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RESISTANCE TO *Flavobacterium psychrophilum* IN RAINBOW TROUT: QTL DETECTION REVEALS EFFECT OF INFECTION ROUTE AND EPISTATIC INTERACTIONS

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Bacterial cold-water disease, caused by *Flavobacterium psychrophilum* (Fp) is one of the most important diseases affecting rainbow trout (*Oncorhynchus mykiss*). Previous studies that used injection as route of infection have revealed that resistance to Fp is controlled by several QTL. However, skin and mucus are recognized as important components of fish defense against infections. Immersion challenge is expected to be closer to natural infection by Fp, and may reveal new defense mechanisms. The objective of this study was to identify and compare QTL associated with resistance to Fp using the two routes of infection.

Three experimental families, one F2 progeny and two gynogenetic doubled haploid, were produced in RESIST and FISHBOOST projects (FUI 15 French and FP7 European) from 6 doubled haploid grand-parents belonging to 6 isogenic lines with opposite resistance to Fp (3 resistant, 3 susceptible). Around 300 to 600 fish/family were individually tagged and challenged using either intramuscular injection or immersion (survival rate from 7% to 50% for injection; from 30% to 80% for immersion). Fish were genotyped with 1,200 to 9,600 markers using the double-digest-RAD or RAD-sequencing methodology. QTL for different resistance traits (i.e. survival, tolerance or endurance) were detected separately for each family and each infection route, using linkage analysis and interval mapping method.

Several chromosome- and genome-wide significant QTL ($P < 0.01$ and $P < 0.05$, respectively) associated with resistance to Fp were detected. Most of them were family specific but the most significant were detected in several families. Many QTL were detected after either immersion or injection. Only a few were found after both infectious challenges, suggesting that different defenses mechanisms may be triggered depending on the infection route. Interestingly, epistatic interactions among resistance QTL were evidenced, highlighting the complexity of the underlying immune pathway.

This study confirms the complex genetic architecture of trout resistance to Fp and demonstrates that different defense mechanisms can be modulated by the infection protocol. Some QTL with large effect were identified consistently across different genetic backgrounds and infectious protocols, paving the way for a better understanding of host defense mechanisms and further implantation of selective breeding for resistance to Fp.

BCWD, QTL, Resistance, Route of infection, Epistasis

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