

Breeds  
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One Region  
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Functional Variants  
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Conclusions  
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## Genomic Differentiation of 5 Danish and French Dairy Breeds

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- Farm animals differentiated into genetically distinct breeds
- Genetic bases of breed differences largely unknown

Breeds ●○○○○○○○	One Region ○○○	Functional Variants ○○○○	Conclusions ○
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## Breeds

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Breeds  
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One Region  
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## Cattle Breeds

- Cattle breeds formed centuries ago
- Founder effect
- Subsequent differential selection
- Recently (very) finite population sizes

Breeds  
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- Local differences in allele frequencies
- Haplotype structure
- Several studies detected numerous selection signals among beef and dairy breeds – mixture of time-scales





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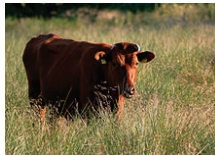
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## Five Breeds



Red Danish



Holstein



Normande



Montbéliarde



Jersey

Images from Wikimedia

Breeds  
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One Region  
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## Whole Genome Sequencing

<b>Breed</b>	<b>Number</b>
Holstein	123
Jersey	27
Montbéliard	28
Normande	24
Red Danish	45

Sequenced at 10X or more  
Characterizing differences between breeds

Breeds  
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## Characterizing Divergence

- Millions of variants
- Wright's  $F_{st}$  measures differentiation between populations
- $F_{st} = 0 \rightarrow$  No differentiation
- $F_{st} = 1 \rightarrow$  Fixed differences
- Weir's weighted  $F_{st}$  in bins of 10 kb
- Weir's weighted  $F_{st}$  for functional variants

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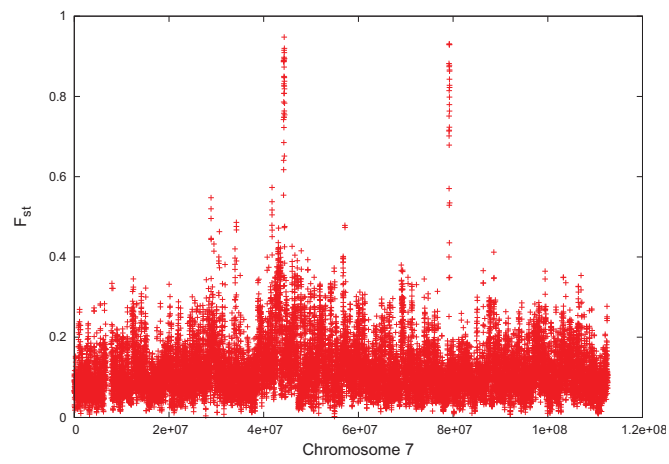
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## Differences in 10kb Bins



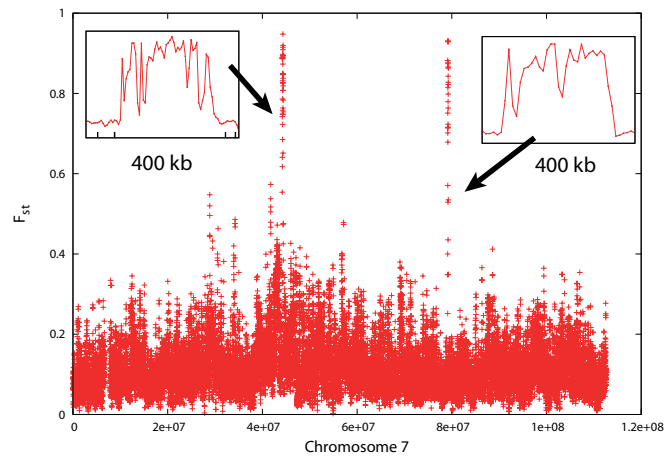
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### Differences in 10kb Bins



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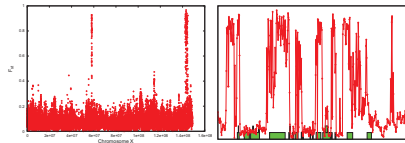
One Region  
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## Summary

- 8 highly differentiated regions across genome
- BTA7(2), BTA13 BTA17(2), BTA22, BTX(2)
- Most are simple regions (250-600 kb)
- On BTX one very large (2.6 Mb), very complex – assembly problem?



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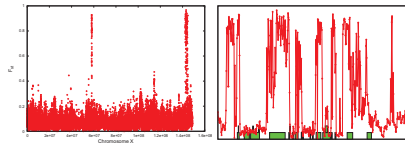
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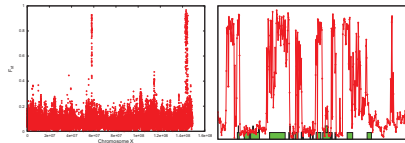
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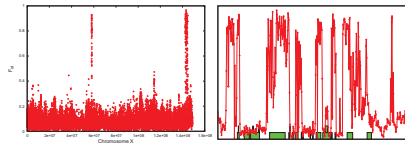
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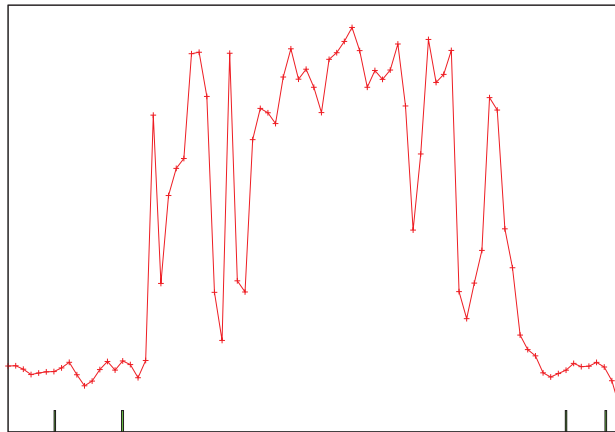
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## Comparisons to Holstein



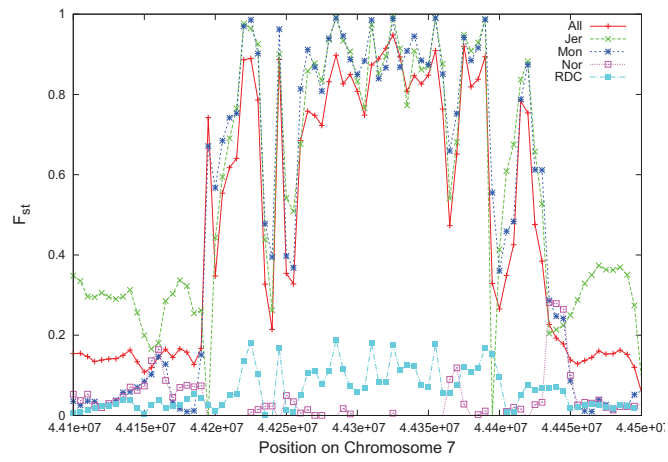
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One Region  
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## Pairwise Comparisons





- Only one region clearly associated with a gene
- Consistent pattern: Hol+Nor+RDC vs. Jer+Mon



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## Functional Annotation

- DNA sequence changes in exons differ in effect
- Effects can be predicted using tools from ENSEMBL (VEP)
- Synonymous, missense (SIFT: tolerated, "deleterious"), drastic (stop gained, stop lost, frame shift)
- Synonymous changes least likely to be subject to selection
- More drastic changes more likely to be subject to selection

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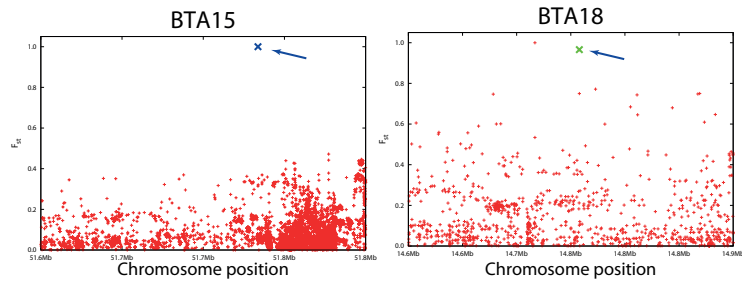
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## Differentiated “Deleterious”



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## Functional Differentiation

Sign. (%)	Functional Annotation Class					
	Tolerated		Deleterious		Drastic (stop etc.)	
	Count	%	Count	%	Count	%
<b>All</b>	56,056		18,516		1,140	
0.1	<b>74</b>	0.13	<b>34</b>	0.18	<b>6</b>	0.50

Synonymous mutations  $F_{st}$  distribution corrected for allele frequency differences used as (conservative) null distribution

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## Functional Differentiation

- Slight excess of differentiation in more extreme mutations
- Conservative test: some synonymous mutations are selected + effect of hitchhiking
- A few genes of recognizable effect, many uncharacterized proteins
- Exception: Black vs. red coat color

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Clear grouping of breeds
2. Many functionally annotated variants are highly differentiated



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