

Whole Genome Association Analysis of Idiopathic Eosinophilic Enteritis in Brown Egg Layers

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Summary and Implications

Idiopathic Eosinophilic Enteritis (IEE) is an intestine disease that affects absorption of nutrients and performance. Hens of a commercial breeding layer line and its two reciprocal crosses with another line were recorded for IEE related traits and genotyped for over 40,000 genetic markers across the genome. Whole genome association analysis was performed on 288 daughters from high and low incidence sire families. Single marker association analyses of IEE incidence in separate lines showed consistent significant regions on chromosomes 4 and 5 ($p < 0.001$). Simultaneous analyses of all SNPs in all 3 lines using Bayesian whole genome selection methods indicated evidence of associations on chromosomes 1, 2 and 4 for additive effects and on chromosome 5 for dominance effects. Line specific regions also appeared on chromosome Z. With further investigation, these results can be used to develop genetic markers to select against this disease and to understand its genetic basis.

Introduction

Idiopathic Eosinophilic Enteritis (IEE) is a rare intestine disease that occurs primarily in brown layer chickens. It affects absorption of nutrients and provokes an interruption in production and the need to cull the birds. Necropsy shows an inflamed, twisted or hemorrhaging intestine in the region of Meckel's Diverticulum. To date, IEE has been observed only in layers and in specific flocks; males under the same conditions are unaffected. The causative agent for this disease has not been identified, nor a treatment to cure or prevent it. However, incidence of IEE has been found to have a genetic basis, with heritability estimates of around 30%. The objective of this study was to identify genetic markers or genomic regions that are associated with IEE incidence, to enable selection to lower the incidence of the IEE disease.

Materials and Methods

Sire-identified hens of a commercial breeding brown layer line and its two reciprocal crosses with another line were placed in a barn that had shown previous incidence of IEE. Cases and unaffected controls for IEE were recorded as mortality or alive within 72 weeks. The diagnosis was confirmed by necropsy to identify the typical intestinal lesion and location that characterizes IEE. In total, 3,219 hens were housed and recorded for IEE. Cases were confirmed by necropsy, and intestine length and lesion length were recorded at that time. Then, 288 daughters from high and low incidence sire families were genotyped using a custom 40k Illumina SNP panel. Two statistical methods were employed to identify genetic markers and genomic regions associated with IEE: 1) single-SNP association analysis by CHI-Square, which was done separately for each of the 3 lines/crosses; 2) simultaneous analysis of all SNPs in all 3 lines using the whole-genome selection analysis method Bayes-C of the *GenSel* program developed at Iowa State University (Fernando and Garrick). The latter was conducted using both categorical and continuous trait analysis, and allowing for both additive and dominance SNP effects.

Results and Discussion

Incidence of IEE differed substantially between the pure line and its two reciprocal crosses: 6.2% affected in the pure line, 16.3% and 7.7% affected in the reciprocal crosses. Single SNP association analyses showed 72 SNPs that were significantly ($p < 0.001$) associated with IEE in the pure line and 206 and 189 significant SNPs in the two crosses. But only 2 regions represented by the significant SNPs were consistent across the three lines, and these were located on chromosomes 4 and 5. The highest significance level in these two regions was 10^{-7} . Line-specific regions were identified on chromosome Z. In the simultaneous analysis of all SNPs in all 3 lines with the Bayes-C method, incidence to IEE of each animal was treated as either a binary or a continuous variable. For the additive model, strong effects were found for regions on chromosomes 1, 2 and 4 for both the binary and the continuous analysis. For the dominance model using continuous variable analysis, a region on chromosome 5 was found to be associated. Comparing results of the single and simultaneous SNP analyses, signals on chromosome 5 agreed well with each other under the two methods. This region shows a strong negative dominant effect in the mixed population, as well as in the cross that had lower incidence of the disease. Line specific regions, such as those on chromosome 6, may be of interest in

indicating an imprinting effect to interpret the big difference of susceptibility in the two reciprocal crosses.

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