Causative gene discovery in bovine dairy traits

Tania Law

Supervisor(s) Russell Snell and Matt Littlejohn

Abstract

Milk is composed of a complex mixture of lipids, proteins, carbohydrates, and various vitamins and minerals to support the growth of the developing neonate. In *Bos taurus*, the composition of milk shows continuous variation across individuals in a population, which has shown to be partly attributable to genetics. In particular, the lipid and protein composition of bovine milk show high levels of heritability, and many studies have highlighted quantitative trait loci (QTL) for these traits on a number of bovine autosomes. However, due to the small effect sizes of these QTL and that most of the causative variants are likely to lie outside of coding regions, few of these signals have been explained.

In order to address our rudimentary understanding of non-coding regulatory regions in the bovine genome, I will utilise the hypersensitivity of these regions to degradation by DNase enzymes to develop a genome-wide map of chromatin accessibility. Several studies have shown that active chromatin is associated with all known classes of active DNA regulatory elements, such as promoters and enhancers, which will enable the profiling of regulatory non-coding DNA in the bovine genome. As such, putative causal variants that lie within or close to these DNase hypersensitive sites are more likely to play a biological role, for example by changing binding affinity of transcription factors, and this information will enable us to predict the consequences of non-coding variants, deciphering those causative variants from neutral polymorphisms.

Given that the genetic variation within non-coding regulatory regions is thought to contribute a significant proportion of the phenotypic variation of milk composition, providing a functional annotation of the non-coding regions of the bovine genome will contribute significantly to the discovery causative genes and variants underpinning bovine dairy traits.