Gene Expression Associated With Virus Resistance in Chickens

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Summary and Implications

We used the powerful contemporary genetic technologies of micrarray and Q-PCR to test global gene expression in a unique population of birds after challenge with infectious bursal disease virus (IBDV). Identification of genes that have differential expression between resistant and susceptible birds helps to determine the mechanisms of host resistance to this virus and may be used to select breeding stock for greater innate resistance to viral infection.

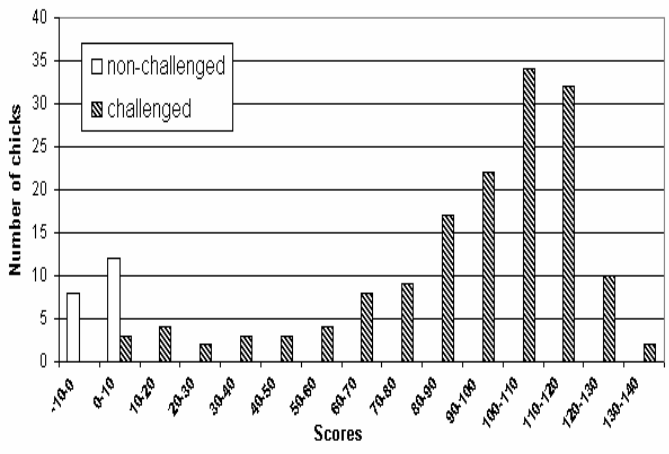
Introduction

Infectious Bursal Disease Virus (IBDV) causes highly contagious, immunosuppressive disease that leads to high mortality in young chickens. IBDV is a double-stranded RNA virus. The main target organ of virus destruction is the bursa of Fabricius, the primary immune organ in which the cells differentiate that will have the capacity to produce antibodies. Therefore, in addition to the morbidity and mortality caused by the acute infection with IBDV, surviving birds can be severely immunosuppressed and later be susceptible to other infections. The objective of our study was to identify genes that are involved in resistance to IBDV infection, so that this information will elucidate the host resistance mechanisms to the virus. This information can be applied to improve animal health by contributing to the rational design of vaccines and by providing gene targets for genetic selection of more resistant breeding stock.

Materials, Methods, and Results

Chicks of an F2 generation of two lines divergently selected for high (HH) or low (LL) antibody (Ab) response to *Escherichia coli* vaccination, were challenged with virulent IBDV. Viral load varied among individual birds, which indicates variation in resistance mechanisms of the individuals (Figure 1).

Figure 1. Distribution of viral-load scores in the bursa of infected and non-infected chicks.

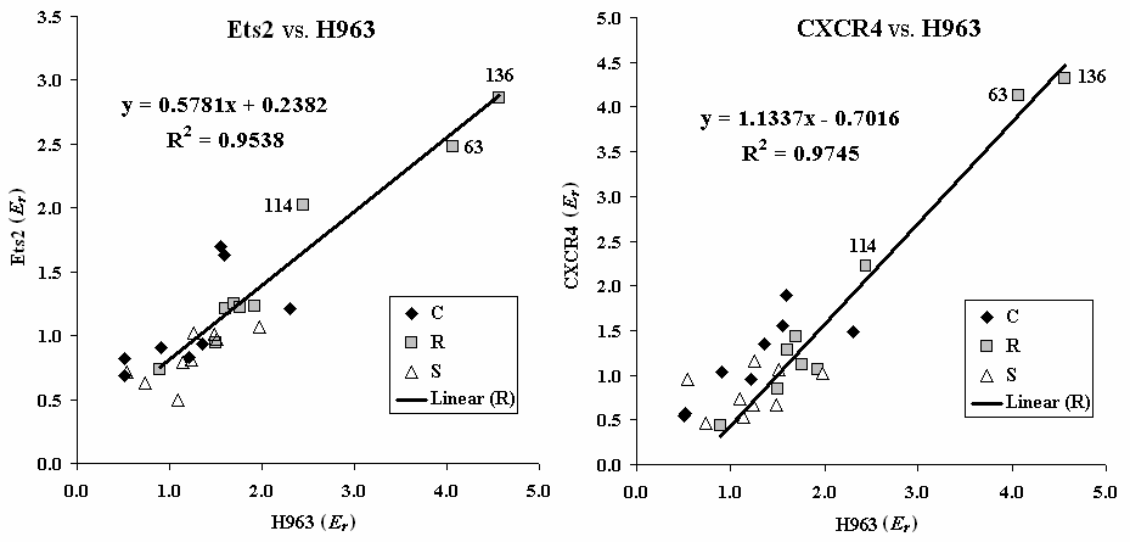


Viral load in infected bursae was used to designate resistant (R, high virus count) and susceptible (S, low virus count) birds. By using a 13K chicken cDNA microarray (Fred Hutchison Cancer Research Center), and pooled spleens of R, S and non-challenged, control (C) chicks, several genes were identified with differential expression associated with host resistance to IBDV. These genes were also subjected to RT-PCR on individual samples to verify the microarray results. The major finding was coordinated upregulation of 7 genes (Ets2, H963, RGS1, ABIN-2, CREM/ICER, DUSP1 and CXCR4) in several R, but not S or C, individuals. There were very high correlations of expression levels among genes (Figures 2 and 3).

Figure 2. Correlations in gene expression in seven co-upregulated genes in virus-resistant chicks. R2 above diagonal, significance of R2 below diagonal.

	H963	ABIN-2	RGS1	CREM/ICER	DUSP1	Ets2	CXCR4
H963		0.938	0.936	0.920	0.758	0.954	0.975
ABIN-2	<<0.01		0.912	0.959	0.738	0.860	0.954
RGS1	<<0.01	<<0.01		0.967	0.914	0.921	0.922
CREM/ICER	<<0.01	<<0.01	<<0.01		0.855	0.895	0.933
DUSP1	0.002	0.003	<<0.01	<<0.01		0.737	0.709
Ets2	<<0.01	<<0.01	<<0.01	<<0.01	0.003		0.959
CXCR4	<<0.01	<<0.01	<<0.01	<<0.01	0.004	<<0.01	

Figure 3. Two examples of the high correlation of gene expression in the IBDV-resistant (but not control or susceptible) chicks.



Discussion

Based on reported functions of these genes, our findings suggest that resistance is mediated by the activation of specific cellular mechanisms, primarily involving macrophages and T-lymphocytes. Early and intense formation and activity of germinal centers in the spleen of resistant birds, followed by the migration of these cells towards the bursa is presumably important for resistance to occur. Identification of genes that have differential expression between resistant and susceptible birds helps to determine the mechanisms of host resistance to this virus and may be used to select breeding stock for greater innate resistance to viral infection

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