Supplementary Information Appendix

Experimental evidence that parasites drive eco-evolutionary feedbacks

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SI Supplementary Methods

SI.1 Further details on parasite exposure

All fish were kept under standard conditions for 24 to 45 days after collection before entering the experiment. All experimental fish were disinfected on the same dates by a 1-hour exposure to 1:4000 Formalin dilution on three consecutive days (modified from [1]). Experimental infection was achieved by manual transfer of *Gyrodactylus spp*. individuals from non-disinfected sticklebacks collected from the same lake and stream populations. All experimental fish were anaesthetized in a 0.1M MS-222 solution before infection or control treatment and non-disinfected parasite source fish were euthanized in a 1M MS-222 solution before parasites were picked off. Two individual parasites from each of the lake and stream environments were transferred. Fifty-eight *Gyrodactylus* individuals from the same parasite source fish were preserved for molecular species identification by sequencing of the ITS1 region [2] and confirmed to be *G. gasterostei* (50 individuals) and *G.arcuatus* (8 individuals), with both parasite species occurring on both host ecotypes in the wild. Control fish were handled similarly without parasite transfer (P contrast). After infection or control treatment, fish were kept in their respective experimental groups in laboratory aquaria for one week before transfer to outdoor mesocosms.

SI.2 Further details on mesocosm setup and sampling at the end of phase 1

The mesocosms were plastic tanks of one cubic meter. They were filled with a 5cm layer of gravel and sand, sediment collected from lake Lucerne and a nearby stream (47^{o}00'45.1"N 8^{o}18'41.4"E). Lake water and a concentrated zooplankton inoculum from Lake Lucerne and Lake Constance were also used. Mesocosms were arranged in blocks of 8 tanks and input material was distributed block-wise. Within each block, we established contrasting nutrient environments by adding nutrient solution aliquots of 20ml containing $NaNO_3$ and HNa_2PO_4. Initial nutrient concentrations were 640μg/L Nitrogen + 40μg/L Phosphorus and 80μg/L Nitrogen + 5μg/L Phosphorus in high and low nutrient tanks respectively (E contrast). For the first phase of the experiment, we introduced three-spined sticklebacks of either lake or stream origin to establish the host ecotype contrast (H). Each mesocosm initially contained a standardized total biomass of fish of 12.5$\pm$4.4g consisting of groups of 6 or 7 fish. We collected ecosystem samples 6 weeks after fish introduction to the mesocosms and removed the fish one week later. Ecosystem samples consisted in measuring a series of physico-chemical parameters (11 parameters including nutrients, NH_4, and DOC concentration, turbidity and DOC-abs), biological parameters (5 parameters including chlorophyll concentration, zooplankton size, and bacterial counts), ecosystem processes (7 parameters including gross primary productivity, bacterial respiration, and sedimentation), and zooplankton community (12 parameters including abundance of cladocerans, copepods, and rotifers). Individual ecosystem parameters are listed in Table S5b. After euthanasia of the fish in 1M MS-222, *Gyrodactylus* specimen were counted on each fish before morphological measurements and dissection. 35 *Gyrodactylus* individuals were successfully sequenced at the ITS region and identified as *G.arcuatus* in 34 cases and *G.gasterostei* in 1 case. Organs were taken out, livers were weighed for estimating metabolic condition (Hepatosomatic index), spleens were stored in RNA later for gene expression analysis, and stomachs were used for diet assessment. For diet analysis, prey items were identified to the lowest possible taxonomic level [3, 4, 5] and counted on a 2.5x2.5mm grid under a binocular. Non-aquatic adult insects were classified together as imagos and digested prey as unidentified material.

SI.3 Further details on preparation and sampling of phase 2

After removal of phase 1 fish, groups of juvenile lab-bred sticklebacks were introduced into the tanks modified throughout phase 1 of the experiment. Each tank received lake, hybrid and stream juvenile fish originating from the same number of different fish families and consistent family distribution within blocks. Juveniles were introduced into mesocosms in two cohorts (7 - 33 days post-hatching, depending on hatching date). The first cohort was introduced one day after removal of first phase fish and the second cohort 32 days later and kept in separate aquaria under common garden conditions for 7 days, after grouping them with an average mortality of 62.5% in that time. Mortality was higher among lake and hybrid juveniles than among stream families (binomial GLM, z_{Stream}=-4.83, P<0.001), but mortality was unrelated to experimental treatments in the destination mesocosms (binomial GLM, all X^2 <1.76, all P>0.19). Juveniles were not treated individually, but the first cohort was exposed group-wise to a euthanized first phase fish from the same tank for 5 hours in a 2L aquarium for potential parasite transmission. The second cohort was introduced to the mesocosms immediately after group assembly and not exposed to parasites at all, such that 16 nave fish entered each mesocosm. Table S6 contains a full description of juvenile fish introduction and survival for each tank.

All surviving fish were caught three months after the first juvenile cohort was introduced to the mesocosms. As with phase 1 fish, after euthanasia in a 1M MS-222 bath *Gyrodactylus* specimen were counted on each fish before length and weight measurements and removal of spleens and livers for gene expression assays. Spleens and livers were pooled for gene expression analysis in this cohort as spleens alone were too small for sufficient RNA yield. Only 10 of the 407 scanned individuals were infected with *Gyrodactylus* at the end of the experiment, with no significant effects of any previous treatment on infection levels in this second generation (binomial GLMMs, all X^2 <2.03, all P>0.15, Table S7). We also confirmed that effects detected in gene expression profiles and body condition were robust to removal of these few infected individuals from analyses (results as presented in Table S7 and S8 do not change qualitatively), and consequently infection intensities were excluded from the analyses of the second fish generation.

SI.4 Further details on common garden experiment

Lab-bred sticklebacks of pure lake and stream origin were raised in the lab for one year on the same diet, namely artemia during the first month of their life and on frozen chironomids later on. These fish were disinfected with formalin on three subsequent days in the same way as the mesocosm fish. We then set up experimental groups of three fish, either of lake or stream origin and either exposed to *Gyrodactylus* from both wild populations as described above or not. Three replicate blocks of these four experimental groups were set up, each of them kept in one of 12 separate black 300 L outdoor tanks for a total of 36 fish. Fish were kept in these groups and fed with frozen chironomids every second day over the course of five weeks. Then they were euthanized and dissected in the same way as the mesocosm fish. One fish died before sample collection and the spleen sample of one fish did not yield good quality gene expression data, so that 34 fish were included in the analyses.

SI.5 Further details on molecular analyses

Because transcriptome analyses have been conducted with lake and stream three-spined sticklebacks [6], we used a target gene approach, measuring relative mRNA levels in microfluidic qPCR assays on Fluidigm 96.96 Dynamic Array IFCs on the BioMark System using EvaGreen DNA Binding Dye (Biotium) according to the Advanced Development Protocol 14 (PN 100-1208 B) by Fluidigm. Gene expression assays included 4 reference genes (ubiquitin (ubc), L13A ribosomal binding protein (*rpl13a*), beta-2-microglobulin (*b2m*), elongation factor *ef1*α (eef1a) [7]) and 28 target genes. These target genes spanned metabolic functions (*fabp2, gapdh, acadsb, rab11al ,ctrc*), the general stress response (*hsp70, hsp90, nr3c1*), innate cellular (*sod2, vegfa, tf, sla1, ogfr, tlr2*) and innate humoral immune response (*f2, saal1*), innate immune signaling (*socs1, cd97, mif, il1b, tgfb1, tnfa*) as well as the complement system (c7, c9,) and the adaptive immune system (*ighm, ly75, il16, mhcII*). Further information on gene functions and primer details can be found in Table S2. Primers for reference genes were previously published [7] as well as primers for mhcII [8]. All new primers were designed in quantprime [9]. The combination of ubc and rpl13a was found to be the most stable composite reference value with geNorm [10] (M=0.721, CV=0.243) and was therefore used to calculated $\triangle$Ct values.

Juveniles were genotyped at 7 microsatellite loci (Stich5196, Stich4170, Stich1125, Stich1097, Stich7033, STN18, STN75) for ecotype determination. All 7 microsatellites was amplified in one multiplex reaction, using the Multiplex PCR Master Mix by Qiagen and previously published primers [11] and the following PCR protocol: 95^{o}C for 15min, 25 cycles of 30s at 94^{o}C,90s at 58^{o}C,60s at 72^{o}C and a final 30min at 60^{o}C. Microsatellite data was then collected on a 3100 Genetic Analyzer (ABI).

SI.6 Further details on statistical analyses

All statistical analyses were performed in R version 3.1.0 [12]. Linear mixed effect models (LMM) and generalized linear mixed effect models (GLMM) were performed with the *lme4* and *MASS* packages (for infection intensity test); while p-values were obtained with Anova (*car*) by performing Type II X^2 or F tests with Kenward-Roger degrees of freedom. The standardized model structure tested for the effects of phase 1 experimental treatments: parasite exposure (P), host ecotype (H), ecosystem nutrient levels (E) and their interactions as fixed structure with block as a random factor. Univariate analyses on individual fish characteristics such as parasite burden, fish condition, gene expression and survival also included tank identity nested within block as a random effect. Significance levels among univariate results were adjusted for multiple testing within each functional parameter group (gene groups, diet, zooplankton, ecosystem parameter groups) by FDR correction according to Benjamini-Yekutieli [13]. Multivariate analyses such as permutational multivariate analysis of variance (perMANOVA) and redundancy analysis (RDA) were performed using the vegan-package and controlled for the effects of block and tank when necessary.

The effects of experimental treatments on individual infection intensity were tested with a Penalized Quasi Maximum Likelihood GLMM (glmmPQL) with negative binomial error distribution, including fish standard length as an offset in MASS R-package (theta = 0.223, link = "sqrt"). Then, we analyzed effects of infection intensity and experimental treatments on individual fish condition. Fish condition was calculated as the hepatosomatic index (HSI) = 1000 x liver wet-mass (mg)/fish mass (mg). HSI was tested with an LMM using infection intensity as well as the experimental treatments as fixed structure (Table S1). Furthermore, we tested if mortality was significantly different between treatments during phase 1 of the experiment with a binomial GLMM, on the live:dead ratio at the end of this phase.

Mean prey preferences and mean zooplankton abundance per tank were Hellinger transformed and then tested in a distance-based redundancy analysis (db-RDA) for treatment effects (60). For multivariate analyses of the ecosystem level, we scaled each ecosystem parameter (mean=0, $\pm$ 1 SD) and then tested for experimental treatment effects in an RDA. Significant effects of each RDA were obtained by permuting treatments 9999 times within each block with the function anova.cca (by=term, strata=block). For univariate analyses, we standardized all LMMs and GLMMs for diet, zooplankton and ecosystem parameters to $\pm$2 SD in a model average framework following Grueber et al [14] and Gelman et al [15], to calculate the relative importance (RI) and standardized effect sized (ES) in Table S5b.

Gene expression was analyzed as ΔCt values [16]. For comparison among biological levels, gene expression data was analyzed in an RDA in the same way as ecosystem parameters. Further gene expression analyses of fish from phase 1 were performed once for the complete dataset to evaluate three-way interactions but interpreted according to separate analyses for lake and stream fish as reference gene expression differed between fish ecotypes. Multivariate effects were assessed with perMANOVA on data averaged within experimental tank. PerMANOVA results were calculated using adonis (*vegan*) with 999 permutations on a Pearson distance matrix obtained with Dist (*amap*) and stratifying data within Blocks (Tables S3a, S4a and S8a). Univariate effects were assessed in LMMs and with Yeo-Johnson transformation where necessary prior to model testing if residual distributions were non-normal or heteroscedastic (λ-values for transformations are listed with the respective LMM output in Tables S3b, S4b and S8b). To correct for the possible dependence of gene expression on fish size we included standard length as prior weights in the linear mixed effect models. Gene expression data from the common garden experiment was analyzed the same way but included only parasite exposure and ecotype as fixed effects and way carried out only in joint models for both ecotypes.

Juvenile stocking differences between tanks (19-39/tank) were statistically accounted for by including tank as a random factor in individual based tests (i.e. survival, body condition and LMMs for gene expression) and by including stocking numbers in tank based tests (i.e. as prior weights in LMMs for selection coefficients and as covariate in perMANOVAs for gene expression). Survival differences between lake, hybrid and stream juveniles (according to their parents origin as determined with microsatellites) were tested with a Pearsons X^2-test. Then we tested for effects of phase 1 treatments on juvenile survival using binomial GLMMs with survival rates from each tank as the response variable and phase 1 experimental treatments as fixed factors. The same model was run for all juveniles together and for each juvenile ecotype individually. We further calculated the selection coefficient S against each juvenile ecotype as the change in frequency of the ecotype relative to the frequency of the fittest genotype, subtracted from 1, within each tank [17]. Effects of phase 1 ecosystem modifications on viability selection were tested in linear mixed models for each juvenile ecotype separately (Table S7). To evaluate second generation fish body condition, we calculated the relative weight W_{rel} [18] as a percentage of the average expected weight for a given fish size according to a logarithmic length-weight regression. These W_{rel} values were analyzed in an LMM using the lme4 package. For fish from phase 2, we analyzed experimental treatment effects on body condition in three subgroups (lake, hybrid or stream) (Table S7). Gene expression data of these fish was analyzed separately for lake, hybrid and stream fish for consistency with phase 1 fish (Table S8a and S8b). Statistical methods for gene expression analysis were the same as for phase 1, except for the inclusion of stocking numbers as a covariate in perMANOVAs.

To determine if differential expression between ecotypes was similar between environments, we calculated the ratio between experiments (mesocosm/common garden) of the difference between ecotypes (stream-lake) and tested (using a 2-tailed t-test) whether the value of this ratio (i.e. the slope see Fig-S2A-B) was significantly different from either 0 or 1. Additionally, we determined whether stream and lake fish showed parallel responses to infection Fig-S2C) by testing whether the directional expression responses across all 28 genes, between our pair of environments (common garden v.s. mesocosm), were more similar than expected by chance using a McNemar test [19, 20].

SI Supplementary Discussion

We found many instances of three-way interactions of parasite exposure x fish ecotype x nutrient loading in the eco-evolutionary feedback from first phase ecosystem manipulations to the relative fitness of juveniles in the second experimental phase. For instance, selection against lake juveniles shows that lake fish are at a selective disadvantage when mesocosms are nutrient poor and have been modified by lake adults under parasite pressure. This indicates that preferred resources of one ecotype can be depleted and might cause a negative feedback for this ecotype in the next generation, particularly under parasite exposure. When nutrient loads are increased (i.e. in eutrophic mesocosms), lake juveniles have similar survival rates as stream and hybrid juveniles in mesocosms modified by parasite exposed lake adults. This suggests that directional selection (driven by parasites) is reduced at higher nutrient levels because compensation is easier to achieve in productive environments. When parasite pressure is low however, lake juveniles are at a selective disadvantage under high nutrient conditions. One possible explanation is that the lake adults in phase 1 benefit from the simultaneous absence (or low level) of parasites and high nutrient levels to the extent that they deplete prey items preferred by lake fish again. Proving these suggested mechanism would require additional experiments, such as laboratory feeding trials of the different ecotypes with and without parasite pressure.

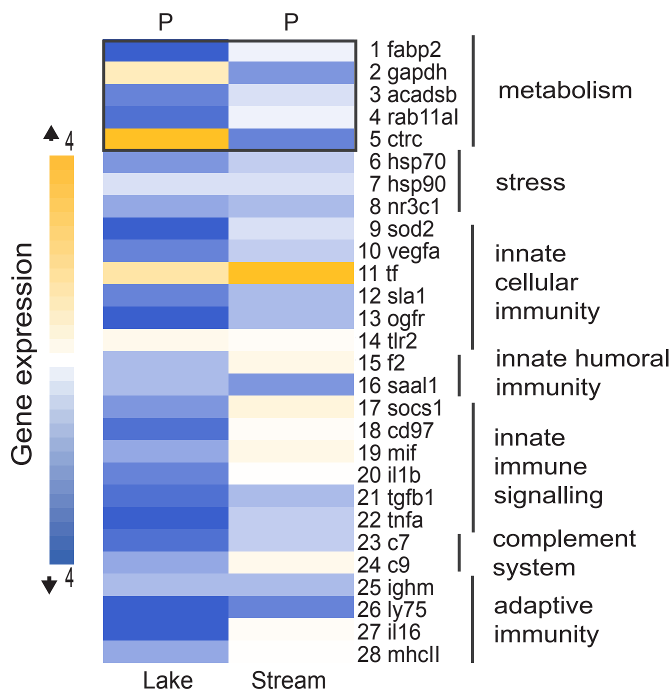
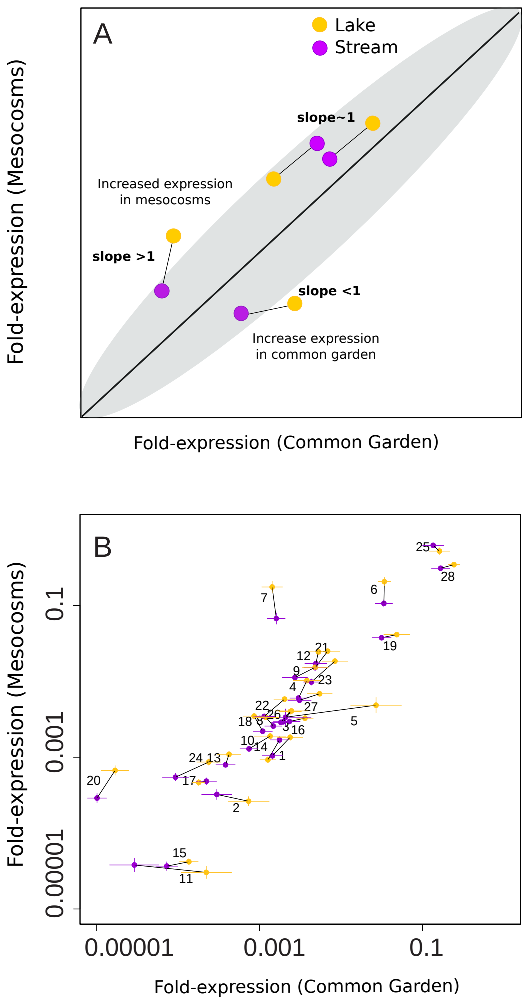


Figure-S1. Gene expression responses of lab-reared adults to parasite exposure in common garden setting, from fourfold down regulation to fourfold up regulation in parasitized vs. control manipulations (P). Significant expression changes for gene groups are highlighted by black outlines (lake: N=6, stream: N=6, test on tank averages). See Table S4a and Table S4b



C

	Gene Name	Lake M	Lake C	Stream M	Stream C	Parallel Expression
	Metabolism					
1	fabp2	+	-	-	-	Stream
2	gapdh	-	+	+	-	
3	acadsb	+	-	-	-	Stream
4	rab11al	-	-	-	-	Both ecotypes
5	ctrc	-	+	+	-	
	Stress					
6	hspa70	+	-	-	-	Stream
7	hsp90	+	-	-	-	Stream
8	nr3c1	-	-	-	-	Both ecotypes
	Innate cellular Immunity					
9	sod2	+	-	-	-	Stream
10	vegfa	+	+	-	-	Both ecotypes
11	tf	-	-	+	+	Both ecotypes
12	sla1	-	-	+	-	Lake
13	ogfr	+	-	-	-	Stream
14	tlr2	-	+	+	+	Stream
	Innate humural immunity					
15	f2	+	-	+	+	Stream
16	saal1	-	-	+	-	Lake
	Innate immune signalling					
17	socs1	+	-	+	+	Stream
18	cd97	-	-	+	-	Lake
19	mif	+	-	-	+	
20	il1b	+	-	+	+	Stream
21	tgfb1	+	-	-	-	Stream
	Complement system					
22	tnfa	+	-	+	-	
23	c7	+	-	-	-	Stream
24	c9	-	-	+	+	Both ecotypes
	Adaptive immunity					
25	ighm	-	-	+	-	Lake
26	ly75	-	-	-	-	Both ecotypes
27	il16	-	-	+	+	Both ecotypes
28	mhcII	-	-	+	+	Both ecotypes

Figure-S2. Panel A: Conceptual figure for comparing patterns of gene expression in two contrasting environmental contexts: wild fish put into experimental mesocosms (M) and lab reared fish from a common garden (C) setting. First, considering both ecotypes together, we expected a positive correlation for gene expression between environments (grey shaded area). Second, we expected variation in the slopes connecting gene expression of lake and stream fish. When the slope is close to 1, we interpret this as evidence for parallel responses, because the divergence in gene expression between ecotypes is similar in both environments. If the slopes are significantly less than or greater than 1, this would indicate that the environmental context (M or C) has a large influence on the differences in gene expression between ecotypes. Panel B: We found support for both of our expectations illustrated in Panel A. First, there was a strong positive relationship (i.e. grey shaded area in Panel A) between levels of expression across all 28 genes (R^2=0.78, t=6.443, p$<$0.001). This is consistent with a limited role for plasticity causing different levels of gene expression between environments (M vs. C). Second, there was variation in the slopes between ecotypes, and the mean slope was not significantly different from 1 (two sided t-test, t= 0.506, df = 27, p-value = 0.617). The slopes were also significantly positive (one sided t-test, t = 1.739, df = 27, p-value = 0.047), which is expected given that expression levels tended to be higher in the lake fish. Panel C: To determine whether stream and lake fish showed parallel responses to parasite (P) infection, we tested whether the directional expression responses across all 28 genes (based on log response ratios (ln[+P/-P]) between our pair of environments (M or C) were more similar than expected by chance [using a McNemar test, 19, 20]. We found that the direction of gene expression responses to parasites was significantly parallel between experiments for stream (McNemar test: b=12, c=4, p-value = 0.077) but not for lake fish (McNemar test: b=12, c=1, p-value = 0.003). Our analyses also show that gene expression was parallel between lake fish in mesocosms and stream fish in common garden (McNemar test: b=5, c=10, p-value = 0.302), but not between stream fish in mesocosms and lake fish in common garden (McNemar test: b=1, c=12, p-value = 0.003).

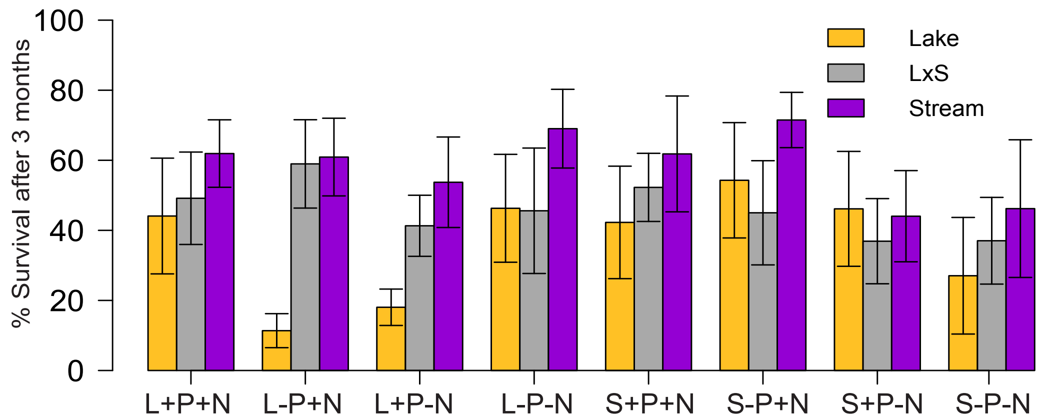


Figure-S3. Effects of phase 1 ecosystem modifications on phase 2 fish survival. Survival percentages of different stickleback genetic backgrounds in ecosystems modified by the phase 1 manipulations. Lake fish survival depends on an interaction of all previous ecosystem modification factors (PxHxE, N=280) and hybrid survival is affected by phase 1 nutrient manipulation (E, hybrids: N=265, stream: N=395). Data is shown as means ± SEM across 5 replicated tanks for each phase 1 treatment. See Table S7

Table S1: Effects of the experimental treatments (in phase 1) on fish mortality, infection intensity (i.i.), and metabolic condition (hepatosomatic index). Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). Significant P values are highlighted in bold, and N is the number of tested individuals

		Mortality		***Gyrodactylus* i.i.**						**Metabolic condition**					
		Both		Both		Lake host		Stream host		Both		Lake host		Stream host	
Treatment	Df	X^2	P	X^2	P	X^2	P	X^2	**P**	X^2	**P**	X^2	**P**	X^2	**P**
Gyrodactylus i.i.	1									3.847	**0.050**	4.454	**0.035**	2.139	0.144
P	1	0.233	0.629	0.008	0.929	6.276	**0.012**	1.190	0.275	3.217	*0.073*	2.454	0.117	0.712	0.399
H	1	4.164	**0.041**	20.262	<**0.001**					3.354	*0.067*				
E	1	0.002	0.966	0.023	0.879	7.470	**0.006**	0.011	0.916	7.047	**0.008**	1.400	0.237	5.919	**0.015**
H:E	1	2.055	0.152	0.015	0.903					1.738	0.187				
H:P	1	1.481	0.224	5.626	**0.018**					0.015	0.902				
E:P	1	0.560	0.454	1.918	0.166	0.354	0.552	2.080	0.149	0.485	0.486	0.742	0.389	0.100	0.752
H:E:P	1	0.535	0.465	1.229	0.268					0.320	0.572				
N		159		159		72		87		159		72		87	

Table S2: Functions and primers for the 28 genes used in this study.

Gene	Putative gene function	ENSEMBL transcript ID	Forward / Reverse Primers	Amplicon size	Reference
ubc	Ubiquitin, basic cell metabolism	ENSGACT00000010662	**AGACGGGCATAGCACTTGC**	218	[7]
			CAGGACAAGGAAGGCATCC		
rpl13a	Ribosomal protein L13a, basic cell metabolism	ENSGACT00000012319	**CACCTTGGTCAACTTGAACAGTG**	218	[7]
			TCCCTCCGCCCTACGAC		
b2m	Beta-2 microgobulin, serum protein associated with MHCI, expressed on all cells	ENSGACT00000025537	**GAAGATGTGTTGAATAGAAGCTGG**	226	[7]
			AGACTATGCCTGGGAATCAAAC		
eef1a	Eukaryotic Elongation factor 1 alpha, basic cell metabolism	ENSGACT00000002833	**CCACCGTTGCCTTTGTCC**	unknown	[7]
			TGGGACTGTTCCAATACCTCC		
Metabolism					
[1]fabp2	Fatty acid binding protein 2 intestinal, growth factor	ENSGACT00000023459	**CGCCGATGGAACAGAACTATCAGG**	102	This study
			CGGGTTGTCGTCAGTTGCTTTC		
[2]gapdh	glyceraldehyde-3-phosphate dehydrogenase, glycolysis	ENSGACT00000013612	**ACAAGTCCCTCAAGGTCGTCAG**	123	This study
			TGGTGGCATGAACTGTGCTCATC		
[3]acadsb	acyl-CoA dehydrogenase, short/branched chain, first step in fatty acid metabolism in cells	ENSGACT00000003295	**ACCAGACAGAGAGTGCAGTTTGG**	60	This study
			TTGATGCTGCATGCCCTGGAAG		
[4]rab11al	member of RAS oncogene family, angiogenesis, protein transport	ENSGACT00000017582	**ATAGTCATCATGCTAGTGGGCAAC**	102	This study
			GAAAGAAAGGCCATGTTTCTCTGC		
[5]ctrc	chymotrypsin C (caldecrin), proteolysis, cellular calcium ion homeostasis	ENSGACT00000008916	**TCATGGGCACCGCTAATATTGTTG**	75	This study
			TGATCAGGGCGATGTCATTACGG		
Stress Response					
[6]hsp70	Heat shock 70kDa protein 8, molecular chaperone	ENSGACT00000013955	**CACCTGGCTTGATGGGAATCAGTC**	60	This study
			TCCTTCTGCTGATGCTCAAACTCC		
[7]hsp90	Heat shock 90kDa protein alpha, molecular chaperone	ENSGACT00000017081	**TCACCGTCAAAGTGGACAACTCC**	79	This study
			TCGATCTGGTCTTCCTTCAAGTGC		
[8]nr3c1	Glucocorticoid receptor, initiates stress response upon cortisol binding	ENSGACT00000024121	**TCTTCAAGAGAGCAGTGGAAGGG**	137	This study
			TTCCAGGTTCATGCCTGCCATC		
Innate Immunity					
[9]sod2	superoxide dismutase 2, superoxide metabolic process,	ENSGACT000000119[7]	**CGTACGTGAACAACCTCAACGTC**	73	This study

Table S2 continued

Gene	Putative gene function	ENSEMBL transcript ID	**Forward** / Reverse Primers	Amplicon size	Reference
	involved in inflammation processes		TGAGCGGTCACATCTCCCTTTG		
[10]vegfa	Vascular endothelial growth factor receptor 2 subtype 1, stimulation of macrophage and monocyte migration	ENSGACT00000018538	**CGAAGCCATGGAGTGTGTTTCC** AGAAGTCTAAGCCGCGTTACCTG	69	This study
[11]tf	transferrin-a, antibacterial, cellular iron homeostasis	ENSGACT00000017999	**ATGCTTCTTGTCACCTGGCCATC** TTGCTGGAACCTAATCTGGTCTGC	115	This study
[12]sla1	Src-like-adaptor, regulates GM-CSFR signaling and monocytic dendritic cell maturation	ENSGACT00000007895	**ACAGAGTCGGCTCCTTCATGATAC** TCACAGAGAGCGAATACAGACCTC	66	This study
[13]ogfr	opioid growth factor receptor, immunocytochemistry, tissue renewal, wound healing	ENSGACT00000020054	**TGAAACGAGCAGACAATTGGAAGG** GCAGGTTGTTGTGCATGTTCCG	66	This study
[14]tlr2	toll-like receptor 2, antigen recognition	ENSGACT00000024730	**CGGAAGGTGATTTTCCTGACC** CTGACCAGGTACGAAGCCG	230	Sascha Hibbeler,
[15]f2	coagulation factor II (thrombin), involved in thrombotic response	ENSGACT00000020418	**ACCTTTGGAGAAGGAGAGAGTGTG** CGACGATGCGTTCTTGTCTGTATG	115	This study
Innate Humoral Immunity					
[16]saal1	Serum amyloid A, acute phase protein	ENSGACT00000007599	**TCGCAGTGAGGCCAAAGATGAG** AAATCTGCCACCGTGTCCTTGG	134	This study
[17]socs1	suppressor of cytokine signaling 1, negative immune regulation	ENSGACT00000018981	**ACTGCAGTGAGAACTAAACGGATG** ATGATGATGACGACGACGACAAGG	138	This study
Innate Immune Signaling					
[18]cd97	cell surface protein, leucocyte recruitment	ENSGACT00000024871	**CTCGTGGCACTCTACGACATGAAG** CAGCCCTATCTTGGTGACCAGTTG	60	This study
[19]mif	macrophage migration inhibitory factor, inflammatory cytokine	ENSGACT00000023656	**ATCAGCGGAGCTCACAACAAGC** TCAGGAGAGATGCTCAGGTGTTTG	77	This study
[20]il1b	interleukin 1 B, inflammation signaling	ENSGACT00000019325	**TGACGATGAAGCAGGTGGTCAAC** ACAGCGTCACGATCTCCTCTTC	150	This study
[21]tgfb1	transforming growth factor beta 1, cytokine, antiflammatory	ENSGACT00000016962	**GGTGGTTGCTTTGTCCTCAT** TGTCCTTCGACGTCACTGAG	190	Marc Ritter,
[22]tnfa	tumor necrosis factor a, cytokine activity	ENSGACT00000013402	**AACTACTACAGAGCCAAGGGCAAG** ACGGCACTCAGCGGTACAATTC	60	This study

Table S2 continued

Gene	Putative gene function	ENSEMBL transcript ID	**Forward** / Reverse Primers	Amplicon size	Reference
Complement System					
[23]c7	bridge btw adaptive and innate immune system	ENSGACT00000009181	**TGGCTCAAGCTCAGCACAACAG** AGCGACACGTGTTTGTTTGATCG	79	This study
[24]c9	bridge btw adaptive and innate immune system	ENSGACT00000020968	**CCGTGACGAACAAAGACTCAGTTG** TCTGACCGATGTCAGCACCTTG	71	This study
Adaptive Immunity					
[25]ighm	immunoglobulin heavy constant mu (ighm), antibody molecule, activates complement system	ENSGACT00000016907, ENSGACT00000016927, ENSGACT00000016947	**AAGGCAGGAGAATGAAACCTTGG** CCGAGTGAGCAGACAGGGACTGG	175	Sascha Hibbeler,
[26]ly75	Lymphocyte antigen 75, reduces B lymphocyte proliferation	ENSGACT00000020067	**TTGTCTGCACAACCGAAGCAAAG** AGGAAGACCACGACGAAGAGAC	70	This study
[27]il16	interleukin 16, T cell activation and proliferation	ENSGACT00000016499	**CTGGTCTGGGCTTCAGTATTGC** CTGGGAAACACTCTGTGGACTG	76	This study
[28]mhcII	Major histocompatibility complex, pathogen recognition	many	**GTCTTTAACTCCACGGAGCTGAAGG** ACTCACCGGACTTAGTCAG	variable	[8]

Table S3a: Multivariate perMANOVAs testing the effects of experimental treatments on gene expression profiles of adult fish in phase 1. We tested the effects on each functional gene group (e.g. stress response, metabolism genes, etc). Tests were performed including both host ecotypes (Both) and splitting them by host ecotype (lake and stream).Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). Significant P values are highlighted in bold.

	Both				Lake				Stream			
Treatment	**DF**	**F**	$\mathbf{R^2}$	**P**	**DF**	**F**	$\mathbf{R^2}$	**P**	**DF**	**F**	$\mathbf{R^2}$	**P**
					All genes							
P	1	-0.111	-0.003	0.771	1	0.585	0.042	0.407	1	2.6	0.134	0.083
H	1	9.136	0.22	**0.002**								
E	1	0.365	0.009	0.514	1	-0.753	-0.054	0.992	1	0.883	0.046	0.406
H:P	1	2.758	0.066	0.061								
P:E	1	-0.18	-0.004	0.822	1	0.156	0.011	0.632	1	-0.149	-0.008	0.874
H:E	1	-0.722	-0.017	0.952								
H:P:E	1	0.279	0.007	0.574								
Residuals	30		0.722		14		1.001		16		0.828	
Total	37		1		17		1		19		1	
					Stress response genes							
P	1	1.168	0.031	0.238	1	-0.036	-0.003	0.572	1	4.788	0.238	0.083
H	1	7.131	0.186	**0.026**								
E	1	0.458	0.012	0.408	1	-0.951	-0.071	0.942	1	-0.188	-0.009	0.649
H:P	1	1.252	0.033	0.23								
P:E	1	0.002	0	0.594	1	0.349	0.026	0.306	1	-0.471	-0.023	0.851
H:E	1	-2.032	-0.053	0.981								
H:P:E	1	0.296	0.008	0.457								
Residuals	30		0.784		14		1.048		16		0.795	
Total	37		1		17		1		19		1	
					Metabolism genes							
P	1	-2.013	-0.075	0.94	1	-0.473	-0.038	0.765	1	-1.526	-0.098	0.911
H	1	0.141	0.005	0.538								
E	1	-0.922	-0.034	0.76	1	-1.68	-0.137	0.952	1	1.329	0.085	0.343
H:P	1	0.709	0.026	0.431								
P:E	1	0.435	0.016	0.479	1	0.451	0.037	0.537	1	-0.156	-0.01	0.594
H:E	1	-1.717	-0.064	0.896								
H:P:E	1	0.334	0.012	0.494								
Residuals	30		1.113		14		1.138		16		1.023	
Total	37		1		17		1		19		1	
					Innate cellular immunity							
P	1	-4.685	-0.08	0.997	1	2.912	0.174	0.173	1	1.149	0.056	0.334
H	1	20.498	0.352	**0.002**								
E	1	1.661	0.029	0.232	1	-0.54	-0.032	0.85	1	3.766	0.185	0.119
H:P	1	7.744	0.133	**0.03**								
P:E	1	0.62	0.011	0.423	1	0.394	0.023	0.494	1	-0.535	-0.026	0.739

Table S3a continued

	Both				Lake				Stream			
Treatment	**DF**	**F**	$\mathbf{R^2}$	**P**	**DF**	**F**	$\mathbf{R^2}$	**P**	**DF**	**F**	$\mathbf{R^2}$	**P**
H:E	1	3.579	0.061	0.11								
H:P:E	1	-1.214	-0.021	0.928								
Residuals	30		0.515		14		0.835		16		0.785	
Total	37		1		17		1		19		1	
					Innate humoral immunity							
P	1	-0.346	-0.012	0.689	1	-0.397	-0.029	0.817	1	-0.063	-0.004	0.64
H	1	0.518	0.018	0.371								
H	1	15.705	0.33	**0.001**								
E	1	2.214	0.076	0.105	1	0.417	0.031	0.394	1	1.114	0.074	0.26
H:P	1	-0.074	-0.003	0.555								
P:E	1	-0.395	-0.014	0.675	1	-0.56	-0.042	0.942	1	-2.044	-0.136	0.987
H:E	1	-0.619	-0.021	0.757								
H:P:E	1	-2.348	-0.081	0.988								
Residuals	30		1.036		14		1.04		16		1.066	
Total	37		1		17		1		19		1	
					Innate immune signaling							
P	1	0.602	0.013	0.379	1	0.52	0.035	0.392	1	-0.922	-0.055	0.825
E	1	0.063	0.001	0.528	1	0.239	0.016	0.508	1	-0.542	-0.032	0.758
H:P	1	-0.249	-0.005	0.635								
P:E	1	1.635	0.034	0.229	1	0.205	0.014	0.52	1	2.293	0.136	0.152
H:E	1	0.041	0.001	0.548								
H:P:E	1	-0.163	-0.003	0.61								
Residuals	30		0.63		14		0.936		16		0.951	
Total	37		1		17		1		19		1	
					Complement system							
P	1	-3.343	-0.053	0.952	1	8.027	0.329	0.111	1	9.339	0.385	**0.024**
H	1	14.765	0.234	**0.009**								
E	1	3.602	0.057	0.158	1	2.145	0.088	0.39	1	0.944	0.039	0.46
H:P	1	20.716	0.328	**0.003**								
P:E	1	-1.655	-0.026	0.835	1	0.194	0.008	0.527	1	-2.054	-0.085	0.89
H:E	1	-0.571	-0.009	0.596								
H:P:E	1	-0.293	-0.005	0.594								
Residuals	30		0.475		14		0.575		16		0.66	
Total	37		1		17		1		19		1	
					Adaptive immunity							
P	1	3.669	0.073	0.127	1	-0.35	-0.02	0.802	1	15.456	0.502	**0.004**
H	1	7.102	0.141	**0.033**								
E	1	3.157	0.063	0.179	1	2.149	0.123	0.263	1	-1.207	-0.039	0.952
H:P	1	3.854	0.077	0.126								
P:E	1	1.108	0.022	0.36	1	1.718	0.098	0.303	1	0.535	0.017	0.446

Table S3a continued

	Both				Lake				Stream			
Treatment	**DF**	**F**	$\mathbf{R^2}$	**P**	**DF**	**F**	$\mathbf{R^2}$	**P**	**DF**	**F**	$\mathbf{R^2}$	**P**
H:E	1	-0.463	-0.009	0.754								
H:P:E	1	1.829	0.036	0.277								
Residuals	30		0.597		14		0.799		16		0.52	
Total	37		1		17		1		19		1	

Table S3b: Univariate LMMs testing the effects of experimental treatments on each gene. Tests were performed including both host ecotypes (Both) and splitting them by host ecotype (lake and stream). Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). P-values lower than 0.05 are highlighted in bold and significant P-values after FDR correction according to Benjamini-Yekutieli are marked with *.

	Both				**Lake**				**Stream**			
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
fabp2												
P	0.051	1	451.062	0.822	0.098	1	127.668	0.754	0.513	1	197.800	0.475
H	15.025	1	473.507	<**0.001**								
E	2.018	1	486.412	0.156	0.631	1	130.191	0.428	0.498	1	212.972	0.481
P:H	0.514	1	465.191	0.474								
P:E	1.253	1	464.094	0.264	2.040	1	125.529	0.156	0.053	1	203.020	0.818
H:E	0.004	1	468.787	0.950								
P:H:E	1.092	1	457.281	0.297								
lambda									-0.411			
gapdh												
P	0.874	1	687.545	0.350	2.500	1	263.066	0.115	0.018	1	258.453	0.893
H	0.443	1	714.801	0.506								
E	1.670	1	726.639	0.197	3.233	1	269.858	0.073	0.165	1	273.321	0.685
H:E	3.375	1	700.484	0.067								
P:H	0.545	1	697.017	0.461								
P:E	2.100	1	701.805	0.148	1.752	1	258.509	0.187	0.560	1	264.089	0.455
P:H:E	0.202	1	688.199	0.653								
lambda	2.612								3.031			
acadsb												
P	0.357	1	271.766	0.551	0.015	1	186.303	0.903	0.387	1	118.822	0.535
H	13.500	1	283.514	< **0.001**								
E	0.608	1	282.652	0.436	0.293	1	190.820	0.589	0.273	1	125.783	0.602
P:H	0.141	1	281.681	0.707								
H:E	0.009	1	285.905	0.927								
P:E	0.787	1	278.108	0.376	3.054	1	183.452	0.082	0.012	1	121.944	0.913
P:H:E	1.174	1	279.484	0.279								
lambda												
rab11al												
P	0.597	1	339.472	0.440	0.207	1	353.980	0.650	0.360	1	85.992	0.550
H	22.718	1	354.017	< **0.001**								
E	1.022	1	354.471	0.313	2.618	1	361.037	0.107	0.000	1	90.499	0.984
H:E	1.023	1	356.352	0.313								
P:H	0.036	1	350.923	0.850								
P:E	0.010	1	347.549	0.922	1.311	1	350.935	0.253	0.458	1	88.081	0.500
P:H:E	1.581	1	347.992	0.209								
lambda												

Table S3b: *Continued*

	Both				Lake				Stream			
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
ctrc												
P	0.006	1	524.456	0.939	0.084	1	129.995	0.773	0.028	1	259.353	0.867
H	0.843	1	544.458	0.359								
E	0.343	1	549.908	0.559	0.016	1	132.244	0.900	0.247	1	276.352	0.619
H:E	0.000	1	543.735	0.988								
P:H	0.032	1	536.615	0.859								
P:E	3.254	1	536.454	0.072	2.582	1	128.987	0.111	0.352	1	265.825	0.554
P:H:E	1.137	1	531.672	0.287								
lambda	1.321								1.484			
hsp70												
P	2.104	1	69.265	0.151	0.310	1	26.062	0.582	4.523	1	35.389	**0.040**
H	8.879	1	71.048	**0.004**								
E	0.411	1	70.230	0.523	0.492	1	25.313	0.489	0.209	1	36.821	0.651
P:H	3.065	1	71.758	0.084								
P:E	1.340	1	70.131	0.251	1.529	1	25.489	0.228	0.286	1	36.011	0.596
H:E	0.013	1	71.954	0.908								
P:H:E	0.201	1	71.050	0.656								
lambda	1.414								1.488			
hsp90												
P	1.694	1	64.255	0.198	0.623	1	28.663	0.437	3.836	1	28.303	0.060
H	7.682	1	65.775	**0.007**								
E	0.413	1	64.944	0.523	0.172	1	27.884	0.682	0.290	1	29.094	0.595
H:E	0.010	1	66.609	0.919								
P:H	3.392	1	66.466	0.070								
P:E	0.739	1	64.974	0.393	2.259	1	27.930	0.144	0.000	1	28.657	0.997
P:H:E	0.871	1	65.842	0.354								
lambda	1.134								1.055			
nr3c1												
P	1.329	1	673.638	0.249	1.550	1	353.028	0.214	0.554	1	188.529	0.458
H	5.463	1	696.482	**0.020**								
E	0.666	1	705.227	0.415	3.816	1	360.038	0.052	0.173	1	200.295	0.678
H:E	2.900	1	688.992	0.089								
P:H	0.005	1	682.619	0.944								
P:E	1.433	1	687.499	0.232	9.628	1	349.871	**0.002***	0.877	1	193.233	0.350
P:H:E	7.557	1	676.061	**0.006***								
lambda	-1.457				-4.058				-0.394			
sod2												
P	0.026	1	321.077	0.873	0.048	1	265.735	0.827	0.276	1	64.343	0.601
H	10.369	1	336.314	**0.001**								
E	2.551	1	340.225	0.111	2.708	1	271.783	0.101	0.351	1	68.147	0.556

Table S3b: *Continued*

	Both				Lake				Stream			
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
H:E	0.568	1	336.079	0.451								
P:H	0.512	1	332.655	0.475								
P:E	1.948	1	329.288	0.164	3.334	1	263.472	0.069	0.058	1	66.001	0.810
P:H:E	1.097	1	328.118	0.296								
lambda												
vegfa												
P	0.983	1	366.714	0.322	0.013	1	290.038	0.910	1.324	1	153.220	0.252
H	16.705	1	382.812	<**0.001**								
E	1.716	1	384.893	0.191	1.746	1	297.119	0.187	0.526	1	162.781	0.469
H:E	0.392	1	383.386	0.532								
P:H	0.785	1	378.528	0.376								
P:E	0.472	1	375.372	0.492	3.974	1	285.359	**0.047**	0.387	1	157.347	0.535
P:H:E	2.507	1	374.685	0.114								
lambda	-1.535											
tf												
P	3.233	1	702.358	0.073	7.004	1	372.070	**0.008***	0.012	1	240.583	0.915
H	0.052	1	723.632	0.820								
E	0.685	1	735.580	0.408	0.726	1	381.215	0.395	3.634	1	255.335	0.058
H:E	4.677	1	719.137	**0.031**								
P:H	3.092	1	710.624	0.079								
P:E	2.067	1	717.846	0.151	2.585	1	369.982	0.109	0.194	1	246.335	0.660
P:H:E	0.501	1	704.017	0.479								
lambda	3.110				3.327				2.918			
sla1												
P	0.473	1	356.204	0.492	1.816	1	372.070	0.179	0.000	1	58.085	0.988
H	17.917	1	371.308	<**0.001**								
E	0.011	1	372.087	0.916	0.415	1	381.215	0.52	0.005	1	60.496	0.946
H:E	0.035	1	373.782	0.851								
P:H	0.599	1	367.961	0.439								
P:E	0.049	1	364.720	0.825	1.120	1	369.982	0.291	1.025	1	59.244	0.316
P:H:E	2.587	1	364.909	0.109								
lambda					-1.698							
ogfr												
P	0.090	1	360.366	0.765	0.013	1	290.543	0.909	0.143	1	97.843	0.707
H	13.883	1	375.893	<**0.001**								
E	1.791	1	377.150	0.182	2.430	1	297.621	0.120	0.234	1	103.510	0.630
H:E	0.298	1	377.428	0.585								
P:H	0.094	1	372.098	0.759								
P:E	0.084	1	368.885	0.772	2.620	1	289.111	0.107	0.583	1	100.391	0.447
P:H:E	2.503	1	368.715	0.114								

Table S3b: *Continued*

	Both				Lake				Stream			
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
lambda												
tlr2												
P	0.031	1	694.018	0.861	1.799	1	343.584	0.181	1.736	1	259.353	0.189
H	18.862	1	717.673	**¡0.001**								
E	0.372	1	726.586	0.542	1.575	1	350.844	0.210	0.347	1	276.352	0.556
P:H	2.859	1	702.345	0.091								
P:E	0.568	1	707.861	0.451	2.314	1	338.612	0.129	0.445	1	265.825	0.505
H:E	1.913	1	708.023	0.167								
P:H:E	2.834	1	695.395	0.093								
lambda												
f2												
P	0.019	1	703.054	0.891	0.077	1	301.646	0.781	0.221	1	258.841	0.639
H	0.792	1	724.161	0.374								
E	0.704	1	736.558	0.402	0.158	1	308.487	0.691	2.090	1	274.441	0.149
H:E	2.168	1	720.092	0.141								
P:H	0.392	1	711.340	0.531								
P:E	1.439	1	718.713	0.231	2.247	1	299.613	0.135	0.000	1	264.784	0.994
P:H:E	1.350	1	704.705	0.246								
lambda	3.485								3.624			
saal1												
P	0.050	1	681.465	0.822	0.326	1	343.635	0.568	0.007	1	251.122	0.934
H	2.117	1	716.539	0.146								
E	0.093	1	746.100	0.760	0.005	1	356.425	0.945	0.001	1	274.988	0.979
H:E	0.019	1	698.551	0.889								
P:H	0.143	1	695.739	0.705								
P:E	0.050	1	703.432	0.823	0.268	1	331.786	0.605	0.132	1	257.314	0.717
P:H:E	0.455	1	682.326	0.500								
lambda	0.526				2.316							
socs1												
P	3.167	1	555.467	0.076	1.629	1	346.213	0.203	1.206	1	208.693	0.273
H	0.546	1	577.258	0.460								
E	0.024	1	583.854	0.877	0.021	1	353.216	0.885	0.387	1	221.240	0.535
H:E	0.576	1	572.820	0.448								
P:H	0.067	1	567.143	0.796								
P:E	1.299	1	567.592	0.255	2.664	1	341.933	0.104	0.023	1	213.682	0.879
P:H:E	1.886	1	561.245	0.170								
lambda												
cd97												
P	0.267	1	459.328	0.606	0.457	1	205.687	0.500	0.000	1	259.353	0.993

Table S3b: *Continued*

			Both				Lake				Stream	
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
H	14.551	1	477.443	$<$**0.001**								
E	0.016	1	481.175	0.900	1.266	1	210.511	0.262	2.260	1	276.352	0.134
H:E	3.589	1	479.419	0.059								
P:H	0.199	1	471.996	0.655								
P:E	0.297	1	470.330	0.586	2.129	1	203.225	0.146	0.946	1	265.825	0.331
P:H:E	3.431	1	467.899	0.065								
lambda	-1.086								-0.916			
mif												
P	0.014	1	407.397	0.907	0.003	1	177.413	0.956	0.107	1	191.038	0.744
H	2.214	1	427.017	0.137								
E	0.675	1	435.445	0.412	0.557	1	181.662	0.456	0.053	1	204.086	0.818
H:E	0.299	1	424.260	0.585								
P:H	0.119	1	420.559	0.730								
P:E	0.191	1	418.287	0.662	0.792	1	174.649	0.375	3.113	1	195.905	0.079
P:H:E	3.969	1	414.152	0.047								
lambda												
il1b												
P	0.688	1	336.065	0.407	1.649	1	145.013	0.201	0.000	1	257.743	0.995
H	10.751	1	352.552	$<$ **0.001**								
E	0.114	1	358.710	0.736	0.480	1	148.925	0.490	0.030	1	271.867	0.862
H:E	0.049	1	351.635	0.825								
P:H	0.683	1	348.336	0.409								
P:E	0.103	1	345.239	0.748	0.000	1	140.890	0.984	0.334	1	262.989	0.564
P:H:E	0.416	1	342.961	0.519								
lambda												
tgfb1												
P	0.222	1	387.874	0.638	0.036	1	161.325	0.850	0.283	1	188.625	0.595
H	19.134	1	405.593	$<$**0.001**								
E	0.045	1	410.252	0.833	0.187	1	165.268	0.666	0.266	1	200.551	0.606
H:E	0.999	1	404.370	0.318								
P:H	0.060	1	400.193	0.806								
P:E	0.098	1	397.349	0.754	2.984	1	158.261	0.086	1.865	1	193.337	0.174
P:H:E	5.331	1	395.175	**0.021**								
lambda	-1.133				-1.825							
tnfa												
P	0.359	1	338.970	0.550	0.208	1	154.090	0.649	0.028	1	259.353	0.867
H	21.231	1	353.452	$<$**0.001**								
E	0.311	1	353.835	0.578	0.059	1	157.674	0.808	0.235	1	276.352	0.628
H:E	0.202	1	355.945	0.653								
P:H	0.009	1	350.429	0.925								

Table S3b: *Continued*

	Both				Lake				Stream			
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
P:E	0.068	1	347.053	0.795	1.731	1	151.356	0.190	1.017	1	265.825	0.314
P:H:E	3.602	1	347.552	0.059								
lambda	-2.135				-2.987							
c7												
P	1.415	1	324.996	0.235	0.001	1	76.885	0.978	3.936	1	233.854	**0.048**
H	17.446	1	339.677	$<$**0.001**								
E	0.034	1	341.469	0.854	0.032	1	77.286	0.859	0.334	1	249.164	0.564
H:E	0.469	1	340.305	0.494								
P:H	1.939	1	336.232	0.165								
P:E	0.428	1	332.776	0.514	0.840	1	77.162	0.362	0.027	1	239.873	0.870
P:H:E	0.714	1	332.556	0.399								
lambda	-0.183											
c9												
P	1.782	1	507.855	0.183	4.143	1	331.673	**0.043**	0.051	1	239.233	0.821
H	9.855	1	527.083	**0.002**								
E	2.493	1	532.368	0.115	0.380	1	338.688	0.538	2.709	1	254.905	0.101
H:E	0.831	1	528.162	0.362								
P:H	1.138	1	520.350	0.286								
P:E	0.019	1	519.865	0.890	0.939	1	327.410	0.333	0.353	1	245.354	0.553
P:H:E	1.038	1	515.730	0.309								
lambda												
ighm												
P	3.607	1	501.626	0.058	0.004	1	358.074	0.948	9.969	1	177.127	**0.002***
H	1.929	1	520.912	0.165								
E	0.953	1	525.823	0.330	0.541	1	365.422	0.462	0.355	1	188.642	0.552
H:E	0.109	1	521.473	0.742								
P:H	3.579	1	514.064	0.059								
P:E	0.283	1	513.358	0.595	0.404	1	355.423	0.525	0.005	1	181.700	0.946
P:H:E	0.224	1	509.450	0.636								
lambda	0.671				0.429							
ly75												
P	0.409	1	477.602	0.523	0.116	1	240.899	0.734	0.308	1	189.951	0.579
H	8.101	1	496.124	**0.005**								
E	0.002	1	500.476	0.967	0.096	1	246.532	0.758	0.062	1	202.030	0.803
H:E	0.195	1	497.937	0.659								
P:H	0.027	1	490.272	0.870								
P:E	0.105	1	489.027	0.746	1.556	1	239.883	0.213	0.618	1	194.953	0.433
P:H:E	2.168	1	485.988	0.142								
lambda	-2.027				-1.769				-1.689			
il16												

Table S3b: *Continued*

	Both				Lake				Stream			
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**	**F**	**Df**	**Df.res**	**P**
P	0.074	1	394.025	0.786	0.139	1	372.070	0.709	0.001	1	57.837	0.976
H	3.833	1	410.374	0.051								
E	0.103	1	412.125	0.749	1.023	1	381.215	0.312	0.023	1	60.231	0.881
H:E	0.333	1	412.747	0.564								
P:H	0.048	1	406.292	0.826								
P:E	0.186	1	403.474	0.666	5.022	1	369.982	**0.026**	1.272	1	58.989	0.264
P:H:E	5.253	1	402.857	0.022								
lambda					-2.206							
mhcII												
P	0.583	1	335.290	0.446	1.518	1	372.070	0.219	4.119	1	70.528	**0.046**
H	1.307	1	349.635	0.254								
E	1.052	1	349.936	0.306	1.578	1	381.215	0.210	0.231	1	74.593	0.632
H:E	0.569	1	352.129	0.451								
P:H	4.962	1	346.680	**0.027**								
P:E	0.495	1	343.280	0.482	0.000	1	369.982	0.986	0.722	1	72.329	0.398
P:H:E	0.314	1	343.840	0.576								
lambda	-0.039				-0.731							

Table S4a. **Multivariate analysis on gene expression profiles for lab-bred adults in a common garden setting.** We tested the effects on each functional gene group (e.g. stress response, metabolism genes, etc). Treatments correspond to the effects of host ecotype (H), parasite exposure (P), and their interaction (H:P). Significant P values are highlighted in bold.

	Df	**F**	R^2	**P**	**F**	R^2	**P**	**F**	R^2	**P**	**F**	R^2	**P**
		All genes			**Stress response**			**Metabolism genes**			**Innate cellular immunity**		
H	1	3.859	0.261	**0.041**	-0.159	-0.018	0.843	13.608	0.356	**0.037**	3.731	0.292	0.124
P	1	1.307	0.088	0.323	2.043	0.229	0.305	5.39	0.141	0.153	0.065	0.005	0.625
H:P	1	1.617	0.109	0.232	-0.955	-0.107	0.927	11.201	0.293	**0.041**	0.998	0.078	0.375
Residuals	8		0.541			0.896			0.209			0.625	
Total	11		1			1			1			1	
		Innate humoral immunity			**Innate immune signalling**			**Complement system**			**Adaptive immunity**		
H	1	0.156	0.015	0.511	0.537	0.067	0.505	-1.036	-0.162	0.923	-0.788	-0.089	0.926
P	1	1.071	0.102	0.314	0.438	0.054	0.545	-0.012	-0.002	0.579	0.585	0.066	0.468
H:P	1	1.247	0.119	0.286	-0.896	-0.111	0.965	-0.535	-0.083	0.785	1.055	0.119	0.326
Residuals	8		0.764			0.99			1.247			0.904	
Total	11		1			1			1			1	

Table S4b. Univariate LMMs testing the effects of parasite exposure in lab-bred adults in a common garden setting. Treatments correspond to the effects of host ecotype (H), parasite exposure (P), and their interaction (H:P). Significant P values are highlighted in bold

	Df	F	Df.res	P	F	Df.res	P	F	Df.res	P	F	Df.res	P
			fabp2			**gapdh**			**acadsb**			**rab11al**	
H	1	0.977	104.945	0.325	1.393	111.557	0.240	0.42	67.577	0.519	0.288	105.24	0.593
P	1	1.824	108.689	0.18	0.025	106.28	0.875	1.392	62.986	0.242	1.2	106.371	0.276
H:P	1	2.095	107.737	0.151	0.503	115.925	0.479	0.315	67.005	0.577	0.453	110.794	0.502
lambda		-			-			3.288			-		
			ctrc			**hsp70**			**hsp90**			**nr3c1**	
H	1	5.07	101.379	**0.027**	0.06	60.663	0.807	0.067	117.808	0.796	0.258	110.669	0.613
P	1	0.026	94.285	0.871	3.027	60.85	0.087	0.322	105.678	0.571	0.494	111.909	0.484
H:P	1	1.133	105.029	0.29	0.518	61.376	0.475	0.071	133.639	0.791	0.025	105.1	0.875
lambda		-			2.505			-			-		
			sod2			**vegfa**			**tf**			**sla1**	
H	1	1.404	103.633	0.239	1.11	110.057	0.294	2.515	21.021	0.128	0.033	106.075	0.857
P	1	1.524	104.66	0.22	1.53	103.181	0.219	0.446	19.994	0.512	1.691	102.879	0.196
H:P	1	0.636	104.226	0.427	0.128	111.079	0.721	0.627	21.302	0.437	0.071	110.877	0.791
lambda		-			2.604			-0.118			-		
			ogfr			**tlr2**			**f2**			**saal1**	
H	1	0.064	98.304	0.801	1.043	110.654	0.309	1.44	88.084	0.233	1.325	107.577	0.252
P	1	3.356	92.871	0.07	0.057	111.062	0.812	0.036	83.746	0.851	1.513	103.11	0.222
H:P	1	0.777	94.094	0.38	0.027	114.405	0.870	0.512	87.919	0.476	0.23	113.792	0.633
lambda		-			-			-			-		
			socs1			**cd97**			**mif**			**il1b**	
H	1	0.343	106.337	0.559	0.088	110.59	0.768	0.511	106.096	0.476	1.243	101.998	0.268
P	1	0.046	101.574	0.83	0.74	101.545	0.392	0.104	106.53	0.747	0.718	101.998	0.399
H:P	1	1.244	106.839	0.267	0.681	121.089	0.411	1.231	106.872	0.270	0.586	104.192	0.446
lambda		-			-			1.794			-		
			tgfb			**tnfa**			**c7**			**c9**	
H	1	0.618	112.957	0.433	2.07	109.68	0.153	2.204	105.151	0.141	2.239	77.447	0.139
P	1	2.162	108.015	0.144	2.963	106.657	0.088	1.067	105.931	0.304	0.127	65.709	0.723
H:P	1	0.304	113.36	0.582	0.551	111.676	0.459	0.335	106.701	0.564	0.299	72.738	0.586
lambda		-			-			-			-		
			IgM			**ly75**			**il16**			**mhcII**	
H	1	0.053	106.105	0.819	0.187	96.186	0.667	1.471	100.644	0.228	1.138	105.828	0.289
P	1	1.027	106.532	0.313	3.641	109.161	0.059	0.959	102.814	0.330	0.804	106.542	0.372
H:P	1	0.015	106.872	0.902	0.296	99.373	0.588	1.637	103.916	0.204	0.584	106.947	0.446
lambda		0.176			-			-			-		

Table S5a: Results of multivariate analyses from genes to ecosystems based on redundancy analyses (RDA). The multivariate response of gene expression (partial-RDA), diet composition (db-RDA), zooplankton community structure (db-RDA), and ecosystem properties (partial-RDA) were tested for the overall effects of the experimental treatment, and for the effects on each host ecotype as well as for each environmental treatment. In addition, ecosystem effects were divided into five major categories (e.g. physico-chemical properties, final nutrient concentrations, ecosystem functions and biological parameters). Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). Significant P values are highlighted in bold.

	All				by host								by environment							
					Lake				Stream				High				Low			
Treatment	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2
										Effects on gene expression										
P	1	0.633	0.660	0.013	1	0.7	0.637	0.034	1	1.008	0.397	0.046	1	0.575	0.633	0.021	1	0.563	0.726	0.025
H	1	9.229	$<$ **0.001**	0.189									1	5.528	**0.003**	0.197	1	4.527	**0.006**	0.203
E	1	0.796	0.515	0.016	1	1.011	0.394	0.050	1	0.691	0.638	0.032								
H:E	1	0.786	0.519	0.016																
H:P	1	1.135	0.294	0.023									1	1.325	0.246	0.047	1	1.482	0.208	0.067
P:E	1	0.476	0.812	0.010	1	1.858	0.096	0.091	1	0.627	0.712	0.029								
H:E:P	1	1.485	0.169	0.030																
Res	26			0.532	10			0.491	12			0.552	11			0.393	11			0.494
										Effects on diet composition										
P	1	2.777	**0.020**	0.064	1	1.311	0.28	0.077	1	1.899	0.118	0.073	1	1.859	0.115	0.092	1	1.054	0.38	0.056
H	1	0.846	0.522	0.020									1	0.345	0.881	0.017	1	0.834	0.503	0.044
E	1	1.145	0.348	0.027	1	0.843	0.539	0.050	1	0.857	0.47	0.033								
H:E	1	0.722	0.635	0.017																
H:P	1	0.435	0.816	0.010									1	0.244	0.942	0.012	1	0.525	0.767	0.028
P:E	1	0.449	0.801	0.010	1	0.208	0.985	0.012	1	0.584	0.737	0.022								
H:E:P	1	0.473	0.794	0.011																
Res	25			0.581	9			0.529	12			0.461	11			0.542	10			0.532
										Effects on zooplankton community structure										
P	1	1.312	0.227	0.028	1	3.734	**0.014**	0.168	1	0.411	0.870	0.018	1	0.18	0.995	0.008	1	3.653	**0.042**	0.154
H	1	1.549	0.162	0.033									1	3.024	**0.033**	0.138	1	2.201	0.085	0.093
E	1	1.003	0.373	0.021	1	1.847	0.117	0.083	1	3.097	**0.027**	0.137								

Table S5a: (continued)

					Lake				Stream				High				Low			
Treatment	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2
H:E	1	3.901	**0.011**	0.083																
H:P	1	3.141	**0.028**	0.067									1	2.834	**0.041**	0.130	1	1.185	0.305	0.050
P:E	1	1.912	0.128	0.041	1	0.925	0.425	0.042	1	2.301	0.079	0.102								
H:E:P	1	1.243	0.247	0.027																
Res	28			0.597	12			0.540	12			0.531	12			0.549	12			0.505
Overall effects on the ecosystem																				
P	1	0.468	0.967	0.008	1	0.777	0.698	0.027	1	0.551	0.890	0.021	1	1	0.436	0.040	1	0.754	0.743	0.035
H	1	1.225	0.227	0.022									1	1.864	**0.030**	0.074	1	1.057	0.344	0.050
E	1	7.443	$<$ **0.001**	0.134	1	3.833	$<$ **0.001**	0.133	1	4.678	**0.003**	0.181								
H:E	1	1.475	0.121	0.027																
H:P	1	0.962	0.476	0.017									1	1.439	0.136	0.057	1	0.445	0.974	0.021
P:E	1	1.415	0.140	0.026	1	1.625	0.093	0.056	1	0.865	0.564	0.033								
H:E:P	1	1.087	0.340	0.020																
Res	27			0.487	11			0.382	12			0.465	11			0.437	12			0.565
Effects on physico-chemical properties of the ecosystem																				
P	1	0.570	0.628	0.008	1	0.669	0.621	0.021	1	0.520	0.657	0.014	1	0.885	0.507	0.038	1	0.507	0.746	0.024
H	1	0.840	0.456	0.012									1	1.364	0.236	0.059	1	1.128	0.347	0.052
E	1	21.750	$<$ **0.001**	0.306	1	7.459	$<$ **0.001**	0.237	1	14.443	**0.003**	0.400								
H:E	1	0.956	0.418	0.013																
H:P	1	0.726	0.532	0.010																
P:E	1	0.811	0.492	0.011	1	1.009	0.435	0.032	1	0.328	0.776	0.009	1	1.100	0.381	0.047	1	0.239	0.922	0.011
H:E:P	1	0.850	0.452	0.012																
Res	27			0.380	11			0.35	12			0.332	11			0.473	12			0.556

Table S5a: (continued)

					Lake				Stream				High				Low			
Treatment	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2	**Df**	**F**	**P**	R^2
Effects on final nutrient concentrations of the ecosystem																				
P	1	0.894	0.482	0.016	1	1.028	0.400	0.044	1	0.419	0.923	0.015	1	1.973	0.059	0.067	1	1.364	0.214	0.060
H	1	2.414	**0.024**	0.044									1	2.371	**0.032**	0.080	1	0.700	0.652	0.031
E	1	2.030	**0.048**	0.037	1	0.982	0.412	0.042	1	1.454	0.200	0.052								
H:E	1	0.443	0.910	0.008																
H:P	1	1.07	0.385	0.020									1	2.328	**0.040**	0.079	1	0.545	0.815	0.024
P:E	1	2.587	**0.019**	0.048	1	1.505	0.149	0.064	1	2.897	**0.003**	0.103								
H:E:P	1	1.683	0.119	0.031																
Res	27			0.497	11			0.470	12			0.428	11			0.371	12			0.523
Effects on ecosystem functions																				
P	1	0.152	0.987	0.003	1	0.486	0.831	0.013	1	0.825	0.511	0.036	1	0.494	0.777	0.018	1	0.261	0.943	0.011
H	1	0.454	0.843	0.009									1	0.601	0.733	0.022	1	1.242	0.296	0.055
E	1	2.399	**0.037**	0.045	1	1.811	0.102	0.049	1	2.155	0.079	0.095								
H:E	1	1.320	0.265	0.025																
H:P	1	1.165	0.327	0.022									1	0.985	0.457	0.035	1	0.531	0.731	0.023
P:E	1	0.545	0.728	0.010	1	0.800	0.569	0.022	1	0.195	0.970	0.009								
H:E:P	1	0.298	0.934	0.006																
Res	27			0.508	11			0.299	12			0.529	11			0.394	12			0.527
Effects on biological parameters of the ecosystem																				
P	1	0.279	0.945	0.006	1	0.796	0.522	0.030	1	0.825	0.511	0.036	1	0.754	0.615	0.036	1	0.892	0.472	0.050
H	1	1.115	0.366	0.024									1	3.111	**0.011**	0.148	1	1.147	0.341	0.064
E	1	7.054	$<$ **0.001**	0.151	1	5.784	$<$ **0.001**	0.218	1	2.155	**0.079**	0.095								
H:E	1	3.107	**0.009**	0.067																
H:P	1	0.822	0.558	0.018									1	1.459	0.236	0.07	1	0.476	0.827	0.027
P:E	1	1.599	0.147	0.034	1	3.123	**0.036**	0.118	1	0.195	0.97	0.009								
H:E:P	1	1.491	0.212	0.032																
Res	27			0.580	11			0.415	12			0.529	11			0.524	12			0.670

Table S5b: Univariate LMMs testing effects of experimental treatments on each prey category, zooplankton category, and ecosystem measurement. Codes represent: confidence intervals ($\mathbf{CI_{lower}}$ and $\mathbf{CI_{upper}}$), standardized effect sizes (ES), standard errors (SE $\pm$), and relative importance (RI). Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. H:E). P-values lower than 0.05 are highlighted in bold and significant P-values after FDR correction according to Benjamini-Yekutieli are marked with *.

Treatment	F	$\mathrm{Df_{res}}$	$\mathrm{CI_{lower}}$	$\mathrm{CI_{upper}}$	ES	SE ($\pm$)	RI	P
				Effects on prey items (Diet)				
Collembola								
P	0.167	717.596	−0.034	0.053	0.010	0.022	0.020	0.683
H	0.023	724.232	−0.046	0.041	−0.003	0.022	0.018	0.879
E	0.977	700.723	−0.021	0.065	0.022	0.022	0.030	0.323
H:E	0.304	723.656	−0.057	0.118	0.030	0.044	0.000	0.582
H:P	0.412	729.860	−0.064	0.112	0.024	0.044	0.000	0.521
P:E	1.257	719.505	−0.136	0.037	−0.050	0.044	0.000	0.263
H:E:P	1.947	730.451	−0.051	0.302	0.126	0.089	0.000	0.163
Nymph								
P	3.777	136.802	−0.137	−0.001	−0.069	0.034	0.178	0.054
H	1.252	144.816	−0.109	0.032	−0.039	0.036	0.051	0.265
E	0.586	136.700	−0.101	0.039	−0.031	0.035	0.042	0.445
H:E	0.007	144.241	−0.163	0.130	−0.017	0.074	0.000	0.931
H:P	0.272	144.257	−0.104	0.179	0.037	0.071	0.001	0.603
P:E	0.254	139.400	−0.102	0.178	0.038	0.071	0.000	0.615
H:E:P	0.123	143.668	−0.251	0.361	0.055	0.154	0.000	0.727
Chironomids								
P	0.319	161.247	−0.184	0.092	−0.046	0.070	0.071	0.573
H	1.876	170.501	−0.045	0.228	0.092	0.069	0.127	0.173
E	4.660	160.792	−0.276	−0.011	−0.144	0.067	0.344	**0.032**
H:E	0.076	169.659	−0.222	0.309	0.044	0.134	0.006	0.784
H:P	0.769	169.918	−0.166	0.387	0.110	0.140	0.001	0.382
P:E	0.425	164.149	−0.348	0.193	−0.078	0.136	0.003	0.516
H:E:P	0.030	169.071	−0.607	0.507	−0.050	0.281	0.000	0.862
Ostracoda								
P	1.341	266.529	−0.156	0.032	−0.062	0.048	0.086	0.248
H	1.849	279.189	−0.026	0.160	0.067	0.047	0.100	0.175
E	1.648	263.634	−0.152	0.034	−0.060	0.047	0.082	0.200
H:E	0.144	277.042	−0.156	0.220	0.032	0.095	0.001	0.704
H:P	0.430	278.751	−0.263	0.117	−0.073	0.096	0.001	0.513
P:E	0.001	269.723	−0.198	0.183	−0.007	0.096	0.000	0.982
H:E:P	0.350	276.967	−0.523	0.280	−0.122	0.202	0.000	0.555
Chydoridae								

Table S5b: continued

Treatment	F	Df_{res}	CI_{lower}	CI_{upper}	ES	SE (±)	RI	P
P	0.082	129.553	−0.128	0.180	0.026	0.078	0.065	0.775
H	1.437	137.162	−0.249	0.051	−0.099	0.076	0.131	0.233
E	0.481	129.534	−0.103	0.203	0.050	0.077	0.077	0.489
H:E	1.429	136.657	−0.489	0.112	−0.188	0.152	0.003	0.234
H:P	0.018	136.614	−0.333	0.288	−0.022	0.157	0.001	0.895
P:E	0.085	132.038	−0.358	0.274	−0.042	0.160	0.001	0.771
H:E:P	0.30	136.100	−0.824	0.462	−0.181	0.324	0.000	0.585
Cyclopoida								
P	3.861	148.078	0.005	0.292	0.149	0.072	0.331	**0.050**
H	0.450	156.688	−0.105	0.191	0.043	0.075	0.072	0.504
E	< 0.01	147.826	−0.144	0.152	0.004	0.074	0.062	1.000
H:E	2.578	155.994	−0.032	0.542	0.255	0.145	0.002	0.110
H:P	0.012	156.115	−0.314	0.277	−0.018	0.149	0.003	0.913
P:E	0.008	150.830	−0.324	0.267	−0.028	0.149	0.002	0.931
H:E:P	0.662	155.407	−0.344	0.840	0.248	0.299	0.000	0.417
				Effects on Zooplankton				
Cladocera								
P	2.566	28	−0.120	0.013	−0.054	0.033	0.664	0.120
H	6.770	28	−0.155	−0.020	−0.088	0.033	0.908	**0.015***
E	0.191	28	−0.052	0.082	0.015	0.033	0.301	0.665
H:E	0.191	28	−0.162	0.104	−0.029	0.065	0.062	0.665
H:P	2.566	28	−0.022	0.238	0.108	0.064	0.326	0.120
P:E	2.065	28	−0.226	0.033	−0.097	0.064	0.096	0.162
H:E:P	2.065	28	−0.052	0.439	0.193	0.120	0.004	0.162
Bosmina								
P	2.158	28	−0.163	0.022	−0.071	0.046	0.520	0.153
H	0.449	28	−0.125	0.061	−0.032	0.046	0.340	0.508
E	1.629	28	−0.031	0.154	0.062	0.046	0.461	0.212
H:E	1.626	28	−0.304	0.058	−0.123	0.089	0.057	0.213
H:P	1.034	28	−0.084	0.280	0.098	0.089	0.049	0.318
P:E	0.029	28	−0.167	0.199	0.016	0.090	0.066	0.866
H:E:P	0.284	28	−0.249	0.455	0.103	0.172	0.000	0.599
Copepoda								
P	< 0.01	28	−0.082	0.081	−0.001	0.040	0.269	0.985
H	1.268	28	−0.126	0.036	−0.045	0.040	0.372	0.270
E	< 0.01	28	−0.081	0.082	0.001	0.040	0.267	0.985
H:E	< 0.01	28	−0.160	0.162	0.001	0.079	0.021	0.991
H:P	0.234	28	−0.200	0.122	−0.039	0.079	0.024	0.632
P:E	2.655	28	−0.290	0.027	−0.131	0.078	0.047	0.114
H:E:P	4.548	28	0.049	0.639	0.344	0.144	0.001	**0.042**

Table S5b: continued

Treatment	F	Df_{res}	CI_{lower}	CI_{upper}	ES	SE (±)	RI	P
Naupli								
P	0.625	28	−0.181	0.449	0.134	0.155	0.343	0.436
H	10.737	28	−0.873	−0.240	−0.556	0.156	0.988	**0.003***
E	0.926	28	−0.478	0.151	−0.163	0.155	0.379	0.344
H:E	0.141	28	−0.755	0.500	−0.127	0.309	0.077	0.710
H:P	0.300	28	−0.814	0.442	−0.186	0.309	0.075	0.588
P:E	0.058	28	−0.707	0.544	−0.082	0.307	0.025	0.812
H:E:P	0.298	28	−0.870	1.611	0.370	0.607	0.000	0.590
Ostracoda								
P	3.549	28	−0.002	0.096	0.047	0.024	0.660	0.070
H	0.149	28	−0.059	0.040	−0.010	0.024	0.293	0.702
E	0.591	28	−0.030	0.069	0.019	0.024	0.344	0.448
H:E	2.254	28	−0.171	0.022	−0.075	0.047	0.042	0.144
H:P	0.149	28	−0.117	0.078	−0.019	0.048	0.054	0.702
P:E	0.591	28	−0.059	0.135	0.038	0.048	0.060	0.448
H:E:P	2.254	28	−0.332	0.032	−0.150	0.089	0.001	0.144
Mix Arthropods								
P	1.084	28	−0.378	0.122	−0.128	0.123	0.377	0.307
H	0.129	28	−0.208	0.296	0.044	0.124	0.291	0.723
E	0.069	28	−0.219	0.284	0.032	0.124	0.263	0.795
H:E	1.334	28	−0.209	0.778	0.284	0.242	0.029	0.258
H:P	0.006	28	−0.516	0.478	−0.019	0.244	0.022	0.939
P:E	2.558	28	−0.093	0.880	0.394	0.239	0.065	0.121
H:E:P	4.034	28	−1.887	−0.090	−0.988	0.440	0.002	0.054
Brachionidae (rotifer)								
P	2.686	28	−1.005	0.075	−0.465	0.265	0.926	0.112
H	5.863	28	−1.235	−0.140	−0.687	0.269	0.971	**0.022**
E	1.725	28	−0.916	0.170	−0.373	0.267	0.882	0.200
H:E	9.463	28	0.669	2.824	1.746	0.530	0.599	**0.005***
H:P	0.022	28	−0.990	1.160	0.085	0.528	0.106	0.883
P:E	0.155	28	−1.289	0.842	−0.224	0.523	0.108	0.697
H:E:P	1.275	28	−0.792	3.357	1.282	1.016	0.006	0.268
Lacanidae (rotifer)								
P	0.890	28	−0.675	0.225	−0.225	0.222	0.349	0.354
H	0.196	28	−0.559	0.347	−0.106	0.223	0.271	0.661
E	0.490	28	−0.618	0.284	−0.167	0.222	0.309	0.489
H:E	0.962	28	−1.357	0.421	−0.468	0.437	0.028	0.335
H:P	0.077	28	−1.031	0.765	−0.133	0.442	0.020	0.783
P:E	0.621	28	−0.512	1.264	0.376	0.437	0.031	0.437
H:E:P	0.212	28	−2.183	1.304	−0.439	0.854	0.000	0.649

Table S5b: continued

Treatment	F	$\mathrm{Df}_{\mathrm{res}}$	$\mathrm{CI}_{\mathrm{lower}}$	$\mathrm{CI}_{\mathrm{upper}}$	ES	SE (±)	RI	P
Euclanidae (rotifer)								
P	0.414	28	−0.656	0.315	−0.170	0.239	0.287	0.525
H	0.005	28	−0.506	0.470	−0.018	0.240	0.241	0.947
E	0.117	28	−0.578	0.397	−0.090	0.240	0.254	0.735
H:E	0.289	28	−1.256	0.686	−0.285	0.478	0.014	0.595
H:P	0.002	28	−0.995	0.950	−0.023	0.478	0.015	0.966
P:E	0.118	28	−0.787	1.152	0.182	0.477	0.016	0.734
H:E:P	0.04	28	−1.724	2.149	0.213	0.948	0.000	0.842
Lepadellidae (rotifer)								
P	3.832	28	−1.594	−0.001	−0.797	0.391	0.914	0.060
H	2.074	28	−1.382	0.209	−0.587	0.390	0.918	0.161
E	0.395	28	−0.532	1.044	0.256	0.387	0.845	0.535
H:E	8.244	28	0.789	3.889	2.339	0.761	0.749	**0.008***
H:P	6.444	28	0.516	3.620	2.068	0.762	0.766	**0.017***
P:E	3.423	28	−3.032	0.017	−1.507	0.748	0.485	0.075
H:E:P	0.316	28	−3.893	2.060	−0.916	1.457	0.068	0.578
Asplanchnidae (rotifer)								
P	0.895	28	−0.451	0.161	−0.145	0.151	0.368	0.352
H	1.511	28	−0.493	0.116	−0.188	0.150	0.448	0.229
E	0.440	28	−0.206	0.409	0.102	0.151	0.306	0.513
H:E	1.386	28	−0.959	0.237	−0.361	0.294	0.052	0.249
H:P	1.942	28	−0.166	1.021	0.427	0.292	0.078	0.174
P:E	0.005	28	−0.629	0.586	−0.022	0.298	0.023	0.944
H:E:P	2.742	28	−0.105	2.136	1.016	0.548	0.001	0.109
Trichotridae								
P	0.128	28	−0.442	0.302	−0.070	0.183	0.277	0.723
H	3.640	28	0.007	0.742	0.374	0.181	0.710	0.067
E	0.023	28	−0.342	0.402	0.030	0.183	0.273	0.880
H:E	0.825	28	−1.084	0.371	−0.357	0.358	0.058	0.371
H:P	0.109	28	−0.863	0.604	−0.129	0.361	0.041	0.744
P:E	1.097	28	−0.322	1.144	0.411	0.360	0.026	0.304
H:E:P	0.007	28	−1.499	1.369	−0.065	0.702	0.000	0.935
Effects on ecosystem properties								
Physico-chemical properties								
UV absorption								
P	0.055	28	−0.393	0.501	0.054	0.220	0.272	0.816
H	0.109	28	−0.371	0.523	0.076	0.220	0.276	0.743
E	0.016	28	−0.417	0.475	0.029	0.220	0.271	0.901
H:E	1.690	28	−0.276	1.472	0.598	0.430	0.034	0.204
H:P	0.929	28	−0.438	1.325	0.443	0.433	0.024	0.343
P:E	2.135	28	−1.542	0.199	−0.672	0.428	0.042	0.155
H:E:P	0.281	28	−1.192	2.167	0.488	0.822	0.000	0.600

Table S5b: continued

Treatment	F	$\mathrm{Df_{res}}$	$\mathrm{CI_{lower}}$	$\mathrm{CI_{upper}}$	ES	SE (±)	RI	P
pH								
P	0.026	28	−0.149	0.126	−0.012	0.068	0.274	0.874
H	0.218	28	−0.170	0.103	−0.034	0.067	0.316	0.644
E	70.088	28	−0.738	−0.463	−0.600	0.068	1.000	$<$ **0.001***
H:E	0.939	28	−0.410	0.132	−0.139	0.133	0.092	0.341
H:P	1.137	28	−0.422	0.116	−0.153	0.132	0.029	0.295
P:E	0.218	28	−0.341	0.207	−0.067	0.135	0.058	0.644
H:E:P	1.228	28	−0.206	0.842	0.318	0.257	0.000	0.277
Dissolved O_2								
P	2.363	28	−0.080	0.711	0.316	0.195	0.572	0.135
H	1.526	28	−0.143	0.650	0.254	0.195	0.464	0.227
E	31.753	28	−1.558	−0.755	−1.157	0.198	1.000	$<$ **0.001***
H:E	0.010	28	−0.835	0.753	−0.041	0.390	0.079	0.921
H:P	0.954	28	−1.176	0.374	−0.401	0.381	0.088	0.337
P:E	0.170	28	−0.960	0.622	−0.169	0.389	0.118	0.684
H:E:P	2.304	28	−0.254	2.746	1.246	0.734	0.002	0.140
Conductivity								
P	0.674	28	−2.538	6.388	1.925	2.196	0.267	0.419
H	1.753	28	−7.518	1.308	−3.105	2.172	0.578	0.196
E	105.187	28	19.559	28.551	24.055	2.214	1.000	$<$ **0.001***
H:E	2.183	28	−1.728	15.588	6.930	4.258	0.344	0.151
H:P	0.286	28	−6.236	11.256	2.510	4.295	0.042	0.597
P:E	0.101	28	−10.425	7.444	−1.490	4.392	0.067	0.753
H:E:P	0.038	28	−18.957	15.317	−1.820	8.391	0.000	0.848
				Final nutrient concentrations				
Dissolved pelagic Phosphorus								
P	1.318	28	−0.096	0.024	−0.036	0.030	0.456	0.261
H	0.070	28	−0.053	0.069	0.008	0.030	0.133	0.793
E	1.318	28	−0.024	0.096	0.036	0.030	0.456	0.261
H:E	0.582	28	−0.072	0.167	0.048	0.059	0.032	0.452
H:P	0.582	28	−0.167	0.072	−0.048	0.059	0.032	0.452
P:E	2.709	28	−0.218	0.013	−0.102	0.057	0.264	0.111
H:E:P	0.070	28	−0.260	0.194	−0.033	0.111	0.000	0.793
Total pelagic phosphorus								
P	1.452	28	−1.179	5.085	1.953	1.542	0.474	0.238
H	4.324	28	−6.507	−0.234	−3.370	1.545	0.770	**0.047**
E	0.067	28	−2.756	3.596	0.420	1.563	0.149	0.797
H:E	0.324	28	−8.097	4.409	−1.844	3.074	0.047	0.574
H:P	1.679	28	−10.299	1.899	−4.200	3.000	0.268	0.206
P:E	0.246	28	−4.641	7.855	1.607	3.070	0.027	0.624
H:E:P	1.678	28	−20.241	3.445	−8.398	5.799	0.001	0.206

Table S5b: continued

Treatment	F	$\mathrm{Df_{res}}$	$\mathrm{CI_{lower}}$	$\mathrm{CI_{upper}}$	ES	SE (±)	RI	P
Total benthic phosphorus								
P	0.078	28	−161.529	119.027	−21.251	69.004	0.950	0.783
H	0.048	28	−159.960	126.545	−16.707	70.416	0.257	0.828
E	4.541	28	20.875	304.442	162.659	69.758	0.876	**0.042**
H:E	0.005	28	−273.361	295.763	11.201	139.716	0.041	0.942
H:P	0.078	28	−238.187	323.583	42.698	137.875	0.043	0.782
P:E	9.205	28	−741.576	−184.812	−463.194	136.928	0.840	**0.005***
H:E:P	0.041	28	−619.302	496.174	−61.564	273.097	0.001	0.842
Dissolved pelagic nitrogen								
P	0.669	28	−21.291	8.665	−6.313	7.371	0.364	0.420
H	9.266	28	−38.550	−8.442	−23.496	7.415	0.966	**0.005***
E	1.034	28	−22.786	7.091	−7.848	7.352	0.409	0.318
H:E	1.066	28	−13.492	45.365	15.937	14.472	0.120	0.311
H:P	1.086	28	−13.411	45.594	16.091	14.507	0.107	0.306
P:E	0.015	28	−27.704	31.533	1.915	14.549	0.028	0.902
H:E:P	1.353	28	−92.318	20.480	−35.919	27.616	0.001	0.255
Total pelagic nitrogen								
P	0.089	28	−26.328	19.439	−3.444	11.258	0.294	0.768
H	6.940	28	−53.285	−7.567	−30.426	11.257	0.918	**0.014***
E	0.411	28	−29.929	15.121	−7.404	11.083	0.476	0.527
H:E	3.765	28	1.000	88.647	44.824	21.552	0.314	0.062
H:P	1.742	28	−14.169	75.148	30.489	21.953	0.110	0.198
P:E	0.356	28	−58.326	30.757	−13.784	21.869	0.033	0.555
H:E:P	0.545	28	−118.492	50.290	−34.101	41.322	0.002	0.467
Ammonium NH_4								
P	0.011	28	−2.818	3.138	0.160	1.466	0.260	0.915
H	< 0.01	28	−2.955	3.003	0.024	1.467	0.257	0.987
E	5.017	28	−6.281	−0.407	−3.344	1.447	0.790	**0.033**
H:E	0.061	28	−5.132	6.608	0.738	2.887	0.042	0.807
H:P	0.778	28	−3.253	8.521	2.634	2.893	0.019	0.385
P:E	0.202	28	−7.200	4.516	−1.342	2.881	0.045	0.657
H:E:P	3.873	28	−22.660	−0.844	−11.752	5.341	0.001	0.059
Dissolved Organic Carbon								
P	0.140	28	−0.846	0.565	−0.141	0.348	0.258	0.711
H	0.882	28	−0.347	1.053	0.353	0.345	0.351	0.356
E	0.645	28	−1.003	0.399	−0.302	0.345	0.323	0.429
H:E	0.582	28	−1.952	0.806	−0.573	0.678	0.032	0.452
H:P	0.006	28	−1.457	1.342	−0.058	0.688	0.019	0.939
P:E	0.178	28	−1.716	1.081	−0.317	0.688	0.019	0.676
H:E:P	0.212	28	−2.055	3.439	0.692	1.345	0.000	0.649

Table S5b: continued

Treatment	F	Df_{res}	CI_{lower}	CI_{upper}	ES	SE (±)	RI	P
				Biological parameters				
Zooplankton average size								
P	3.403	28	−0.837	0.027	−0.405	0.212	0.694	0.076
H	4.738	28	−0.913	−0.044	−0.478	0.214	0.883	**0.038**
E	0.408	28	−0.567	0.287	−0.140	0.210	0.688	0.528
H:E	6.605	28	0.294	1.964	1.129	0.411	0.573	**0.016***
H:P	1.396	28	−0.320	1.359	0.519	0.412	0.204	0.247
P:E	0.660	28	−1.188	0.475	−0.357	0.408	0.120	0.424
H:E:P	0.089	28	−1.343	1.867	0.262	0.786	0.005	0.768
Pelagic chlorophyll *a*								
P	0.399	28	−0.231	0.468	0.118	0.172	0.301	0.533
H	0.036	28	−0.315	0.386	0.036	0.173	0.257	0.85
E	2.863	28	−0.663	0.029	−0.317	0.170	0.628	0.102
H:E	0.367	28	−0.916	0.462	−0.227	0.339	0.039	0.55
H:P	0.001	28	−0.688	0.711	0.012	0.344	0.015	0.975
P:E	0.432	28	−0.932	0.439	−0.246	0.337	0.048	0.516
H:E:P	0.006	28	−1.427	1.312	−0.057	0.670	0.000	0.939
Benthic chlorophyll *a*								
P	0.554	28	−0.534	0.237	−0.148	0.190	0.294	0.463
H	0.755	28	−0.207	0.553	0.173	0.187	0.502	0.392
E	43.534	28	−1.702	−0.928	−1.315	0.191	1.000	<**0.001***
H:E	3.156	28	−1.454	0.038	−0.708	0.367	0.322	0.087
H:P	0.005	28	−0.731	0.784	0.027	0.372	0.030	0.947
P:E	0.190	28	−0.944	0.596	−0.174	0.378	0.066	0.666
H:E:P	1.088	28	−2.287	0.625	−0.831	0.713	0.001	0.306
LNA (small) bacteria								
P	0.323	28	−12450.075	7145.400	−2652.338	4819.114	0.479	0.574
H	2.127	28	−16661.385	3055.660	−6802.863	4851.024	0.609	0.156
E	0.131	28	−8139.602	11519.610	1690.004	4834.177	0.281	0.720
H:E	3.358	28	−1540.376	35730.093	17094.858	9149.112	0.173	0.078
H:P	5.262	28	2597.050	40200.967	21399.008	9237.427	0.395	**0.030**
P:E	2.885	28	−2569.672	34262.088	15846.208	9036.201	0.134	0.100
H:E:P	3.766	28	−70291.674	−2128.093	−36209.883	16688.170	0.044	0.062
HNA (big) bacteria								
P	0.983	28	−1232.979	3867.779	1317.400	1254.563	0.375	0.330
H	0.716	28	−3633.085	1384.018	−1124.533	1234.090	0.952	0.405
E	7.549	28	−6211.264	−1090.736	−3651.000	1260.436	0.603	**0.010***
H:E	4.486	28	724.204	10534.062	5629.133	2412.134	0.442	**0.043**
H:P	0.009	28	−5229.036	4728.370	−250.333	2444.572	0.041	0.926
P:E	0.236	28	−3779.302	6361.302	1291.000	2491.762	0.074	0.631

Table S5b: continued

Treatment	F	Df_{res}	CI_{lower}	CI_{upper}	ES	SE (±)	RI	P
H:E:P	< 0.01	28	−9785.789	9632.722	−76.533	4754.143	0.001	0.989
			Ecosystem processes					
Gross Primary Productivity								
P	0.062	28	−320.658	415.678	47.510	181.359	0.255	0.805
H	0.687	28	−206.523	522.543	158.010	179.571	0.354	0.414
E	0.190	28	−448.851	282.795	−83.028	180.192	0.295	0.666
H:E	2.405	28	−114.344	1296.572	591.114	346.971	0.066	0.132
H:P	0.954	28	−347.672	1092.127	372.227	354.001	0.030	0.337
P:E	0.001	28	−742.831	720.773	−11.029	359.779	0.015	0.977
H:E:P	0.079	28	−1607.177	1177.742	−214.717	681.819	0.000	0.78
Ecosystem Respiration								
P	0.107	28	−306.559	425.350	59.395	180.182	0.357	0.746
H	0.077	28	−312.896	413.614	50.359	178.836	0.303	0.784
E	1.070	28	−175.843	551.440	187.799	179.076	0.412	0.310
H:E	3.510	28	−15.540	1376.192	680.326	342.131	0.118	0.071
H:P	3.232	28	−45.820	1351.322	652.751	343.354	0.082	0.083
P:E	0.285	28	−521.740	909.674	193.967	351.699	0.030	0.597
H:E:P	0.302	28	−1725.360	927.752	−398.804	649.549	0.001	0.587
Carbon-oxygen mass exchange								
P	0.570	28	−66.403	145.384	39.491	52.088	0.474	0.457
H	0.023	28	−98.218	114.075	7.929	52.202	0.212	0.881
E	19.737	28	−340.522	−124.196	−232.359	53.265	0.998	$<$**0.001***
H:E	0.218	28	−259.781	162.177	−48.802	103.653	0.077	0.644
H:P	4.246	28	−418.137	−12.954	−215.546	99.493	0.151	**0.049**
P:E	2.412	28	−369.929	45.006	−162.462	101.982	0.362	0.132
H:E:P	2.297	28	−65.070	699.238	317.084	187.122	0.007	0.141
Ecosystem Respiration 20°C								
P	0.102	28	−17.502	24.027	3.262	10.223	0.370	0.752
H	0.054	28	−18.225	22.998	2.387	10.146	0.313	0.817
E	1.022	28	−10.303	31.006	10.352	10.170	0.416	0.321
H:E	3.821	28	0.590	79.469	40.030	19.389	0.132	0.061
H:P	3.550	28	−0.953	78.115	38.581	19.430	0.095	0.070
P:E	0.424	28	−27.101	53.777	13.338	19.869	0.033	0.520
H:E:P	0.371	28	−99.749	49.871	−24.939	36.631	0.001	0.547
Bacterial Respiration 16°C								
P	0.075	28	−0.005	0.007	0.001	0.003	0.294	0.786
H	1.336	28	−0.002	0.010	0.004	0.003	0.416	0.257
E	0.879	28	−0.003	0.009	0.003	0.003	0.360	0.356
H:E	0.568	28	−0.007	0.016	0.005	0.006	0.045	0.457
H:P	1.747	28	−0.004	0.020	0.008	0.006	0.055	0.197

Table S5b: continued

Treatment	F	$\mathrm{Df_{res}}$	$\mathrm{CI_{lower}}$	$\mathrm{CI_{upper}}$	ES	SE ($\pm$)	RI	P
P:E	1.628	28	-0.020	0.004	-0.008	0.006	0.040	0.213
H:E:P	0.084	28	-0.019	0.026	0.004	0.011	0.000	0.774
Sedimentation								
P	0.346	28	-0.417	0.215	-0.101	0.156	0.279	0.561
H	0.004	28	-0.328	0.306	-0.011	0.156	0.241	0.949
E	0.020	28	-0.341	0.293	-0.024	0.156	0.241	0.890
H:E	0.057	28	-0.717	0.553	-0.082	0.312	0.012	0.813
H:P	0.262	28	-0.454	0.806	0.176	0.310	0.016	0.612
P:E	0.029	28	-0.574	0.690	0.058	0.311	0.014	0.867
H:E:P	0.381	28	-1.679	0.831	-0.424	0.615	0.000	0.542
Light diffusion ($\mathrm{K_d}$)								
P	< 0.01	28	-0.153	0.154	0.000	0.076	0.185	0.997
H	1.096	28	-0.066	0.235	0.084	0.074	0.464	0.304
E	6.782	28	0.058	0.362	0.210	0.075	0.925	**0.015***
H:E	1.837	28	-0.513	0.076	-0.219	0.145	0.257	0.186
H:P	0.104	28	-0.354	0.250	-0.052	0.148	0.023	0.750
P:E	0.031	28	-0.277	0.334	0.029	0.150	0.046	0.861
H:E:P	0.019	28	-0.545	0.635	0.045	0.289	0.000	0.890

Table S6: Introduction and survival of phase 2 fish. Two cohorts of juvenile fish (i.e. lake, hybrids, and stream) were added to each tank after removing the adult fish (i.e. lake and stream) of phase 1. Survival of juveniles at the end of phase 2 is shown for each tank.

		1^{st} cohort introduced				2^{sd} cohort introduced				Total$_1$	Survival					Phase 1 treatment			
Tank	**Block**	**Lake$_1$**	**Hybrid$_1$**	**Stream$_1$**	**N$_1$**	**Lake$_2$**	**Hybrid$_2$**	**Stream$_2$**	**N$_2$**	**N$_{1+2}$**	**Lake**	**Hybrid**	**Stream**	**Unidentified**	**Total**	**H**	**E**	**P**	**Sex**
1	1	2	2	4	8	4	8	4	16	24	0	5	4	0	9	Lake	+N	+P	Female
2	1	2	1	3	5	4	8	4	16	21	2	4	4	4	14	Lake	-N	-P	Female
3	1	3	0	2	3	4	8	4	16	19	0	4	5	2	11	Stream	-N	-P	Female
4	1	3	2	4	7	4	8	4	16	23	3	4	11	5	23	Stream	+N	+P	Female
5	4	2	1	3	5	4	8	4	16	21	1	8	4	3	16	Lake	+N	-P	Female
6	1	3	5	7	10	4	8	4	16	26	1	3	8	2	14	Stream	-N	+P	Female
7	1	0	3	5	11	4	8	4	16	27	1	2	9	1	13	Lake	-N	+P	Female
8	1	4	0	2	6	4	8	4	16	22	1	4	4	1	10	Lake	+N	-P	Female
9	2	0	8	10	9	4	8	4	16	25	2	5	4	4	15	Stream	-N	+P	Male
10	2	3	5	7	11	4	8	4	16	27	0	3	9	1	13	Lake	+N	-P	Male
11	2	4	8	10	15	4	8	4	16	31	2	5	7	1	15	Lake	+N	+P	Male
12	2	2	4	6	11	4	8	4	16	27	1	10	9	1	21	Lake	-N	-P	Male
13	2	5	7	9	21	4	8	4	16	37	1	5	8	2	16	Stream	+N	+P	Male
14	2	7	6	8	23	4	8	4	16	39	2	4	4	3	13	Lake	-N	+P	Male
15	2	3	8	10	17	4	8	4	16	33	1	5	7	3	16	Stream	+N	-P	Male
16	2	6	5	7	20	4	8	4	16	36	0	1	1	2	4	Stream	-N	-P	Male
17	3	1	2	4	11	4	8	4	16	27	2	2	4	3	11	Stream	+N	+P	Male
18	3	5	6	8	14	4	8	4	16	30	6	2	3	1	12	Stream	-N	-P	Male
19	3	0	3	5	6	4	8	4	16	22	4	0	1	4	9	Stream	-N	+P	Male
20	3	1	4	6	12	4	8	4	16	28	4	1	4	1	10	Lake	-N	-P	Male
21	3	0	8	10	18	4	8	4	16	34	5	4	6	4	19	Stream	+N	-P	Male
22	3	2	8	10	20	4	8	4	16	36	0	2	4	7	13	Lake	-N	+P	Male
23	3	0	4	6	13	4	8	4	16	29	0	4	2	2	8	Lake	+N	-P	Male
24	3	2	4	6	13	4	8	4	16	29	2	3	4	2	11	Lake	+N	+P	Male
25	1	1	3	5	8	4	8	4	16	24	2	0	9	2	13	Stream	+N	-P	Female
26	4	1	3	5	5	4	8	4	16	21	1	6	1	3	11	Stream	-N	+P	Female
27	4	3	2	4	8	4	8	4	16	24	0	6	4	4	14	Stream	+N	+P	Female
28	4	4	3	5	6	4	8	4	16	22	5	8	0	0	13	Stream	-N	-P	Female
29	4	1	4	6	9	4	8	4	16	25	0	0	0			Lake	-N	-P	Female
30	4	5	3	5	12	4	8	4	16	28	2	6	2	2	12	Lake	-N	+P	Female
31	4	2	0	2	6	4	8	4	16	22	1	5	3	3	12	Stream	+N	-P	Female
32	4	1	1	3	6	4	8	4	16	22	5	9	4	0	18	Lake	+N	+P	Female
33	5	0	3	5	8	4	8	4	16	24	1	2	4	2	9	Lake	-N	-P	Male
34	5	6	2	4	9	4	8	4	16	25	5	3	9	1	18	Lake	+N	+P	Male
35	5	0	3	5	10	4	8	4	16	26	3	7	6	2	18	Stream	+N	-P	Male
36	5	6	1	3	7	4	8	4	16	23	1	4	2	2	9	Lake	-N	+P	Male
37	5	2	4	6	11	4	8	4	16	27	0	2	7	2	11	Stream	-N	-P	Male
38	5	3	1	3	9	4	8	4	16	25	1	4	2	4	11	Lake	+N	-P	Male
39	5	2	3	5	9	4	8	4	16	25	1	4	5	1	11	Stream	-N	+P	Male
40	5	2	3	5	8	4	8	4	16	24	4	5	0	3	12	Stream	+N	+P	Male

Table S7: Effects of phase 1 on survival, selection and body condition of juveniles in phase 2. Effects on survival and selection tested by GLMMs. Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). Significant P values are highlighted in bold.

		Survival			Selection			Infection intensity			Condition		
Juvenile Group	**Factor**	**X^2**	**Df**	**P**	**X^2**	**Df**	**P**	**X^2**	**Df**	**P**	**F**	**Df_{res}**	**P**
All	P	0.084	1	0.771				1.815	1	0.178			
	H	0.242	1	0.622				2.027	1	0.155			
	E	3.697	1	0.055				0.46	1	0.498			
	P:H	1.197	1	0.274				1.819	1	0.177			
	P:E	0.607	1	0.436				0.333	1	0.564			
	H:E	0.816	1	0.366				0.392	1	0.531			
	P:H:E	3.177	1	0.075				0.395	1	0.530			
Lake	P	0.31	1	0.578	0.174	1	0.677				0.003	18.493	0.955
	H	1.609	1	0.205	1.145	1	0.285				2.183	18.06	0.157
	E	0.234	1	0.628	0.005	1	0.943				0.273	18.406	0.607
	P:H	0.001	1	0.979	0.083	1	0.774				2.897	19.86	0.104
	P:E	0.92	1	0.338	0.521	1	0.471				0.789	17.362	0.387
	H:E	0.108	1	0.743	0.351	1	0.554				0.538	19.458	0.472
	P:H:E	4.835	1	**0.028**	6.109	1	**0.013**				1.065	18.899	0.315
Hybrids	P	0.198	1	0.656	0.014	1	0.904	1.482	1	0.223	0.006	16.028	0.938
	H	0.084	1	0.771	2.988	1	0.084	1.245	1	0.264	0.655	16.87	0.430
	E	4.358	1	**0.037**	0.25	1	0.617	0.979	1	0.322	0.147	17.011	0.706
	P:H	1.622	1	0.203	0.007	1	0.933	1.335	1	0.248	2.086	16.788	0.167
	P:E	0.007	1	0.932	0.051	1	0.821	0.825	1	0.364	17.606	16.613	**0.001**
	H:E	0.164	1	0.686	0.247	1	0.619	0.881	1	0.348	1.477	19.173	0.239
	P:H:E	0.722	1	0.396	0.676	1	0.411	0.749	1	0.387	0.063	17.901	0.804
Stream	P	0.164	1	0.685	0.038	1	0.845	0.963	1	0.326	2.248	18.156	0.151
	H	0.606	1	0.436	2.014	1	0.156	0.761	1	0.383	4.127	18.711	0.057
	E	1.815	1	0.178	0.948	1	0.330	0.772	1	0.380	0.038	20.082	0.848
	P:H	0.006	1	0.941	0.572	1	0.449	0.857	1	0.355	5.438	19.376	**0.031**
	P:E	0.042	1	0.837	0.415	1	0.520	0.772	1	0.380	0.047	19.24	0.831
	H:E	0.55	1	0.458	0.449	1	0.503	0.696	1	0.404	0.012	19.93	0.914
	P:H:E	0.032	1	0.859	0.009	1	0.924	0.672	1	0.412	0.44	19.376	0.515

Table S8a: Multivariate perMANOVAs testing the effects of the experimental treatments from phase 1 on gene expression profiles of juvenile fish in phase 2. We tested the effects on each functional gene group (e.g. stress response, metabolism genes, etc). Tests were performed for each juvenile ecotype separately (i.e. lake, hybrid, and stream). Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). Stocking, in the **Factor** column, refers to the number of juveniles introduced at the start of phase 2 and is therefore tank specific. Significant P values are highlighted in bold.

	Lake				Hybrid				Stream			
Factor	**Df**	**F**	**R2**	**P**	**Df**	**F**	**R2**	**P**	**Df**	**F**	**R2**	**P**
					All genes							
P	1	1.466	0.065	0.323	1	6.787	0.181	**0.006**	1	1.26	0.028	0.374
H	1	4.021	0.18	**0.027**	1	0.637	0.017	0.537	1	6.201	0.138	**0.011**
E	1	2.503	0.112	0.176	1	0.45	0.012	0.582	1	3.38	0.075	0.11
P:H	1	0.106	0.005	0.728	1	-0.326	-0.009	0.92	1	3.342	0.075	0.1
P:E	1	1.311	0.059	0.372	1	0.776	0.021	0.463	1	1.155	0.026	0.425
H:E	1	-0.433	-0.019	0.948	1	2.348	0.062	0.146	1	2.098	0.047	0.272
P:H:E	1	0.897	0.04	0.369	1	0.112	0.003	0.785	1	2.017	0.045	0.276
Residuals	13		0.581		23		0.612		25		0.558	
Total	21		1		31		1		33		1	
stocking	1	-0.478	-0.021	0.822	1	3.808	0.101	**0.001**	1	0.341	0.008	0.904
					Stress response genes							
P	1	-2.652	-0.063	0.981	1	2.115	0.048	0.211	1	5.153	0.127	**0.024**
H	1	10.708	0.254	**0.020**	1	1.871	0.043	0.216	1	1.144	0.028	0.311
E	1	7.925	0.188	0.052	1	2.73	0.062	0.212	1	-0.075	-0.002	0.686
P:H	1	-3.689	-0.087	0.995	1	0.05	0.001	0.64	1	-1.009	-0.025	0.887
P:E	1	-0.035	-0.001	0.656	1	-0.861	-0.02	0.817	1	-0.894	-0.022	0.87
H:E	1	5.559	0.132	0.105	1	3.442	0.079	0.128	1	0.599	0.015	0.392
P:H:E	1	4.714	0.112	0.086	1	1.629	0.037	0.3	1	10.234	0.252	**0.007**
Residuals	13		0.308		23		0.526		25		0.616	
Total	21		1		31		1		33		1	
stocking	1	6.682	0.158	0.067	1	9.715	0.222	0.226	1	0.424	0.01	0.118
					Metabolism genes							
P	1	0.83	0.026	0.547	1	17.314	0.354	**0.007**	1	2.047	0.045	0.332
H	1	12.305	0.381	**0.009**	1	-0.736	-0.015	0.82	1	10.364	0.226	0.061
E	1	5.911	0.183	0.105	1	0.849	0.017	0.363	1	5.807	0.127	0.153
P:H	1	-0.337	-0.01	0.646	1	1.608	0.033	0.238	1	5.955	0.13	0.162
P:E	1	3.311	0.103	0.193	1	1.921	0.039	0.265	1	-2.663	-0.058	0.914
H:E	1	-3.314	-0.103	0.998	1	-1.159	-0.024	0.912	1	-3.646	-0.08	0.954
P:H:E	1	1.763	0.055	0.272	1	-1.458	-0.03	0.925	1	3.097	0.068	0.259
Residuals	13		0.403		23		0.47		25		0.545	
Total	21		1		31		1		33		1	
stocking	1	-1.2	-0.037	0.887	1	7.579	0.155	**0.001**	1	-0.115	-0.003	0.892
					Innate cellular immunity							

Table S8a continued

		Lake				Hybrid				Stream		
Factor	**Df**	**F**	**R2**	**P**	**Df**	**F**	**R2**	**P**	**Df**	**F**	**R2**	**P**
P	1	0.159	0.009	0.665	1	-0.106	-0.004	0.731	1	1.608	0.048	0.381
H	1	2.369	0.136	0.21	1	-0.299	-0.012	0.771	1	4.427	0.131	0.124
E	1	-0.549	-0.031	0.878	1	1.114	0.046	0.423	1	4.504	0.133	0.125
P:H	1	-0.332	-0.019	0.867	1	-0.453	-0.019	0.823	1	-2.483	-0.073	0.958
P:E	1	1.759	0.101	0.207	1	-0.477	-0.02	0.795	1	-0.156	-0.005	0.62
H:E	1	0.25	0.014	0.637	1	-0.183	-0.008	0.680	1	-1.696	-0.05	0.892
P:H:E	1	1.036	0.059	0.26	1	0.33	0.014	0.550	1	2.765	0.082	0.24
Residuals	13		0.745		23		0.953		25		0.739	
Total	21		1		31		1		33		1	
stocking	1	-0.251	-0.014	0.697	1	1.206	0.05	0.376	1	-0.135	-0.004	0.9
Innate humoral immunity												
P	1	0.787	0.053	0.507	1	-0.128	-0.004	0.526	1	6.882	0.191	0.115
H	1	0.929	0.063	0.44	1	2.689	0.086	0.240	1	8.718	0.241	0.06
E	1	-0.915	-0.062	0.843	1	-2.326	-0.074	0.914	1	6.213	0.172	0.106
P:H	1	-0.185	-0.013	0.712	1	0.241	0.008	0.455	1	-3.672	-0.102	0.962
P:E	1	-0.387	-0.026	0.709	1	0.468	0.015	0.412	1	-5.496	-0.152	0.988
H:E	1	0.516	0.035	0.395	1	2.995	0.096	0.156	1	-2.11	-0.058	0.862
P:H:E	1	1.459	0.099	0.424	1	-0.951	-0.03	0.754	1	0.409	0.011	0.441
Residuals	13		0.878		23		0.736		25		0.692	
Total	21		1		31		1		33		1	
stocking	1	-0.401	-0.027	0.925	1	5.243	0.168	**0.023**	1	0.178	0.005	0.265
Innate immune signalling												
P	1	-0.445	-0.017	0.658	1	-0.074	-0.003	0.743	1	0.147	0.003	0.626
H	1	2.467	0.094	0.168	1	0.511	0.018	0.564	1	2.454	0.043	0.253
E	1	-1.278	-0.049	0.927	1	-2.605	-0.093	0.993	1	-1.296	-0.023	0.88
P:H	1	2.061	0.079	0.238	1	0.056	0.002	0.678	1	-0.815	-0.014	0.775
P:E	1	2.108	0.08	0.114	1	-0.735	-0.026	0.864	1	9.496	0.166	**0.020**
H:E	1	6.792	0.259	0.067	1	8.489	0.303	**0.020**	1	13.45	0.235	0.009
P:H:E	1	1.306	0.05	0.177	1	-0.298	-0.011	0.788	1	4.852	0.085	0.105
Residuals	13		0.496		23		0.82		25		0.436	
Total	21		1		31		1		33		1	
stocking	1	0.198	0.008	0.827	1	-0.301	-0.011	0.853	1	3.989	0.07	0.159
Complement system												
P	1	1.033	0.066	0.426	1	0.459	0.019	0.399	1	2.523	0.065	0.213
H	1	-0.189	-0.012	0.66	1	0.53	0.022	0.416	1	6.877	0.177	**0.050**
E	1	0.145	0.009	0.531	1	-4.507	-0.187	0.987	1	6.683	0.172	**0.047**
P:H	1	-0.321	-0.02	0.746	1	0.288	0.012	0.431	1	-3.586	-0.092	0.983
P:E	1	-0.276	-0.018	0.774	1	-0.148	-0.006	0.557	1	-1.689	-0.043	0.892
H:E	1	0.005	0	0.462	1	-0.4	-0.017	0.630	1	1.714	0.044	0.258
P:H:E	1	2.297	0.146	0.315	1	0.495	0.021	0.460	1	1.362	0.035	0.262
Residuals	13		0.828		23		0.956		25		0.643	

Table S8a continued

	Lake				Hybrid				Stream			
Factor	**Df**	**F**	**R2**	**P**	**Df**	**F**	**R2**	**P**	**Df**	**F**	**R2**	**P**
Total	21		1		31		1		33		1	
stocking	1	0.003	0	0.756	1	4.354	0.181	**0.037**	1	-0.003	0	0.478
					Adaptive immunity							
P	1	0.374	0.024	0.506	1	7.433	0.158	**0.015**	1	-2.342	-0.063	0.948
H	1	1.712	0.111	0.352	1	5.98	0.127	**0.014**	1	4.329	0.117	0.129
E	1	-1.419	-0.092	0.824	1	-0.508	-0.011	0.805	1	1.49	0.04	0.371
P:H	1	0.544	0.035	0.634	1	-2.748	-0.059	0.999	1	1.784	0.048	0.317
P:E	1	-0.407	-0.027	0.659	1	11.902	0.253	**0.002**	1	2.18	0.059	0.259
H:E	1	1.214	0.079	0.416	1	0.162	0.003	0.601	1	0.495	0.013	0.458
P:H:E	1	0.628	0.041	0.45	1	0.221	0.005	0.537	1	3.077	0.083	0.167
Residuals	13		0.847		23		0.49		25		0.677	
Total	21		1		31		1		33		1	
stocking	1	-0.289	-0.019	0.522	1	1.516	0.032	0.147	1	0.893	0.024	0.468

Table S8b: Univariate LMMs testing the effects of experimental treatments from phase 1 on each gene of juvenile fish in phase 2. Tests were performed for each juvenile ecotype separately (i.e. lake, hybrid, and stream). Treatments correspond to the effects of host (H), environment (E), parasite exposure (P), and their interactions (e.g. HxE). P-values lower than 0.05 are highlighted in bold and significant P-values after FDR correction according to Benjamini-Yekutieli are marked with *.

			Lake			Hybrid			Stream	
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df.res**	**P**	**F**	**Df.res**	**P**
fabp2										
P	0.379	1	88.829	0.540	0.030	144.156	0.863	1.072	205.739	0.302
H	1.562	1	130.261	0.214	0.021	149.616	0.885	0.013	202.295	0.908
E	1.085	1	96.322	0.300	0.512	196.342	0.475	0.845	202.254	0.359
H:E	0.001	1	144.039	0.978	0.673	201.116	0.413	0.152	215.250	0.697
P:H	0.006	1	149.611	0.940	0.055	152.153	0.815	0.093	219.162	0.761
P:E	0.869	1	89.241	0.354	3.186	220.696	0.076	0.574	233.549	0.450
P:H:E	0.095	1	139.143	0.759	0.092	221.812	0.762	0.654	211.046	0.420
lambda	3.073				4.731			3.979		
gapdh										
P	0.863	1	41.546	0.358	0.037	124.467	0.847	4.614	206.118	**0.033**
H	0.152	1	52.095	0.699	0.471	126.057	0.494	1.472	202.493	0.226
E	0.079	1	45.519	0.779	0.304	166.413	0.582	0.871	202.809	0.352
H:E	0.140	1	58.561	0.709	1.506	164.669	0.221	1.274	214.998	0.260
P:H	0.300	1	61.867	0.586	0.226	127.300	0.635	3.749	218.848	0.054
P:E	0.176	1	41.570	0.677	0.054	182.535	0.816	1.164	232.548	0.282
P:H:E	0.005	1	55.316	0.946	0.536	182.521	0.465	0.442	211.017	0.507
lambda								0.586		
acadsb										
P	2.211	1	67.140	0.142	0.033	71.577	0.856	0.932	206.133	0.335
E	0.733	1	68.379	0.395	0.001	88.961	0.971	0.200	202.833	0.655
H	0.161	1	90.329	0.689	0.043	71.650	0.836	2.526	202.501	0.114
H:E	1.210	1	98.833	0.274	0.438	91.865	0.510	0.005	214.989	0.942
P:H	0.247	1	100.777	0.621	0.799	74.375	0.374	0.335	218.837	0.564
P:E	0.000	1	61.803	0.995	0.272	98.894	0.603	0.237	232.511	0.627
P:H:E	0.886	1	108.899	0.349	0.570	97.534	0.452	0.370	211.017	0.544
lambda										
rab11al										
P	1.239	1	66.383	0.270	0.002	132.302	0.962	0.801	112.212	0.373
H	0.108	1	91.679	0.743	0.030	136.965	0.863	1.286	106.237	0.259
E	0.749	1	71.969	0.390	0.734	179.219	0.393	0.008	115.188	0.93
H:E	0.851	1	104.103	0.358	0.029	184.910	0.864	0.182	114.787	0.67
P:H	0.060	1	108.648	0.807	1.901	140.115	0.170	0.039	113.593	0.844
P:E	1.264	1	65.945	0.265	3.898	202.313	**0.050**	0.426	121.136	0.515
P:H:E	0.187	1	99.985	0.666	0.034	201.536	0.853	0.077	112.670	0.782
lambda								3.384		

Table S8b: continued

	Lake				Hybrid			Stream		
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df.res**	**P**	**F**	**Df.res**	**P**
ctrc										
P	0.374	1	97.119	0.542	2.499	144.426	0.116	0.530	65.667	0.469
H	2.982	1	144.416	0.086	0.058	150.160	0.81	2.585	61.969	0.113
E	1.352	1	105.400	0.247	2.319	197.250	0.129	1.100	68.779	0.298
H:E	0.005	1	157.422	0.944	0.471	202.754	0.493	0.004	67.159	0.953
P:H	0.004	1	163.387	0.950	5.639	152.944	**0.019***	2.132	65.221	0.149
P:E	1.353	1	98.068	0.248	0.025	222.034	0.875	2.333	70.294	0.131
P:H:E	0.858	1	152.203	0.356	0.226	222.634	0.635	1.301	65.988	0.258
lambda	-0.149									
hsp70										
P	0.021	1	48.219	0.885	1.492	136.522	0.224	1.343	205.658	0.248
H	2.781	1	61.334	0.101	1.631	136.133	0.204	0.693	202.252	0.406
E	1.986	1	51.817	0.165	0.468	187.224	0.495	0.000	202.137	0.999
H:E	0.014	1	69.751	0.905	0.980	174.978	0.323	0.862	215.314	0.354
P:H	0.191	1	72.080	0.663	1.167	135.632	0.282	0.004	219.242	0.948
P:E	0.785	1	46.873	0.380	2.649	198.130	0.105	0.281	233.786	0.597
P:H:E	0.301	1	68.177	0.585	1.262	190.327	0.263	5.331	211.059	**0.022***
lambda					1.457					
hsp90										
P	0.012	1	96.526	0.912	2.098	142.652	0.150	0.074	206.313	0.785
H	0.756	1	140.989	0.386	2.853	146.645	0.093	0.000	202.594	0.988
E	0.116	1	104.142	0.734	0.118	192.449	0.731	0.003	203.101	0.957
H:E	0.991	1	155.702	0.321	0.171	193.503	0.679	0.243	214.895	0.623
P:H	0.348	1	160.792	0.556	1.325	148.128	0.252	0.176	218.720	0.675
P:E	11.320	1	96.943	<**0.001***	1.333	214.009	0.250	0.028	232.098	0.868
P:H:E	0.409	1	151.429	0.524	0.018	216.577	0.892	0.601	211.022	0.439
lambda								5.096		
nr3c1										
P	0.956	1	76.133	0.331	0.008	111.918	0.930	2.809	150.075	0.096
H	0.760	1	104.823	0.385	0.665	114.575	0.416	1.433	144.571	0.233
E	0.005	1	81.063	0.944	0.248	148.256	0.619	0.385	151.217	0.536
H:E	1.633	1	120.155	0.204	1.524	152.988	0.219	0.275	154.927	0.600
P:H	0.188	1	122.885	0.666	0.888	117.796	0.348	0.178	155.546	0.674
P:E	1.515	1	74.294	0.222	0.484	167.284	0.488	0.163	164.619	0.687
P:H:E	1.160	1	118.889	0.284	0.050	165.687	0.823	0.062	151.928	0.803
lambda										
sod2										
P	0.425	1	97.119	0.516	0.412	79.348	0.523	1.142	218.126	0.286
H	1.425	1	144.416	0.234	0.446	79.726	0.506	0.805	206.939	0.371
E	0.424	1	105.400	0.516	0.658	100.089	0.419	0.482	218.889	0.488

Table S8b: continued

	Lake				Hybrid			Stream		
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df.res**	**P**	**F**	**Df.res**	**P**
H:E	0.260	1	157.422	0.611	0.689	103.310	0.409	0.563	220.853	0.454
P:H	0.019	1	163.387	0.89	4.590	82.629	0.035	1.075	225.158	0.301
P:E	0.149	1	98.068	0.701	0.270	111.771	0.604	0.102	237.367	0.749
P:H:E	0.517	1	152.203	0.473	0.005	110.184	0.943	0.060	217.921	0.806
lambda										
vegfa										
P	1.903	1	43.975	0.175	0.063	106.168	0.803	3.200	173.733	0.075
H	0.213	1	54.675	0.646	0.398	108.324	0.529	0.016	170.321	0.900
E	1.375	1	45.246	0.247	0.607	139.610	0.437	0.000	171.943	0.984
H:E	1.598	1	60.264	0.211	0.325	144.063	0.569	0.116	183.652	0.734
P:H	0.442	1	61.480	0.508	0.170	111.532	0.681	0.092	186.045	0.762
P:E	3.622	1	40.608	0.064	0.887	157.382	0.348	0.020	199.584	0.889
P:H:E	0.128	1	65.477	0.721	0.576	155.673	0.449	0.001	178.994	0.977
lambda								3.099		
tf										
P	0.092	1	36.543	0.763	2.089	84.373	0.152	0.000	111.859	0.989
H	0.368	1	44.941	0.547	0.130	84.294	0.719	2.944	105.606	0.089
E	0.122	1	40.239	0.728	0.609	107.878	0.437	0.039	114.954	0.844
H:E	0.516	1	50.024	0.476	0.194	108.791	0.661	0.580	114.141	0.448
P:H	0.292	1	52.996	0.591	2.675	86.309	0.106	0.035	112.892	0.852
P:E	0.192	1	36.808	0.664	0.079	118.853	0.779	1.313	120.459	0.254
P:H:E	0.704	1	46.980	0.406	0.043	116.789	0.836	0.009	112.084	0.923
lambda	0.286									
sla1										
P	0.742	1	90.452	0.391	0.263	71.863	0.61	3.107	215.820	0.079
H	1.428	1	124.595	0.234	1.014	71.945	0.317	0.024	206.285	0.878
E	0.023	1	93.112	0.879	0.863	89.367	0.355	1.196	216.237	0.275
H:E	1.047	1	136.440	0.308	0.128	92.283	0.722	3.389	219.024	0.067
P:H	0.548	1	138.229	0.461	0.026	74.678	0.872	1.310	223.121	0.254
P:E	0.261	1	86.100	0.611	0.775	99.365	0.381	7.234	234.269	**0.008***
P:H:E	0.081	1	144.197	0.777	0.100	97.994	0.753	0.804	216.337	0.371
lambda								-0.792		
ogfr										
P	0.306	1	67.806	0.582	0.003	144.674	0.959	3.941	150.834	**0.049**
H	0.005	1	91.209	0.941	0.602	150.665	0.439	1.215	146.841	0.272
E	0.161	1	71.910	0.689	0.021	198.158	0.885	0.203	150.751	0.653
H:E	0.758	1	104.836	0.386	1.099	204.355	0.296	0.387	158.347	0.535
P:H	0.036	1	106.893	0.849	0.208	153.696	0.649	0.436	159.328	0.510
P:E	2.183	1	65.397	0.144	1.396	223.308	0.239	0.054	169.997	0.816
P:H:E	0.167	1	104.612	0.683	0.040	223.352	0.842	0.060	154.477	0.806

Table S8b: continued

	Lake				Hybrid			Stream		
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df.res**	**P**	**F**	**Df.res**	**P**
lambda								3.549		
tlr2										
P	0.002	1	96.654	0.964	0.271	142.307	0.603	3.972	175.819	0.048
H	0.542	1	141.690	0.463	0.166	145.986	0.684	0.008	166.932	0.927
E	0.492	1	104.410	0.485	2.553	191.786	0.112	1.109	177.601	0.294
H:E	1.039	1	156.078	0.310	2.088	192.057	0.15	0.190	178.655	0.663
P:H	0.006	1	161.351	0.940	2.608	147.289	0.108	0.139	180.396	0.710
P:E	4.214	1	97.186	**0.043**	0.352	212.663	0.553	1.320	190.542	0.252
P:H:E	0.323	1	151.597	0.571	1.532	215.264	0.217	0.036	175.935	0.849
lambda										
f2										
P	0.659	1	40.707	0.422	0.429	114.090	0.514	2.382	198.135	0.124
H	0.073	1	50.873	0.788	0.091	116.945	0.763	3.366	189.333	0.068
E	0.002	1	44.633	0.968	0.088	151.534	0.767	0.467	199.011	0.495
H:E	0.162	1	57.105	0.689	1.078	156.371	0.301	0.004	201.429	0.948
P:H	0.117	1	60.359	0.733	1.329	120.167	0.251	1.029	204.473	0.312
P:E	0.335	1	40.769	0.566	0.008	171.026	0.927	0.274	214.992	0.601
P:H:E	0.106	1	53.894	0.746	0.112	169.485	0.738	0.120	198.709	0.729
lambda								0.545		
saal1										
P	0.258	1	49.124	0.614	1.692	137.150	0.195	0.205	130.049	0.651
H	0.553	1	62.303	0.460	0.053	142.328	0.818	0.108	125.021	0.743
E	1.554	1	51.487	0.218	0.476	186.634	0.491	1.175	131.800	0.280
H:E	0.009	1	70.047	0.925	1.484	192.533	0.225	0.408	134.709	0.524
P:H	1.478	1	71.064	0.228	2.718	145.438	0.101	0.011	134.437	0.917
P:E	0.013	1	46.161	0.909	3.687	210.577	0.056	0.168	142.871	0.683
P:H:E	0.491	1	72.425	0.486	0.757	210.093	0.385	0.776	131.880	0.380
lambda								-0.389		
socs1										
P	0.075	1	83.125	0.785	0.256	107.463	0.614	1.824	208.591	0.178
H	0.009	1	115.213	0.924	4.206	109.729	**0.043**	0.378	203.695	0.539
E	2.694	1	83.389	0.104	2.373	141.554	0.126	0.414	206.561	0.521
H:E	1.316	1	121.051	0.254	2.397	146.069	0.124	0.001	214.712	0.970
P:H	0.006	1	127.476	0.937	0.019	112.942	0.89	3.164	218.434	0.077
P:E	0.016	1	76.768	0.901	1.817	159.612	0.180	2.155	229.390	0.143
P:H:E	2.512	1	136.560	0.115	1.683	157.923	0.196	0.980	211.722	0.323
lambda										
cd97										
P	2.028	1	87.229	0.158	0.022	103.945	0.883	0.835	205.536	0.362

Table S8b: continued

	Lake				Hybrid			Stream		
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df.res**	**P**	**F**	**Df.res**	**P**
H	0.525	1	120.998	0.470	1.428	104.534	0.235	0.125	202.050	0.724
E	2.201	1	88.149	0.141	0.173	136.564	0.678	0.098	202.105	0.755
H:E	2.085	1	127.563	0.151	0.363	136.252	0.548	0.799	214.902	0.372
P:H	0.196	1	132.568	0.659	0.554	106.287	0.459	0.039	218.785	0.844
P:E	0.601	1	81.363	0.441	0.177	150.182	0.674	2.323	233.002	0.129
P:H:E	0.025	1	141.556	0.874	0.071	148.628	0.79	0.039	210.744	0.844
lambda										
mif										
P	4.121	1	92.226	**0.045**	2.237	140.486	0.137	1.674	218.126	0.197
H	1.681	1	127.141	0.197	0.012	146.022	0.913	0.296	206.939	0.587
E	0.005	1	96.053	0.941	1.885	191.740	0.171	3.605	218.889	0.059
H:E	0.169	1	142.094	0.682	0.780	197.776	0.378	2.354	220.853	0.126
P:H	0.450	1	143.615	0.504	1.852	149.099	0.176	0.279	225.158	0.598
P:E	2.100	1	89.013	0.151	0.566	216.235	0.453	0.062	237.367	0.804
P:H:E	0.909	1	146.031	0.342	0.233	215.974	0.630	0.530	217.921	0.467
lambda	5.788							-1.934		
il1b										
P	0.076	1	64.391	0.784	0.510	84.175	0.477	1.030	193.528	0.311
H	0.000	1	85.681	0.984	1.918	84.289	0.170	0.191	186.375	0.663
E	0.988	1	66.360	0.324	3.051	107.404	0.084	1.556	193.833	0.214
H:E	1.809	1	95.588	0.182	5.161	109.048	**0.025**	4.859	197.647	**0.029**
P:H	0.758	1	96.575	0.386	0.626	86.579	0.431	0.279	200.455	0.598
P:E	0.977	1	59.814	0.327	1.653	118.883	0.201	0.724	210.395	0.396
P:H:E	0.016	1	102.188	0.899	0.880	117.029	0.350	1.916	194.912	0.168
lambda										
tgfb1										
P	2.433	1	34.113	0.128	0.008	102.058	0.928	4.224	157.727	**0.042**
H	0.358	1	40.750	0.553	0.280	103.879	0.598	0.479	153.302	0.490
E	0.170	1	36.178	0.683	0.349	133.463	0.556	0.011	157.634	0.916
H:E	1.803	1	44.820	0.186	1.005	137.718	0.318	1.072	164.515	0.302
P:H	0.235	1	46.002	0.630	0.106	107.068	0.746	0.103	165.718	0.748
P:E	3.062	1	32.656	0.090	0.872	150.319	0.352	0.148	176.042	0.701
P:H:E	0.200	1	45.438	0.657	0.160	148.560	0.690	0.000	160.882	0.994
lambda								2.633		
tnfa										
P	1.223	1	59.360	0.273	0.016	67.851	0.900	2.998	206.437	0.085
H	0.459	1	77.816	0.500	1.231	67.816	0.271	0.086	202.659	0.769
E	0.161	1	61.717	0.689	0.001	83.688	0.974	0.144	203.288	0.705
H:E	0.967	1	87.705	0.328	0.051	86.449	0.823	0.654	214.839	0.420
P:H	0.011	1	88.573	0.918	0.044	70.440	0.834	0.287	218.649	0.592

Table S8b: continued

Treatment	Lake F	Df	Df.res	P	Hybrid F	Df.res	P	Stream F	Df.res	P
P:E	0.776	1	55.482	0.382	0.043	92.797	0.836	2.780	231.832	0.097
P:H:E	0.053	1	91.917	0.818	0.015	91.576	0.904	0.005	211.031	0.946
lambda										
c7										
P	0.271	1	97.119	0.604	0.002	81.072	0.963	1.250	202.109	0.265
H	1.696	1	144.416	0.195	0.289	81.532	0.593	0.838	191.610	0.361
E	2.820	1	105.400	0.096	0.374	102.582	0.542	0.016	203.337	0.899
H:E	0.010	1	157.422	0.921	1.219	105.876	0.272	0.047	204.787	0.828
P:H	0.577	1	163.387	0.448	0.268	84.469	0.606	1.985	208.084	0.160
P:E	2.187	1	98.068	0.142	0.534	114.656	0.466	1.550	219.580	0.214
P:H:E	0.266	1	152.203	0.606	5.802	113.030	**0.018***	0.188	201.920	0.665
lambda										
c9										
P	0.480	1	66.395	0.491	0.917	109.114	0.340	1.141	153.358	0.287
H	0.188	1	91.698	0.666	0.049	109.466	0.826	2.852	148.444	0.093
E	0.090	1	71.981	0.765	0.630	144.534	0.429	0.850	153.895	0.358
H:E	0.266	1	104.124	0.607	0.780	142.264	0.379	1.003	159.141	0.318
P:H	0.134	1	108.670	0.715	0.953	110.728	0.331	0.537	160.021	0.465
P:E	0.557	1	65.956	0.458	0.029	157.496	0.865	0.012	169.590	0.914
P:H:E	0.216	1	100.006	0.643	0.007	155.574	0.935	0.004	155.848	0.949
lambda										
ighm										
P	0.317	1	43.708	0.577	1.307	141.344	0.255	1.008	201.596	0.317
H	0.790	1	54.373	0.378	1.072	144.184	0.302	0.045	191.119	0.833
E	0.027	1	46.316	0.870	1.064	190.264	0.304	0.049	202.838	0.825
H:E	1.257	1	61.027	0.267	0.937	188.428	0.334	2.068	204.272	0.152
P:H	1.115	1	62.322	0.295	0.182	145.069	0.670	0.018	207.537	0.894
P:E	0.027	1	41.621	0.869	0.207	209.231	0.650	0.461	219.011	0.498
P:H:E	0.282	1	61.688	0.597	0.465	211.431	0.496	0.005	201.408	0.946
lambda					-0.451			-0.088		
ly75										
P	1.082	1	20.530	0.310	0.005	104.048	0.945	1.351	205.572	0.246
H	0.001	1	23.980	0.978	0.530	105.204	0.468	0.246	202.208	0.620
E	0.006	1	23.084	0.937	0.277	136.426	0.600	0.064	202.014	0.801
H:E	0.147	1	25.202	0.705	0.158	137.991	0.692	0.036	215.385	0.851
P:H	0.009	1	26.684	0.924	0.173	107.499	0.678	1.586	219.331	0.209
P:E	0.166	1	21.272	0.688	1.523	151.594	0.219	0.014	234.045	0.904
P:H:E	0.044	1	23.066	0.835	0.268	150.342	0.606	1.447	211.076	0.230
lambda										

Table S8b: continued

	Lake				Hybrid			Stream		
Treatment	**F**	**Df**	**Df.res**	**P**	**F**	**Df.res**	**P**	**F**	**Df.res**	**P**
il16										
P	0.684	1	59.795	0.411	0.132	92.735	0.717	2.472	146.101	0.118
H	1.053	1	78.525	0.308	2.944	93.873	0.089	0.445	138.140	0.506
E	0.309	1	61.986	0.581	0.260	119.627	0.611	1.280	148.670	0.260
H:E	0.251	1	88.203	0.618	0.110	123.442	0.741	1.353	148.595	0.247
P:H	0.681	1	89.067	0.411	0.127	96.984	0.722	1.574	148.745	0.212
P:E	0.298	1	55.717	0.587	1.317	134.369	0.253	4.190	157.833	**0.042**
P:H:E	0.295	1	93.123	0.588	0.077	132.590	0.782	0.327	146.106	0.568
lambda										
mhcII										
P	0.514	1	97.119	0.475	2.101	72.616	0.152	4.971	160.281	**0.027**
H	1.857	1	144.416	0.175	6.114	72.724	**0.016***	1.894	151.653	0.171
E	0.221	1	105.400	0.639	1.600	90.439	0.209	1.862	162.559	0.174
H:E	0.007	1	157.422	0.936	0.014	93.384	0.907	1.816	162.830	0.180
P:H	0.032	1	163.387	0.859	0.011	75.476	0.917	3.340	163.700	0.069
P:E	2.535	1	98.068	0.115	2.074	100.604	0.153	8.706	173.394	**0.004***
P:H:E	1.847	1	152.203	0.176	0.463	99.208	0.498	4.335	160.214	0.039
lambda										

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