Genomic selection for bacterial cold water disease resistance in rainbow trout reveals large within-family variation that cannot be exploited in “traditional” family-based selective breeding.

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BACTERIAL COLD WATER DISEASE (BCWD)

- High priority disease problem in US trout aquaculture
- Caused by Flavobacterium psychrophilum (Fp)
- There is no licensed vaccine available
- Treatment with antibiotics: Florfenicol & Oxytetracycline
- Antimicrobial resistance is a growing concern

BCWD SYMPTOMS

- Fry-lethargy, lack of feeding, darkened skin, enlarged spleen, anaemia and high mortality

OBJECTIVES

1. Demonstrate with EMPIRICAL DATA the power of GS to exploit within-family genetic variation for BCWD resistance in commercial rainbow trout population (Troutlodge, Inc.)

2. Evaluate accuracy of BREEDING VALUE PREDICTION for BCWD resistance using “PROGENY TESTING DATA” with pedigree-based and GS models

3. Explore genetic architecture of BCWD resistance in this “commercial population” with GWAS

SIB-SELECTION IN RAINBOW TROUT

- Many important traits selected for breeding cannot be recorded directly in SELECTION CANDIDATES:
  - Disease resistance traits (BCWD, IPNV, etc.)
  - Meat quality traits (fillet yield)
- Sib-selection is common practice (between-family selection)
  - We need pathogen-free NUCLEUS population
  - Estimated Breeding Value (EBV) has limited reliability <0.5
  - Strong co-selection of family members (inbreeding)
- Genomic breeding value (GEBV) enables within-family individual selection
  - Reliability of GEBV can be >0.5

GENETIC RESISTANCE PHENOTYPES

- Survival days (DAYS)
  - Number of days to death post-challenge with Fp
  - Fish survival was evaluated for 21 days post-challenge
- Binary survival status (STATUS)
  - 1 = fish died during the 21 d post-challenge evaluation
  - 2 = fish was alive on day 22 post-challenge

GS IN COMMERCIAL RAINBOW TROUT

- Rainbow trout growth strain TUUM (Troutlodge, Inc.; USA; May)
- TRAINING sample:
  - Offspring from 2013 year-class (YC)
  - Full-sib families = 102
  - Genotyped animals = 3,370
  - Phenotyped & Genotyped animals = 1,473
  - Total phenotyped animals = 7,893
- TESTING sample:
  - Offspring from 2013 YC families (full-sibs of training animals)
  - Full-sib Families = 25
  - Genotyped animals = 102 (selection candidates with GEBVs)
- Genotyping platform:
  - 57K SNP chip (Affymetrix: Axiom® Trout Genotyping Array)
Accuracy of EBV & GEBV predictions

Predictive ability (PA) of EBV and GEBV estimated using "PROGENY TESTING DATA" from 127 progeny testing families

Predictive ability:

\[ P_{\text{EBV}} = \text{CORR}(\text{MPP}, \text{MidParent EBV}) \]
\[ P_{\text{GEBV}} = \text{CORR}(\text{MPP}, \text{MidParent GEBV}) \]

Bias:

\[ \beta_{\text{MPP-EBV}} = \text{REGRESS}(\text{MPP on MidParent EBV}) \]
\[ \beta_{\text{MPP-GEBV}} = \text{REGRESS}(\text{MPP on MidParent GEBV}) \]

MPP = mean progeny phenotype; \( \beta > 0 \) unbiased; \( \beta < 0 \) biased

Response to one generation of GS for BCWD resistance (19.6%)

Correlation of EBV/GEBV with survival phenotype (Families= 127)


days

\[ r = 0.30 \]

\[ r = 0.71 \]

\[ r = 0.69 \]

\[ r = 0.30 \]

PEDIGREE and GS MODELS

1) Pedigree-based model (BLUP) (BLUPF90; Misztal et al., 2002, 2014)
2) Single-step GBLUP (ssGBLUP) (BLUPF90; Aguilar et al., 2010)
3) Weighted ssGBLUP (ssGBLUP) (BLUPF90; Wang et al., 2012)
4) Bayesian method (BayesB) (GENSEL; Fernando & Garrick, 2009)

ANIMAL MIXED LINEAR MODEL

\[ y = X \beta + Z \alpha + e \]

- \( y \) is a \( n \times 1 \) vector of traits values;
- \( X \) is a \( n \times p \) incidence matrix relating vector \( \beta \) of fixed genetic effects to \( y \);
- \( Z \) is a \( n \times k \) matrix of genotype covariates for \( k \) SNPs; \( \alpha \) is a \( k \times 1 \) vector of random partial regression coefficients of \( k \) SNPs (additive genetic effects), and \( e \) is vector of residuals.

- \( \alpha \) ~ N(0, \( \mathbf{A} \sigma^2 \))
- \( \mathbf{H} = A + G \) (ssGBLUP, wangGBLUP)
- \( \alpha \) ~ N(0, \( \mathbf{A} \sigma^2 \)) (BayesB)

- Response to one generation of GS for BCWD resistance (19.6%)

- Testing fish sampled from 25 training families
Correlation of GEBV with survival phenotype (Families= 127)

ACCURACY OF EBV & GEBV PREDICTIONS

<table>
<thead>
<tr>
<th>Model</th>
<th>DAYS Accracy</th>
<th>DAYS Bias</th>
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<td>BayesB</td>
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</table>

GWAS for BCWD Resistance with wssGBLUP (Iteration 2)

GWAS for BCWD Resistance with BayesB (π = 0.97)

CONCLUSION (1)

Average BCWD survival in progeny from HIGH-GEBV dams was 79% greater than in progeny from LOW-GEBV dams.

This response to one generation of GS is solely due to within-family variation that cannot be exploited in “traditional” family-based breeding programs.

CONCLUSION (2)

All GS models are much better performance predictors for BCWD resistance than “traditional” pedigree-based BLUP model.

Genomic predictions for DAYS with BayesB are the most accurate, followed by wssGBLUP and ssGBLUP.

GWAS identified moderate-large effect QTL on 17 chromosomes explaining up to 53% of genetic variance.
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