

**REGIONS IMPACTING INBREEDING DEPRESSION AND THEIR  
ASSOCIATION WITH ADDITIVE GENETIC EFFECTS FOR JERSEY CATTLE FROM  
THE UNITED STATES OF AMERICA AND AUSTRALIA**

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**SUMMARY**

The advent of dense genotype platforms allow for the identification of specific regions that give rise to inbreeding depression and characterize their relationship with the additive effect of that region. Utilizing a run of homozygosity (ROH) metric the first study objective is to identify regions having an impact on inbreeding depression for United States (US) and Australia (AU) Jersey cows. The second objective is to determine the relationship between the additive and ROH SNP effects. Genotyped cows with phenotypes on milk yield traits (US=6751; AU=3974) and calving interval (US=5816; AU=3905) were utilized. A ROH based metric (ROH4Mb) was calculated across the genome. Residuals from a model that accounted for the fixed and additive genetic effects were regressed on ROH4Mb using a single marker regression or a machine-learning tree based model. The relationship between ROH4Mb and additive effect was characterized based on sliding window (500kb) direct genomic value derived from a Bayesian-LASSO analysis. Genomic regions across multiple traits were found to be associated with ROH4Mb for the US on BTA13, BTA23 and BTA25 and AU on BTA3, BTA7 and BTA17. Multiple potential epistatic interactions were characterized. The covariance between ROH4Mb and the additive effect depended on the genomic region.

**INTRODUCTION**

High levels of inbreeding result in a reduction in fitness and overall performance at the phenotypic level (Leroy, 2014). Previous research has shown that inbreeding depression is heterogeneous across founders (Gulisija *et al.* 2006), which implies that the genetic load is not distributed evenly among genomes. Utilizing a run of homozygosity (ROH) metric, Pryce *et al.* (2014) confirmed heterogeneity in inbreeding depression by identifying multiple regions that resulted in reduction in milk yield and fertility traits in Australian (AU) Holstein and Jersey cows. Furthermore, regions with multiplicative effects, which individually may have a minor effect but which have significant impact on fitness when combined, might provide clues about the previously identified non-linear relationship of inbreeding depression (Gulisija *et al.* 2007).

Characterizing regions that give rise to inbreeding depression in dairy cattle is advantageous due the increasingly large number of genotyped cows and the extensive list of recorded phenotypes. It has been shown by Howard *et al.* (2015) that ROH frequency differs across the Australian (AU) and United States (US) Jersey populations, which could potentially give rise to different regions that have an impact on inbreeding depression. Also, Howard *et al.* (2015) found that regions of the genome with high ROH frequency are most likely the result of directional selection. Here we hypothesize that the covariance between the additive effect and ROH status of a SNP is variable across the genome, and characterizing this may provide clues about the relationship between the two metrics. Therefore the





have previously been found to be under positive directional selection (Howard *et al.* 2015). Homozygosity at certain regions of the genome is beneficial such that homozygosity based on the ROH4Mb status gives rise to a higher additive genomic estimated breeding value. Conversely, homozygosity at certain regions is unfavorable giving rise to lower additive genomic estimated breeding values. The majority of the regions with the largest absolute covariance value across traits were positive, which is not surprising due to a low frequency of ROH4Mb status for regions with a large ROH4Mb effect (mean ROH4Mb frequency = 0.089) in comparison to the regions that displayed a large positive covariance (mean ROH4Mb frequency = 0.235). These results provide evidence that it is possible to distinguish between two individuals that have the same inbreeding coefficient, but different overall genomic loads. This would have in turn important consequences in the management of genomic diversity and the implementations of effective mating design.

**Table 1. Regions of the genome associated with inbreeding depression for milk traits.**

Country	Traits	BTA (Region Mb)	Frequency	Candidate Gene
United States	MY-PY	13 (19.3-19.9)	0.10	PARD3
	MY-FY-PY	23 (32.7-33.3)	0.18	ALDH5A1
	MY-PY	25 (24.8-30.7)	0.05	IL4R, CALN1
Australia	FY-PY	3 (113.4-114.6)	0.06	UGT1A1
	FY-PY	7 (6.6-16.7)	0.17	NOTCH3
	MY-FY-PY	17 (68.9-75.0)	0.04	IGLL1

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