Evidence of major genes affecting resistance to bacterial cold water disease in rainbow trout using Bayesian methods of segregation analysis


*National Center for Cool and Cold Water Aquaculture, USDA/ARS, 11861 Leetown Rd., Kearneysville, WV 25430; and †Department of Genetics and Biotechnology, University of Aarhus, DK-8830 Tjele, Denmark

ABSTRACT: Bacterial cold water disease (BCWD) causes significant economic loss in salmonid aquaculture. We previously detected genetic variation for BCWD resistance in our rainbow trout population, and a family-based selection program to improve resistance was initiated at the National Center for Cool and Cold Water Aquaculture (NCCCWA). This study investigated evidence of major trait loci affecting BCWD resistance using only phenotypic data (without using genetic markers) and Bayesian methods of segregation analysis (BMSA). A total of 10,603 juvenile fish from 101 full-sib families corresponding to 3 generations (2005, 2007, and 2009 hatch years) of the NCCCWA population were challenged by intraperitoneal injection with Flavobacterium psychrophilum, the bacterium that causes BCWD. The results from single- and multiple-QTL models of BMSA suggest that 6 to 10 QTL explaining 83 to 89% of phenotypic variance with either codominant or dominant disease-resistant alleles plus polygenic effects may underlie the genetic architecture of BCWD resistance. This study also highlights the importance of polygenic background effects in the genetic variation of BCWD resistance. The polygenic heritability on the observed scale of survival status \( h^2_{\text{observed}} = 0.45 \) is slightly larger than that previously reported for rainbow trout BCWD resistance. These findings provide the basis for designing informative crosses for QTL mapping and carrying out genome scans for QTL affecting BCWD resistance in rainbow trout.

Key words: bacterial cold water disease, Bayesian analysis, disease resistance, major gene, rainbow trout, segregation analysis

INTRODUCTION

Bacterial cold water disease (BCWD) causes significant economic loss in worldwide salmonid aquaculture.

It is a common-chronic disease in rainbow trout (Oncorhynchus mykiss) in US aquaculture that is caused by Flavobacterium psychrophilum (Fp). This bacterium also causes acute losses in young fish known as rainbow trout fry syndrome. There are limited methods for prevention of BCWD, and no licensed vaccine is currently available. In 2005, a rainbow trout breeding program was initiated at the National Center for Cool and Cold Water Aquaculture (NCCCWA), Agricultural Research Service, USDA, to select for increased resistance to BCWD.

The main objectives of this study were to determine the mode of inheritance of BCWD resistance and to detect evidence of major trait loci affecting BCWD resistance using Bayesian methods of complex segregation analysis (CSA) and large full-sib (FS) families from a 3-generation pedigree of the NCCCWA rainbow trout population. The CSA is a statistical method to determine whether a mixed mode of inheritance of a major gene (MG) plus polygenic background effects is consis-
tent with the inheritance of a trait using only phenotypic data without using marker genotype data (Guo and Thompson, 1992; Thaller et al., 1996; Janss et al., 1997). We evaluated whether a mixed-inheritance of a MG and polygenic background effects was consistent with the inheritance of resistance to BCWD. This study provides the basis for designing informative crosses for QTL mapping, and carrying out genome linkage scans for QTL underlying the genetic variation of resistance to BCWD in rainbow trout.

MATERIALS AND METHODS

The institutional Animal Care and Use Committee protocol used in this research was NCCCWA Animal Care and Use Committee Protocol Number 049.

Population Sample

A total of 10,603 fish comprising 3 generations spawned in 2005, 2007, and 2009 were evaluated for BCWD resistance under laboratory experimental conditions (Table 1 and Figure 1). Details on developing this synthetic population are described in Silverstein et al. (2009). In 2005, a random sample of 40 to 80 fish from each of 71 families was challenged with Fp strain CSF259–93 in 1 or 2 replicates per family (40 fish per tank; 43 families had 80 fish and 28 families had 40 fish). A sample of 52 sires and 61 dams unselected for BCWD resistance was used to generate the 71 families. These families were composed of 14 paternal half-sib (HS) families, 10 maternal HS families, and 27 FS families with no maternal or paternal half sibs.

Fish mortality was monitored over 21 d postchallenge. In this parental generation population (G₀), 4,498 fish had individual records on survival status and survival days (Figure 1). Three families with greatest and 3 families with least relative survival rate were selected for further study. Non-disease-challenged siblings from the 6 selected families were used as breeders to generate the 2007 population (Figure 1).

In 2007, a total of 15 FS families from greatest × greatest (5 FS), greatest × least (RxS; 5 FS), and least × least (SxS; 5FS) relative survival rate were evaluated for survival to BCWD. From each family, a random sample of 200 fish was challenged with Fp strain CSF259–93 in 4 replicates per family (50 fish per tank). Fish mortality was monitored over 21 d postchallenge. In this first generation population (G₁), 2,960 fish had individual records on survival status and survival days (Figure 1). Two RxS families with high survival rate postchallenge (HRxS; 3 RxS families with medium survival (MRxS), and 3 SxS families with least survival (LSxS) were selected. Non-disease-challenged siblings from the 8 selected families were used as breeders to generate the 2009 population (Figure 1).

In 2009, a total of 15 FS families from H₁RxS × L₁SxS (backcross (BC); 10 FS) and M₁RxS × M₁SxS [F₁ intercross (F₂); 5 FS] were evaluated. From each family, a ran-
A sample of 200 fish was challenged in 4 replicates per family (50 fish per tank). In addition, 3 of the BC families that were challenged in the first 2009 experiment were also challenged in the second experiment using a random sample of 60 fish per family (30 fish per tank; Table 1). Fish mortality was monitored over 21 d postchallenge. In this second generation population (G2), 3,145 fish had individual records on survival status and survival days (Figure 1).

**Fish Challenge with Fp Strain CSF259–93**

The *Fp* challenge was carried out in the NCCCWA challenge facility. The fish were allowed 1 to 2 wk to
acclimatize before challenge and were fed by hand to apparent satiation. Fish were challenged with the virulent Fp strain CSF-259–93. The bacterial culture was prepared as described previously (Hadidi et al., 2008). All fish were challenged by intraperitoneal injection, with dose and volume adjusted for BW (Table 1). Fish that died during the 21-d period after challenge were recorded for day of mortality, removed from the tank, and examined for clinical signs of disease. Fish that did not die during the 21-d challenge were recorded as censored observations.

**Measured BCWD-Related Traits**

Each individual fish had records of survival days (i.e., number of days to death) postchallenge with Fp. Fish survival was evaluated for 21 d postchallenge with Fp. Each individual fish also had records on binary trait survival status. The binary survival status had 2 classes: 0 = fish was normal or alive through the evaluation period, and 1 = fish had BCWD and was dead during the study.

**Statistical Analysis of Nongenetic Effects**

Before performing CSA, to identify significant predictors of response variables “survival status” and “survival days,” we performed multivariable regression analysis by year (and combined data set) using 2 linear models that included random (family, sire, and dam), fixed effect tank, and continuous covariates (BW and age) using STEPWISE model selection with Proc REG (SAS Inst. Inc., Cary, NC). Model A included all 6 variables, and model B included fixed effects and continuous covariates (tank, age, and weight). Next, the variables with a significant effect (potential variables to include in CSA models) on response variables were tested for family effect using SAS Proc MIXED. This test helps avoid wrongly adjusting response variables for fixed effects and covariates that had significant family effects.

At STEPWISE model selection, the following fixed effects and covariates had significant effect on BCWD traits: BW in 2005; tank, BW, and age in 2007; BW and age in 2009; and tank, BW, age, and year in combined 2005–2007–2009 data set (results not presented). Next with SAS Proc Mixed, we found out that the covariates BW and age had significant family effect in all data sets (2005, 2007, 2009, and combined). These results indicate that BW and age should not be used as covariates in the models of CSA. Subsequently, we decided to include the fixed effect tank in the mixed-inheritance model used in CSA of 2007 data set to minimize the variance in the sampled population; also, the fixed effects tank and year were included in the mixed-inheritance model used in CSA of combined data set. The CSA models used with 2005 and 2009 data sets did not include any fixed effects and covariates.

**Bayesian Segregation Analysis with iBay**

The binary survival status was used to perform Bayesian segregation analysis (BMSA) in the underlying scale of liability fitting a mixed-inheritance threshold model (MITM). The binary survival status and survival days were also used to perform BMSA on the observed scale fitting a mixed-inheritance linear model (MILM). Janss et al. (1995) have presented a BMSA approach for livestock species. This BMSA method was used to fit MITM and MILM using the software iBay version 1.46 (Janss, 2008).

**Polygenic Model.** The pure polygenic model was used to supply an overall quantification of genetic variance for the binary survival status in the underlying scale of liability. A threshold model postulating pure polygenic inheritance was specified as

\[ \lambda_{nx1} = X_{nxq} b_{qxl} + Z_{nxr} u_{rx1} + e_{nx1}, \]

where \( \lambda_{nx1} \) is the vector of liability to survival status, \( n \) is the number of records, \( b_{qxl} \) is the vector of nongenetic effects (tank), \( q \) is the number of levels for nongenetic effects, \( u_{rx1} \) is the vector of polygenic effects, \( r \) is the number of levels for random animal effects, \( e_{nx1} \) is the vector of random residual effects, and \( X_{nxq} \) and \( Z_{nxr} \) are incidence matrices connecting the unknowns in \( b_{qxl} \) and \( u_{rx1} \) to the observations.

Threshold-liability models for analysis of binary data were first proposed by Wright (1934) and were later adapted for the analysis of a mixed-inheritance by Morton and Maclean (1974). Threshold models have been also used in QTL detection and mapping in BC and F2 populations (Rebai, 1997) and in outbred populations on a within-family basis (Kadarmideen et al., 2000; Kadarmideen and Dekkers, 2001; Kadarmideen and Janss, 2005). These models assume the presence of an underlying continuous random variable called the liability, \( \lambda = \{ \lambda_i \} \). The liability \( \lambda \) in model [1] is such that the observed discrete (survival status) responses \( y = \{ y_i \} \) are the result of the relationship

\[ y_i = \begin{cases} 0 & \text{if } \lambda_i \leq T_i \\ 1 & \text{if } \lambda_i > T_i \end{cases}, \]

where \( T \) is a fixed threshold. Here, \( y_i = 0 \) denotes a healthy animal and \( y_i = 1 \) denotes a diseased animal, depending on whether their liability \( \lambda_i \) exceeded the threshold point \( T \) for manifestation of the disease. The \( \lambda_i \) is not observed and is used to simplify the likelihood and the construction of the Markov chain Monte Carlo (MCMC; Kadarmideen and Janss, 2005). Liabilities were assumed to be normally distributed with mean \( \mu \) and variance \( \text{variance } R_{nx1} = I \sigma^2_s \), where \( I \) is the identity matrix. The threshold and the dispersion parameters were set to \( T_i = 0 \) and \( \sigma^2_s = 1 \), respectively.

The fixed effects were assumed distributed as \( b \sim N(0, 2) \). This normal distribution with relatively large
transmits the allele were calculated as $u \sim N(0, A\sigma^2_u)$, where $A$ is the numerator relationship matrix. In the implementation of the threshold model, the prior distribution for polygenic variance $\sigma^2_u$ was set as a uniform on $[0, 10]$.

Statistical inference was based on a Bayesian approach computing marginal posterior densities of the unknown parameters by the MCMC method known as Gibbs sampling (Gelman et al., 2004). The theory and methodology of BMSA are explained in more detail by Janss et al. (1995), Sorensen (1996), and Janss (2008). The Bayesian approach for CSA allowed the estimation of marginal posterior distributions for nongenetic effects, polygenic variance $\sigma^2_u$, error variance $\sigma^2_e$, and polygenic heritability in the underlying scale of liability defined as $h^2_p = \sigma^2_u / (\sigma^2_u + \sigma^2_e)$. The polygenic heritability on the observed scale was estimated as $h^2_{\text{observed}} = (\hat{h}^2_p)^2 / (1 - p)$, where $i$ is the mean deviation of affected individuals from their group mean, and $p$ is the incidence of mortality (Falconer and Mackay, 1996).

**MITM.** A MITM describing nongenetic effects, effect of 1 MG and effects of background polygons was used to detect the presence of a MG in the inheritance of the binary survival status. As indicated in polygenic model, threshold-liability models assume the presence of an underlying continuous random variable called the liability, $\lambda = \{\lambda_i\}$. Under the liability scale, the MITM applied to survival status was

$$\lambda_{\text{nxl}} = X_{\text{nxl}}b_{\text{qxl}} + Z_{\text{nxl}}u_{\text{nxl}} + Z_{\text{nxr}} W_{\text{rx3}} g_{\text{rx3}} + e_{\text{nxl}},$$

where $\lambda_{\text{nxl}}$ is the vector of liability to survival status, $n$ is the number of individuals, $b_{\text{qxl}}$ is the vector of nongenetic effects that included fixed effect tank, $q$ is the number of levels for nongenetic effects, $u_{\text{nxl}}$ is the vector of polygenic effects, $r$ is the number of levels for random animal effects, $W_{\text{rx3}}$ is the incidence matrix for MG genotypes, $b_{\text{qxl}}$ is the vector of genotype means, $e_{\text{nxl}}$ is the vector of random residuals for $\lambda$, and $X_{\text{nxl}}$ and $Z_{\text{nxr}}$ are incidence matrices connecting the unknowns in $b_{\text{qxl}}, u_{\text{nxl}},$ and $W_{\text{rx3}}g_{\text{rx3}}$ to the observations.

The fixed, polygenic, and residual effects were assumed distributed as indicated in polygenic model. The MG effect is assumed to result from the segregation at a single locus with 2 alleles ($A_1$, $A_2$). The allele $A_1$ is associated with “low” values on the underlying scale of liability $\lambda$ and the allele $A_2$ with “high” values of $\lambda$. The frequency of $A_1$ and $A_2$ in the sample population was denoted as $p$ and $q = (1 - p)$, respectively. The prior distribution for genotypes can be specified as founder genotypes to have prior probabilities of $p^2$, $2pq$, and $q^2$ for genotypes $A_1A_1$, $A_1A_2/A_2A_1$, and $A_2A_2$, respectively, and as nonfounder genotypes to have prior probabilities conditional on parental genotypes given Mendelian transmission. Hence, this parameterization assumes a single population and Hardy-Weinberg equilibrium for prior probabilities in founders, although evidences for subpopulations within founders of the NCCCWA rainbow trout population was suggested (Johnson et al., 2007). For founder allele frequency, only $p$ is estimated and a flat prior distribution on $[0, 1]$ was assigned for $p$. Effects of the 3 genotypes $A_1A_1$, $A_1A_2$, and $A_2A_2$ were modeled as $g^* = (-a, d, a)$. The prior distribution for the additive $a$ and dominant $d$ effect at the major locus was set as $\sim N(0, 5)$, which applies a moderate shrinkage to the MG effects.

The MITM was analyzed under Mendelian and non-Mendelian inheritance of the MG. This model included 3 transmission probabilities $\{\tau_{A_1/A_1}, \tau_{A_1/A_2}, \tau_{A_2/A_1}\}$ defined as the probability that a parent with any of the 3 genotypes $\{A_1A_1, A_1A_2, A_2A_2\}$ transmits the allele $A_1$ to its offspring. If Mendelian inheritance was assumed, the transmission probabilities were fixed to $\tau_{A_1/A_1} = 1$, $\tau_{A_1/A_2} = 0.5$, and $\tau_{A_2/A_1} = 0$. By estimation of the transmission probabilities with a flat prior distribution on $[0, 1]$ extra safeguards against detection of false-positive MG can be made: a robust indication for the segregation of a MG is obtained only when estimated transmission probabilities do not deviate significantly from Mendelian, but do differ significantly from equal transmission probabilities (Elston and Stewart, 1971), in conjunction with overall significance of the MG component in the model. Estimation of transmission probabilities was done by fixing obtained MG parameters $a$, $d$, and $p$ and polygenic variance $\sigma^2_u$ to estimated values with best-fitting MITM, allowing the estimation of transmission probabilities to indicate whether the inferred MG might have been caused by other sources.

**The Gibbs Sampler.** Statistical inference was based on a Bayesian approach as indicated in polygenic model. The Bayesian approach for CSA allowed the estimation of marginal posterior distributions for nongenetic effects, genotypic values from the MG component in the model. Estimation of marginal posterior distributions for nongenetic effects, genotypic values from the MG component in the model. Estimation of transmission probabilities was done by fixing obtained MG parameters $a$, $d$, and $p$ and polygenic variance $\sigma^2_u$ to estimated values with best-fitting MITM, allowing the estimation of transmission probabilities to indicate whether the inferred MG might have been caused by other sources.
a MG expressed in genetic SD (GSD) units
\[ a_{GSD} = \frac{1}{\left(\sigma_u^2 + \sigma_g^2\right)^{1/2}} \]
were estimated and their marginal posterior distributions were computed.

After exploratory BMSA with binary survival status and survival days, the length of each chain was set to 1,200,000 iterations. The first half of each chain was discarded (burn-in period of 600,000 iterations) to diminish the effect of the starting distribution and allow convergence of the Gibbs sampler (Gelman et al., 2004). On the last half of the chain, samples were saved every 10,000 iterations (thinning parameter \( k = 10,000 \)) to ensure that independent samples were collected. This Gibbs sampler allowed collecting 60 virtually independent samples per chain. Estimation of posterior distributions of parameters for each model was based on at least 20 replicated Gibbs chains.

Postanalysis and Statistical Inference. Convergence of the Gibbs sampler was judged by using at least 1,200 independent samples from 20 chains in an ANOVA testing for a significant chain effect. Significant differences between chains indicated that the Gibbs sampler did not converge and that generated samples were not from the correct posterior distribution. Convergence was also tested using the criterion outlined by Gelman et al. (2004). For each unknown parameter in the model, a scale reduction factor \( \hat{R} \), which involves variance between and within chains, was computed. The \( \hat{R} \) can be interpreted as the factor by which the scale of the marginal posterior distribution of each variable would be reduced if the simulations were continued in the limit \( n \to \infty \). The \( \hat{R} \) should be around \( \approx 1 \) (or at most \( \leq 1.1 \)) to indicate convergence of the iterative simulation for the unknown parameter.

Statistical inferences were based on summarizing the generated samples in the form of estimated marginal posterior distributions. As features of the marginal posterior distributions, estimated means and SD were computed. Posterior means were used as point estimates for the parameters. Statistical inferences focused on the genetic variance components \( \left(\sigma_u^2, \sigma_g^2\right) \) to determine significance of the MG in the model. Conclusions were also based on the shapes of estimated posterior distributions of variance components (Janss et al., 1995), where a nonsignificant variance shows a distribution with global mode at \( \sigma^2 = 0 \) and a significant variance shows a global mode at \( \sigma^2 > 0 \). Major gene variance was concluded to be significant when the global mode had a density 20 times larger than the density at \( \sigma^2 = 0 \).

Once significant MG variance was found, further inferences focused on the effects at the major locus and on estimable functions of allele frequencies. The highest posterior density region at 95% (HPDR95) was also calculated from the marginal posterior distributions for each unknown parameter.

Mode of Inheritance of BCWD Resistance. We determined the likely mode of inheritance of resistance to BCWD by defining 8 mixed-inheritance models and sub-models or nested models using data on binary survival status evaluated in 71 families from 2005. The models were categorized into 4 model sets. 1) The first set is non-Mendelian (unrestricted \( \tau \)), which assumes non-Mendelian segregation. This set included the general model that maximizes \( \sigma_u^2 \) (model 1) and the general model with fixed \( \sigma_u^2 = 0 \) (model 2). 2) The second set is sporadic, which assumes no genetic effects or absence of MG and polygenic effects \( \left( p = 0, \sigma_g^2 = 0 \right) \), which is equivalent to the assumption of equal transmission probabilities \( \left( \tau_{A_1/A_1}, \tau_{A_1/A_2}, \tau_{A_2/A_2} \right) \) (model 3). 3) The third set is polygenic, which assumes no MG but polygenic background (model 4). 4) The fourth set is Mendelian mixed-inheritance of a MG plus the polygenic background, which is divided into 4 models: dominance of the increasing BCWD phenotype allele \( A_2 \) (i.e., disease susceptibility allele; model 5, \( a = d \)), additive (model 6, \( a = d \)), additive (model 6, \( a = d \)), dominance of the decreasing disease phenotype allele \( A_1 \) (i.e., disease resistance allele) (model 7, \( a = -d \)), and codominant (model 8, \( d \neq 0 \)).

In the model comparisons, we combined the use of Bayes factors (BF) with approaches that measure the distance of the data to each of the approximate models by comparing nested models. Let \( \theta \) be the vector of parameters in the smaller model and \( \psi \) be the additional parameters in the expanded model. Then we compared the 2 posterior distributions, \( p(\theta|y) \) and \( p(\theta,\psi|y) \), along with their predictive distributions for replicated data chains.

The loge of the marginal distribution of the data under each model, \( \log \left[ p(y|H_i) \right] \), is estimated, which is basically the normalization constant for the marginalized posterior density (Janss, 2008). Here, given 2 competing models \( H_1 \) and \( H_2 \), we estimated BF \( (H_2; H_1) = p(y|H_2)/p(y|H_1) \), which is the ratio of the marginal likelihood under 1 model to the marginal likelihood under a second model (Gelman et al., 2004). In this study, the guidelines provided by Janss (2008) were used to assess the amount of evidence in the data that supported the difference between compared models, BF \( (H_2; H_1) \).

Inference on Transmission Probabilities. After determining the most likely mode of inheritance for BCWD resistance, we analyzed a MG model under non-Mendelian assumptions, defined as
\[ \lambda_{nx1} = X_{nx1}b_{nx1} + Z_{nx1}W_{nx1}g_{nx1} + e_{nx1}, \]
with the specifications equal to those defined for model [2]. The parameters \( a, d, \) and \( p \) were fixed to the values estimated for the best fitting mixed-inheritance model, the polygenic variance was set to \( \sigma_g^2 = 0 \), and the transmission probabilities \( \left( \tau_{A_1/A_1}, \tau_{A_1/A_2}, \tau_{A_2/A_2} \right) \) were given a flat prior for parameter estimation (best-fitting MG model). After running the Gibbs sampler as previously specified, the parameters \( \mu, \sigma_g^2, \sigma_u^2 \), and transmission-
sion probabilities \((\tau_{A_A/A_A}, \tau_{A_A/A_A}, \tau_{A_A/A_A})\) were estimated from the marginal posterior distributions of the unknown parameters. For comparison purposes, we also analyzed a MG general model (General fixed model) with all the above parameters treated as unknowns \((a, b, p, \tau_{A_A/A_A}, \tau_{A_A/A_A}, \tau_{A_A/A_A}, \mu, \sigma^2_p, \sigma^2_e)\) with the polygenic variance set to \(\sigma^2_e = 0\). We also analyzed the mixed-inheritance threshold model [2] to assess the effect of the polygenic background in the estimation of Mendelian transmission probabilities. In this model, the MG parameters \(a, d, p, \) and polygenic variance \(\sigma^2_e\) were fixed to values estimated with the most plausible mixed-inheritance model for BCWD resistance (best-fitting mixed-inheritance model). The unknown parameters were the transmission probabilities \(\tau_{A_A/A_A}, \tau_{A_A/A_A}, \tau_{A_A/A_A}\).

**BMSA on the Observed Scale.** An MILM was applied to the observed binary survival status \((0 = \text{alive}, 1 = \text{dead})\) to estimate genetic parameters on the observed scale. The MILM applied to survival status was equal to those defined for model [2] with the exception that here the MILM was applied to the observed data of survival status \((y)\), instead of to liability \((x)\).

**Inference on Number and Size of QTL with LOKI**

In comparison with the software iBay version 1.46 (Janss, 2008), which runs only single-QTL model, the software LOKI version 2.4.5 (Heath, 1997) can perform BMSA using multiple-QTL models. However, LOKI is tailored to perform BMSA only with continuous quantitative traits. So, we decided also to perform BMSA of survival days with the software LOKI with the aims of predicting the number of segregating QTL in the studied population, estimating the size of the QTL effect in units of survival days, and other relevant QTL parameters. We reasoned that by using 2 complementary Bayesian methods of CSA was going to safeguard against potential computational errors and provide a means of results validation.

The number of segregating QTL for BCWD resistance and the size of QTL effects were determined by performing BMSA on survival days with the software LOKI version 2.4.5 (Heath, 1997). Fish survival days postchallenge with \(F_p\) were modeled as a quantitative trait in a Bayesian MCMC segregation analysis. The analysis model included an unknown but estimated number of underlying biallelic QTL that contribute additively to survival days. Each locus is modeled as a biallelic locus, according to standard QTL methods, with genotype effects for QTL \(i\) parameterized as \(\pm a\) and \(d\) for the 2 homozygous and the heterozygous genotypes, respectively (Falconer and Mackay, 1996). The overall model is a standard MILM that combines QTL effects, animal polygenic effects, covariate effects, and environmental effects, with no interactions (Heath, 1997).

The segregation analyses were based on 8 independent MCMC runs with a total of 800,000 iterations. Each MCMC run had these general characteristics: total iterations = 100,000; burn-in period = 20,000 (the first portion of the total iterations that was discarded before starting the sampling of iterations); skip = 5 (a sample was saved from every 5 iterations); sampled iterations = 16,000; LM ratio = 0.2 (the LM ratio is a parameter in the LOKI program that sets the proportion of meiosis updates vs. locus updates); trait mean = 12; and residual variance = 45. Over many iterations, the parameter values accepted can be regarded as being drawn from the marginal posterior parameter distribution, which can be used to draw inferences about parameters of interest (Tierney, 1994). For our analyses, we used default values for the prior distribution on QTL locations (uniform over the genome) and for QTL allele frequencies (uniform on 0–1). The prior distribution on the number of QTL \((k)\) was assumed to be Poisson with mean 4. The prior for \(k\) was uniform on \([0, 20]\). The prior distribution of the QTL genotype effects \(a_i\) and \(d_i\) were assumed sampled from a normal distribution with mean 0 and variance \(\tau\), where \(\tau\) is determined by an interaction between the internal LOKI variables \(\tau_{\text{mode}}\) and \(\tau_{\beta} (\tau_{\beta})\). The value used for \(\tau_{\beta}\) was 45 because this parameter should be set approximately to the variance of the analyzed trait (Heath, 1997); the variance of survival days was ~44.6. The parameter \(\tau_{\text{mode}}\) was set to 2. We evaluated the impact of starting \(k\) values (0 and 10) and priors of \(\tau\) (1 and 45) on the posterior distribution of unknown model parameters. A graphical analysis was used to assess the mixing of MCMC iterations.

The records of survival days from 2005 families were fitted using this MILM, \(\mu = X_{n\times k} b_{q \times k} + Z_{n \times r} u_{r \times k} + \sum_{i=1}^{k} Q_{i} \alpha_{i} + e_{n \times k}\) [4], where \(y_{n \times k}\) is the vector of observations on survival days, \(n\) is the number of records, \(\mu\) is the overall mean, \(b_{q \times k}\) is the vector that included founder or genetic group as the fixed effect, \(q\) is the number of levels for the fixed effect, \(u_{r \times k}\) is the vector of polygenic effects, \(r\) is the number of levels for random animal effects, \(\alpha_{i}\) is a \((2 \times 1)\) vector of effects for the \(i\)th QTL (e.g., \(a_i\) and \(d_i\)), \(k\) is the number of QTL in the model, \(Q_{i}\) \((n \times 2)\) is the incidence matrix for the QTL effects, \(X_{n \times q}\) and \(Z_{n \times r}\) are incidence matrices connecting the unknowns in \(u_{r \times k}\) to the observations, and \(e_{n \times k}\) is the vector of random residual effects. We did not include tank in the BMSA model because the tank effect on survival days was nonsignificant in the 2005 data set. Although the continuous covariate BW had a significant effect on survival days of 2005 families, BW also had significant family effects.

The records on fish survival days are right-censored observations because survival data were recorded for 21 d postchallenge with \(F_p\), and about 30% of fish were alive at the end of the 2005 experiment. To account for
In the polygenic inheritance threshold model, the error variance was set to \(1.0\) of liability for the binary survival status.

The results from performing BMSA in the underlying scale of liability were approximately converted into the BMSA with the software iBay, we will only present parameters (results not presented). Thus, for the remaining of variance components and major locus parameters (results not presented). Thus, for the remaining of the MCMC iterations (results not presented).

### RESULTS

In the 2005 parental generation \(G_0\), the average mortality rate postchallenge with BCWD was \(\sim 0.70\). However, the mortality rates postchallenge with BCWD were much less in the 2007 first generation \(G_1\) and 2009 second generation \(G_2\). The average mortality rate was \(\sim 0.29\) and \(\sim 0.42\) for the 2007 and 2009 evaluations, respectively.

The BMSA on the observed scale of survival status and survival days resulted in poor mixing and convergence of the MCMC iterations for the unknown parameters (results not presented). Thus, for the remaining of the BMSA with the software iBay, we will only present results from performing BMSA in the underlying scale of liability for the binary survival status.

### Polygenic Model

Analysis of the 35 to 40 Gibbs chains with virtually 60 independent samples per chain indicated very good convergence for the unknown parameters polygenic variance and heritability because 1) the scale reduction factor for these 2 unknown parameters reached \(R = 1.0\); 2) the estimates of between-chain variance was smaller or close to the within-chain variance for each parameter across analyzed data sets; and 3) a relatively large effective number of samples per parameter was observed (Table 2). The estimated SD of the marginal posterior means of the polygenic heritability for survival status in the underlying scale of liability were \(0.53\) and \(0.73\) for the 2005 and combined 2005–2007–2009 data sets, respectively. These heritability estimates were significantly different from their corresponding HPDR\(_{95}\) boundaries (Table 2).

The difference in heritability estimates is likely due to the use of different methods and disease phenotypes (binary disease status vs. survival days).

### Mode of Inheritance of BCWD Resistance

A summary of estimated marginal posterior means for variance components and major locus parameters using nongenetic, polygenic, and mixed-inheritance models of binary survival status evaluated in 2005 families is presented in Table 3. Comparing the log of \(\log \left[ p(y|H_i) \right] \) of the tested models, there was not substantial statistical evidence to reject the hypothesis of no polygenic background [test model 1 vs. 2, BF \((H_2; H_1) = −0.3\)]. However, there was strong evidence to support the polygenic background or polygenic heritability.
In the mixed-inheritance threshold model the error variance was set to χ². Chains per model was variable and they are indicated in the table.

### Table 3. Estimated marginal posterior means for variance components and major gene (MG) parameters of binary survival status evaluated in 2005 families using mixed-inheritance threshold models in Bayesian segregation analysis

<table>
<thead>
<tr>
<th>Model</th>
<th>σ²</th>
<th>σ²</th>
<th>a</th>
<th>d</th>
<th>p</th>
<th>2 * (log_e [p(y/H)])</th>
<th>Model tested</th>
<th>BF</th>
<th>Chains</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. General</td>
<td>4.127</td>
<td>3.408</td>
<td>2.169</td>
<td>-0.007</td>
<td>0.56</td>
<td>0.74</td>
<td>-1.017.4</td>
<td>1 vs. 2</td>
<td>-0.3</td>
</tr>
<tr>
<td>2. General fixed</td>
<td>[0]^1</td>
<td>5.206</td>
<td>1.598</td>
<td>0.394</td>
<td>0.47</td>
<td>[0]</td>
<td>-1.017.1</td>
<td>2 vs. 3</td>
<td>281.8</td>
</tr>
<tr>
<td>3. Sporadic</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>-1.298.9</td>
<td>4 vs. 3</td>
<td>227.7</td>
</tr>
<tr>
<td>4. Polygenic</td>
<td>1.209</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>[0]</td>
<td>-1.071.3</td>
<td>8 vs. 7</td>
<td>6.0</td>
</tr>
<tr>
<td>5. Dominant A₂</td>
<td>1.087</td>
<td>1.383</td>
<td>1.131</td>
<td>1.131</td>
<td>0.50</td>
<td>0.49</td>
<td>-1.081.0</td>
<td>5 vs. 1</td>
<td>-63.6</td>
</tr>
<tr>
<td>6. Additive</td>
<td>1.061</td>
<td>0.319</td>
<td>1.007</td>
<td>[0]</td>
<td>0.55</td>
<td>0.48</td>
<td>-1.070.9</td>
<td>6 vs. 1</td>
<td>-53.5</td>
</tr>
<tr>
<td>7. Dominant A₁</td>
<td>1.185</td>
<td>2.313</td>
<td>1.143</td>
<td>-1.143</td>
<td>0.61</td>
<td>0.52</td>
<td>-1.064.9</td>
<td>7 vs. 1</td>
<td>-47.5</td>
</tr>
<tr>
<td>8. Codominant</td>
<td>1.135</td>
<td>1.149</td>
<td>1.412</td>
<td>0.132</td>
<td>0.56</td>
<td>0.50</td>
<td>-1.059.0</td>
<td>8 vs. 1</td>
<td>-41.5</td>
</tr>
</tbody>
</table>

1Bayesian segregation analysis of survival status performed with software iBay version 1.46 (Janss, 2008). The Gibbs sampler had these characteristics: number of iterations per chain = 1,200,000; burn-in period = 600,000; thinning = 10,000; and collected independent samples per chain = 60.

2Parameters: polygenic variance σ²; MG variance σ²; MG additive effect a; MG dominance effect d; p is frequency of disease-decreasing allele A₁; and b² is the polygenic model heritability σ² / (σ² + σ²). In the mixed-inheritance threshold model the error variance was set to σ² = 1.

3log_e of the marginal density under the fitted model H.

4Bayes factor BF (H₂; H₁) = p(y/H₂) / p(y/H₁) is the ratio of the marginal likelihood under one model to the marginal likelihood under a second model, and H₁ and H₂ are the 2 competing models.

5Value between brackets indicates the parameter was fixed to the value shown.

Model when compared with the sporadic or nongenetic effects model [test model 4 vs. 3, BF (H₂; H₁) = 227.7]. This last model comparison and results presented in Table 2 support the significant contribution of polygenic background effects in the inheritance of BCWD resistance.

To infer Mendelian transmission of a MG, 3 model comparisons were sequentially performed. First, the hypothesis of no MG effects was rejected [Table 3, test model 2 vs. 3, BF (H₂; H₁) = 281.8]. Second, the hypothesis of an environmental model can be ruled out because the estimated transmission probabilities (although with slight departure from expected Mendelian proportions) clearly do not overlap (Figure 2). This indicates that there is genetic transmission of BCWD resistance but this trait might have a complex mode of inheritance and be controlled by more than 1 MG.

Third, the 4 mixed-inheritance models (model 5 to 8) were rejected when tested against the general model 1 (Table 3), which suggests a lack of statistical support for a purely Mendelian transmission of 1 MG plus polygenic background effects in the inheritance of BCWD resistance. Although the hypothesis of a mixed-inheritance of 1 MG with codominant alleles plus polygenic background (model 8) was rejected (test model 8 vs. 1, BF (H₂; H₁) = -41.5), model 8 had the best log_e [p(y/H₁)] estimates among the 4 mixed-inheritance models. In the BMSA of the 2009 families (results not presented), the mixed-inheritance model of one MG with dominant A₁ resistance allele plus polygenic background effects had the best fit {log_e [p(y/H₁)] = -798.3} and the model of one MG with codominant alleles plus polygenic background effects had the second best fit {log_e [p(y/H₁)] = -810.4}. Although the 2007 and 2009 families were less informative for BMSA due to a reduced number of families that were selected for BCWD response, we performed BMSA of survival status in the 2009 families to determine the most likely mode of inheritance and to predict MG genotypes of the 2009 parents.

Overall, these results suggest that the inheritance of BCWD resistance might be controlled by 1 or more major loci with codominant alleles or dominant disease-resistance A₁ allele, or both, plus polygenic background effects in the studied population.

**Evidence of Major Genes Affecting BCWD Resistance**

The estimated marginal posterior mean, SD, left and right HPDR₉₅ for variance components, and MG parameters for survival status data evaluated in 2005 families for 5 mixed-inheritance models, with the exception of general fixed, polygenic, and sporadic models, are presented in Table 4. For the most plausible mixed-inheritance model for survival status, a MG with codominant alleles plus polygenic background effects (codominant model), the MG variance σ² is nonsignificant because the HPDR₉₅ for its variance does include zero. Similarly, the posterior distribution of additive
Figure 2. Estimated marginal posterior density of Mendelian transmission probabilities $\tau_{A_1/A_2A_2}, \tau_{A_1/A_2A_1}, \tau_{A_1/A_1A_2}, \tau_{A_1/A_1A_1}$ for binary survival status evaluated in 2005 families using a major gene (MG) inheritance threshold model in Bayesian segregation analysis (BMSA). A) General fixed model: the polygenic variance was fixed to $\sigma^2_u = 0$. The unknown parameters were as follows: MG additive effect $a$, MG dominance effect $d$, $p$ the frequency of disease-decreasing allele $A_1$, MG variance $\sigma^2_g$, and transmission probabilities $\tau_{A_1/A_1A_1}, \tau_{A_1/A_1A_2}, \tau_{A_1/A_2A_1}, \tau_{A_1/A_2A_2}$. B) Best-fitting MG model: The polygenic variance was fixed to $\sigma^2_u = 0$. The MG parameters $a$, $d$, and $p$ were fixed to values estimated with the best-fitting mixed-heritance threshold model (MG with codominant alleles $A_1$ and $A_2$ plus polygenic effects). The unknown parameters were $\tau_{A_1/A_1A_1}, \tau_{A_1/A_1A_2}, \tau_{A_1/A_2A_1}, \tau_{A_1/A_2A_2}$. A MG inheritance threshold model with codominant alleles $A_1$ and $A_2$ was used in BMSA with software iBay version 1.46 (Janss, 2008). The Gibbs sampler had these characteristics: number of iterations per chain = 1,200,000; burn-in period per chain = 600,000; thinning = 10,000; collected samples per chain = 60; total chains = 20; and total collected samples = 1,200. Color version available in the online PDF.
### Table 4. Estimated marginal posterior mean, 95% highest posterior density regions, and convergence assessment of iterative simulations for unknown model parameters\(^1\) of survival status using mixed-inheritance threshold model in BMSA\(^2\) of 2005 families

<table>
<thead>
<tr>
<th>Model and statistic</th>
<th>(\sigma_u^2)</th>
<th>(\sigma_g^2)</th>
<th>(a)</th>
<th>(d)</th>
<th>(p)</th>
<th>(a_{GSD})</th>
<th>(\sigma_a^2)</th>
<th>(R_g)</th>
<th>(R_u)</th>
<th>(R_{pu})</th>
<th>(h^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td>4.13</td>
<td>3.41</td>
<td>2.17</td>
<td>-0.01</td>
<td>0.56</td>
<td>0.83</td>
<td>2.29</td>
<td>0.33</td>
<td>0.50</td>
<td>0.83</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>2.61</td>
<td>3.71</td>
<td>1.45</td>
<td>2.46</td>
<td>0.28</td>
<td>0.47</td>
<td>3.18</td>
<td>0.20</td>
<td>0.18</td>
<td>0.11</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Left</strong></td>
<td>0.48</td>
<td>0.00</td>
<td>0.00</td>
<td>-4.74</td>
<td>0.08</td>
<td>-0.04</td>
<td>-0.76</td>
<td>-0.02</td>
<td>0.16</td>
<td>0.59</td>
<td>0.49</td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Right</strong></td>
<td>9.22</td>
<td>10.52</td>
<td>4.78</td>
<td>4.59</td>
<td>1.00</td>
<td>1.62</td>
<td>8.49</td>
<td>0.71</td>
<td>0.84</td>
<td>0.97</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Within-chain (\sigma^2)</strong></td>
<td>6.70</td>
<td>13.6</td>
<td>3.5</td>
<td>2.21</td>
<td>0.099</td>
<td>0.218</td>
<td>10.02</td>
<td>0.041</td>
<td>0.030</td>
<td>0.012</td>
<td>0.017</td>
</tr>
<tr>
<td><strong>Between-chain (\sigma^2)</strong></td>
<td>12.60</td>
<td>21.5</td>
<td>3.5</td>
<td>2.21</td>
<td>0.099</td>
<td>0.218</td>
<td>10.02</td>
<td>0.041</td>
<td>0.030</td>
<td>0.012</td>
<td>0.017</td>
</tr>
<tr>
<td><strong>Effective No. of samples</strong></td>
<td>1,116</td>
<td>1,331</td>
<td>1,244</td>
<td>549</td>
<td>1,640</td>
<td>1,091</td>
<td>1,557</td>
<td>1,251</td>
<td>1,129</td>
<td>1,300</td>
<td>1,083</td>
</tr>
<tr>
<td><strong>Additive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>1.06</td>
<td>0.32</td>
<td>1.01</td>
<td>0.55</td>
<td>0.86</td>
<td>0.32</td>
<td>0.12</td>
<td>0.43</td>
<td>0.55</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>0.65</td>
<td>0.56</td>
<td>0.88</td>
<td>0.32</td>
<td>0.67</td>
<td>0.56</td>
<td>0.14</td>
<td>0.14</td>
<td>0.10</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Left</strong></td>
<td>0.13</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.08</td>
<td>-0.15</td>
<td>-0.03</td>
<td>0.16</td>
<td>0.36</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Right</strong></td>
<td>2.17</td>
<td>1.13</td>
<td>2.76</td>
<td>0.97</td>
<td>2.10</td>
<td>1.13</td>
<td>0.40</td>
<td>0.69</td>
<td>0.74</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td><strong>Within-chain (\sigma^2)</strong></td>
<td>0.415</td>
<td>0.308</td>
<td>0.7</td>
<td>0.102</td>
<td>0.432</td>
<td>0.3</td>
<td>0.018</td>
<td>0.018</td>
<td>0.009</td>
<td>0.014</td>
<td></td>
</tr>
<tr>
<td><strong>Between-chain (\sigma^2)</strong></td>
<td>0.583</td>
<td>0.524</td>
<td>2.4</td>
<td>0.306</td>
<td>1.517</td>
<td>0.5</td>
<td>0.028</td>
<td>0.029</td>
<td>0.013</td>
<td>0.020</td>
<td></td>
</tr>
<tr>
<td><strong>Effective No. of samples</strong></td>
<td>1,495</td>
<td>1,235</td>
<td>663</td>
<td>Ne</td>
<td>698</td>
<td>508</td>
<td>1,235</td>
<td>1,342</td>
<td>1,361</td>
<td>1,509</td>
<td>1,430</td>
</tr>
<tr>
<td><strong>Dominant (A_1)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>1.18</td>
<td>2.31</td>
<td>1.14</td>
<td>-1.14</td>
<td>0.61</td>
<td>0.60</td>
<td>0.92</td>
<td>0.25</td>
<td>0.39</td>
<td>0.64</td>
<td>0.52</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>0.60</td>
<td>5.05</td>
<td>1.24</td>
<td>1.24</td>
<td>0.27</td>
<td>0.44</td>
<td>2.01</td>
<td>0.30</td>
<td>0.17</td>
<td>0.16</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Left</strong></td>
<td>0.40</td>
<td>0.00</td>
<td>0.00</td>
<td>-3.93</td>
<td>0.07</td>
<td>-0.06</td>
<td>-0.49</td>
<td>-0.06</td>
<td>0.03</td>
<td>0.40</td>
<td>0.34</td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Right</strong></td>
<td>2.30</td>
<td>12.62</td>
<td>3.88</td>
<td>0.25</td>
<td>1.00</td>
<td>1.16</td>
<td>4.96</td>
<td>0.86</td>
<td>0.66</td>
<td>0.97</td>
<td>0.72</td>
</tr>
<tr>
<td><strong>Within-chain (\sigma^2)</strong></td>
<td>0.362</td>
<td>24.376</td>
<td>1.475</td>
<td>0.071</td>
<td>0.187</td>
<td>3.878</td>
<td>0.086</td>
<td>0.029</td>
<td>0.026</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td><strong>Between-chain (\sigma^2)</strong></td>
<td>0.392</td>
<td>93.734</td>
<td>4.800</td>
<td>4.800</td>
<td>0.237</td>
<td>0.484</td>
<td>12.80</td>
<td>0.265</td>
<td>0.070</td>
<td>0.011</td>
<td></td>
</tr>
<tr>
<td><strong>Effective No. of samples</strong></td>
<td>2,052</td>
<td>577</td>
<td>682</td>
<td>682</td>
<td>670</td>
<td>856</td>
<td>672</td>
<td>720</td>
<td>918</td>
<td>751</td>
<td>1,862</td>
</tr>
<tr>
<td><strong>Codominant</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>1.13</td>
<td>1.15</td>
<td>1.13</td>
<td>0.50</td>
<td>0.78</td>
<td>0.68</td>
<td>0.18</td>
<td>0.41</td>
<td>0.59</td>
<td>0.49</td>
<td></td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>0.59</td>
<td>3.79</td>
<td>1.21</td>
<td>1.21</td>
<td>0.32</td>
<td>0.74</td>
<td>1.56</td>
<td>0.26</td>
<td>0.16</td>
<td>0.15</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Left</strong></td>
<td>0.23</td>
<td>0.00</td>
<td>0.00</td>
<td>-0.26</td>
<td>0.05</td>
<td>-0.16</td>
<td>-0.41</td>
<td>-0.06</td>
<td>0.04</td>
<td>0.35</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>HPDR(_{95}) Right</strong></td>
<td>2.11</td>
<td>7.84</td>
<td>3.69</td>
<td>3.71</td>
<td>1.00</td>
<td>2.37</td>
<td>3.23</td>
<td>0.81</td>
<td>0.66</td>
<td>0.93</td>
<td>0.71</td>
</tr>
<tr>
<td><strong>Within-chain (\sigma^2)</strong></td>
<td>0.352</td>
<td>13.744</td>
<td>1.403</td>
<td>0.096</td>
<td>0.524</td>
<td>2.3</td>
<td>0.064</td>
<td>0.026</td>
<td>0.022</td>
<td>0.011</td>
<td></td>
</tr>
<tr>
<td><strong>Between-chain (\sigma^2)</strong></td>
<td>0.336</td>
<td>52.184</td>
<td>5.533</td>
<td>5.533</td>
<td>0.569</td>
<td>2.191</td>
<td>11.1</td>
<td>0.252</td>
<td>0.080</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td><strong>Effective No. of samples</strong></td>
<td>2,202</td>
<td>553</td>
<td>533</td>
<td>533</td>
<td>502</td>
<td>435</td>
<td>538</td>
<td>675</td>
<td>755</td>
<td>1,926</td>
<td></td>
</tr>
</tbody>
</table>

Continued
vance due to the MG \(\left(\sigma_a^2\right)\) is nonsignificant because the HPDR\(_{95}\) for its variance does include zero.

The posterior mean and posterior SD (PSD) for the additive effect \(\hat{a}\) in genetic SD units was \(\sigma_{a_GSD} = 1.03 \pm 0.87\), which suggests that this is a relatively large size MG, although this effect might be nonsignificant given its relatively large PSD. In addition, the posterior distribution of \(\hat{a}\) and \(\sigma_{a_GSD}\) was nonsignificant because their HPDR\(_{95}\) did include zero. However, the posterior mean of the disease-resistance \(A_1\) allele frequency was \(p_{A_1} = 0.56\) and marginally significant because its HPDR\(_{95}\) does not include zero (Table 4). The proportion of phenotypic variance attributed to the MG effect was about \(R_g = 0.23\), which is nonsignificant because of its large PSD with HPDR\(_{95}\) that included zero (Table 4). The proportion of genetic variance explained by this MG is about 0.46.

In Figure 3, it is also shown that the phenotypic variance explained by this relatively large MG does not reach significance because the posterior density of the parameter \(R_g\) includes zero. However, the contribution of \(R_g\) on the proportion of phenotypic variance due to total genetic effects (\(R_g = R_p + R_s\)) is clearly supported by the posterior density of the parameter \(R_{gs}\), which has a larger global mode than the parameter \(R_g\).

Major trait loci that display either codominance of \(A_1\) and \(A_2\) alleles or a complete dominance of the \(A_1\) resistance allele plus polygenic background might affect resistance to BCWD in the NCCCWA rainbow trout breeding program based on the following results: 1) for the codominant model, partial or incomplete dominance of \(A_1\) or \(A_2\) alleles is ruled out because the HPDR\(_{95}\) for the difference between the additive effect and absolute dominance effect \(\left(\sigma_a - |\sigma_d|\right)\) covers zero (results not presented); and 2) the codominant and dominance of \(A_1\) resistance allele plus polygenic effect models were the mixed-inheritance models with best fit to survival status (Table 3).

In addition, we estimated the within- and between-chain variances, the effective number of samples, and the scale reduction factor \(\hat{R}\) for each estimated scalar parameter with the mixed-inheritance models (Table 4). For all the estimated parameters within each evaluated model, the difference between the within- and between-chain variances was relatively small. Also, the average number of effective samples was about 50\% (average = 1,058; minimum = 162; maximum = 2,202) from the expected 2,100 total independent samples when using the Gibbs sampler outlined in the methods section. From the 4 mixed-inheritance models, the codominant model had one of the largest number of effective samples (\(n = 1,155\)). Furthermore, all the unknown parameters for all the evaluated mixed-inheritance models had a scale reduction factor of \(\hat{R} = 1.0\). Overall, these results indicate that the mixing and con-
vergence of the MCMC iterations for the unknown parameters were very good in the BMSA of survival status.

**Inference on Transmission Probabilities**

For further validation of the evidence of MG for BCWD resistance, the Mendelian transmission probabilities \( \tau_{AA/AA}, \tau_{AA/AY}, \tau_{AY/AY} \) were estimated fitting MG and mixed-inheritance models in the BMSA of survival status evaluated in 2005 families (Table 5). For the MG models (general fixed model and best fitting MG model), clearly the left-right bounds of HPDR95 of the Mendelian transmission probabilities do not overlap. However, when using the best-fitting mixed-inheritance model, the transmission probabilities depart somewhat from the expected Mendelian transmissions and partially overlap. This can be attributed to effects of the polygenic variance on the marginal posterior distributions of the transmission probabilities.

The transmission probabilities resembled much closer to those expected under Mendelian transmission when using the best fitting MG model (Table 5). Under this MG model, the posterior mean (and PSD) transmission probabilities were 0.91 (0.06), 0.51 (0.06), and 0.06 (0.04), respectively (Table 5). Furthermore, when using the best-fitting MG model, we show conclusively that the posterior distributions of the transmission probabilities do not overlap (Figure 2B).

The simulated iterations to estimate the transmission probabilities reached convergence \( (\hat{R} = 1.0) \) when using the best-fitting MG and best-fitting mixed-inheritance models (Table 5). However, the convergence of the simulated iterations to estimate the transmission probabilities had poor convergence \( (\hat{R} > 1.1) \) when fitting the general fixed model.

Overall, because these transmission probabilities do not overlap, an environmental hypothesis for the inferred mixture distribution for BCWD resistance can be rejected. In this case, there is strong evidence in support of a genetic transmission of BCWD resistance, although it may not be strictly Mendelian. The distortion can be of genetic origin (i.e., the MG may be X-linked), the MG can have multiple alleles, or the true model can be digenic, and this results in an apparent distortion in the Mendelian transmission when the data

![Figure 3. Estimated marginal posterior density of proportion of total variance due to major gene (MG) effect \( (R_g) \), proportion of total variance due to polygenic effect \( (R_u) \), proportion of total variance due to MG effect plus polygenic effect \( (R_{gu}) \), and heritability due to polygenic effect \( (h^2_p) \) for binary survival status evaluated in 2005 families using a mixed-inheritance threshold model (MITM) in Bayesian segregation analysis (BMSA). A MITM of a MG with codominant alleles plus polygenic effects was used in BMSA with software iBay version 1.46 (Janss, 2008). The Gibbs sampler had these characteristics: number of iterations per chain = 1,200,000; burn-in period per chain = 600,000; thinning = 10,000; collected samples per chain = 60; total chains >20; and total collected samples >1,200. Color version available in the online PDF.](image-url)
Table 5. Mendelian transmission probabilities estimated from the marginal posterior distributions after Bayesian segregation analysis\(^1\) of binary survival status in 2005 families

<table>
<thead>
<tr>
<th>Statistic</th>
<th>General fixed model(^2)</th>
<th>Best fitting MG model(^3)</th>
<th>Best-fitting mixed-inheritance model(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(t_{AA/AA})</td>
<td>(t_{AA/Ab})</td>
<td>(t_{Ab/Ab})</td>
</tr>
<tr>
<td>Mean</td>
<td>0.89</td>
<td>0.48</td>
<td>0.08</td>
</tr>
<tr>
<td>SD</td>
<td>0.08</td>
<td>0.17</td>
<td>0.08</td>
</tr>
<tr>
<td>Left HPDR(^5)</td>
<td>0.75</td>
<td>0.22</td>
<td>0.00</td>
</tr>
<tr>
<td>Right HPDR(^6)</td>
<td>1.00</td>
<td>0.75</td>
<td>0.25</td>
</tr>
<tr>
<td>Within-chain (s^2)</td>
<td>0.0038</td>
<td>0.0084</td>
<td>0.0031</td>
</tr>
<tr>
<td>Between-chain (s^2)</td>
<td>0.1772</td>
<td>1.2540</td>
<td>0.1604</td>
</tr>
<tr>
<td>Effective No. samples</td>
<td>56</td>
<td>18</td>
<td>51</td>
</tr>
</tbody>
</table>

\(^1\) Bayesian segregation analysis of binary survival status was performed with software iBay version 1.46 (Janss, 2008). The Gibbs sampler had these characteristics: number of iterations per chain = 1,200,000; burn-in period per chain = 600,000; thinning = 10,000; collected samples per chain = 60; total chains = 20; and total collected samples = 1,200.

\(^2\) General fixed model. The polygenic variance was fixed to \(s_u^2 = 0\). The unknown parameters were MG additive effect \(a\), MG dominance effect \(d\), \(p\) the frequency of disease-decreasing allele \(A_1\), MG variance \(\sigma^2_u\) and transmission probabilities \(t_{AA/AA}, t_{AA/Ab}, t_{Ab/Ab}\).

\(^3\) Best-fitting major gene (MG) model. The MG parameters \(a\), \(d\), and \(p\) were fixed to values estimated with the best-fitting mixed-heritance model (codominant MG alleles plus polygenic effects), and polygenic variance was fixed to \(s_u^2 = 0\). The unknown parameters were \(t_{AA/AA}, t_{AA/Ab}, t_{Ab/Ab}\).

\(^4\) Best-fitting mixed-inheritance model. The MG parameters \(a\), \(d\), \(p\), and \(\sigma^2_u\) were fixed to values estimated with the best-fitting mixed heritance model (codominant MG alleles plus polygenic effects). The unknown parameters were \(t_{AA/AA}, t_{AA/Ab}, t_{Ab/Ab}\).

\(^5\) HPDR\(^95\) is the 95% highest posterior density region.

\(^6\) \(\hat{\text{R}}\) is the scale reduction factor. The \(\hat{\text{R}}\) should be around ~1.0 (or at most ≤1.1) to indicate convergence of the iterative simulations for the unknown parameter.
Figure 4. Assessing the mixing of Markov chain Monte Carlo (MCMC) iterations for unknown parameter total genetic variance (variance due to all QTL plus additive polygenic variance) in Bayesian segregation analysis (BMSA) of survival days evaluated in 2005 families. The BMSA of survival days was performed with software LOKI version 2.4.5 (Heath, 1997). The MCMC sampler had these general characteristics per run: total iterations = 100,000; burn-in period = 20,000 (the first portion of the total iterations that was discarded before starting the sampling of iterations); skip = 5 (a sample was saved from every 5 iterations); sampled iterations = 16,000; number of QTL currently estimated $k \in [0, 20]$; LM ratio = 0.2 (the LM ratio is a parameter in the LOKI program that sets the proportion of “meiosis” updates vs. “locus” updates); tau mode = 2; trait mean = 12.0; residual variance = 45.0; and mean $k = 4$. The mixing of MCMC iterations for runs with 2 different priors for parameters $\tau_\beta$ and starting value of $k$ is shown in panels A to D: (A) $\tau_\beta = 45$ and $k = 0$; (B) $\tau_\beta = 45$ and $k = 10$; (C) $\tau_\beta = 1$ and $k = 0$; and (D) $\tau_\beta = 1$ and $k = 10$.

Table 6. Estimated marginal posterior mean of unknown model parameters from Bayesian segregation analysis\(^1\) of survival days in 2005 families

<table>
<thead>
<tr>
<th>MCMC sampler(^2)</th>
<th>QTL(^3)</th>
<th>Variance(^4)</th>
<th>Variance due to all QTL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Run $\tau_3$</td>
<td>Start $k$</td>
<td>$k$ SD Size SD</td>
<td>Total genetic SD Polygenic SD Residual SD</td>
</tr>
<tr>
<td>1</td>
<td>45 0</td>
<td>10 1.4 1.8 2.1</td>
<td>90.5 2.0 9.4 1.5 0.17 0.07 0.10</td>
</tr>
<tr>
<td>2</td>
<td>45 0</td>
<td>8 1.3 1.8 1.7</td>
<td>58.4 0.7 7.6 1.0 0.25 0.13 0.13</td>
</tr>
<tr>
<td>3</td>
<td>45 10</td>
<td>6 0.2 2.1 1.7</td>
<td>49.5 0.7 5.1 0.2 0.24 0.12 0.10</td>
</tr>
<tr>
<td>4</td>
<td>45 10</td>
<td>6 0.2 2.1 1.7</td>
<td>49.7 0.7 5.1 0.2 0.24 0.11 0.10</td>
</tr>
<tr>
<td>5</td>
<td>1 0</td>
<td>7 2.0 1.7 1.9</td>
<td>58.7 2.4 9.4 1.1 0.33 0.13 0.16</td>
</tr>
<tr>
<td>6</td>
<td>1 0</td>
<td>7 2.0 1.7 1.9</td>
<td>58.6 2.4 9.4 1.1 0.33 0.13 0.16</td>
</tr>
<tr>
<td>7</td>
<td>1 10</td>
<td>9 2.3 1.6 1.6</td>
<td>56.4 2.7 9.2 1.2 0.34 0.13 0.16</td>
</tr>
<tr>
<td>8</td>
<td>1 10</td>
<td>9 2.3 1.6 1.6</td>
<td>56.2 2.6 9.3 1.2 0.34 0.13 0.16</td>
</tr>
</tbody>
</table>

\(^1\) Bayesian segregation analysis of survival days was performed with software LOKI version 2.4.5 (Heath, 1997).

\(^2\) The Markov chain Monte Carlo (MCMC) sampler had these general characteristics per run: total iterations = 100,000; burn-in period = 20,000 (the first portion of the total iterations that was discarded before starting the sampling of iterations); skip = 5 (a sample was saved from every 5 iterations); sampled iterations = 16,000; number of QTL currently estimated $k \in [0, 20]$; LM ratio = 0.2 (the LM ratio is a parameter in the LOKI program that sets the proportion of “meiosis” updates vs. “locus” updates); tau mode = 2; trait mean = 12.0; residual variance = 45.0; and mean $k = 4$. We evaluated 2 values for $\tau_\beta$ ($\tau_3$) = 45.0 and 1.0; we also evaluated 2 starting values of $k$ = 0 and 10. The trait loci effects have a normal prior which by default is $N(0; \tau)$, where $\tau$ is determined by an interaction between the internal LOKI variables tau mode and $\tau_\beta$.

\(^3\) Posterior mean of $k$ number of QTL; size of QTL in survival days; and SD is SD of posterior mean.

\(^4\) Total genetic variance is equal to variance due to all QTL plus additive polygenic variance. $R_{\text{polyg}}$ is proportion of phenotypic variance due to additive polygenic effects.
are fitted using an autosomal biallelic model. Thus, it can be accepted that a simple autosomal codominant gene is not the most plausible mode of inheritance for BCWD resistance.

**Inference on Number and Size of QTL Effects with LOKI**

In general, the graphical analysis of the MCMC iterations suggests a good mixing for all unknown parameters when performing BMSA with LOKI software. In Figure 4, we present the mixing of MCMC iterations for the most relevant parameter in this study: total genetic variance (variance due to all QTL plus additive polygenic variance). For this parameter, the mixing of MCMC iterations was better when using \( \tau_\beta = 45 \) (Figure 4A, B) than when using \( \tau_\beta = 1 \) (Figure 4C, D).

Based on results of BMSA with LOKI, the estimated marginal posterior means for evaluated MCMC samplers support that 6 to 10 QTL might be segregating in this rainbow trout population (Table 6). The size of the QTL effect is between 1.6 and 2.1 survival days, and the allele frequency of this relatively large effect QTL is about 0.50. These QTL explained 83 to 89% of the phenotypic variance of BCWD survival. The genetic variance explained by these QTL is only marginally greater than the phenotypic variance due to the relatively small estimate of additive polygenic variance and very small estimate of residual variance (Table 6). The posterior means of these parameters have significant support because their corresponding 95% empirical confidence limits did not include zero (results not presented). Overall, the results from performing BMSA with the software LOKI provide additional statistical evidence that supports the contribution of 6 to 10 QTL in the inheritance of BCWD resistance in this rainbow trout population.

**DISCUSSION**

This study presents the first evidence of major trait loci affecting BCWD resistance in rainbow trout using large FS families and Bayesian methods of segregation analysis. The results from BMSA of survival traits suggest that BCWD resistance in rainbow trout is hereditary and is influenced by genetic factors transmitted from parents to offspring. The BMSA of BCWD survival traits supports that 6 to 10 QTL of relatively large effect with either codominant or dominant disease-resistant alleles plus polygenic background effects might be underlying the genetic variation of BCWD resistance in the sampled rainbow trout families.

**Average Mortality Rate Across Generations**

The mortality rate due to BCWD was much greater in 2005 families in comparison with evaluations performed in 2007 and 2009. The mortality rates were 0.70, 0.29, and 0.42 in families evaluated during 2005, 2007, and 2009, respectively. The changes in mortality rate across generations might be due to selection effects and differences in environmental exposure to disease (e.g., challenge dose, BW). The 2005 families were randomly sampled from the NCCCWA selective breeding program, and they were neither evaluated nor selected for BCWD performance. In subsequent analyses, we selected families that were highly resistant and highly susceptible to BCWD after 2005 and 2007 family evaluations because we wanted to develop informative families to map QTL for BCWD.

**Mode of Inheritance of BCWD Resistance**

In the 2005 base population, the most likely mode of inheritance for BCWD was the mixed inheritance of a codominant MG plus polygenic background effects, and the second best competing model was a mixed inheritance of a dominant MG for disease resistance plus polygenic effects. However, after 2 generations of breeding to produce BC and F2 crosses for QTL mapping, we observed in the 2009 families that the most likely mode of inheritance was the mixed inheritance of a dominant MG for disease resistance plus polygenic effects, and the second best competing model was a mixed inheritance of a codominant MG plus polygenic effects. These changes in the predicted QTL mode of inheritance across generations suggest that the population under study might be segregating more than one major QTL, each with a distinct mode of inheritance. It is likely that these QTL may have alleles interacting either as codominant or dominant alleles in determining the degree of BCWD resistance.

Given these competing QTL modes of inheritance, the degree of dominance \((D = d / a)\) ranged from \(-1.0\) to 0.1 in this population. Based on the criteria proposed by Stuber et al. (1987), the BCWD QTL mode of inheritance ranged from complete dominance of \(A_1\) allele to partial dominance of \(A_2\) allele (software iBay uses the \(A_2\) phenotype increasing allele as reference allele). This range of degree of dominance for detected QTL was also observed for QTL affecting vegetative traits of tomatoes (deVicente and Tanksley, 1993). Similarly, most of the QTL affecting Marek’s disease susceptibility in chickens were recessive with a few exhibiting partial dominance, dominance, and overdominance (Vallejo et al., 1998).

The range of degree of dominance for QTL that might be segregating in this rainbow trout population contrasts with the complete dominance or recessivity normally shown by mutations with major phenotypic effects. Presumably, the alleles of QTL responsible for quantitative variation actually produce quantitative differences in, rather than total absence of, the protein produced by the locus (Falconer and Mackay, 1996). Based on our BMSA results, we should not expect detecting a single major QTL for resistance to BCWD.
In this rainbow trout population as recently reported for infectious pancreatic necrosis in Atlantic salmon (Houston et al., 2009; Moen et al., 2009). Instead, we expect mapping 6 to 10 QTL explaining 83 to 89% of the phenotypic variance in this rainbow trout population. These QTL will enhance selective breeding efforts to develop rainbow trout resistant to BCWD.

The results from performing BMSA with different algorithms implemented in computer applications iBay and LOKI complemented well in revealing the genetic architecture of BCWD resistance in rainbow trout. A single-QTL model of BMSA with software iBay suggests that more than one MG with codominant or dominant disease-resistance alleles plus polygenic background effects may be controlling the inheritance of BCWD resistance, with each QTL explaining about 23% of the phenotypic variance of BCWD. Similarly, a multiple-QTL model of BMSA with LOKI suggests that the resistance to BCWD might be controlled by 6 to 10 QTL, with largest effect QTL explaining about 15% of the phenotypic variance (results not presented). However, in contrast to iBay which provides strong support for polygenic background effects in the inheritance of BCWD resistance, the QTL estimated with LOKI explains large portion of the phenotypic variance (89%), and provides small polygenic variance and very small residual variance. In this study, we might have carry-over tank effects confounded with family effects because fish families are initially raised in separate tanks. These confounded effects may have up-biased the estimate of genetic variance and decreased the residual variance.

In the 2005–07–09 combined families, tank had a significant effect on survival days and was included in the BMSA model run with LOKI. In this BMSA, the residual variance was also very small in comparison with the total genetic variance (results not presented). This highlights that whether tank is included or not in the BMSA model, the results will remain more or less the same: the genetic variation of BCWD resistance may be controlled by few QTL that explain a large portion of phenotypic trait variance. Whether there are 6 or 10 loci may remain somewhat elusive, but we would say that there is good evidence for oligogenic inheritance of BCWD in these rainbow trout families.

Because all 3-generation animals are linked by pedigrees, we thought the combined data set 2005–07–09 was the most informative for BMSA. However, we observed 2 main drawbacks in the 2007 and 2009 families. First, the proportion of censored data was much greater in 2007 (0.71) and 2009 (0.58) families in contrast to 2005 (0.30) families. Second, the number of parents that were selected for BCWD survival in 2007 (24) and 2009 (19) families was reduced in comparison with the 2005 (113) families. Thus, we consider that the 2005 families are the most informative for BMSA of BCWD in this study. The BMSA results from 2007 and 2009 families were mainly useful to predict QTL genotypes and design crosses to develop informative families for QTL mapping.

In general, the results presented here support a pedigree-based linkage analysis approach for the discovery of QTL underlying the genetic variance of BCWD resistance in rainbow trout. The F2 and BC families identified with BMSA of 2009 families will be used in genome-wide linkage scans for QTL affecting BCWD resistance in this NCCWA rainbow trout population.

**Nonsignificant Major QTL Effects**

In this study with the software iBay, we have shown evidence for major QTL effects on the inheritance of BCWD resistance, which were nonsignificant in BMSA of binary survival status. We think this outcome can be attributed to several constraints in the BMSA of this binary trait. First, in comparison with the analysis of well-behaved normally distributed continuous quantitative traits, the segregation and linkage analysis of binary observations is a more challenging task that requires the use of appropriate modeling methods as the MITM used in this study. There is also a general consensus that segregation/linkage and QTL analysis using continuous quantitative trait is more powerful than using dichotomous observations. So, there is still a need of further improvements on current methods of segregation/linkage analyses using binary data in complex pedigrees of arbitrary size to increase statistical power.

Second, there were several limitations in the current implementation of the software iBay. This software only allows the use of single-QTL models. In the likely event that multiple QTL are controlling the inheritance of BCWD resistance, then this application might have a limitation on the BMSA. In addition, the current version of iBay does not account for the use of censored data in the BMSA. We should note that the 2005 data set had about 30% of right-censored observations. We do not know the consequences of not accounting for the use of censored data on the BMSA results, and this type of research is out of the scope of this study. However, we noticed that the estimated posterior density of most of the unknown MG parameters have a right-skewed distribution and we wonder if this might be a consequence of using right-censored data.

Third, in making a more in-depth study of the family mean-variance patterns, because this is the main source of information for the CSA, there was a significant scale of measurement effect or scaling effect (i.e., there is not family mean-variance independence) in survival status and survival days (results not presented). As suggested by Lynch and Walsh (1997), we performed a Kleckowski’s data transformation with the hope of eliminating that mean-variance linear relationship with unsuccessful outcome. Therefore, we decided to use survival raw data in the BMSA, reasoning also that if a MG was segregating in the studied sample, we did not want to erase that MG effect by performing a data transformation. Intuitively, regardless of randomizing every experimental variable to diminish this scaling effect, it seems that this mean-variance linear relationship is
expected in disease survival data when using highly heterozygous and segregating individuals sampled from outbred populations; the variance of survival days is expected to be larger in susceptible families relative to resistant families.

**Implications of Poor Mixing and Convergence of MCMC Iterations**

Poor convergence observed for a few parameters estimated with general fixed models has minimal impact on the conclusions. Poor mixing of the MCMC iterations is a potential problem for the fit of MG models; mixing refers to the possibility of the Markov chain to move through the parameter space; for the genotypes, this implies that the chain should be able to make transitions between different genotypic configurations (Janss, 2008). It is unlikely that lock-up of Gibbs chains in subspaces of the parameter space occurred because multiple chains were run and compared and the general model had better support than the mixed-inheritance models 5 to 8. Furthermore, the evidence to support MG and polygenic effects and variance components was based on analysis of marginal posterior distributions of polygenic and mixed-inheritance models that had very good mixing and convergence in the MCMC computations. However, we are aware of the risk on predicting incorrect genetic models when using methods of CSA that are usually not robust to violations of assumptions (Lynch and Walsh, 1997). Ultimately, the molecular approach will allow confirming or rejecting the presence of a Mendelian locus (Jarvik, 1998).

**Parameter Estimates Varies with MCMC Sampler**

We evaluated 4 MCMC samplers in the BMSA of survival days with the software LOKI to 1) identify samplers with good mixing of the MCMC iterations for the unknown parameters and 2) determine the impact of priors set for unknown model parameters on the results of the BMSA. Overall, the mixing of the MCMC iterations using long runs of 100,000 total iterations was good for all MCMC sampling schemes. Wijssman et al. (2004) performed segregation and linkage analyses on late-onset Alzheimer disease based on 500,000 MCMC iterations with the software LOKI; they suggested that long runs are needed for analysis of censored traits and that runs of this length give highly reproducible results. However, we noticed that the mixing of iterations was much better when setting the parameter $\tau_3 = 45$ (prior variance of QTL genotype effects), which should be set approximately to the variance of the trait in study (Heath, 1997). So, we consider that the results from the runs 1 to 4 with parameter $\tau_3 = 45$ should provide results that better describe the underlying genetics of QTL affecting BCWD resistance in this rainbow trout population.

**Poor Mixing of MCMC Iterations for BMSA on Observed Scale**

With the software iBay, we decided to perform BMSA on the observed scale of survival status and survival days to have estimates of their unknown parameters on the observed scale using a MILM. However, after testing few MCMC sampling schemes, we noticed that the mixing of the MCMC iterations was poor when performing BMSA of both traits on the observed scale (results not presented). The poor mixing of MCMC iterations when performing BMSA of survival status on the observed scale can be expected because the MILM incorrectly treats this binary trait as a continuous quantitative trait. In contrast, as shown in this study, the MCMC iterations had very good mixing and convergence when using an appropriate MITM in the BMSA of binary survival status.

The poor mixing of the MCMC iterations on BMSA of survival days using MILM with iBay might have been caused by the use of censored data in the BMSA. We should note that the failure time data used in the BMSA had 30 and 58% of right-censored observations in 2005 and 2009 family evaluations, respectively. We did not account for this fact in the BMSA model because the current implementation of iBay does not allow accounting for the use of censored data. We expect to include this improvement in a new release of the software iBay. In addition, survival days had a significant scale of measurements effect (i.e., family mean-variance linear relationship), and this might have also contributed toward a poor mixing of the MCMC iterations.

**Conclusions**

In this study, Bayesian methods of CSA are shown to be informative to detect statistical evidence for major trait loci that might affect the genetic variation of BCWD resistance, an economically important disease in rainbow trout aquaculture. The BMSA of BCWD survival data provided information on the likely mode of inheritance of BCWD resistance, number of segregating QTL, size of the QTL and polygenic background effects, and heritability of survival to postchallenge with $F_p$ in the studied rainbow trout population. These findings support a pedigree-based linkage analysis approach, and genome wide association scans if tools and reagents are available, to the discovery of major trait loci underlying the genetic variation of resistance to BCWD in rainbow trout.

**LITERATURE CITED**


