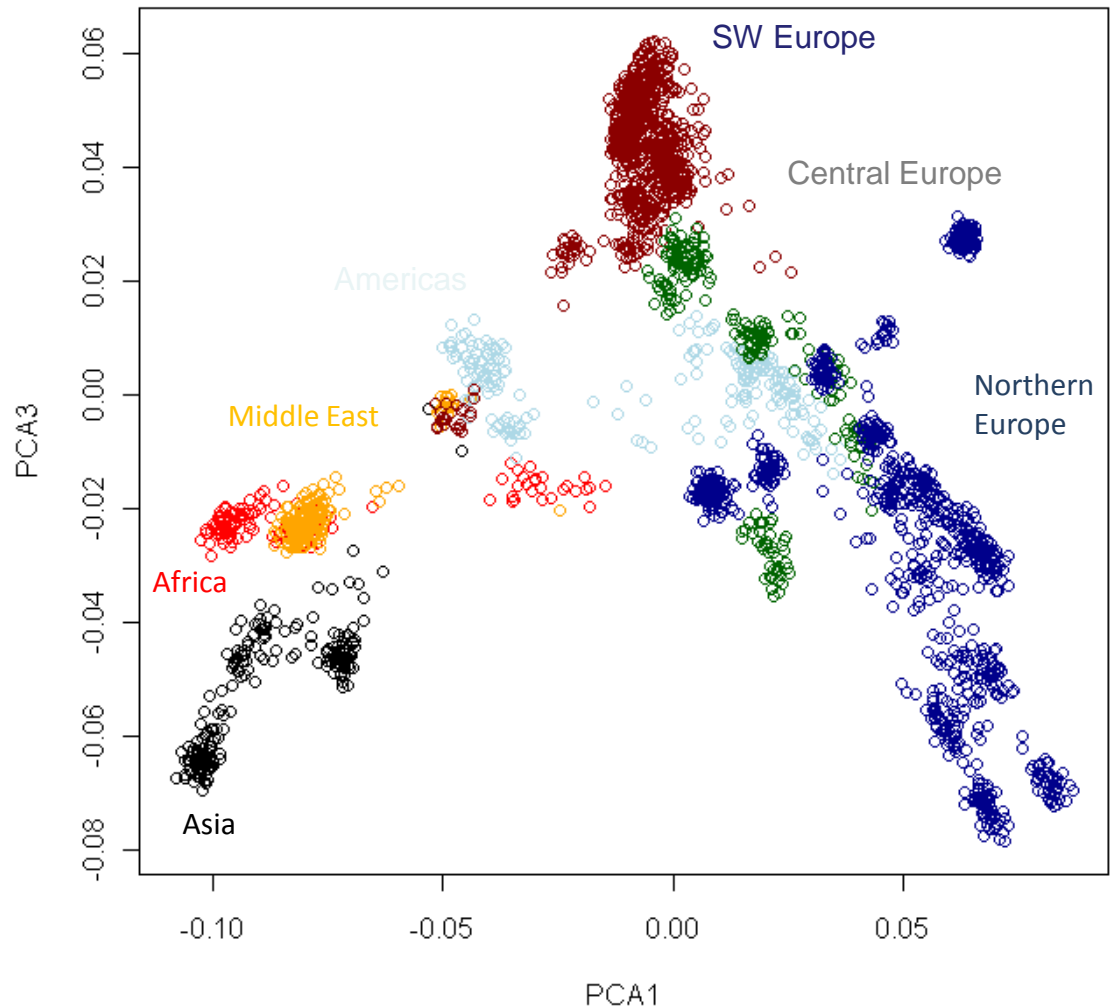
Wild sheep (argali, urial, mouflon, bighorn, thinhorn)
Out-group species (barbary, goat, thar, cattle..)

Distribution of Gene Diversity within 74 Breeds

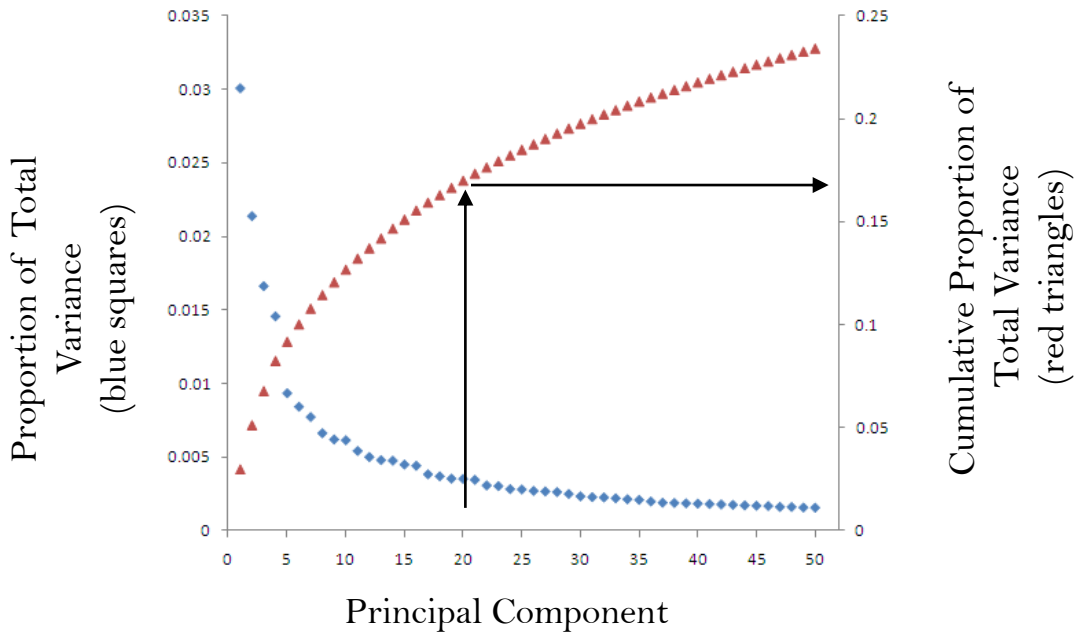
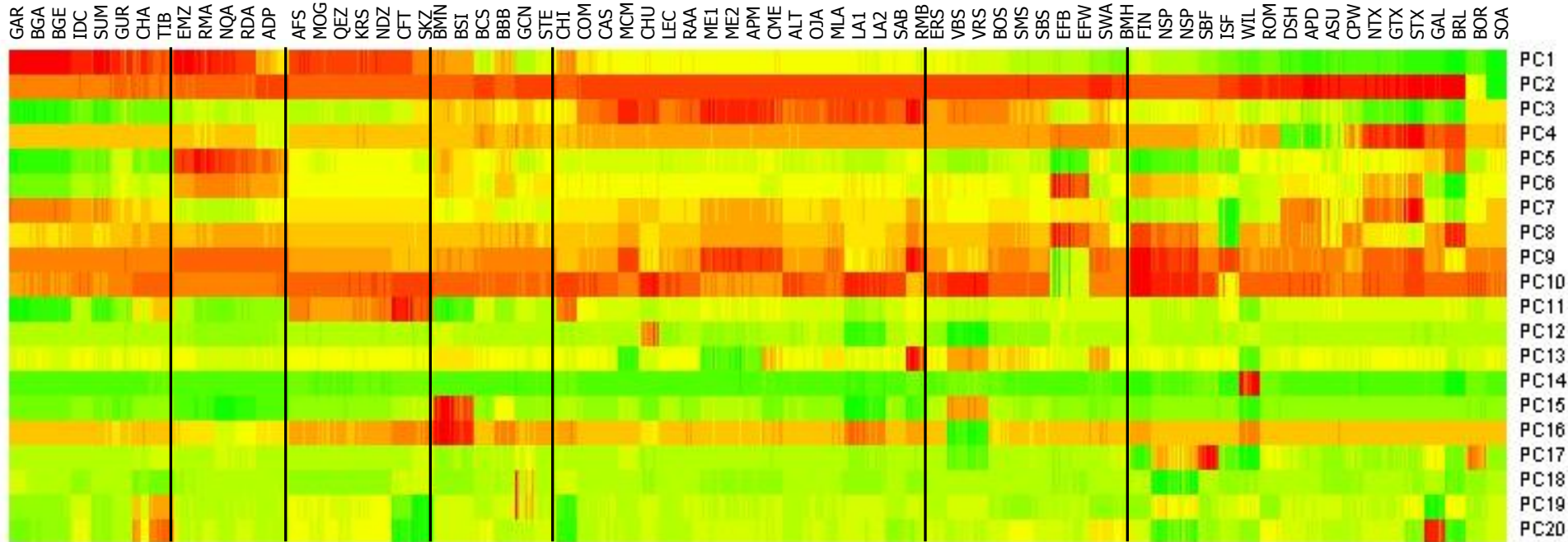




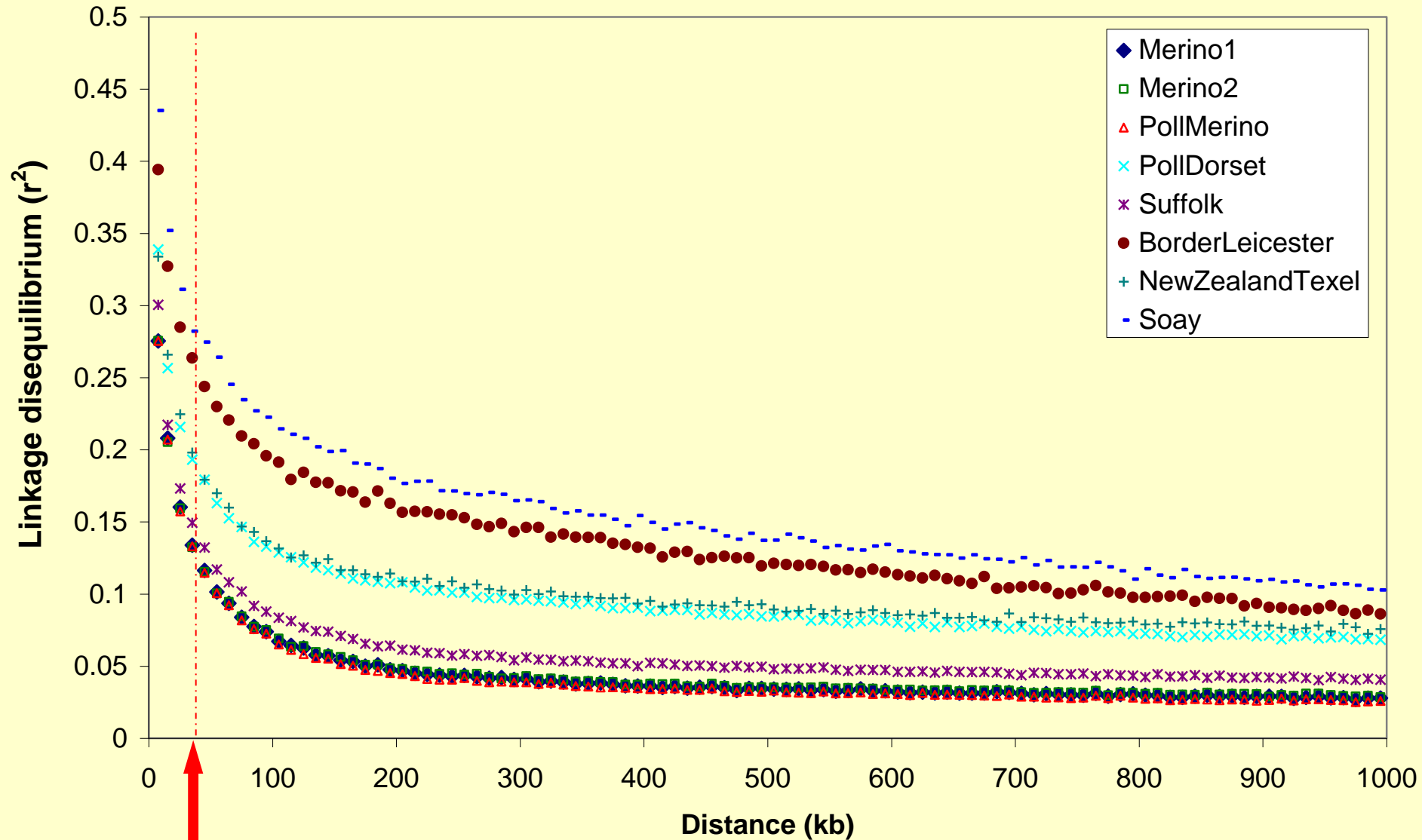
- Asian, African, Middle Eastern, European breeds can be differentiated
- European breeds cluster according to geographical location



Asia Africa Middle East Americas SW Europe Central Europe Northern Europe



Range of LD profiles among 73 breeds- selected sample representing extremes



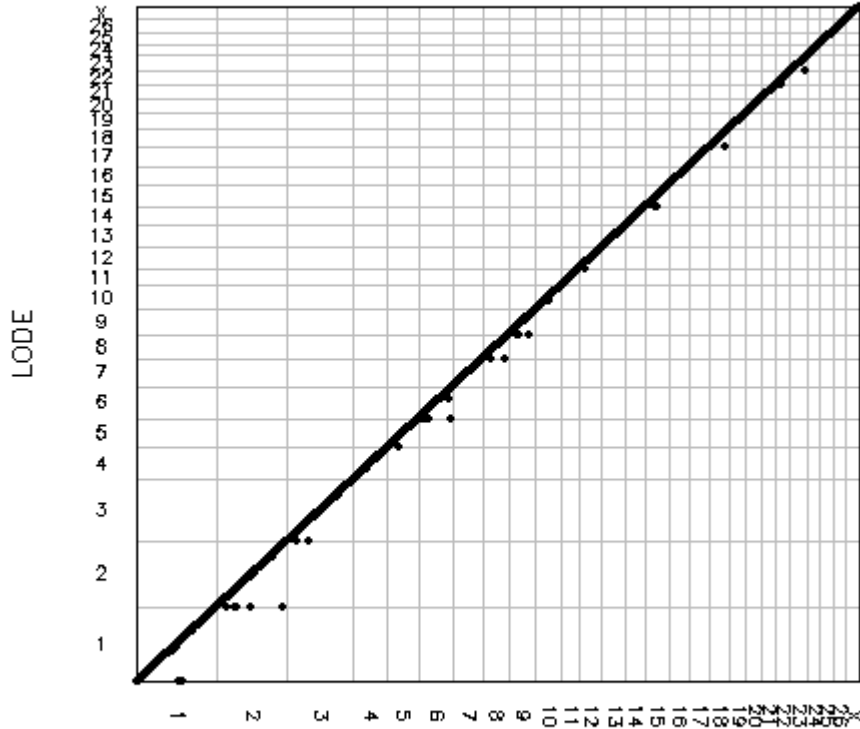
Average SNP spacing of 50K

Effective population size ~ 50 generations ago

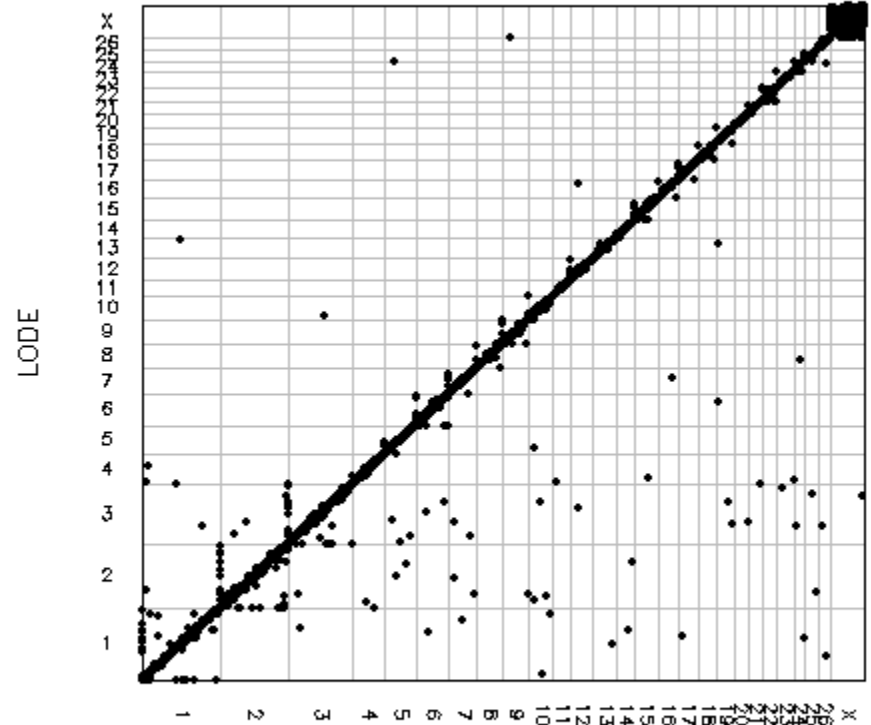
AfricanDorper	264	Comisana	589	NewZealandRomney	405
Afshari	465	CyprusFatTail	203	NewZealandTexel	282
Altamura	469	Deccari	837	Norduz	285
AustralianIndustryMe	853	DorsetHorn	134	Ojalada	588
AustralianMerino	833	EastFriesianBrown	186	Qezel	1317
AustralianPollDorset	318	EngadineRedSheep	482	Rambouillet	709
AustralianPollMerino	918	EthiopianMenz	1260	Rasaaragonesa	780
AustralianSuffolk	569	Finnsheep	795	RedMaasai	1070
BangladeshiBGE	582	Galway	322	Sakiz	165
BangladeshiGarole	437	Garut	337	Santalnes	520
BarbadosBlackBelly	374	GermanTexel	448	SardinianAncestralBI	306
BlackHeadedMountain	247	GulfCoastNative	611	ScottishBlackface	528
BorderLeicester	242	IndianGarole	364	ScottishTexel	305
BrazilianCreole	371	IrishSuffolk	300	Soay	194
BundnerOberlanderShe	253	Leccese	556	Spael-white	339
Castellana	546	MeatLacaune	835	Sumatra	336
Changthangi	684	Merinolandschaf	407	SwissBlack-BrownMoun	333
ChineseMerino	397	MilkLacaune	714	SwissMirrorSheep	262
Chios	334	Moghani	825	SwissWhiteAlpineShee	374
Churra	600	MoradaNova	327	Tibetan	903
				ValaisBlacknoseSheep	288
				ValaisRedSheep	173
				Wiltshire	100

Agreement marker positioning LOD vs VSG

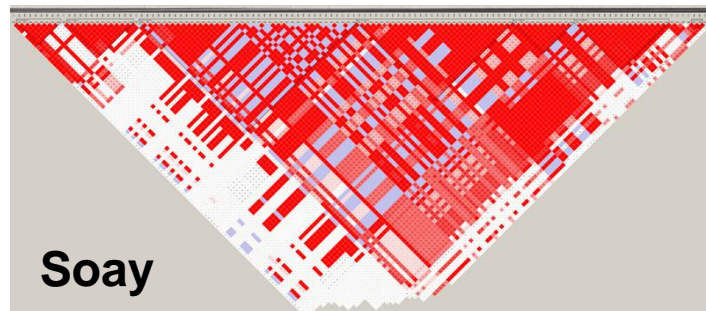
O. aries genome (Soay)



O. aries genome (Churra)



ISGC



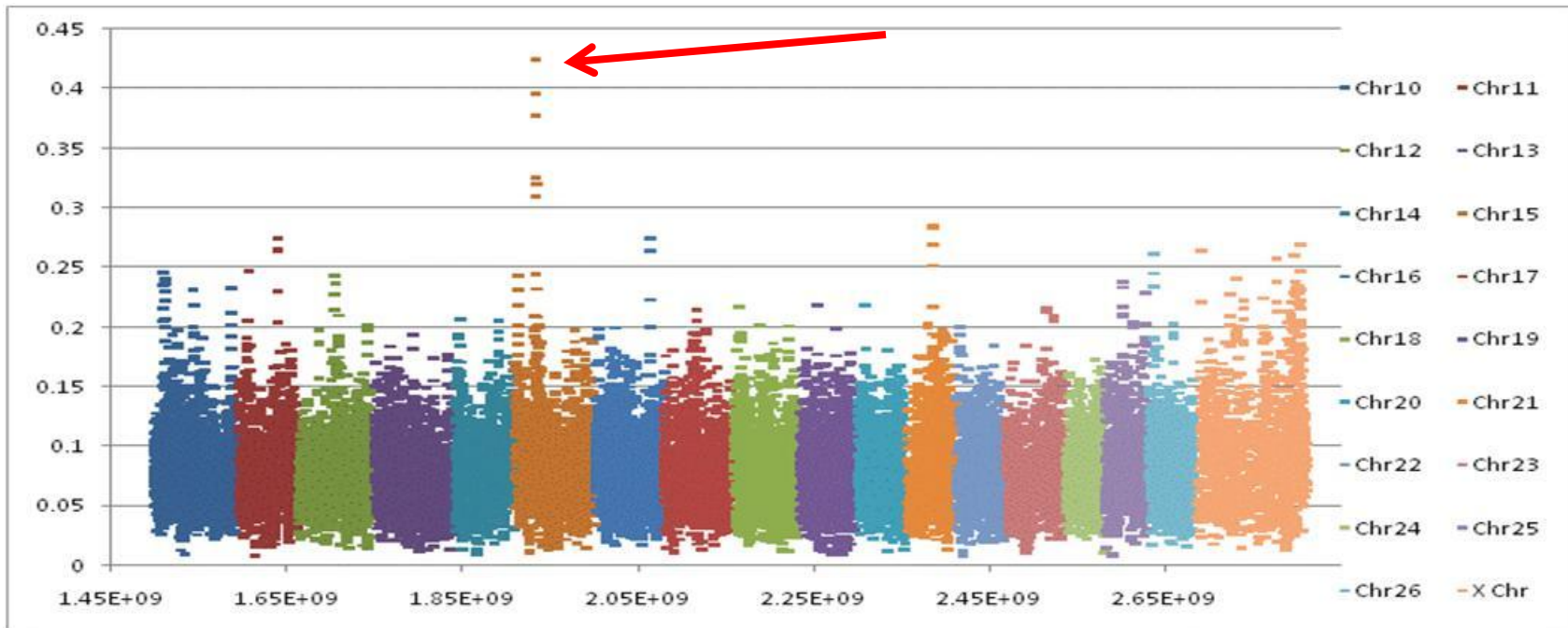
Soay

ISGC



Churra

Yellow fat in Perendales
Single mutation
Partially recessive
30 affected, 30 controls
Gene on OAR21





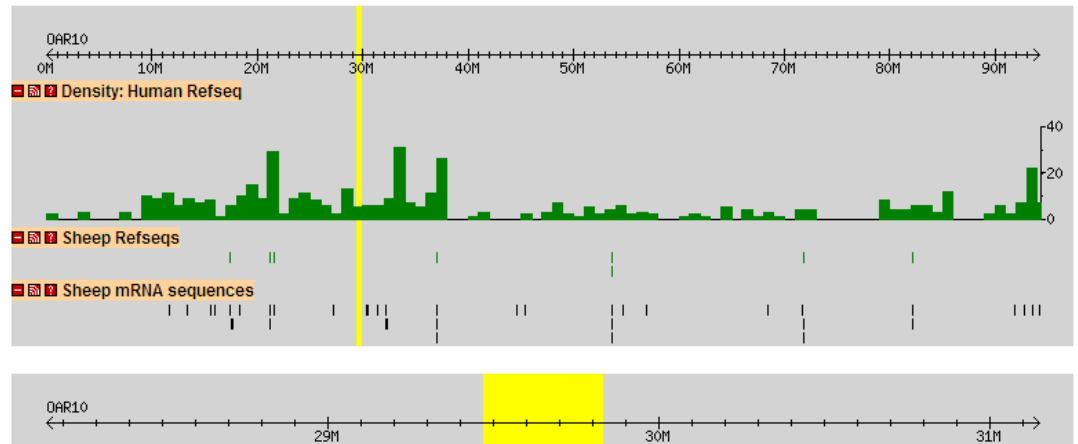
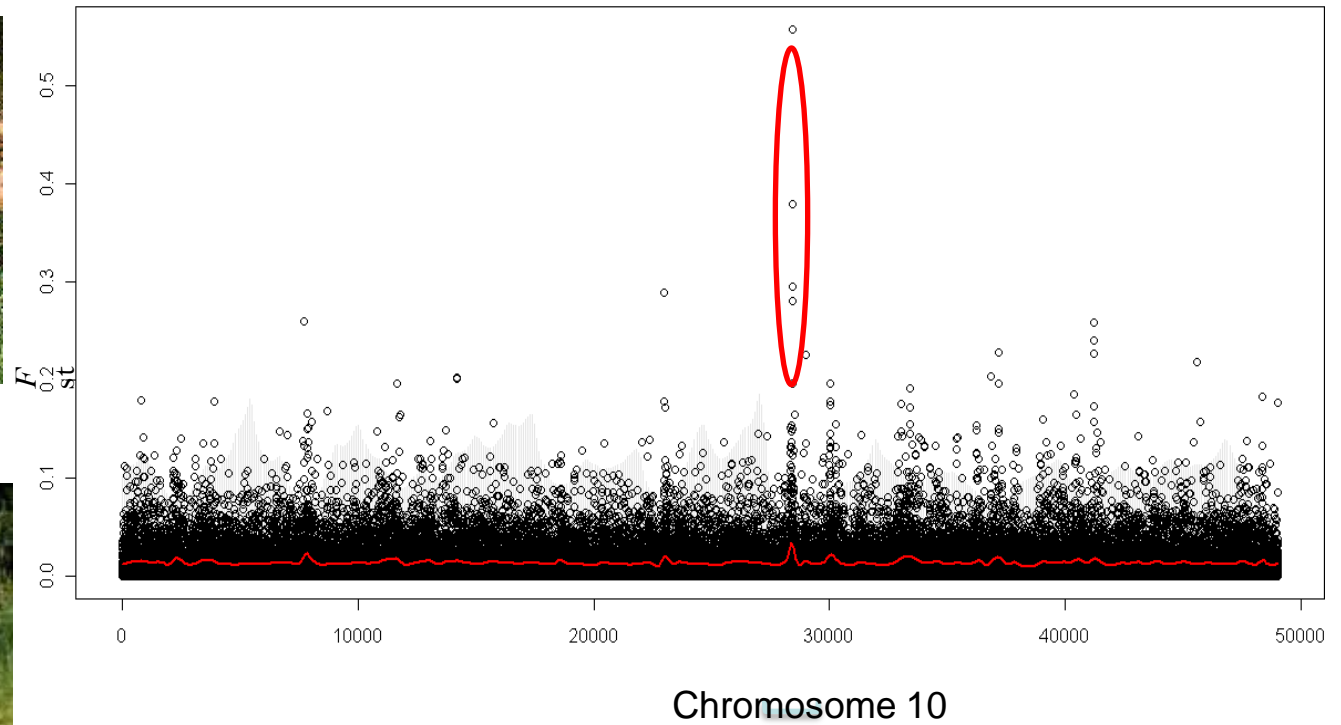
Australian Merino



Polled Merino

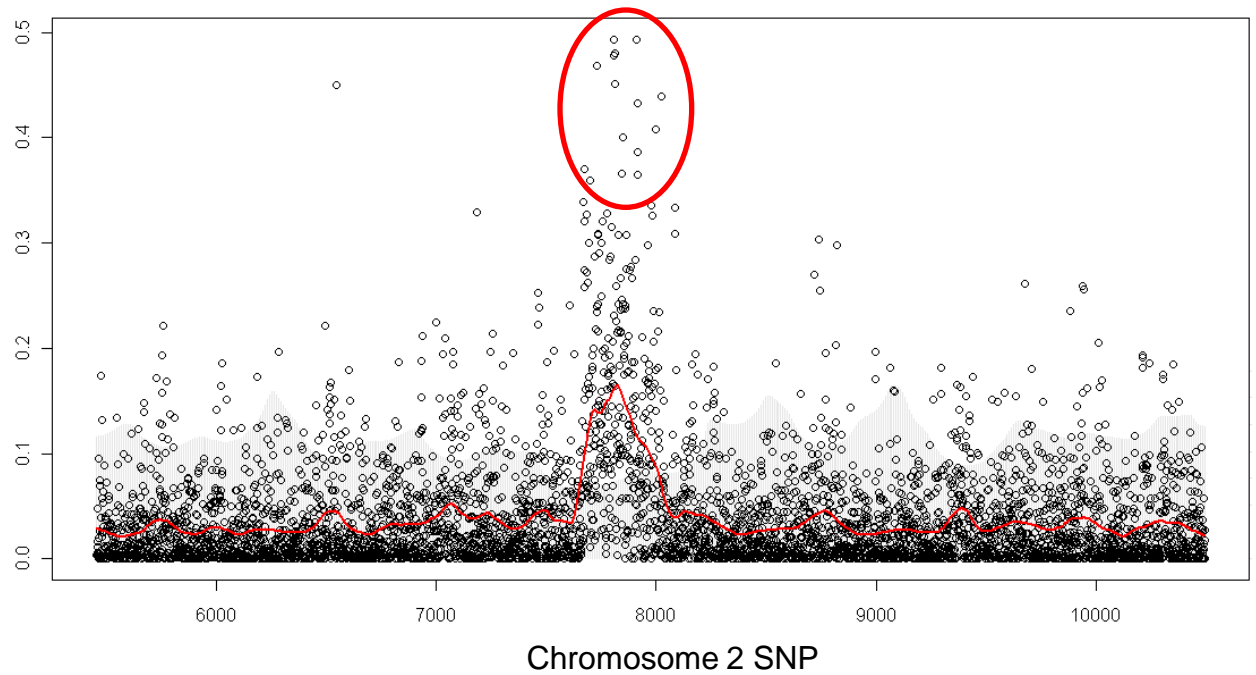
350 kB region
on OAR10

1 gene within the
interval



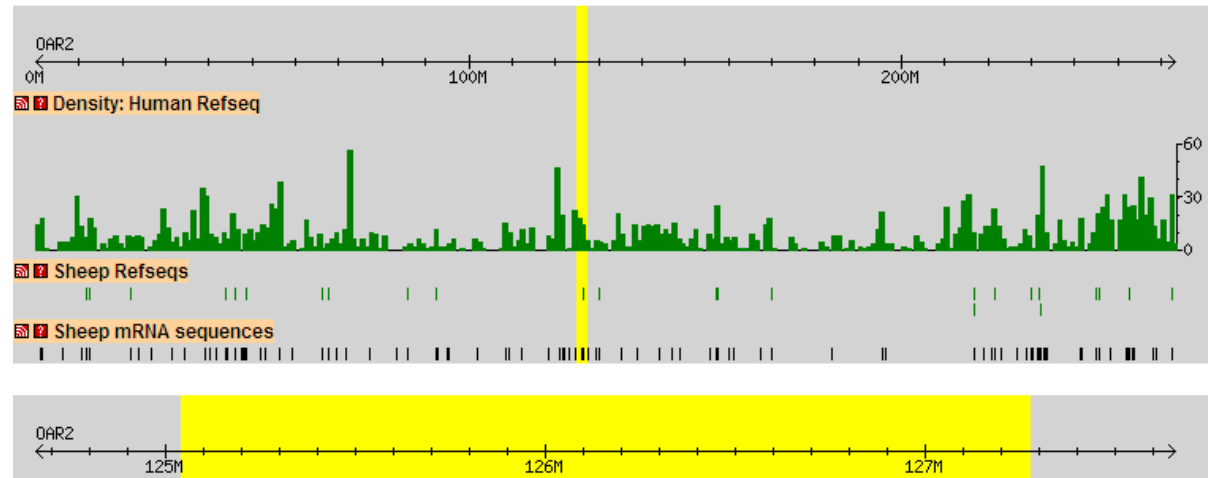


Texel

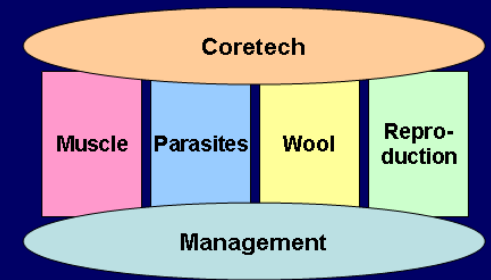


2.2 Mb region on
OAR2

15 human Refseqs
including *myostatin*



Whole Genome Selection Australia's Falkiner Flock



- Largest fine mapping flock in the world
- 15 industry and 5 research sires
- 5,300+ lambs by AI on 4,000+ ewes
- Characterised for 491 traits
- 4,058 progeny genotyped with 50k SNPs
- Funding from MLA and AWI

Ovine Whole Genome Reference Sequence

- Sequence generated from Texel ram used for the CHORI-243 BAC library
 - ~90 Gbp (30X coverage) on Illumina GAI platform (Roslin Institute)
 - ~6 Gbp (2X coverage) on Roche 454 FLX and ABI SOLiD platforms (BCM-HGSC)
 - Gaps will be covered using BAC tiling path on ABI SOLiD platform
- End result will be a whole genome reference sequence equivalent to 7X Sanger sequence and covering 95% of the unique ovine genome

International Sheep Genome Consortium



Funding Sources:

- USDA – ARS (USA)
- USDA – NRICGP (USA)
- USDA – NRSP-8 (USA)
- SheepGenomics (Australia)
- Australian Government ISL
- AgResearch (New Zealand)
- INRA (France)
- 7th Framework Program (EC)