Variance and covariance estimates for resistance to bacterial cold water disease and columnaris disease in two rainbow trout breeding populations¹

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ABSTRACT: Family-based selective breeding can be an effective strategy for controlling diseases in aquaculture. This study aimed to estimate (co) variance components for resistance to bacterial cold water disease (BCWD) and columnaris disease (CD) in two unrelated rainbow trout nucleus breeding populations: the USDA, ARS, National Center for Cool and Cold Water Aquaculture odd-year line (ARS-Fp-R), which has been subjected to five generations of selection for improved resistance to BCWD, and the Troutlodge, Inc., May-spawning odd-year line (TLUM), which has been selected for improved growth performance but not for disease resistance. A total of 46,805 and 27,821 pedigree records were available from both populations, respectively. Between 44 and 138 families per generation and population were evaluated under controlled BCWD and CD challenges, providing 32,311 and 17,861 phenotypic

records for BCWD resistance, and 13,603 and 9,413 for CD resistance, in the ARS-Fp-R and TLUM populations, respectively. A two-trait animal threshold model assuming an underlying normal distribution for the binary survival phenotypes was used to estimate (co)variance components separately for each population. Resistance to BCWD (h^2 = 0.27 ± 0.04 and 0.43 ± 0.08) and CD (h^2 = 0.23 ± 0.07 and 0.34 ± 0.09) was moderately heritable in the ARS-Fp-R and TLUM populations, respectively. The genetic correlation between the resistance to BCWD and CD was favorably positive in the ARS-Fp-R (0.40 ± 0.17) and TLUM (0.39 ± 0.18) populations. These findings suggest that both disease resistance traits can be improved simultaneously even if genetic selection pressure is applied to only one of the two traits.

Key words: bacterial cold water disease, columnaris disease, disease resistance, genetic correlation, heritability, rainbow trout

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INTRODUCTION

Infectious diseases accounted for 94% of the total loss of all trout intended for sale in the United States during 2017 (NASS, 2018). Bacterial cold water disease (BCWD), caused by the Gram-negative bacterium *Flavobacterium psychrophilum*, affects a broad range of host species and is one of the most important salmonid pathogens due to its high mortality rate and economic impact (Nematollahi et al., 2003; Starliper 2011; Wahli and Madsen 2018). The disease often occurs at colder temperatures (4 to 10 °C) and is also referred to as rainbow trout fry syndrome due to elevated mortality in young trout. Columnaris disease (CD), caused by the Gram-negative bacterium *Flavobacterium columnare*, is an emerging problem in rainbow trout aquaculture. It also affects a broad range of host species, but the disease occurs at warmer temperatures (≥ 12 °C) compared to BCWD (Declercq et al., 2013). Currently, there are no licensed vaccines for *F. psychrophilum* or *F. columnare* in rainbow trout (USDA 2016), and prevention and control of these diseases have generally been limited to management practices and application of chemical and antibiotic treatments. Previous studies have demonstrated that BCWD resistance is heritable and can be improved in rainbow trout populations by selective breeding (Henry et al., 2005; Silverstein et al., 2009; Leeds et al., 2010; Wiens et al., 2013a, 2018; Vallejo et al., 2017), but only limited data are available to support selective breeding for CD resistance and to assess the genetic correlation of resistance to these two diseases in rainbow trout (Evenhuis et al. 2015). Objectives of the current study were to estimate (co)variance parameters for BCWD and CD resistance using multi-generation data from two unrelated nucleus rainbow trout populations: the ARS-Fp-R line (Evenhuis et al. 2015), which has undergone selection for improved BCWD resistance, and a commercial nucleus population that has not been previously selected for disease resistance.

MATERIALS AND METHODS

Resource Populations

The Institutional Animal Care and Use Committee (Leetown, WV) reviewed and approved

all animal husbandry practices and disease challenge protocols per standards set forth in the USDA, ARS Policies and Procedures 130.4.v.3 titled “Institutional Animal Care and Use Committee.”

Resistance to BCWD and CD was assessed in two pedigreed, commercially relevant rainbow trout nucleus populations: the USDA, ARS, National Center for Cool and Cold Water Aquaculture (NCCCWA; Leetown, WV) odd-year line (ARS-Fp-R) and the Troutlodge, Inc., Sumner Lake, WA, May-spawning odd-year line (TLUM). Both populations have been closed to outside germplasm and propagated by producing a target of 100 nucleus families each generation. The ARS-Fp-R line was developed by scientists at the NCCCWA beginning in 2005 and to date has been subjected to five generations of family-based selective breeding for improved BCWD resistance (Silverstein et al., 2009; Leeds et al., 2010). Germplasm from the ARS-Fp-R line has been released to domestic stakeholders for commercial propagation. The TLUM odd-year line is one of eight domestic rainbow trout nucleus populations maintained by Troutlodge, Inc., the world’s leading supplier of eyed salmonid eggs. Breeding objectives in the TLUM line have historically focused on growth-related traits, and to date this line has not been selected for improved disease resistance.

Disease Resistance Phenotyping

All posthatch rearing practices and disease challenges were conducted at the NCCCWA as previously described for BCWD (Silverstein et al., 2009; Leeds et al., 2010; Vallejo et al., 2017) and CD (Evenhuis et al., 2015). Nucleus TLUM families were shipped to the NCCCWA as eyed eggs and reared as separate families following standard NCCCWA culture practices until the time of disease challenge. Briefly, pathogen-naïve fry were challenged with CD by immersion in a 1-h static bath of a virulent strain (CSF298-10) of *F. columnare*, a genomovar I isolate (Evenhuis et al., 2014), at ~63 d posthatch (BW ~1.3 g). The target challenge dose was 2.0×10^6 cfu/mL of water. Fry were reared in heated flow-through spring water (16 °C) for the duration of the 21-d CD challenge period and mortalities were removed from each

tank and recorded daily. A separate sample of pathogen-naïve fry from each family were anesthetized in 90 mg·L⁻¹ of tricaine methanesulfonate (Tricaine-S; Western Chemical, Ferndale, WA) and challenged with BCWD by intraperitoneal injection of a virulent strain (CSF259-93) of *F. psychrophilum* at ~84 d posthatch (BW ~2.9 g). The target challenge dose was $\sim 3.1 \times 10^6$ cfu/g of BW. Fry were reared in flow-through spring water at ambient temperature (~12.9 °C) for the duration of the 21-d BCWD challenge period and mortalities were removed from each tank and recorded daily. For both disease challenges, fry that survived for the 21-d postchallenge period were categorized as 2, and categorized as 1 if the fry died as a result of the challenge. Table 1 summarizes the number of families, the number of challenge tanks, average BW at the time of challenge, and average survival rate for each disease challenge $\times$ population $\times$ generation subclass. Variance attributable to challenge tank effects is generally larger for the immersion-based CD challenge (Evenhuis et al., 2015) than the injection-based BCWD challenge (Leeds et al., 2010), thus the number of challenge tank replicates per family was larger for the CD challenge (two or three replicates) than the BCWD challenge (one or two replicates). The disease challenges also included families from additional reference genetic lines that are not reported in the current study, therefore not every family was replicated in two and three tanks for the BCWD and CD challenges, respectively, due to the finite number of challenge tanks available. The number of replicates per family was based on fry availability and to ensure adequate representation of sires and parental families. All disease challenges had a target of 40 fry per challenge tank with

the exception of the 2015 TLUM CD challenge (20 fry per challenge tank).

Data and Analyses

Survival data were available from a total of 32,311 and 17,861 fry from the BCWD challenges, and 13,603 and 9,413 fry from the CD challenges, for the ARS-Fp-R and TLUM populations, respectively. A total of 46,805 and 27,821 animals were included in the pedigree for the ARS-Fp-R and TLUM populations, respectively.

An animal threshold model assumed an underlying normal distribution to estimate the (co)variance components of BCWD and CD resistance status. (Co)variance components were estimated separately for the ARS-Fp-R and TLUM populations. For both disease challenges, the models included the fixed effects of year and random effects of animal, full-sib family, and challenge tank nested within family (family/tank). In addition, fixed effects of row and system for the CD challenge were included in the models to account for potential systematic environmental effects on the waterborne challenge. The underlying distribution (U) was determined using the following model:

$$U = \mu + Xb + Wf + Zt + Ha + e$$

where U is the vector of underlying distribution of phenotype y , μ is the mean, b is the vector of fixed effects, f is the vector of random effect of family, t is the vector of random effect of tank/family, a is the vector of random additive direct genetic effects, and e is the vector of unknown residual random effects; X , W , Z , and H are the incidence matrices, and relate to the effects in b , f , t , a and e , respectively. The

Table 1. Descriptive statistics for the disease challenge studies conducted using the National Center for Cool and Cold Water Aquaculture (ARS-Fp-R) and Troutlodge (TLUM) populations

Population	Item	Year and disease resistance trait ¹							
		2005 (0)	2007 (1)	2009 (2)	2011 (3)	2013 (4)		2015 (5)	
		BCWD	BCWD	BCWD	BCWD	BCWD	CD	BCWD	CD
ARS-Fp-R	No. of records	4,496	3,921	5,472	4,578	7,018	5,229	6,826	8,374
	Survival rate	30%	75%	82%	71%	77%	12%	85%	74%
	No. of families	71	63	96	75	100	44	97	99
	No. of tanks	114	99	137	116	177	132	173	213
	Mean BW, g	2.34	2.38	4.20	3.32	2.52	0.70	2.97	1.30
TLUM	No. of records	—	—	—	—	7,893	5,427	9,968	3,986
	Survival rate	—	—	—	—	45%	12%	33%	38%
	No. of families	—	—	—	—	102	52	138	100
	No. of tanks	—	—	—	—	202	142	250	200
	Mean BW, g	—	—	—	—	2.19	0.93	3.45	2.81

¹Generations of selection for improved resistance to bacterial cold water disease (BCWD) for the ARS-Fp-R population are given in parenthesis. CD = columnaris disease.

response variable y was modeled with the following distribution:

$$f(y|U) = \prod_{i=1}^n I(U_i < t_1) I(y_i = 1) + I(t_1 < U_i) I(y_i = 2)$$

where n is the number of records, t_1 is the threshold that defined the two categories and I is an indicator function that takes value 1 if the fish died in the disease challenge, otherwise the value is 2. The procedure is a nonlinear transformation of best linear unbiased estimation and best linear unbiased prediction. The additive direct genetic component was assumed to be correlated, whereas random family, family/tank, and residual effects were assumed to be uncorrelated.

Using Bayesian inference, a uniform prior distribution was adopted for the fixed effects, whereas an inverted Wishart distribution was a priori assumed for the additive genetic direct, family, tank/family and residual covariance structures:

$$F|_{\nu_f}, V_f \sim IW(\nu_f V_f, \nu_f),$$

$$T|_{\nu_t}, V_t \sim IW(\nu_t V_t, \nu_t),$$

$$G|_{\nu_a}, V_a \sim IW(\nu_a V_a, \nu_a),$$

and

$$R|_{\nu_e}, V_e \sim IW(\nu_e V_e, \nu_e)$$

where we assumed the known hyperparameters of ν_i and V_i ($i \in \{f, t, a, e\}$). The inverted Wishart distribution is reduced to an improper uniform distribution if $\nu_i \rightarrow 0$; $-(k-1)$ and $V_i \rightarrow 0$ with $k \rightarrow 3$ (Sorensen and Gianola, 2002). The prior distributions of the additive genetic direct and residual effects followed a multivariate normal distribution. To make the parameters in the model identifiable, the residual variances for CD and BCWD were set to 1 (Sorensen et al., 1995).

The analysis consisted of a single chain of 1 million cycles with a conservative burn-in of 500,000 cycles, taking a sample every 10 iterations. Therefore, 50,000 samples were used to obtain the parameters. The bivariate analyses to estimate the (co)variance components and breeding values were run using the THRGIBBS1F90 program (Tsuruta and Misztal 2006) with an option to store solutions, whereas the POSTGIBBSF90 program (Tsuruta and Misztal 2006) was used to check convergence and to calculate posterior means.

Table 2. Heritabilities (diagonal) and genetic correlations (above diagonal) of resistance to bacterial cold water disease (BCWD) and columnaris disease (CD) in the National Center for Cool and Cold Water Aquaculture (ARS-Fp-R) and Troutlodge (TLUM) populations

	ARS-Fp-R		TLUM	
	BCWD	CD	BCWD	CD
BCWD	0.27 ± 0.04	0.40 ± 0.17	0.43 ± 0.08	0.39 ± 0.18
CD		0.23 ± 0.07		0.34 ± 0.09

RESULTS AND DISCUSSION

Heritabilities

Resistance to bacterial, viral, and parasitic diseases have generally been found to be heritable in salmonid populations, and thus selective breeding can be effective in mitigating the severity of disease outbreaks in aquaculture (for reviews, see Yáñez and Martínez 2010; Ødegård et al., 2011; Yáñez et al., 2014; Houston 2017). The heritable nature of BCWD resistance has been well documented in the ARS-Fp-R line (Silverstein et al., 2009; Leeds et al., 2010), the TLUM population (Vallejo et al., 2017), and in other populations of rainbow trout (Henryon et al., 2005; Wiens et al., 2013b). Thus, the moderate heritability estimates for BCWD resistance in the ARS-Fp-R (0.27) and TLUM (0.43) populations were anticipated (Table 2).

Evenhuis et al. (2015) characterized CD resistance in 44 full-sib families (22 paternal half-sib families) from the 2013 year class in the ARS-Fp-R line (Table 1) and reported a heritability estimate of 0.17 from a linear animal model and 0.45 when rescaled to the underlying continuous scale. In agreement with Evenhuis et al. (2015), heritability estimates for CD resistance in the current study (Table 2) using data from two generations of nucleus families each from ARS-Fp-R and TLUM populations were moderate (0.23 and 0.34, respectively) and provide further evidence that selective breeding can be an effective control strategy for losses due to CD in rainbow trout aquaculture. To our knowledge, these are the only heritability estimates currently available in the literature for CD resistance for salmonids, although Wonmongkol et al. (2018) recently reported a heritability estimate of 0.15 for CD resistance in a tilapia population using a threshold animal model. It remains important, however, to confirm that resistance measured using the current laboratory-based CD challenge model is predictive of resistance to the pathogen during

Table 3. Numbers of effective samples (N) and posterior means, modes, medians, and 95% confidence intervals (CI) of variance components for disease resistance traits in the National Center for Cool and Cold Water Aquaculture (ARS-Fp-R) and Troutlodge (TLUM) populations

Trait ¹	Variance component ²	ARS-Fp-R					TLUM				
		N	Mean (SE)	Median	Mode	95% CI	N	Mean (SE)	Median	Mode	95% CI
BCWD	σ_a^2	22	0.40 $\pm$ 0.07	0.38	0.37	0.26 to 0.53	39	0.94 $\pm$ 0.32	0.88	0.80	0.43 to 1.61
	σ_F^2	33	0.05 $\pm$ 0.01	0.05	0.05	0.02 to 0.08	125	0.17 $\pm$ 0.04	0.17	0.17	0.08 to 0.25
	$\sigma_{T/F}^2$	738	0.01 $\pm$ 0.01	0.01	0.01	0.00 to 0.02	1,126	0.02 $\pm$ 0.01	0.02	0.02	0.00 to 0.03
CD	σ_e^2	40k	1.00 $\pm$ 0.01	1.00	1.00	0.98 to 1.02	40k	1.00 $\pm$ 0.01	1.00	1.00	0.98 to 1.03
	σ_a^2	20	0.34 $\pm$ 0.12	0.33	0.37	0.11 to 0.56	73	0.78 $\pm$ 0.04	0.74	0.67	0.22 to 1.37
	σ_F^2	48	0.07 $\pm$ 0.03	0.07	0.07	0.01 to 0.13	245	0.24 $\pm$ 0.01	0.23	0.21	0.01 to 0.38
	$\sigma_{T/F}^2$	3,201	0.06 $\pm$ 0.01	0.06	0.06	0.03 to 0.09	262	0.16 $\pm$ 0.01	0.16	0.15	0.01 to 0.24
	σ_e^2	40k	1.00 $\pm$ 0.01	1.00	1.00	0.98 to 1.02	40k	1.00 $\pm$ 0.01	1.00	1.00	0.98 to 1.03

¹BCWD = bacterial cold water disease; CD = columnaris disease.

² σ_a^2 = additive genetic variance; σ_F^2 = variance of full-sib family; $\sigma_{T/F}^2$ = variance of disease challenge tank nested within family; σ_e^2 = residual variance.

Figure 1. Average family inbreeding coefficients by year of the National Center for Cool and Cold Water Aquaculture (ARS-Fp-R) and Troutlodge (TLUM) populations.

natural exposure in a production environment as has been previously demonstrated for *F. psychrophilum* in rainbow trout (Wiens et al., 2013a; Wiens et al., 2018) and *Aeromonas salmonicida* in Atlantic salmon (Gjen et al., 1997).

The variance component estimates for effects of animal, full-sib family, and challenge tank nested within family had low standard error and consistent values for mean, median, mode, and low range of 95% confidence intervals for both populations and disease resistance traits (Table 3). The good pedigree structure accounting for seven generations in each population, with almost 100% of nonfounders with known sire and dam, and low inbreeding accumulation (Figure 1) likely contributed to good adjustment of the model. Furthermore, reliable estimates of (co)variance parameters necessitate having high throughput and repeatable laboratory challenge models to provide accurate phenotypes for a large number of animals and families. Compared to the

injection-based BCWD challenge model, which evades the host's intrinsic mucosal, skin, gill, and gut defense mechanisms (Decostere et al., 2000), the waterborne-based CD challenge model would seem to better mimic natural exposure to the pathogen in the production environment and thus provide a more appropriate assessment of host resistance. However, the CD challenge model consistently had larger variance attributable to the effect of tank nested within family compared to the BCWD challenge model (Table 3). As a result of this comparatively poorer repeatability, the current CD challenge model may result in downward-biased heritability estimates and less accurate genetic merit predictions compared to the BCWD challenge model. The larger estimate of variance attributable to the effect of tank nested within family (Table 3) for the TLUM CD challenge (0.16), compared to ARS-Fp-R (0.06), was likely exacerbated by challenging fewer fish per tank (20 vs. 40) in 2015 (Table 1).

In general, the variance component estimates for both disease resistance traits in the TLUM population were larger than those for ARS-Fp-R (Table 3). The larger additive genetic variances, and heritabilities (Table 2), found in the TLUM population suggests great potential for improving resistance against the two bacterial diseases through family-based selection in this population, as has already been demonstrated for the ARS-Fp-R line (Leeds et al., 2010; Wiens et al., 2013a; Wiens et al., 2018). Variance component estimates are subject to large range of factors, including the model used to analyze the data, the presence of selection pressure, the number and quality of phenotypic records, and relationships among families. The reduced number of phenotyped generations of TLUM families may have impacted the precision of the variance component estimates in that population, but this is not likely the main reason for the observed differences among the two populations. The intense selective pressure for BCWD resistance applied on the ARS-Fp-R line over the last five generations, and more rapid increase in inbreeding (Figure 1), has likely contributed to the decreased genetic variability for the two disease resistance traits in that line compared to the TLUM line, although the use of an animal model and a complete relationship matrix is expected to result in unbiased estimates in the base population (Sorensen and Kennedy, 1984).

Genetic Correlations

The moderate and favorable genetic correlation between resistance to BCWD and CD in the ARS-Fp-R (0.40 ± 0.17) and TLUM (0.39 ± 0.18) lines is consistent with the correlation (0.35) previously reported by Evenhuis et al (2015). As a result of this genetic correlation and selection for BCWD resistance in the ARS-Fp-R line, the genetic trend for CD resistance in Figure 2 differed from 0 for the ARS-Fp-R line ($P = 0.001$; two-tailed t -test with 4 df). Further support for this favorable genetic correlation was given in Evenhuis et al. (2015) by comparing survival of the ARS-Fp-R and ARS-Fp-S lines after CD challenges. The ARS-Fp-S line was derived from the same base population as the ARS-Fp-R line, but was subjected to one generation of selection for increased BCWD susceptibility and thereafter maintained as a reference susceptible line (Wiens et al., 2013a; Evenhuis et al., 2015). After three and four generations of BCWD resistance selection, survival in the ARS-Fp-R line after CD challenge was 15.0 and 18.2 percentage points greater, respectively, compared to

the ARS-Fp-S line (Evenhuis et al., 2015). In 2015 (fifth generation of BCWD resistance selection), 21 ARS-Fp-S families were challenged with CD alongside the 99 ARS-Fp-R families in the current study (data not shown), and the survival difference increased to 24.2 percentage points. Collectively, the genetic correlation (Table 2) and genetic trend estimates from the ARS-Fp-R and TLUM lines (Figure 2), and the increased divergence between the ARS-Fp-R and -S lines for CD resistance, provide convincing evidence of a favorable genetic correlation between resistance to BCWD and CD in rainbow trout. In summary, the current study and that of Evenhuis et al. (2015) are the only literature reports of genetic correlation between BCWD and CD resistance in salmonids.

The estimates of genetic correlations from two unrelated populations and correlated selection response in the current study are encouraging because they suggest that both traits can be improved simultaneously if genetic selection is applied in only one of the traits. However, it is currently unknown if the correlation is due to pleiotropic effects or linked QTL. Regardless of the nature of the genetic correlation, the lack of previous CD or BCWD resistance selection, and large estimates of additive genetic variance, in the commercially relevant TLUM population, suggests that substantial genetic gains can be realized for these disease resistance traits in this population via family-based selective breeding. It is important to note that disease resistance was assessed using only single isolates of *F. psychrophilum* (CSF259-93) and *F. columnare* (CSF298-10), and the favorable genetic correlation reported herein may not extend to other strains within these two pathogen species. Multiple genetic

Figure 2. Genetic trends for bacterial cold water disease (BCWD) and columnaris disease (CD) resistance in the National Center for Cool and Cold Water Aquaculture (ARS-Fp-R) and Troutlodge (TLUM) populations.

strains of *F. psychrophilum* cause BCWD in North American aquaculture facilities (Van Vliet et al., 2016) and genetic diversity has also been identified between rainbow trout isolates of *F. columnare* (Evenhuis et al., 2016). The magnitude of host $\times$ pathogen interaction effects on resistance is currently unresolved.

The estimation of genetic correlations for resistance among diseases is important for developing sound breeding objectives, but only a limited number of studies have aimed to estimate correlations among and between multiple disease agents in salmonids (Yáñez et al., 2014). Genetic correlations have generally been found to be favorable or neutral among and between bacterial and viral diseases (Ødegård et al., 2007; Kjøglum et al., 2008; Drangsholt et al., 2011). In cases where genetic correlation estimates were antagonistic, the magnitude of the correlations was weak, leading scientists to conclude that both resistance traits could be improved simultaneously (Gjøen et al., 1997; Henryon et al., 2005). Divergent selection for BCWD resistance in the ARS-Fp-R and ARS-Fp-S lines has not provided any evidence of genetic correlation—favorable or antagonistic—between BCWD and infectious hematopoietic necrosis virus (Wiens et al., 2013a) or Weisselosis (Marancik et al., 2013). These studies, however, were conducted using a limited number of second- and third-generation families, respectively, and should be interpreted with caution.

Selection Response

Although the genetic selection has provided significant genetic gain over the past five generations in the ARS-Fp-R line (Figure 1; $P < 0.001$; two-tailed t -test with 4 df), the genetic gain for BCWD resistance tended to stabilize after two generations of selection. Fitting a negative quadratic term (-0.033 ± 0.011) to the regression model approached significance ($P = 0.054$; two-tailed t -test with 3 df). Whereas selection intensity was greater in the first two generations (12 and 16 families were selected, respectively; Leeds et al., 2010), it was decreased in the latter three generations (26 to 34 families selected) to limit inbreeding accumulation (Figure 1). The corresponding weighted phenotypic selection differentials for survival in generations 1 through 5 were 30.2, 15.6, 12.8, 13.3, and 13.0 percentage points, respectively. In addition, it is likely that the genetic variability for the trait has decreased after the initial generations of selection and then stabilized because of the Bulmer effect (Bulmer

1971). The stabilization of the genetic trend might also be affected by the limited phenotypic scale (i.e., 0 to 100%), given that the average BCWD survival in the ARS-Fp-R line reached 85% by the last generation of selection (Table 1). The genetic trends of BCWD and CD resistance in TLUM (Figure 1) did not differ from 0 ($P = 0.35$ and 0.32 , respectively; two-tailed t -tests with 4 df), suggesting that the selective pressure applied for growth-related traits in this line has not negatively impacted the resistance against the two diseases. Conversely, four generations of selection for BCWD did not result in divergent growth performance between the ARS-Fp-R and -S lines (Evenhuis et al., 2015), and fifth-generation fish from these lines did not differ in BW at 12 months of age ($P = 0.95$; data not shown). Data from these two breeding programs therefore support previous reports that resistance to BCWD and CD and growth-related traits are genetically independent in rainbow trout (Silverstein et al., 2009; Evenhuis et al., 2015).

In conclusion, controlling infectious diseases has been one of the principal issues in aquaculture for decades. Based on our results and studies reported in the literature, genetic selection is a viable approach to increase the resistance of a population to BCWD and CD in rainbow trout (Leeds et al., 2010; Wiens et al., 2013a; Evenhuis et al., 2015) that can complement good biosecurity practices and vaccination strategies in a comprehensive disease management plan. Data from the current study from multiple generations in two unrelated populations further suggest that both resistance traits can be simultaneously improved when selection is applied to only 1 of the traits. The observed genetic correlation between BWCD and CD resistance implies that there is a certain proportion of common genes with pleiotropic effects acting to improve the resistance to both pathogens. However, the exact nature of this genetic correlation is currently unresolved. It is also possible that the correlation is caused in part by physical linkage of QTL that affect each trait separately, as was previously found for BCWD resistance and spleen size in rainbow trout (Wiens et al., 2013b; Vallejo et al., 2014; Liu et al., 2015). Either way, the identification of QTL with significant effects on the two traits in each population will enable better assessment of the genetic architecture of the traits and the nature of the observed genetic correlation. Further investigation to identify the causative genome variants and to elucidate the molecular and immunological or physiological pathways that are involved in resistance to these

pathogens will aid our understanding of the broad-based vs. pathogen-specific nature of host resistance mechanisms.

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