Supplementary Information

Piecyk *et al.* 2021 Cross-continental experimental infections reveal distinct defence mechanisms in populations of the three-spined stickleback *Gasterosteus aculeatus*

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SI.1. Further information on infection rates

Table S1. Host and parasite population effects on infection rates. Results from Type III chisquare tests of generalized linear mixed effect models; the effect of sympatry was tested with a GLMM using sympatry as fixed effect and round and worm sibship as random intercepts.

In copepods (first intermediate host)	Chisq	Df	Pr(>Chisq)
(Intercept)	11.6737	1	0.0006339
Parasite population	2.9572	2	0.2279
Round	3.8827	2	0.1435
Parasite population : round	7.2386	4	0.1238
In sticklebacks	Chisq	Df	Pr(>Chisq)
(Intercept)	2.1497	1	0.1426
Parasite population	2.7889	2	0.2480
Host population	7.7672	2	0.0206
Parasite : host population	14.4449	4	0.0060
Alaskan populations	Chisq	Df	Pr(>Chisq)
(Intercept)	10.1170	1	0.00147
sympatry	5.6504	1	0.0175

SI.2. Further information on parasite indices

Linear mixed models (LMMs) with parasite origin as fixed effect did not differ significantly from the respective Nullmodels.

Table S2. Effect of host population on parasite indices. Linear mixed models (LMMs) included host population as fixed effect and fish sex and tank as crossed random terms. Bold numbers indicate significance post fdr correction according to Benjamini and Hochberg (1995) with an alpha of 0.05. The effect of sympatry was tested with a GLMM in comparison to the Nullmodel.

Parasite		Contrast (Hos	it)	Estimate	Std. Error	z value	Pr(> z)	
NO	DE	-	Walby	8.924	1.592	5.607	<0.0001	***
Walby	Wolf	-	Walby	-3.072	2.459	-1.249	0.424	
	DE	-	Walby	11.778	2.378	4.954	<0.0001	***
	DE	-	Wolf	14.850	2.631	5.643	<0.0001	***
Wolf	Wolf	-	Walby	-2.199	2.020	-1.089	0.51712	
	DE	-	Walby	6.816	2.774	2.457	0.0363	*
	DE	-	Wolf	9.015	2.624	3.436	0.0018	**
Alaskan pop	ulations				Chisq	Df	Pr(>Chisq)	
Comparison	to Nullm	odel			0.0278	1	0.8676	

SI.3. Further information on host condition and immunological parameters

Table S3. Effect of host population on condition and immunological indices in controls. Response variables were the condition factor (CF) and hepatosomatic index (HSI) as well as the splenosomatic index (SSI) and head kidney index (HKI). LMMs included host population as fixed effect and fish sex and tank as crossed random terms. Bold numbers indicate significance post fdr correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Index		Contrast (Host	:)	Estimate	Std. Error	z value	Pr(> z)	
CF	Wolf	-	Walby	-0.362	0.059	-6.187	<0.0001	***
	DE	-	Walby	1.024	0.058	17.777	<0.0001	***
	DE	-	Wolf	1.386	0.057	24.200	<0.0001	***
HSI	Wolf	-	Walby	-1.293	0.274	-4.717	< 0.001	***
	DE	-	Walby	-0.924	0.278	-3.330	0.002	**
	DE	-	Wolf	0.369	0.277	1.331	0.378	
SSI	Wolf	-	Walby	-0.013	0.008	-1.581	0.254	
	DE	-	Walby	0.016	0.008	1.873	0.147	
	DE	-	Wolf	0.029	0.008	3.411	0.002	**
HKI	Wolf	-	Walby	-0.036	0.021	-1.705	0.203	
	DE	-	Walby	0.084	0.021	3.937	<0.0001	***
	DE	-	Wolf	0.120	0.021	5.667	<0.0001	***



Figure S2. Stickleback condition (condition factor, CF, and hepatosomatic index, HSI). Fish originated from Walby Lake (Walby), Wolf Lake (Wolf), and Großer Plöner See (DE); *S. solidus* came from Walby, Wolf, and Lake Skogseidvatnet (NO); controls were sham-exposed; 'exposed' fish were exposed but uninfected.



Figure S3. Stickleback immunological parameters (splenosomatic index, SSI, and head kidney index, HKI). Fish originated from Walby Lake (Walby), Wolf Lake (Wolf), and Großer Plöner See (DE); *S. solidus* came from Walby, Wolf, and Lake Skogseidvatnet (NO); controls were sham-exposed; 'exposed' fish were exposed but uninfected.

Table S4. Effect of host population on condition and immunological indices in *S. solidus* **exposed but uninfected stickleback.** Response variables were condition factor (CF), hepatosomatic index (HSI), splenosomatic index (SSI) and head kidney index (HKI). LMMs included host population as fixed effect and fish sex and tank as crossed random effects. Bold numbers indicate significance post FDR correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Index		Contrast (Host)	Estimate	Std. Error	z value	Pr(> z)	
CF	Wolf	-	Walby	-0.329	0.021	-15.300	<0.0001	***
	DE	-	Walby	0.899	0.022	41.600	<0.0001	***
	DE	-	Wolf	1.227	0.020	62.100	<0.0001	***
HSI	Wolf	-	Walby	-0.979	0.140	-7.003	<0.001	***
	DE	-	Walby	-0.635	0.141	-4.512	<0.001	***
	DE	-	Wolf	0.344	0.129	2.674	0.020	*
SSI	Wolf	-	Walby	-0.005	0.006	-0.911	0.633	
	DE	-	Walby	0.026	0.006	4.521	<0.0001	***
	DE	-	Wolf	0.031	0.005	5.927	<0.0001	***
HKI	Wolf	-	Walby	-0.037	0.014	-2.658	0.021	*
	DE	-	Walby	0.064	0.014	4.578	<0.0001	***
	DE	-	Wolf	0.101	0.013	7.905	<0.0001	***

Table S5. Effect of host population on condition and immunological indices in *S. solidus* **infected stickleback.** Response variables were condition factor (CF), hepatosomatic index (HSI), splenosomatic index (SSI) and head kidney index (HKI). LMMs included host population as fixed effect and fish sex and tank as crossed random terms. Bold numbers indicate significance post fdr correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Index		Contrast (Host	:)	Estimate	Std. Error	z value	Pr(> z)	
CF	Wolf	-	Walby	-0.386	0.059	-6.585	<0.0001	***
	DE	-	Walby	0.651	0.053	12.300	<0.0001	***
	DE	-	Wolf	1.037	0.062	16.658	<0.0001	***
HSI	Wolf	-	Walby	-0.780	0.261	-2.986	0.008	**
	DE	-	Walby	-1.165	0.235	-4.957	< 0.001	***
	DE	-	Wolf	-0.385	0.282	-1.366	0.357	
SSI	Wolf	-	Walby	0.005	0.039	0.139	0.989	
	DE	-	Walby	0.012	0.036	0.338	0.939	
	DE	-	Wolf	0.007	0.040	0.165	0.985	
HKI	Wolf	-	Walby	-0.093	0.048	-1.922	0.132	
	DE	-	Walby	-0.043	0.045	-0.975	0.592	
	DE	-	Wolf	0.049	0.050	0.980	0.589	

Table S6. Effect of *S. solidus* **exposure and infection on host condition (condition factor, CF).** Sticklebacks were either sham-exposed (control), *S. solidus* exposed but uninfected (exposed), or *S. solidus* infected (infected). We further tested the effect of parasite origin in infected versus control stickleback. LMMs included either infection status or parasite origin as fixed effects and fish sex and tank as crossed random terms. Bold numbers indicate significance post FDR correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Host		Contrast		Estimate	Std. Error	z value	Pr(> z)	
DE	infected	-	control	-0.462	0.068	-6.818	<0.001	***
	exposed	-	control	-0.205	0.048	-4.233	<0.001	***
	exposed	-	infected	0.258	0.058	4.457	<0.001	***
Wolf	infected	-	control	-0.087	0.031	-2.781	0.0143	*
	exposed	-	control	-0.040	0.020	-1.983	0.1119	
	exposed	-	infected	0.047	0.027	1.728	0.1881	
Walby	infected	-	control	-0.144	0.035	-4.140	< 0.001	***
	exposed	-	control	-0.055	0.026	-2.072	0.094	
	exposed	-	infected	0.089	0.031	2.838	0.013	*
Parasite		Contrast		Estimate	Std. Error	z value	Pr(> z)	
NO	exposed	-	infected	-0.234	0.119	-1.972	0.0486	*
Walby	exposed	-	infected	0.055	0.113	0.486	0.627	
Wolf	exposed	-	infected	0.345	0.118	2.937	0.0033	**
Host	Cont	rast (Para	site)	Estimate	Std. Error	z value	Pr(> z)	
DE	Walby	-	CTRL	-0.461	0.126	-3.671	0.001	**
	Wolf	-	CTRL	-0.298	0.161	-1.856	0.231	
	NO	-	CTRL	-0.424	0.104	-4.059	< 0.001	***
	Wolf	-	Walby	0.163	0.200	0.814	0.836	
	NO	-	Walby	0.037	0.158	0.237	0.995	
	NO	-	Wolf	-0.126	0.187	-0.671	0.900	
Wolf	Walby	-	CTRL	-0.049	0.061	-0.803	0.693	
	Wolf	-	CTRL	-0.116	0.046	-2.502	0.031	*
	Wolf	-	Walby	-0.067	0.073	-0.930	0.612	
Walby	Walby	-	CTRL	-0.113	0.066	-1.716	0.298	
	Wolf	-	CTRL	-0.213	0.079	-2.688	0.034	*
	NO	-	CTRL	-0.149	0.081	-1.849	0.236	
	Wolf	-	Walby	-0.099	0.100	-0.992	0.739	
	NO	-	Walby	-0.036	0.101	-0.353	0.984	
	NO	-	Wolf	0.064	0.110	0.576	0.934	

Table S7. Effect of *S. solidus* **exposure and infection on host condition (hepatosomatic index, HSI).** Sticklebacks were either sham-exposed (control), *S. solidus* exposed but uninfected (exposed), or *S. solidus* infected (infected). We further tested the effect of parasite origin in infected versus control stickleback. LMMs included either infection status or parasite origin as fixed effects and fish sex and tank as crossed random terms. Bold numbers indicate significance post FDR correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Host		Contrast		Estimate	Std. Error	z value	Pr(> z)	
DE	infected	-	control	-2.119	0.245	-8.642	<0.001	***
	exposed	-	control	-0.425	0.174	-2.438	0.038	*
	exposed	-	infected	1.695	0.210	8.073	<0.001	***
Walby	infected	-	control	-2.592	0.272	-9.541	<0.001	***
	exposed	-	control	-0.626	0.209	-2.995	0.008	**
	exposed	-	infected	1.966	0.240	8.194	<0.001	***
Wolf	infected	-	control	-1.651	0.269	-6.129	<0.001	***
	exposed	-	control	-0.292	0.172	-1.700	0.181	
	exposed	-	infected	1.360	0.235	5.780	<0.001	***
Parasite		Contrast		Estimate	Std. Error	z value	Pr(> z)	
NO	exposed	-	infected	1.875	0.265	7.081	<0.0001	***
Walby	exposed	-	infected	1.473	0.257	5.723	<0.0001	***
Wolf	exposed	-	infected	1.386	0.256	5.421	<0.0001	***
Host	Cont	rast (Para	site)	Estimate	Std. Error	z value	Pr(> z)	
DE	Walby	-	CTRL	-2.018	0.284	-7.109	<0.0001	***
	Wolf	-	CTRL	-2.047	0.375	-5.459	<0.0001	***
	NO	-	CTRL	-2.265	0.234	-9.678	<0.0001	***
	Wolf	-	Walby	-0.029	0.454	-0.064	1.000	
	NO	-	Walby	-0.247	0.346	-0.714	0.884	
	NO	-	Wolf	-0.218	0.424	-0.513	0.953	
Wolf	Walby	-	CTRL	-1.128	0.458	-2.465	0.034	**
	Wolf	-	CTRL	-2.303	0.345	-6.677	<0.001	***
	Wolf	-	Walby	-1.175	0.556	-2.112	0.082	
Walby	Walby	-	CTRL	-2.620	0.408	-6.427	<0.001	***
	Wolf	-	CTRL	-1.597	0.485	-3.291	0.005	**
	NO	-	CTRL	-2.411	0.497	-4.852	<0.001	***
	Wolf	-	Walby	1.023	0.598	1.711	0.304	
	NO	-	Walby	0.209	0.607	0.345	0.985	
	NO	-	Wolf	-0.814	0.660	-1.233	0.591	

Table S8. Effect of *S. solidus* **exposure and infection on host immunity (splenosomatic index, SSI).** Sticklebacks were either sham-exposed (control), *S. solidus* exposed but uninfected (exposed), or *S. solidus* infected (infected). We further tested the effect of parasite origin in infected versus control stickleback. LMMs included either infection status or parasite origin as fixed effects and fish sex and tank as crossed random terms. Bold numbers indicate significance post fdr correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Host		Contrast		Estimate	Std. Error	z value	Pr(> z)	
DE	infected	-	control	0.048	0.013	3.763	<0.001	***
	exposed	-	control	0.007	0.009	0.720	0.747	
	exposed	-	infected	-0.041	0.011	-3.895	<0.001	***
Walby	infected	-	control	0.072	0.024	3.041	0.007	**
	exposed	-	control	0.002	0.019	0.113	0.993	
	exposed	-	infected	-0.070	0.020	-3.468	0.001	**
Wolf	infected	-	control	0.083	0.011	7.472	<0.0001	***
	exposed	-	control	0.009	0.007	1.163	0.467	
	exposed	-	infected	-0.075	0.010	-7.791	<0.0001	***
Parasite		Contrast		Estimate	Std. Error	z value	Pr(> z)	
NO	exposed	-	infected	-0.044	0.010	-4.652	<0.0001	***
Walby	exposed	-	infected	-0.087	0.021	4.083	<0.0001	***
Wolf	exposed	-	infected	-0.051	0.010	-5.148	<0.0001	***
Host	Cont	rast (Para	isite)	Estimate	Std. Error	z value	Pr(> z)	
DE	Walby	-	CTRL	0.014	0.016	0.851	0.821	
	Wolf	-	CTRL	0.140	0.022	6.412	<0.001	***
	NO	-	CTRL	0.043	0.013	3.275	0.005	**
	Wolf	-	Walby	0.127	0.025	4.981	<0.001	***
	NO	-	Walby	0.029	0.018	1.594	0.367	
	NO	-	Wolf	-0.097	0.024	-4.101	<0.001	***
Wolf	Walby	-	CTRL	0.108	0.017	6.537	<0.001	***
	Wolf	-	CTRL	0.069	0.012	5.592	<0.001	***
	Wolf	-	Walby	-0.039	0.019	-2.044	0.098	
Walby	Walby	-	CTRL	0.140	0.047	2.947	0.016	*
	Wolf	-	CTRL	0.029	0.058	0.505	0.956	
	NO	-	CTRL	0.013	0.058	0.215	0.996	
	Wolf	-	Walby	-0.110	0.067	-1.646	0.344	
	NO	-	Walby	-0.127	0.067	-1.898	0.222	
	NO	-	Wolf	-0.017	0.075	-0.225	0.996	

Table S9. Effect of *S. solidus* **exposure and infection on host immunity (head kidney index, HKI).** Sticklebacks were either sham-exposed (control), *S. solidus* exposed but uninfected (exposed), or *S. solidus* infected (infected). We further tested the effect of parasite origin in infected versus control stickleback. LMMs included either infection status or parasite origin as fixed effects and fish sex and tank as crossed random terms. Bold numbers indicate significance post fdr correction according to Benjamini and Hochberg (1995) with an alpha of 0.05.

Host		Contrast		Estimate	Std. Error	z value	Pr(> z)	
DE	infected	-	control	0.011	0.030	0.370	0.926	
	exposed	-	control	-0.008	0.022	-0.390	0.918	
	exposed	-	infected	-0.019	0.025	-0.783	0.709	
Walby	infected	-	control	0.150	0.033	4.513	<0.0001	***
	exposed	-	control	0.015	0.026	0.588	0.825	
	exposed	-	infected	-0.135	0.029	-4.715	<0.0001	***
Wolf	infected	-	control	0.095	0.024	3.915	<0.001	***
	exposed	-	control	0.018	0.016	1.143	0.497	
	exposed	-	infected	-0.077	0.021	-3.674	<0.001	***
Host		Contrast		Estimate	Std. Error	z value	Pr(> z)	
NO	exposed	-	infected	-0.105	0.028	-3.851	0.0001	***
Walby	exposed	-	infected	-0.111	0.030	-3.748	0.0002	***
Wolf	exposed	-	infected	-0.052	0.026	-2.028	0.0425	
Host	Cont	rast (Para	site)	Estimate	Std. Error	z value	Pr(> z)	
DE	Walby	-	CTRL	0.044	0.044	0.990	0.742	
	Wolf	-	CTRL	0.003	0.060	0.047	1.000	
	NO	-	CTRL	-0.012	0.036	-0.335	0.986	
	Wolf	-	Walby	-0.041	0.071	-0.576	0.935	
	NO	-	Walby	-0.056	0.053	-1.052	0.704	
	NO	-	Wolf	-0.015	0.067	-0.224	0.996	
Wolf	Walby	-	CTRL	0.041	0.041	0.989	0.563	
	Wolf	-	CTRL	0.120	0.031	3.843	<0.001	***
	Wolf	-	Walby	0.079	0.048	1.662	0.213	
Walby	Walby	-	CTRL	0.177	0.057	3.110	0.009	**
	Wolf	-	CTRL	0.096	0.067	1.427	0.471	
	NO	-	CTRL	0.145	0.070	2.087	0.151	
	Wolf	-	Walby	-0.081	0.080	-1.012	0.734	
	NO	-	Walby	-0.032	0.082	-0.385	0.980	

SI.4. Further information on stickleback gene expression

Non-parametric permutational multivariate analyses of variance (PERMANOVA (Anderson, 2001) using the function adonis() from the *vegan* package (Oksanen et al., 2015)) were based on Euclidian distance matrices and 10,000 permutations. The weight of the fish was included as covariate to account for size-related effects. Permutations were constrained within tank. Pairwise PERMANOVAs were used *a posteriori* to identify significantly different groups (Anderson, 2001). The False Discovery Rate (FDR) (Benjamini and Hochberg, 1995) was used to account for multiple testing.

Multivariate patterns in gene expression were visualized by non-metric multidimensional scaling (NMDS) on Euclidian distances and two dimensions (function metaMDS()); the contribution of each gene was plotted by use of the envfit() function (both implemented in *vegan*).

Linear mixed models to compare expression levels of single genes were fit with Imer() from *Ime4* (Bates et al., 2014); pseudo R² were calculated with sem.model.fits() from the R package *piecewiseSEM* (Lefcheck, 2016); the glht() function from *multcomp* (Hothorn et al., 2008) was used for post hoc pairwise comparisons. The R² includes the effect of the random term and was calculated according to (Nakagawa and Schielzeth, 2013; Johnson, 2014).

Table S10. Effects of host and parasite population and infection status on stickleback gene expression profiles. The PERMANOVA included host (H) and parasite (P) population and infection status (group: control, exposed, infected) and all interactions as explanatories and the weight of the fish as covariate. Permutations (10,000) were constrained within tank.

Explanatories	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
Fish weight	1	25.92	25.9154	7.9633	0.02762	0.0542	•
Stickleback population (H)	2	38.77	19.3855	5.9568	0.04131	0.0005	***
S. solidus population (P)	3	11.79	3.9293	1.2074	0.01256	0.3596	
group	2	22.22	11.1076	3.4132	0.02367	0.0004	***
H:P interaction	6	22.65	3.7746	1.1599	0.02413	0.3885	
H:group interaction	2	9.08	4.5407	1.3953	0.00968	0.1048	
P:group interaction	2	9.63	4.8172	1.4802	0.01027	0.2120	
H:P:group interaction	3	7.59	2.5284	0.7769	0.00808	0.4672	
Residuals	243	790.81	3.2544		0.84268		
Total	264	938.45			1		



SI.4.1. Baseline gene expression profiles of the host populations (n = 84)

Figure S4. Gene expression profiles of sham-exposed stickleback. Sticklebacks originated from Walby Lake (Walby; Alaska), Wolf Lake (Wolf; Alaska), and Großer Plöner See (DE; Germany) and were 10 months old. Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total*) including eleven innate immune genes (*innate*: *marco*, *mst1ra*, *mif*, *tnfr1*, *saal1*, *tlr2*, *csf3r*, *p22^{phox}*, *nkef-b*, *sla1*, *cd97*), eight adaptive immune genes (*adaptive: stat4*, *stat6*, *igm*, *cd83*, *foxp3*, *il-16*, *mhcII*, *tcr-β*), three complement component genes (*complement: cfb*, *c7*, *c9*), and three regulatory genes (*regulatory: abtb1*, *kat2a*, *mapk13*). NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Table S11.

Table S11. Population effect on gene expression profiles of sham-exposed stickleback. Sticklebacks originated from Walby Lake (Alaska), Wolf Lake (Alaska), and Großer Plöner See (Germany). Bold numbers indicate significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	5.344	5.3438	1.6574	0.0192	0.0330	*
	fish_origin	2	14.468	7.2342	2.2437	0.0521	0.0081	**
	Residuals	80	257.944	3.2243		0.9287		
	Total	83	277.757			1		
innate	fish_weight	1	2.961	2.96106	3.0167	0.0350	0.0005	***
	fish_origin	2	3.03	1.51516	1.5436	0.0359	0.0239	*
	Residuals	80	78.525	0.98156		0.9291		
	Total	83	84.516			1		
adaptive	fish_weight	1	2.107	2.1066	2.3098	0.0262	0.0334	*
	fish_origin	2	5.437	2.7187	2.981	0.0675	0.0072	**
	Residuals	80	72.96	0.912		0.9063		
	Total	83	80.504			1		
complement	fish_weight	1	0.237	0.23698	0.19546	0.0023	0.7881	
	fish_origin	2	5.219	2.60955	2.15231	0.0509	0.1398	
	Residuals	80	96.995	1.21244		0.9467		
	Total	83	102.451			1		
regulatory	fish_weight	1	0.0514	0.05138	0.33116	0.0039	0.6183	
	fish_origin	2	0.8496	0.42479	2.73814	0.0638	0.0040	**
	Residuals	80	12.4112	0.15514		0.9323		
	Total	83	13.3122			1		

 Table S12. Population effect on gene expression profiles of sham-exposed Alaskan stickleback.
 Sold numbers indicate significance post FDR correction.

Walby vs Wolf	•	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	6.43	6.4301	2.1272	0.0389	0.0524	
	fish_origin	1	7.863	7.8629	2.6012	0.0475	0.0034	**
	Residuals	50	151.142	3.0228		0.9136		
	Total	52	165.435			1		
innate	fish_weight	1	0.867	0.86735	0.9995	0.0195	0.1886	
	fish_origin	1	0.27	0.26998	0.3111	0.0061	0.6797	
	Residuals	50	43.388	0.86776		0.9745		
	Total	52	44.525			1		
adaptive	fish_weight	1	4.124	4.1243	4.2979	0.0758	0.0958	
	fish_origin	1	2.281	2.2806	2.3766	0.0419	0.042	*
	Residuals	50	47.98	0.9596		0.8822		
	Total	52	54.385			1		
complement	fish_weight	1	1.435	1.4355	1.3204	0.0235	0.2328	
	fish_origin	1	5.23	5.2299	4.8107	0.0857	0.0072	**
	Residuals	50	54.357	1.0871		0.8908		
	Total	52	61.022			1		
regulatory	fish_weight	1	0.0485	0.04846	0.3212	0.0063	0.555	
	fish_origin	1	0.1157	0.11574	0.7669	0.0150	0.1643	
	Residuals	50	7.5455	0.15091		0.9787		
	Total	52	7.7097			1		

Walby vs DE		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	3.7390	3.7389	1.2052	0.0203	0.1892	
	fish_origin	1	4.0240	4.0237	1.2970	0.0218	0.1502	
	Residuals	57	176.84	3.1024		0.9580		
	Total	59	184.60			1		
innate	fish_weight	1	2.5680	2.5683	2.5805	0.0423	0.0016	**
	fish_origin	1	1.4540	1.4539	1.4608	0.0239	0.0456	*
	Residuals	57	56.732	0.9953		0.9338		
	Total	59	60.754			1		
adaptive	fish_weight	1	0.6740	0.6739	0.9776	0.0165	0.0647	
	fish_origin	1	0.9030	0.9035	1.3107	0.0221	0.0555	
	Residuals	57	39.292	0.6893		0.9614		
	Total	59	40.869			1		
complement	fish_weight	1	0.3800	0.3801	0.2911	0.0050	0.7961	
	fish_origin	1	1.2940	1.2940	0.9909	0.0170	0.3490	
	Residuals	57	74.434	1.3059		0.9780		
	Total	59	76.108			1		
regulatory	fish_weight	1	0.1224	0.1224	0.8214	0.0136	0.2395	
	fish_origin	1	0.3833	0.3833	2.5726	0.0426	0.0117	*
	Residuals	57	8.4918	0.1490		0.9438		
	Total	59	8.9974			1		

Table S13. Population effect on gene expression profiles of sham-exposed Alaskan (Walby) and European (DE) stickleback. Bold numbers indicate significance post FDR correction.

Table S14. Population effect on gene expression profiles of sham-exposed Alaskan (Wolf) and European (DE) stickleback. Bold numbers indicate significance post FDR correction.

Wolf vs DE		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	5.129	5.1287	1.5268	0.0267	0.1318	
	fish_origin	1	12.005	12.0048	3.5738	0.0626	0.0070	**
	Residuals	52	174.674	3.3591		0.9107		
	Total	54	191.808			1		
innate	fish_weight	1	3.244	3.2435	3.0500	0.0528	0.0024	**
	fish_origin	1	2.893	2.8934	2.7208	0.0471	0.0260	*
	Residuals	52	55.300	1.0635		0.9001		
	Total	54	61.437			1		
adaptive	fish_weight	1	1.371	1.3709	1.2700	0.0218	0.2930	
	fish_origin	1	5.483	5.4827	5.0790	0.0871	0.0352	*
	Residuals	52	56.133	1.0795		0.8912		
	Total	54	62.987			1		
complement	fish_weight	1	0.764	0.7641	0.6447	0.0116	0.6050	
	fish_origin	1	3.280	3.2797	2.7670	0.0499	0.0229	*
	Residuals	52	61.635	1.1853		0.9384		
	Total	54	65.679			1		
regulatory	fish_weight	1	0.092	0.0924	0.5686	0.0098	0.2769	
	fish_origin	1	0.938	0.9381	5.7720	0.0989	0.0132	*
	Residuals	52	8.451	0.1625		0.8913		
	Total	54	9.482			1		

Table S15. Differentially expressed genes between sham-exposed controls. LMMs included the origin of the fish as fixed effect, the weight of the fish as covariate and tank as random term. Bold letters indicate significance.

	contrast		Estimate	Std. Error	z value	Pr(> z)		R2	
regulatory									
abtb1	Wolf	-	Walby	-0.0496	0.0397	-1.249	0.423		0.579
	DE	-	Walby	0.0089	0.0437	0.205	0.977		
	DE	-	Wolf	0.0585	0.0379	1.543	0.27		
kat2a	Wolf	-	Walby	-0.0754	0.0524	-1.4410	0.319		0.381
	DE	-	Walby	0.0263	0.0569	0.4630	0.888		
	DE	-	Wolf	0.1018	0.0502	2.0270	0.105		
mapk13	Wolf	-	Walby	0.0060	0.0596	0.1010	0.994		0.535
	DE	-	Walby	0.2000	0.0653	3.0640	0.006	**	
	DE	-	Wolf	0.1940	0.0570	3.4040	0.002	**	
innate									
cd97	Wolf	-	Walby	-0.03379	0.08173	-0.413	0.91		0.783
	DE	-	Walby	0.11055	0.09082	1.217	0.441		
	DE	-	Wolf	0.14434	0.07783	1.855	0.151		
csf3r	Wolf	-	Walby	-0.0197	0.0593	-0.3320	0.941		0.308
	DE	-	Walby	-0.1393	0.0635	-2.1930	0.072	•	
	DE	-	Wolf	-0.1197	0.0571	-2.0950	0.091		
marco	Wolf	-	Walby	-0.1026	0.0698	-1.4700	0.304		0.675
	DE	-	Walby	-0.0889	0.0771	-1.1540	0.480		
	DE	-	Wolf	0.0137	0.0666	0.2060	0.977		
mif1	Wolf	-	Walby	0.0150	0.0337	0.4460	0.896		0.582
	DE	-	Walby	0.0557	0.0371	1.5020	0.289		
	DE	-	Wolf	0.0406	0.0322	1.2630	0.415		
mst1ra	Wolf	-	Walby	-0.0361	0.0478	-0.7560	0.729		0.399
	DE	-	Walby	-0.0978	0.0517	-1.8900	0.141		
	DE	-	Wolf	-0.0616	0.0459	-1.3430	0.371		
nkefb	Wolf	-	Walby	0.0120	0.0718	0.1670	0.985		0.523
	DE	-	Walby	0.0664	0.0788	0.8430	0.675		
	DE	-	Wolf	0.0544	0.0687	0.7920	0.707		
p22phox	Wolf	-	Walby	-0.0444	0.0443	-1.0040	0.574		0.306
	DE	-	Walby	0.1072	0.0477	2.2490	0.063	•	
	DE	-	Wolf	0.1516	0.0425	3.5640	0.001	**	
saal1	Wolf	-	Walby	0.0839	0.0607	1.3840	0.349		0.376
	DE	-	Walby	-0.0941	0.0658	-1.4300	0.325		
	DE	-	Wolf	-0.1780	0.0582	-3.0580	0.006	**	
sla	Wolf	-	Walby	-0.0579	0.0396	-1.4620	0.308		0.419
	DE	-	Walby	-0.0644	0.0430	-1.4960	0.292		
	DE	-	Wolf	-0.0065	0.0379	-0.1710	0.984		
tlr2	Wolf	-	Walby	-0.0193	0.0783	-0.2470	0.967		0.206
	DE	-	Walby	0.2142	0.0837	2.5580	0.028	*	
	DE	-	Wolf	0.2335	0.0755	3.0940	0.006	**	
tnfr1	Wolf	-	Walby	-0.0016	0.0693	-0.0230	1.000		0.684
	DE	-	Walby	-0.1406	0.0765	-1.8370	0.157		
	DE	-	Wolf	-0.1390	0.0661	-2.1030	0.089		

Table S15 (continued). Differentially expressed genes between sham-exposed controls. LMMs included the origin of the fish as fixed effect, the weight of the fish as covariate and tank as random term.

	contrast		Estimate	Std. Error	z value	Pr(> 2	z)	R2	
adaptive									
stat4	Wolf	-	Walby	-0.0661	0.0568	-1.1640	0.474		0.709
	DE	-	Walby	-0.0563	0.0629	-0.8960	0.641		
	DE	-	Wolf	0.0097	0.0541	0.1800	0.982		
cd83	Wolf	-	Walby	-0.0821	0.0397	-2.0670	0.096		0.481
	DE	-	Walby	-0.1276	0.0434	-2.9410	0.009	**	
	DE	-	Wolf	-0.0455	0.0380	-1.1950	0.455		
igm	Wolf	-	Walby	-0.4509	0.1667	-2.7060	0.019	*	0.169
	DE	-	Walby	0.0681	0.1767	0.3850	0.921		
	DE	-	Wolf	0.5190	0.1609	3.2260	0.004	**	
stat6	Wolf	-	Walby	-0.0476	0.0404	-1.1780	0.465		0.654
	DE	-	Walby	-0.0856	0.0446	-1.9220	0.132		
	DE	-	Wolf	-0.0380	0.0386	-0.9850	0.585		
foxp3	Wolf	-	Walby	-0.0399	0.0813	-0.4900	0.876		0.693
	DE	-	Walby	0.0674	0.0900	0.7480	0.734		
	DE	-	Wolf	0.1072	0.0776	1.3830	0.349		
il16	Wolf	-	Walby	-0.0632	0.0468	-1.3500	0.367		0.370
	DE	-	Walby	0.0196	0.0509	0.3850	0.921		
	DE	-	Wolf	0.0828	0.0449	1.8430	0.155		
mhcII	Wolf	-	Walby	-0.1014	0.0474	-2.1370	0.082	•	0.115
	DE	-	Walby	-0.0154	0.0503	-0.3060	0.950		
	DE	-	Wolf	0.0860	0.0458	1.8780	0.145		
tcr-β	Wolf	-	Walby	-0.0369	0.1004	-0.3680	0.928		0.192
	DE	-	Walby	-0.2093	0.1077	-1.9430	0.126		
	DE	-	Wolf	-0.1724	0.0966	-1.7840	0.174		
complement									
с7	Wolf	-	Walby	0.0300	0.0412	0.728	0.746		0.564
	DE	-	Walby	-0.0291	0.0453	-0.643	0.795		
	DE	-	Wolf	-0.0591	0.0394	-1.502	0.289		
c9	Wolf	-	Walby	-0.3773	0.1361	-2.773	0.015	*	0.134
	DE	-	Walby	0.0323	0.1443	0.224	0.973		
	DE	-	Wolf	0.4097	0.1314	3.119	0.005	**	
cfb	Wolf	-	Walby	-0.5242	0.2711	-1.933	0.129		0.172
	DE	-	Walby	-0.4092	0.2906	-1.408	0.336		
	DE	-	Wolf	0.1150	0.2610	0.441	0.898		



Figure S5. Gene expression profiles of *S. solidus* **exposed stickleback.** Sticklebacks originated from Walby Lake (Walby; Alaska), Wolf Lake (Wolf; Alaska), and Großer Plöner See (DE; Germany); *S. solidus* came from Walby Lake, Wolf Lake, and Lake Skogseidvatnet (NO; Norway). Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total*) including eleven innate immune genes (*innate: marco, mst1ra, mif, tnfr1, saal1, tlr2, csf3r, p22^{phox}, nkef-b, sla1, cd97*), eight adaptive immune genes (*adaptive: stat4, stat6, igm, cd83, foxp3, il-16, mhcII, tcr-* β), three complement component genes (*complement: cfb, c7, c9*), and three regulatory genes (*regulatory: abtb1, kat2a, mapk13*). NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Tables S16-S18.

Host effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	7.28	7.2800	2.2054	0.0670	0.0205	*
	Host origin	2	8.937	4.4685	1.3537	0.0823	0.2190	
	Residuals	28	92.426	3.3009		0.8507		
	Total	31	108.643			1		
innate	fish_weight	1	3.4334	3.4334	4.0349	0.1155	0.0294	*
	Host origin	2	2.4653	1.2327	1.4486	0.0829	0.4385	
	Residuals	28	23.8263	0.8509		0.8016		
	Total	31	29.725			1		
adaptive	fish_weight	1	1.938	1.9378	2.1494	0.0606	0.0993	
	Host origin	2	4.817	2.4086	2.6717	0.1506	0.0120	*
	Residuals	28	25.243	0.9015		0.7889		
	Total	31	31.998			1		
complement	fish_weight	1	1.629	1.6286	1.1505	0.0385	0.1158	
	Host origin	2	1.055	0.5275	0.3726	0.0249	0.7936	
	Residuals	28	39.636	1.4156		0.9366		
	Total	31	42.319			1		
regulatory	fish_weight	1	0.3905	0.3905	2.0664	0.0621	0.1452	
	Host origin	2	0.6109	0.3054	1.6160	0.0971	0.3973	
	Residuals	28	5.2919	0.1890		0.8409		
	Total	31	6.2933			1		

Table S16. Differences between Walby *S. solidus* exposed hosts (Walby, Wolf, and DE stickleback). The effect of host origin was not significant after FDR correction.

Table S17. Differences between Wolf *S. solidus* exposed hosts (Walby, Wolf, and DE stickleback). Bold numbers indicate significance post FDR correction.

Host effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	4.346	4.3461	1.1329	0.0340	0.9072	
	Host origin	2	16.117	8.0585	2.1007	0.1260	0.0042	**
	Residuals	28	107.411	3.8361		0.8400		
	Total	31	127.874			1		
innate	fish_weight	1	2.134	2.1336	1.9541	0.0577	0.7368	
	Host origin	2	4.263	2.1314	1.9520	0.1153	0.0102	*
	Residuals	28	30.573	1.0919		0.8270		
	Total	31	36.969			1		
adaptive	fish_weight	1	1.253	1.2534	1.4202	0.0392	0.7389	
	Host origin	2	6.032	3.0158	3.4170	0.1885	0.0005	***
	Residuals	28	24.713	0.8826		0.7723		
	Total	31	31.998			1		
complement	fish_weight	1	0.436	0.4356	0.2558	0.0082	0.9643	
	Host origin	2	5.145	2.5726	1.5108	0.0966	0.1592	
	Residuals	28	47.68	1.7029		0.8952		
	Total	31	53.261			1		
regulatory	fish_weight	1	0.5496	0.5496	2.8073	0.0791	0.4291	
	Host origin	2	0.9131	0.4566	2.3319	0.1315	0.0289	*
	Residuals	28	5.4821	0.1958		0.7894		
	Total	31	6.9449			1		

Table S18. Differences between NO *S. solidus* exposed hosts (Walby, Wolf, and DE stickleback). The bold number indicates significance post FDR.

Host effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	9.014	9.0145	2.4115	0.0640	0.0113	*
	Host origin	2	8.582	4.2908	1.1478	0.0609	0.1455	
	Residuals	33	123.359	3.7381		0.8752		
	Total	36	140.955			1.0000		
innate	fish_weight	1	5.164	5.1636	6.3459	0.1544	0.0007	***
	Host origin	2	1.431	0.7155	0.8793	0.0428	0.3010	
	Residuals	33	26.852	0.8137		0.8028		
	Total	36	33.446			1.0000		
adaptive	fish_weight	1	2.0438	2.0438	3.3566	0.0732	0.0208	*
	Host origin	2	5.7858	2.8929	4.7511	0.2072	0.0007	***
	Residuals	33	20.0934	0.6089		0.7196		
	Total	36	27.923			1.0000		
complement	fish_weight	1	1.502	1.5022	0.6753	0.0198	0.2633	
	Host origin	2	1.131	0.5656	0.2543	0.0149	0.8305	
	Residuals	33	73.402	2.2243		0.9654		
	Total	36	76.036			1.0000		
regulatory	fish_weight	1	0.4202	0.4202	3.4071	0.0878	0.0864	
	Host origin	2	0.294	0.1470	1.1919	0.0615	0.1907	
	Residuals	33	4.0696	0.1233		0.8507		
	Total	36	4.7838			1.0000		

Table	S19.	Differences	between	exposed	Walby	stickleback	(Walby,	Wolf,	and	NO	S .
solidu	s)										

Parasite effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	3.331	3.3309	0.9475	0.0274	0.4707
	S. solidus	2	5.9	2.9498	0.8391	0.0485	0.1198
	Residuals	32	112.494	3.5154		0.9242	
	Total	35	121.724			1	
innate	fish_weight	1	1.5996	1.5996	2.0020	0.0540	0.0612 .
	S. solidus	2	2.4722	1.2361	1.5471	0.0834	0.0775 .
	Residuals	32	25.5676	0.7990		0.8626	
	Total	35	29.6394			1	
adaptive	fish_weight	1	0.891	0.8910	2.2327	0.0591	0.2207
	S. solidus	2	1.4086	0.7043	1.7649	0.0935	0.2487
	Residuals	32	12.77	0.3991		0.8474	
	Total	35	15.0696			1	
complement	fish_weight	1	0.806	0.8060	0.3636	0.0110	0.9538
	S. solidus	2	1.476	0.7382	0.3330	0.0202	0.0619 .
	Residuals	32	70.934	2.2167		0.9688	
	Total	35	73.216			1	
regulatory	fish_weight	1	0.0533	0.0533	0.4025	0.0110	0.2357
	S. solidus	2	0.5706	0.2853	2.1563	0.1175	0.3171
	Residuals	32	4.2335	0.1323		0.8716	
	Total	35	4.8574			1	

Parasite effect	t	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	9.538	9.5385	1.9458	0.0736	0.75
	S. solidus	2	7.249	3.6245	0.7394	0.0560	0.25
	Residuals	23	112.747	4.9021		0.8704	
	Total	26	129.535			1	
innate	fish_weight	1	4.8607	4.8607	5.7926	0.1911	0.875
	S. solidus	2	1.2729	0.6365	0.7585	0.0501	1
	Residuals	23	19.2995	0.8391		0.7588	
	Total	26	25.4331			1	
adaptive	fish_weight	1	3.026	3.0259	1.9475	0.0750	0.75
	S. solidus	2	1.573	0.7866	0.5063	0.0390	0.375
	Residuals	23	35.736	1.5537		0.8860	
	Total	26	40.335			1	
complement	fish_weight	1	0.38	0.3797	0.1610	0.0065	0.375
	S. solidus	2	4.252	2.1258	0.9011	0.0722	0.25
	Residuals	23	54.257	2.3590		0.9214	
	Total	26	58.889			1	
regulatory	fish_weight	1	1.5814	1.5814	8.6223	0.2647	0.875
	S. solidus	2	0.1754	0.0877	0.4782	0.0294	1
	Residuals	23	4.2184	0.1834		0.7060	
	Total	26	5.9753			1	

Table S20. Differences between exposed Wolf stickleback (Walby, Wolf, and NO S. solidus)

Table S21. Differences between exposed DE stickleback (Walby, Wolf, and NO S. solidus)

Parasite effect	t	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	5.533	5.5334	1.9471	0.0518	0.5
	S. solidus	2	4.749	2.3745	0.8356	0.0444	0.4844
	Residuals	34	96.622	2.8418		0.9038	
	Total	37	106.904			1	
innate	fish_weight	1	2.708	2.7076	2.5718	0.0672	0.5117
	S. solidus	2	1.82	0.9101	0.8644	0.0451	0.4766
	Residuals	34	35.796	1.0528		0.8877	
	Total	37	40.324			1	
adaptive	fish_weight	1	1.4861	1.4861	2.3920	0.0625	0.4844
	S. solidus	2	1.1784	0.5892	0.9484	0.0495	0.4844
	Residuals	34	21.1236	0.6213		0.8880	
	Total	37	23.7881			1	
complement	fish_weight	1	1.106	1.1057	1.0615	0.0290	0.6094
	S. solidus	2	1.571	0.7857	0.7543	0.0413	0.5664
	Residuals	34	35.416	1.0416		0.9297	
	Total	37	38.093			1	
regulatory	fish_weight	1	0.237	0.2370	1.3304	0.0364	0.5312
	S. solidus	2	0.2252	0.1126	0.6322	0.0346	0.5586
	Residuals	34	6.0561	0.1781		0.9291	
	Total	37	6.5182			1	

Table	S22.	Diffe	rentially	expresse	da	adapti	ive	imn	nune	gen	es l	betw	een	Wo	olf-	expo	sed
stickle	back.	LMMs	included	the origin o	of th	ne fish	as	fixed	effect,	the	weig	ght of	the	fish	as	covar	riate
and tar	nk as r	andom	term. Bo	old letters in	ndic	ate sig	Jnifi	icance	e.								

	CO	ontras	st	Estimate	Std. Error	z value Pr(> z)			R2
adaptive									
stat4	Wolf	-	Walby	-0.2384	0.0782	-3.0500	0.007	**	0.729
	DE	-	Walby	-0.2553	0.0781	-3.2680	0.003	**	
	DE	-	Wolf	-0.0169	0.0754	-0.2240	0.973		
cd83	Wolf	-	Walby	-0.2117	0.0629	-3.3660	0.002	**	0.545
	DE	-	Walby	-0.3393	0.0632	-5.3720	< 1e-04	***	
	DE	-	Wolf	-0.1276	0.0619	-2.0610	0.098		
igm	Wolf	-	Walby	-0.6746	0.2247	-3.0020	0.008	**	0.239
	DE	-	Walby	-0.3588	0.2270	-1.5800	0.254		
	DE	-	Wolf	0.3158	0.2226	1.4190	0.331		
stat6	Wolf	-	Walby	-0.1869	0.0761	-2.4550	0.038	*	0.617
	DE	-	Walby	-0.2993	0.0761	-3.9310	< 0.001	***	
	DE	-	Wolf	-0.1124	0.0739	-1.5200	0.282		
foxp3	Wolf	-	Walby	-0.1712	0.0856	-1.9990	0.112		0.84
	DE	-	Walby	-0.1662	0.0855	-1.9430	0.127		
	DE	-	Wolf	0.0050	0.0821	0.0610	0.998		
il16	Wolf	-	Walby	-0.1326	0.0747	-1.7750	0.178		0.416
	DE	-	Walby	-0.1194	0.0748	-1.5960	0.247		
	DE	-	Wolf	0.0132	0.0730	0.1810	0.982		
mhcII	Wolf	-	Walby	-0.0680	0.0573	-1.1870	0.461		0.493
	DE	-	Walby	-0.0731	0.0573	-1.2760	0.408		
	DE	-	Wolf	-0.0051	0.0558	-0.0920	0.995		
tcr-β	Wolf	-	Walby	-0.3580	0.1583	-2.2620	0.061		0.611
	DE	-	Walby	-0.5859	0.1582	-3.7030	< 0.001	***	
	DE	-	Wolf	-0.2279	0.1536	-1.4830	0.299		

Table S23. Differentially expressed genes between NO-exposed stickleback. LMMs included the origin of the fish as fixed effect, the weight of the fish as covariate and tank as random term. Bold letters indicate significance.

	CC	ontra	ast	Estimate	Std. Error	z value	Pr(> z)	R2
adaptive								
stat4	Wolf	-	Walby	-0.0743	0.0694	-1.0710	0.531	0.797
	DE	-	Walby	-0.1401	0.0682	-2.0540	0.099 .	
	DE	-	Wolf	-0.0658	0.0748	-0.8800	0.653	
cd83	Wolf	-	Walby	-0.1885	0.0531	-3.5500	0.002 **	0.618
	DE	-	Walby	-0.1812	0.0513	-3.5350	0.001 **	
	DE	-	Wolf	0.0073	0.0573	0.1280	0.991	
igm	Wolf	-	Walby	-1.0326	0.2173	-4.7530	< 1e-04 ***	0.417
	DE	-	Walby	-0.2372	0.2053	-1.1550	0.479	
	DE	-	Wolf	0.7955	0.2346	3.3910	0.002 **	
stat6	Wolf	-	Walby	-0.1008	0.0604	-1.6680	0.217	0.72
	DE	-	Walby	-0.1646	0.0591	-2.7870	0.015 *	
	DE	-	Wolf	-0.0638	0.0651	-0.9790	0.589	
foxp3	Wolf	-	Walby	0.0508	0.1053	0.4830	0.879	0.72
	DE	-	Walby	0.0747	0.1030	0.7250	0.748	
	DE	-	Wolf	0.0239	0.1135	0.2110	0.976	
il16	Wolf	-	Walby	-0.0991	0.0602	-1.6460	0.226	
	DE	-	Walby	0.0242	0.0581	0.4170	0.908	0.553
	DE	-	Wolf	0.1233	0.0650	1.8990	0.139	
mhcII	Wolf	-	Walby	-0.1898	0.0626	-3.0320	0.007 **	
	DE	-	Walby	-0.0257	0.0590	-0.4360	0.900	0.269
	DE	-	Wolf	0.1640	0.0676	2.4270	0.040 *	
tcr-β	Wolf	-	Walby	0.0288	0.0892	0.3230	0.944	0.103
	DE	-	Walby	-0.0501	0.0844	-0.5930	0.823	
	DE	-	Wolf	-0.0789	0.0963	-0.8190	0.691	



Figure S6. Gene expression profiles of *S. solidus* **infected stickleback.** Sticklebacks originated from Walby Lake (Walby; Alaska), Wolf Lake (Wolf; Alaska), and Großer Plöner See (DE; Germany); *S. solidus* came from Walby Lake, Wolf Lake, and Lake Skogseidvatnet (NO; Norway). Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total*) including eleven innate immune genes (*innate: marco, mst1ra, mif, tnfr1, saal1, tlr2, csf3r, p22^{phox}, nkef-b, sla1, cd97*), eight adaptive immune genes (*adaptive: stat4, stat6, igm, cd83, foxp3, il-16, mhcII, tcr-* β), three complement component genes (*complement: cfb, c7, c9*), and three regulatory genes (*regulatory: abtb1, kat2a, mapk13*). NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Tables S24-S26.

Host effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	6.386	6.3857	1.8526	0.0550	0.9598
	Host origin	2	23.498	11.7488	3.4085	0.2025	0.3609
	Residuals	25	86.172	3.4469		0.7425	
	Total	28	116.056			1.0000	
innate	fish_weight	1	2.454	2.4538	2.2138	0.0635	0.9888
	Host origin	2	8.505	4.2526	3.8367	0.2200	0.6109
	Residuals	25	27.710	1.1084		0.7166	
	Total	28	38.669			1.0000	
adaptive	fish_weight	1	1.184	1.1837	0.9495	0.0292	0.9912
	Host origin	2	8.250	4.1252	3.3089	0.2032	0.1478
	Residuals	25	31.167	1.2467		0.7676	
	Total	28	40.601			1.0000	
complement	fish_weight	1	2.565	2.5655	2.6524	0.0804	0.6217
	Host origin	2	5.158	2.5789	2.6662	0.1617	0.4456
	Residuals	25	24.181	0.9672		0.7579	
	Total	28	31.904			1.0000	
regulatory	fish_weight	1	0.187	0.1867	1.1336	0.0306	0.8198
	Host origin	2	1.802	0.9010	5.4700	0.2951	0.1265
	Residuals	25	4.118	0.1647		0.6743	
	Total	28	6.107			1.0000	

Table S24. Differences between Walby *S. solidus* infected stickleback (Walby, Wolf, and DE fish)

Table S25. Differences between Wolf *S. solidus* infected stickleback (Walby, Wolf, and DE fish)

Host effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	5.078	5.0779	1.8928	0.0691	0.0439	*
	Host origin	2	4.018	2.0088	0.7488	0.0547	0.6715	
	Residuals	24	64.388	2.6828		0.8762		
	Total	27	73.484			1.0000		
innate	fish_weight	1	1.638	1.6380	2.2817	0.0823	0.0149	*
	Host origin	2	1.037	0.5185	0.7222	0.0521	0.5848	
	Residuals	24	17.229	0.7179		0.8656		
	Total	27	19.904			1.0000		
adaptive	fish_weight	1	1.494	1.4943	1.8558	0.0643	0.2052	
	Host origin	2	2.430	1.2152	1.5092	0.1045	0.1276	
	Residuals	24	19.324	0.8052		0.8312		
	Total	27	23.249			1.0000		
complement	fish_weight	1	1.557	1.5569	1.5115	0.0585	0.0990	
	Host origin	2	0.331	0.1654	0.1606	0.0124	0.9778	
	Residuals	24	24.722	1.0301		0.9291		
	Total	27	26.610			1.0000		
regulatory	fish_weight	1	0.431	0.4313	2.9054	0.1015	0.0957	
	Host origin	2	0.255	0.1275	0.8589	0.0600	0.3375	
	Residuals	24	3.562	0.1484		0.8385		
	Total	27	4.249			1.0000		

Host effect		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	2.454	2.4536	1.3598	0.0558	0.0049	**
	Host origin	1	7.236	7.2363	4.0103	0.1646	0.1351	
	Residuals	19	34.284	1.8044		0.7796		
	Total	21	43.974			1		
innate	fish_weight	1	0.546	0.5456	1.1197	0.0534	0.0789	
	Host origin	1	0.423	0.4228	0.8677	0.0413	0.7984	
	Residuals	19	9.258	0.4873		0.9053		
	Total	21	10.226			1		
adaptive	fish_weight	1	1.357	1.3571	4.9834	0.1628	0.0007	***
	Host origin	1	1.807	1.8071	6.6357	0.2167	0.0001	***
	Residuals	19	5.174	0.2723		0.6205		
	Total	21	8.338			1		
complement	fish_weight	1	0.430	0.4302	0.4306	0.0177	0.3339	
	Host origin	1	4.934	4.9342	4.9395	0.2027	0.2282	
	Residuals	19	18.980	0.9989		0.7796		
	Total	21	24.344			1		
regulatory	fish_weight	1	0.224	0.2240	3.3187	0.1418	0.0125	*
	Host origin	1	0.073	0.0732	1.0847	0.0464	0.4042	
	Residuals	19	1.282	0.0675		0.8119		
	Total	21	1.580			1		

Table S26. Differences between NO S. solidus infected stickleback (Walby and DE fish)

Table S27. Differences within infected Walby stickleback (Walby, Wolf, and NO S. solidus)

Parasite effec	t	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	6.002	6.0021	2.3392	0.0701	0.7481
	S. solidus	3	10.370	3.4567	1.3472	0.1211	0.4597
	Residuals	27	69.279	2.5659		0.8089	
	Total	31	85.651			1	
innate	fish_weight	1	1.482	1.4822	1.7465	0.0542	0.9548
	S. solidus	3	2.965	0.9882	1.1644	0.1084	0.9748
	Residuals	27	22.914	0.8487		0.8375	
	Total	31	27.361			1	
adaptive	fish_weight	1	0.870	0.8700	1.6518	0.0539	0.9899
	S. solidus	3	1.058	0.3528	0.6698	0.0655	0.9938
	Residuals	27	14.221	0.5267		0.8806	
	Total	31	16.150			1	
complement	fish_weight	1	3.598	3.5976	3.2771	0.0918	0.3526
	S. solidus	3	5.953	1.9842	1.8074	0.1519	0.2859
	Residuals	27	29.641	1.0978		0.7563	
	Total	31	39.191			1	
regulatory	fish_weight	1	0.054	0.0539	0.4342	0.0139	0.5675
	S. solidus	3	0.466	0.1554	1.2520	0.1204	0.6147
	Residuals	27	3.351	0.1241		0.8657	
	Total	31	3.871			1	

Parasite effect	t	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	5.200	5.1995	1.7172	0.0818	0.1793
	S. solidus	1	0.802	0.8018	0.2648	0.0126	0.8034
	Residuals	19	57.531	3.0279		0.9055	
	Total	21	63.532			1	
innate	fish_weight	1	1.956	1.9563	2.4438	0.1117	0.2391
	S. solidus	1	0.353	0.3532	0.4413	0.0202	0.4171
	Residuals	19	15.210	0.8005		0.8682	
	Total	21	17.519			1	
adaptive	fish_weight	1	1.367	1.3674	1.0375	0.0510	0.1332
	S. solidus	1	0.408	0.4078	0.3094	0.0152	0.7487
	Residuals	19	25.042	1.3180		0.9338	
	Total	21	26.817			1	
complement	fish_weight	1	1.085	1.0850	1.4085	0.0689	0.2339
	S. solidus	1	0.037	0.0367	0.0476	0.0023	0.7639
	Residuals	19	14.636	0.7703		0.9288	
	Total	21	15.758			1	
regulatory	fish_weight	1	0.853	0.8526	5.2762	0.2171	0.1198
	S. solidus	1	0.004	0.0041	0.0252	0.0010	0.9015
	Residuals	19	3.070	0.1616		0.7819	
	Total	21	3.927			1	

Table S28. Differences within infected Wolf stickleback (Walby and Wolf S. solidus)

Table S29. Differences within infected DE stickleback (Walby, Wolf, and NO S. solidus)

Parasite effec	t	Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	14.578	14.5779	5.9882	0.1708	0.9688
	S. solidus	2	17.216	8.6080	3.5359	0.2017	0.9727
	Residuals	22	53.558	2.4344		0.6275	
	Total	25	85.352			1	
innate	fish_weight	1	5.053	5.0533	7.4936	0.1907	0.7695
	S. solidus	2	6.605	3.3023	4.8970	0.2493	0.7956
	Residuals	22	14.836	0.6743		0.5600	
	Total	25	26.494			1	
adaptive	fish_weight	1	3.183	3.1830	4.7654	0.1402	0.6302
	S. solidus	2	4.829	2.4143	3.6145	0.2127	0.4518
	Residuals	22	14.695	0.6680		0.6472	
	Total	25	22.707			1	
complement	fish_weight	1	5.874	5.8743	5.8582	0.1821	0.9766
	S. solidus	2	4.322	2.1609	2.1550	0.1340	0.9701
	Residuals	22	22.060	1.0027		0.6839	
	Total	25	32.257			1	
regulatory	fish_weight	1	0.639	0.6393	5.7377	0.1337	0.8385
	S. solidus	2	1.691	0.8455	7.5892	0.3537	0.8385
	Residuals	22	2.451	0.1114		0.5126	
	Total	25	4.781			1	

	contrast		Estimate	Std. Error	z value	z value Pr(> z)		
adaptive								
stat4	DE	-	Walby	-0.1941	0.1152	-1.6860	0.092 .	0.746
cd83	DE	-	Walby	-0.3716	0.0730	-5.0890	<0.0001 ***	0.873
igm	DE	-	Walby	-0.5029	0.1209	-4.1600	<0.0001 ***	0.811
stat6	DE	-	Walby	-0.1812	0.0928	-1.9530	0.051 .	0.841
foxp3	DE	-	Walby	0.0576	0.1058	0.5440	0.586	0.753
il16	DE	-	Walby	-0.0709	0.1208	-0.5870	0.557	0.52
mhcII	DE	-	Walby	-0.2617	0.0967	-2.7070	0.007 **	0.845
tcr-β	DE	-	Walby	-0.4820	0.1089	-4.4260	<0.0001 ***	0.683

Table S30. Differentially expressed genes between NO infected stickleback. LMMs included the origin of the fish as fixed effect, the weight of the fish as covariate and tank as random term. Bold letters indicate significance.



SI.4.4. Effect of infection status on stickleback gene expression profiles

Figure S7. Immune and regulatory gene expression profiles of sham-exposed and *S. solidus* **exposed and infected stickleback.** Statistics follow Tables S31-S39.



Figure S8. Gene expression profiles of eleven innate immune genes of sham-exposed and *S. solidus* exposed and infected stickleback. Statistics follow Tables S31-S39.



Figure S9. Gene expression profiles of eight adaptive immune genes of sham-exposed and *S. solidus* exposed and infected stickleback. Statistics follow Tables S31-S39.



Figure S10. Gene expression profiles of three complement components of sham-exposed and *S. solidus* exposed and infected stickleback. Statistics follow Tables S31-S39.



Figure S11. Gene expression profiles of three regulatory genes of sham-exposed and *S. solidus* exposed and infected stickleback. Statistics follow Statistics follow Tables S31-S39.

Table S31. Differences between gene expression profiles of control, exposed, and infected Walby stickleback. Fish were sham-exposed controls or exposed or infected with Walby *S. solidus* (group).

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	3.031	3.0312	1.0666	0.0210	0.5288
	group	2	4.950	2.4751	0.8709	0.0343	0.2645
	Residuals	48	136.411	2.8419		0.9447	
	Total	51	144.392			1	
innate	fish_weight	1	1.364	1.3641	1.5119	0.0294	0.6948
	group	2	1.691	0.8456	0.9372	0.0365	0.1353
	Residuals	48	43.306	0.9022		0.9341	
	Total	51	46.361			1	
adaptive	fish_weight	1	0.652	0.6516	1.1036	0.0219	0.5106
	group	2	0.800	0.4000	0.6776	0.0269	0.3213
	Residuals	48	28.338	0.5904		0.9513	
	Total	51	29.790			1	
complement	fish_weight	1	1.055	1.0549	0.8017	0.0159	0.2139
	group	2	2.330	1.1649	0.8852	0.0350	0.3458
	Residuals	48	63.165	1.3159		0.9491	
	Total	51	66.550			1	
regulatory	fish_weight	1	0.050	0.0500	0.3205	0.0064	0.8136
	group	2	0.298	0.1487	0.9534	0.0380	0.2550
	Residuals	48	7.488	0.1560		0.9557	
	Total	51	7.836			1	

Table S32. Differences between gene expression profiles of control, exposed, and infected Walby stickleback. Fish were sham-exposed controls or exposed or infected with Wolf *S. solidus* (group).

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	1.245	1.2451	0.4291	0.0092	0.3613
	group	2	6.693	3.3463	1.1532	0.0494	0.5808
	Residuals	44	127.679	2.9018		0.9415	
	Total	47	135.616			1	
innate	fish_weight	1	0.053	0.0526	0.0634	0.0014	0.9592
	group	2	1.545	0.7725	0.9320	0.0406	0.1795
	Residuals	44	36.471	0.8289		0.9580	
	Total	47	38.069			1	
adaptive	fish_weight	1	0.079	0.0785	0.1495	0.0032	0.7754
	S. solidus	2	1.193	0.5966	1.1359	0.0489	0.3767
	Residuals	44	23.110	0.5252		0.9478	
	Total	47	24.382			1	
complement	fish_weight	1	1.070	1.0704	0.6838	0.0145	0.2890
	S. solidus	2	4.131	2.0654	1.3193	0.0558	0.6280
	Residuals	44	68.881	1.5655		0.9298	
	Total	47	74.083			1	
regulatory	fish_weight	1	0.080	0.0801	0.6122	0.0135	0.2859
	S. solidus	2	0.114	0.0572	0.4373	0.0192	0.9546
	Residuals	44	5.753	0.1308		0.9673	
	Total	47	5.948			1	

Table S33. Differences between gene expression profiles of control, exposed, and infected Walby stickleback. Fish were sham-exposed controls or exposed or infected with NO *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	0.578	0.5779	0.2183	0.0040	0.8177	
	group	2	12.273	6.1365	2.3180	0.0845	0.0368	*
	Residuals	50	132.364	2.6473		0.9115		
	Total	53	145.215			1		
innate	fish_weight	1	0.289	0.2893	0.4015	0.0075	0.5965	
	group	2	2.182	1.0910	1.5143	0.0567	0.3911	
	Residuals	50	36.023	0.7205		0.9358		
	Total	53	38.494			1		
adaptive	fish_weight	1	0.124	0.1235	0.2757	0.0053	0.9571	
	group	2	0.815	0.4074	0.9098	0.0349	0.8004	
	Residuals	50	22.389	0.4478		0.9598		
	Total	53	23.327			1		
complement	fish_weight	1	0.236	0.2365	0.1594	0.0028	0.6362	
	group	2	9.299	4.6496	3.1341	0.1111	0.0256	*
	Residuals	50	74.176	1.4835		0.8861		
	Total	53	83.712			1		
regulatory	fish_weight	1	0.002	0.0022	0.0200	0.0004	0.9186	
	group	2	0.256	0.1280	1.1838	0.0452	0.5136	
	Residuals	50	5.405	0.1081		0.9544		
	Total	53	5.663			1		

Table S34. Differences between gene expression profiles of control, exposed, and infected Wolf stickleback. Fish were sham-exposed controls or exposed or infected with Walby *S. solidus* (group). The bold number indicates significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	11.021	11.0211	2.9893	0.0744	0.2602	
	group	2	4.295	2.1475	0.5825	0.0290	0.5933	
	Residuals	36	132.727	3.6869		0.8965		
	Total	39	148.043			1		
innate	fish_weight	1	4.651	4.6514	5.6953	0.1285	0.0875	
	group	2	2.143	1.0717	1.3122	0.0592	0.0065	**
	Residuals	36	29.402	0.8167		0.8123		
	Total	39	36.196			1		
adaptive	fish_weight	1	5.655	5.6555	3.6176	0.0890	0.3947	
	S. solidus	2	1.638	0.8191	0.5240	0.0258	0.5937	
	Residuals	36	56.279	1.5633		0.8853		
	Total	39	63.572			1		
complement	fish_weight	1	0.192	0.1918	0.1494	0.0040	0.3888	
	S. solidus	2	1.127	0.5633	0.4387	0.0237	0.6859	
	Residuals	36	46.221	1.2839		0.9723		
	Total	39	47.540			1		
regulatory	fish_weight	1	0.914	0.9137	6.3502	0.1487	0.0523	
	S. solidus	2	0.053	0.0264	0.1836	0.0086	0.8540	
	Residuals	36	5.180	0.1439		0.8428		
	Total	39	6.147			1		

Table S35. Differences between gene expression profiles of control, exposed, and infected Wolf stickleback. Fish were sham-exposed controls or exposed or infected with Wolf *S. solidus* (group).

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	10.066	10.0657	2.9645	0.0589	0.1415
	group	2	4.735	2.3677	0.6973	0.0277	0.3738
	Residuals	46	156.191	3.3954		0.9134	
	Total	49	170.992			1	
innate	fish_weight	1	3.777	3.7772	3.8419	0.0745	0.1931
	group	2	1.710	0.8548	0.8695	0.0337	0.2303
	Residuals	46	45.225	0.9831		0.8918	
	Total	49	50.712			1	
adaptive	fish_weight	1	4.335	4.3351	3.3082	0.0656	0.0540 .
	group	2	1.485	0.7425	0.5666	0.0225	0.4414
	Residuals	46	60.279	1.3104		0.9120	
	Total	49	66.099			1	
complement	fish_weight	1	0.727	0.7272	0.7086	0.0147	0.7433
	group	2	1.599	0.7995	0.7791	0.0323	0.3456
	Residuals	46	47.208	1.0263		0.9530	
	Total	49	49.535			1	
regulatory	fish_weight	1	1.581	1.5809	7.8492	0.1451	0.1677
	group	2	0.053	0.0264	0.1309	0.0048	0.9583
	Residuals	46	9.265	0.2014		0.8501	
	Total	49	10.898			1	

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	6.631	6.6314	1.7100	0.0550	0.3281
	group	1	5.453	5.4528	1.4061	0.0452	0.3516
	Residuals	28	108.583	3.8780		0.8999	
	Total	30	120.667			1	
innate	fish_weight	1	2.290	2.2901	2.5767	0.0837	0.4766
	group	1	0.187	0.1870	0.2104	0.0068	0.9531
	Residuals	28	24.886	0.8888		0.9095	
	Total	30	27.363			1	
adaptive	fish_weight	1	3.462	3.4618	2.4024	0.0763	0.0938 .
	S. solidus	1	1.538	1.5382	1.0675	0.0339	0.7344
	Residuals	28	40.346	1.4409		0.8897	
	Total	30	45.346			1	
complement	fish_weight	1	0.729	0.7286	0.4798	0.0156	0.5859
	S. solidus	1	3.614	3.6140	2.3801	0.0771	0.1797
	Residuals	28	42.517	1.5185		0.9073	
	Total	30	46.860			1	
regulatory	fish_weight	1	0.446	0.4463	2.9607	0.0931	0.3359
	S. solidus	1	0.129	0.1292	0.8572	0.0269	0.2109
	Residuals	28	4.220	0.1507		0.8800	
	Total	30	4.796			1	

Table S36. Differences between gene expression profiles of control and NO *S. solidus* exposed Wolf stickleback. Wolf stickleback were not infected with NO *S. solidus*.

Table S37. Differences between gene expression profiles of control, exposed, and infected DE stickleback. Fish were sham-exposed controls or exposed or infected with Walby *S. solidus* (group). Bold numbers indicate significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	11.946	11.9459	3.9016	0.0653	0.3403	
	group	2	20.889	10.4445	3.4112	0.1142	0.0043	**
	Residuals	49	150.029	3.0618		0.8204		
	Total	52	182.864			1		
innate	fish_weight	1	4.450	4.4501	3.9716	0.0620	0.1039	
	group	2	12.399	6.1993	5.5328	0.1728	<0.001	***
	Residuals	49	54.903	1.1205		0.7652		
	Total	52	71.751			1		
adaptive	fish_weight	1	2.975	2.9746	3.4904	0.0588	0.06189	
	group	2	5.862	2.9310	3.4393	0.1159	0.0005	***
	Residuals	49	41.758	0.8522		0.8254		
	Total	52	50.595			1		
complement	fish_weight	1	3.934	3.9338	3.6625	0.0672	0.786	
	group	2	1.945	0.9725	0.9054	0.0332	0.6162	
	Residuals	49	52.630	1.0741		0.8995		
	Total	52	58.508			1		
regulatory	fish_weight	1	0.807	0.8068	4.6221	0.0745	0.1263	
	group	2	1.466	0.7332	4.2003	0.1354	0.0026	**
	Residuals	49	8.554	0.1746		0.7900		
	Total	52	10.827			1		

Table S38. Differences between gene expression profiles of control, exposed, and infected DE stickleback. Fish were sham-exposed controls or exposed or infected with Wolf *S. solidus* (group). The bold number indicates significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	5.507	5.5071	1.7895	0.0384	0.8428	
	group	2	8.586	4.2931	1.3950	0.0599	0.1168	
	Residuals	42	129.254	3.0775		0.9017		
	Total	45	143.347			1		
innate	fish_weight	1	1.455	1.4545	1.3561	0.0293	0.9809	
	group	2	3.178	1.5888	1.4813	0.0640	0.0083	**
	Residuals	42	45.048	1.0726		0.9068		
	Total	45	49.681			1		
adaptive	fish_weight	1	1.247	1.2467	1.6061	0.0349	0.3561	
	S. solidus	2	1.895	0.9475	1.2206	0.0530	0.0274	*
	Residuals	42	32.602	0.7762		0.9121		
	Total	45	35.743			1		
complement	fish_weight	1	2.725	2.7252	2.2092	0.0470	0.5687	
	S. solidus	2	3.399	1.6995	1.3777	0.0587	0.6120	
	Residuals	42	51.810	1.2336		0.8943		
	Total	45	57.934			1		
regulatory	fish_weight	1	0.127	0.1273	0.9078	0.0186	0.8146	
	S. solidus	2	0.834	0.4168	2.9731	0.1217	0.0376	*
	Residuals	42	5.888	0.1402		0.8597		
	Total	45	6.849			1.0000		

Table S39. Differences between gene expression profiles of control, exposed, and infected DE stickleback. Fish were sham-exposed controls or exposed or infected with NO *S. solidus* (group). Bold numbers indicate significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	14.391	14.3907	5.0082	0.0800	0.6693	
	group	2	10.406	5.2028	1.8106	0.0578	0.0233	*
	Residuals	54	155.165	2.8734		0.8622		
	Total	57	179.961			1		
innate	fish_weight	1	4.918	4.9176	4.9989	0.0769	0.6139	
	group	2	5.903	2.9516	3.004	0.0923	0.0006	***
	Residuals	54	53.122	0.9837		0.8308		
	Total	57	63.942			1		
adaptive	fish_weight	1	3.383	3.3828	5.4544	0.0844	0.3361	
	group	2	3.201	1.6004	2.5805	0.0799	0.0091	**
	Residuals	54	33.490	0.6202		0.8357		
	Total	57	40.074			1		
complement	fish_weight	1	5.784	5.7842	4.5459	0.0767	0.7208	
	group	2	0.921	0.4604	0.3618	0.0122	0.6871	
	Residuals	54	68.710	1.2724		0.9111		
	Total	57	75.415			1		
regulatory	fish_weight	1	0.684	0.6843	4.7639	0.0765	0.6673	
	group	2	0.509	0.2545	1.7719	0.0569	0.0750	
	Residuals	54	7.757	0.1436		0.8667		
	Total	57	8.950			1		



SI.4.5. Gene expression differences between infected and control fish



Figure S12. Gene expression profiles of *S. solidus* infected and control Walby stickleback. Stickleback originated from Walby Lake (Walby; Alaska); *S. solidus* came from Walby Lake (Walby; Alaska), Wolf Lake (Wolf; Alaska), and Lake Skogseidvatnet (NO; Norway). Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total*) including eleven innate immune genes (*innate: marco, mst1ra, mif, tnfr1, saal1, tlr2, csf3r, p22^{phox}, nkef-b, sla1, cd97*), eight adaptive immune genes (*adaptive: stat4, stat6, igm, cd83, foxp3, il-16, mhcII, tcr-* β), three complement component genes (*complement: cfb, c7, c9*), and three regulatory genes (*regulatory: abtb1, kat2a, mapk13*). NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Tables S40-S42.



Figure S13. Gene expression profiles of *S. solidus* infected and control Wolf stickleback. Stickleback originated from Wolf Lake (ALX; Alaska); *S. solidus* came from Walby Lake (ALO; Alaska) and Wolf Lake (ALX; Alaska); *S. solidus* from Lake Skogseidvatnet (NO; Norway) did not infect ALX stickleback (as indicated by 'na'). Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total*) including eleven innate immune genes (*innate: marco, mst1ra, mif, tnfr1, saal1, tlr2, csf3r, p22^{phox}, nkef-b, sla1, cd97),* eight adaptive immune genes (*adaptive: stat4, stat6, igm, cd83, foxp3, il-16, mhcII, tcr-β*), three complement component genes (*complement: cfb, c7, c9*), and three regulatory genes (*regulatory: abtb1, kat2a, mapk13*). NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Tables S43 and S44.



Figure S14. Gene expression profiles of *S. solidus* **infected and control DE stickleback.** Stickleback originated from Lake Großer Plöner See (DE; Germany); *S. solidus* came from Walby Lake (ALO; Alaska), Wolf Lake (ALX; Alaska), and Lake Skogseidvatnet (NO; Norway). Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total***)** including eleven innate immune genes (*innate: marco, mst1ra, mif, tnfr1, saal1, tlr2, csf3r, p22*^{phox}, *nkef-b, sla1, cd97***)**, eight adaptive immune genes (*adaptive: stat4, stat6, igm, cd83, foxp3, il-16, mhcII, tcr-* β **)**, three complement component genes (*complement: cfb, c7, c9***)**, and three regulatory genes (*regulatory: abtb1, kat2a, mapk13***)**. NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Tables S45-S47.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	2.133	2.1327	0.6891	0.0163	0.9963
	group	1	1.862	1.8621	0.6017	0.0142	0.3698
	Residuals	41	126.886	3.0948		0.9695	
	Total	43	130.881			1	
innate	fish_weight	1	1.318	1.3177	1.3903	0.0323	0.9988
	group	1	0.657	0.6566	0.6928	0.0161	0.2437
	Residuals	41	38.858	0.9478		0.9517	
	Total	43	40.832			1	
adaptive	fish_weight	1	0.599	0.5993	0.9358	0.0221	0.7174
	S. solidus	1	0.226	0.2257	0.3524	0.0083	0.6274
	Residuals	41	26.259	0.6405		0.9695	
	Total	43	27.084			1	
complement	fish_weight	1	0.188	0.1882	0.1339	0.0032	0.8866
	S. solidus	1	0.885	0.8846	0.6297	0.0151	0.3622
	Residuals	41	57.598	1.4048		0.9817	
	Total	43	58.670			1	
regulatory	fish_weight	1	0.036	0.0362	0.2428	0.0058	0.9730
	S. solidus	1	0.119	0.1193	0.8010	0.0191	0.2096
	Residuals	41	6.108	0.1490		0.9752	
	Total	43	6.264			1	

Table S40. Differences between gene expression profiles of infected and control Walbystickleback. Fish were sham-exposed controls or infected with Walby S. solidus (group).

Table S41. Differences between gene expression profiles of infected and control Walby stickleback. Fish were sham-exposed controls or infected with Wolf *S. solidus* (group). The bold number indicates significance after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	1.160	1.1603	0.4352	0.0114	0.3980	
	group	1	4.508	4.5079	1.6906	0.0443	0.4541	
	Residuals	36	95.995	2.6665		0.9443		
	Total	38	101.663			1		
innate	fish_weight	1	0.147	0.1467	0.2013	0.0054	0.6771	
	group	1	1.005	1.0053	1.3802	0.0367	0.0090	**
	Residuals	36	26.221	0.7284		0.9579		
	Total	38	27.373			1		
adaptive	fish_weight	1	0.343	0.3433	0.6978	0.0186	0.0379	*
	group	1	0.405	0.4051	0.8235	0.0220	0.8805	
	Residuals	36	17.711	0.4920		0.9595		
	Total	38	18.460			1		
complement	fish_weight	1	0.574	0.5737	0.4177	0.0108	0.4690	
	group	1	3.093	3.0929	2.2517	0.0582	0.5590	
	Residuals	36	49.449	1.3736		0.9310		
	Total	38	53.115			1		
regulatory	fish_weight	1	0.117	0.1170	1.0272	0.0275	0.0768	
	group	1	0.032	0.0324	0.2841	0.0076	0.9902	
	Residuals	36	4.102	0.1139		0.9649		
	Total	38	4.251			1		

Table S42. Differences between gene expression profiles of infected and control Walby stickleback. Fish were sham-exposed controls or infected with NO *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	0.995	0.9947	0.4151	0.0104	0.6204	
	group	1	10.697	10.6970	4.4643	0.1119	0.0203	*
	Residuals	35	83.864	2.3961		0.8777		
	Total	37	95.556			1		
innate	fish_weight	1	0.102	0.1017	0.1459	0.0039	1.0000	
	group	1	1.597	1.5974	2.2918	0.0612	0.5648	
	Residuals	35	24.395	0.6970		0.9349		
	Total	37	26.094			1		
adaptive	fish_weight	1	0.122	0.1222	0.2625	0.0071	0.9497	
	S. solidus	1	0.805	0.8048	1.7289	0.0467	0.5625	
	Residuals	35	16.292	0.4655		0.9462		
	Total	37	17.219			1		
complement	fish_weight	1	0.730	0.7297	0.6271	0.0147	0.4363	
	S. solidus	1	8.040	8.0400	6.9098	0.1624	0.0104	*
	Residuals	35	40.725	1.1636		0.8228		
	Total	37	49.494			1		
regulatory	fish_weight	1	0.063	0.0625	0.5705	0.0151	0.0232	*
	S. solidus	1	0.256	0.2557	2.3347	0.0616	0.5347	
	Residuals	35	3.834	0.1095		0.9234		
	Total	37	4.152			1		

Table	S43.	Differences	between	gene	expression	profiles	of infected	and cont	rol Wolf
stickle	back	Fish were sha	am-expose	d contr	rols or infected	d with Wal	by S. solidus	(group). Di	fferences
were n	ot sigi	nificant after F	DR correct	tion.					

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	7.152	7.1516	2.1166	0.0682	0.8229
	group	1	3.078	3.0779	0.9109	0.0294	0.0729 .
	Residuals	28	94.609	3.3789		0.9024	
	Total	30	104.839			1	
innate	fish_weight	1	2.278	2.2777	2.5748	0.0803	0.5417
	group	1	1.315	1.3152	1.4868	0.0464	0.0417 *
	Residuals	28	24.769	0.8846		0.8733	
	Total	30	28.362			1	
adaptive	fish_weight	1	4.411	4.4114	3.0605	0.0954	0.6562
	group	1	1.464	1.4643	1.0159	0.0317	0.1042
	Residuals	28	40.359	1.4414		0.8729	
	Total	30	46.234			1	
complement	fish_weight	1	0.256	0.2557	0.2756	0.0096	0.9583
	group	1	0.293	0.2933	0.3161	0.0111	0.8333
	Residuals	28	25.974	0.9277		0.9793	
	Total	30	26.523			1	
regulatory	fish_weight	1	0.379	0.3794	2.4279	0.0795	0.2500
	group	1	0.018	0.0182	0.1165	0.0038	0.9271
	Residuals	28	4.375	0.1563		0.9167	
	Total	30	4.773			1	

Table S44. Differences between gene expression profiles of infected and control Wolf stickleback. Fish were sham-exposed controls or infected with Wolf *S. solidus* (group). The bold number indicates significance after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	5.975	5.9753	1.7647	0.0454	0.2080	
	group	1	3.875	3.8746	1.1443	0.0294	0.0889	
	Residuals	36	121.899	3.3861		0.9252		
	Total	38	131.749			1		
innate	fish_weight	1	2.080	2.0800	2.2077	0.0555	0.2492	
	group	1	1.476	1.4761	1.5667	0.0394	0.0068	**
	Residuals	36	33.917	0.9421		0.9051		
	Total	38	37.473			1		
adaptive	fish_weight	1	2.712	2.7116	1.9910	0.0512	0.2688	
	S. solidus	1	1.226	1.2262	0.9003	0.0232	0.1829	
	Residuals	36	49.030	1.3620		0.9257		
	Total	38	52.968			1		
complement	fish_weight	1	0.532	0.5317	0.5694	0.0151	0.1959	
	S. solidus	1	1.134	1.1344	1.2149	0.0322	0.3905	
	Residuals	36	33.614	0.9337		0.9528		
	Total	38	35.280			1		
regulatory	fish_weight	1	0.874	0.8737	5.0337	0.1220	0.2320	
	S. solidus	1	0.040	0.0404	0.2326	0.0056	0.9103	
	Residuals	36	6.248	0.1736		0.8724		
	Total	38	7.162			1		

Table S45. Differences between gene expression profiles of infected and control DE stickleback. Fish were sham-exposed controls or infected with Walby *S. solidus* (group). Bold numbers indicate significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	8.066	8.0658	2.3646	0.0537	0.8715	
	group	1	19.474	19.4736	5.7089	0.1295	0.0208	*
	Residuals	36	122.799	3.4111		0.8168		
	Total	38	150.338			1		
innate	fish_weight	1	2.098	2.0977	1.8393	0.0385	0.8623	
	group	1	11.310	11.3102	9.9169	0.2077	0.0035	**
	Residuals	36	41.058	1.1405		0.7538		
	Total	38	54.466			1		
adaptive	fish_weight	1	2.428	2.4276	2.5712	0.0587	0.2512	
	group	1	4.949	4.9492	5.2419	0.1196	0.0428	*
	Residuals	36	33.989	0.9441		0.8217		
	Total	38	41.366			1		
complement	fish_weight	1	3.133	3.1331	2.6167	0.0647	0.9051	
	group	1	2.196	2.1964	1.8343	0.0454	0.4826	
	Residuals	36	43.105	1.1974		0.8900		
	Total	38	48.435			1		
regulatory	fish_weight	1	0.408	0.4076	2.5843	0.0565	0.2882	
	group	1	1.124	1.1235	7.1236	0.1559	0.0093	**
	Residuals	36	5.678	0.1577		0.7876		
	Total	38	7.209			1		

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	9.986	9.9861	3.0997	0.0854	0.8125
	group	1	3.826	3.8265	1.1878	0.0327	0.1250
	Residuals	32	103.093	3.2216		0.8819	
	Total	34	116.905			1	
innate	fish_weight	1	2.996	2.9959	2.7547	0.0763	0.9375
	group	1	1.446	1.4465	1.3300	0.0369	0.0625 .
	Residuals	32	34.802	1.0876		0.8868	
	Total	34	39.244			1	
adaptive	fish_weight	1	1.689	1.6887	2.2126	0.0625	0.4375
	S. solidus	1	0.893	0.8929	1.1700	0.0331	0.0625 .
	Residuals	32	24.423	0.7632		0.9044	
	Total	34	27.004			1	
complement	fish_weight	1	4.835	4.8350	3.8864	0.1054	0.5625
	S. solidus	1	1.232	1.2321	0.9904	0.0269	0.1875
	Residuals	32	39.810	1.2441		0.8678	
	Total	34	45.877			1	
regulatory	fish_weight	1	0.472	0.4716	3.0850	0.0832	0.4375
	S. solidus	1	0.305	0.3052	1.9966	0.0538	0.1875
	Residuals	32	4.892	0.1529		0.8630	
	Total	34	5.669			1	

Table S46. Differences between gene expression profiles of infected and control DEstickleback. Fish were sham-exposed controls or infected with ALX S. solidus (group).

Table S47. Differences between gene expression profiles of infected and control DE stickleback. Fish were sham-exposed controls or infected with NO *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	12.128	12.1285	4.0019	0.0833	0.5112	
	group	1	6.235	6.2346	2.0572	0.0428	0.1946	
	Residuals	42	127.287	3.0306		0.8739		
	Total	44	145.650			1		
innate	fish_weight	1	3.883	3.8832	3.9387	0.0804	0.6023	
	group	1	3.033	3.0334	3.0767	0.0628	0.0281	*
	Residuals	42	41.408	0.9859		0.8569		
	Total	44	48.325			1		
adaptive	fish_weight	1	2.709	2.7085	4.1020	0.0822	0.1821	
	group	1	2.527	2.5266	3.8266	0.0766	0.1562	
	Residuals	42	27.732	0.6603		0.8412		
	Total	44	32.967			1		
complement	fish_weight	1	4.978	4.9776	3.8988	0.0841	0.5153	
	group	1	0.571	0.5707	0.4470	0.0097	0.8372	
	Residuals	42	53.621	1.2767		0.9062		
	Total	44	59.170			1		
regulatory	fish_weight	1	0.611	0.6112	4.4978	0.0949	0.6968	
	group	1	0.121	0.1211	0.8914	0.0188	0.0893	
	Residuals	42	5.708	0.1359		0.8863		
	Total	44	6.440			1		



Figure S15. Gene expression profiles of *S. solidus* infected and exposed (but uninfected) **DE stickleback.** Sticklebacks originated from Lake Großer Plöner See (DE; Germany); *S. solidus* came from Walby Lake (ALO; Alaska), Wolf Lake (ALX; Alaska), and Lake Skogseidvatnet (NO; Norway). Total RNA was extracted from head kidneys. We quantified expression levels of 25 targets (*total*) including eleven innate immune genes (*innate: marco, mst1ra, mif, tnfr1, saal1, tlr2, csf3r, p22^{phox}, nkef-b, sla1, cd97)*, eight adaptive immune genes (*adaptive: stat4, stat6, igm, cd83, foxp3, il-16, mhcII, tcr-* β), three complement component genes (*complement: cfb, c7, c9*), and three regulatory genes (*regulatory: abtb1, kat2a, mapk13*). NMDS plots are based on log10 transformed calibrated normalized relative quantities (CNRQ). Statistics follow Tables S53-S55.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	3.744	3.7438	1.1424	0.0518	0.9960
	group	1	3.030	3.0303	0.9246	0.0419	0.4391
	Residuals	20	65.545	3.2772		0.9063	
	Total	22	72.319			1	
innate	fish_weight	1	2.193	2.1929	2.1110	0.0890	0.9925
	group	1	1.674	1.6735	1.6110	0.0679	0.1539
	Residuals	20	20.776	1.0388		0.8431	
	Total	22	24.643			1	
adaptive	fish_weight	1	1.300	1.3003	2.0822	0.0886	0.9664
	S. solidus	1	0.888	0.8882	1.4222	0.0605	0.2198
	Residuals	20	12.490	0.6245		0.8509	
	Total	22	14.679			1	
complement	fish_weight	1	0.056	0.0559	0.0380	0.0019	0.9991
	S. solidus	1	0.140	0.1400	0.0951	0.0047	0.8333
	Residuals	20	29.466	1.4733		0.9934	
	Total	22	29.662			1	
regulatory	fish_weight	1	0.201	0.2007	1.1034	0.0477	0.6881
	S. solidus	1	0.366	0.3664	2.0140	0.0871	0.3365
	Residuals	20	3.638	0.1819		0.8652	
	Total	22	4.205			1	

Table S48. Differences between gene expression profiles of infected and exposed Walbystickleback. Fish were exposed to or infected with Walby S. solidus (group).

Table S49. Differences between gene expression profiles of infected and exposed Walby stickleback. Fish were exposed to or infected with Wolf *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	2.093	2.0934	0.5888	0.0321	0.0463	*
	group	1	6.328	6.3278	1.7797	0.0969	0.0521	
	Residuals	16	56.888	3.5555		0.8711		
	Total	18	65.309			1		
innate	fish_weight	1	1.149	1.1490	1.2899	0.0721	0.0362	*
	group	1	0.546	0.5460	0.6129	0.0342	0.5697	
	Residuals	16	14.252	0.8908		0.8937		
	Total	18	15.947			1		
adaptive	fish_weight	1	0.192	0.1917	0.3768	0.0208	0.5388	
	group	1	0.884	0.8838	1.7373	0.0959	0.5101	
	Residuals	16	8.140	0.5087		0.8833		
	Total	18	9.215			1		
complement	fish_weight	1	0.733	0.7334	0.3555	0.0190	0.1030	
	group	1	4.801	4.8010	2.3275	0.1246	0.0182	*
	Residuals	16	33.004	2.0627		0.8564		
	Total	18	38.538			1		
regulatory	fish_weight	1	0.021	0.0208	0.1568	0.0092	0.8108	
	group	1	0.117	0.1174	0.8862	0.0520	0.8941	
	Residuals	16	2.120	0.1325		0.9388		
	Total	18	2.258			1		

Table S50. Differences between gene expression profiles of infected and exposed Walby stickleback. Fish were exposed to or infected with NO *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	3.812	3.8116	1.3526	0.0521	0.0548	
	group	1	7.416	7.4157	2.6316	0.1013	0.0730	
	Residuals	22	61.994	2.8179		0.8467		
	Total	24	73.221			1		
innate	fish_weight	1	0.790	0.7900	1.2090	0.0481	0.2931	
	group	1	1.270	1.2696	1.9430	0.0773	0.3760	
	Residuals	22	14.375	0.6534		0.8747		
	Total	24	16.434			1		
adaptive	fish_weight	1	0.316	0.3155	0.9342	0.0385	0.2899	
	S. solidus	1	0.447	0.4466	1.3224	0.0545	0.6950	
	Residuals	22	7.429	0.3377		0.9070		
	Total	24	8.191			1		
complement	fish_weight	1	2.674	2.6739	1.5154	0.0568	0.0498	*
	S. solidus	1	5.598	5.5981	3.1726	0.1189	0.0744	
	Residuals	22	38.819	1.7645		0.8243		
	Total	24	47.091			1		
regulatory	fish_weight	1	0.045	0.0445	0.5501	0.0231	0.3499	
	S. solidus	1	0.102	0.1021	1.2604	0.0529	0.5936	
	Residuals	22	1.781	0.0810		0.9240		
	Total	24	1.928			1		

Table S51. Differences between gene expression profiles of infected and exposed Wolf stickleback. Fish were exposed to or infected with Walby *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	7.045	7.0449	1.6032	0.1049	0.3403	
	group	1	3.022	3.0223	0.6878	0.0450	0.5000	
	Residuals	13	57.125	4.3942		0.8502		
	Total	15	67.192			1		
innate	fish_weight	1	3.490	3.4896	5.8074	0.2659	0.0139	*
	group	1	1.823	1.8234	3.0344	0.1389	0.0278	*
	Residuals	13	7.812	0.6009		0.5952		
	Total	15	13.125			1		
adaptive	fish_weight	1	2.472	2.4717	1.3020	0.0895	0.5729	
	group	1	0.472	0.4720	0.2486	0.0171	0.7326	
	Residuals	13	24.679	1.8984		0.8934		
	Total	15	27.622			1		
complement	fish_weight	1	0.415	0.4146	0.2272	0.0167	0.1424	
	group	1	0.726	0.7258	0.3976	0.0292	0.6944	
	Residuals	13	23.728	1.8252		0.9541		
	Total	15	24.868			1		
regulatory	fish_weight	1	0.764	0.7644	7.2611	0.3523	0.4097	
	group	1	0.037	0.0368	0.3498	0.0170	0.6806	
	Residuals	13	1.369	0.1053		0.6307		
	Total	15	2.170			1		

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	6.182	6.1819	1.7463	0.0689	0.4977
	group	1	2.104	2.1040	0.5944	0.0235	0.4953
	Residuals	23	81.422	3.5401		0.9076	
	Total	25	89.708			1	
innate	fish_weight	1	2.756	2.7562	2.6581	0.1006	0.3264
	group	1	0.783	0.7828	0.7549	0.0286	0.2768
	Residuals	23	23.849	1.0369		0.8708	
	Total	25	27.388			1	
adaptive	fish_weight	1	1.811	1.8114	1.4903	0.0592	0.4515
	S. solidus	1	0.845	0.8453	0.6954	0.0276	0.4633
	Residuals	23	27.956	1.2155		0.9132	
	Total	25	30.613			1	
complement	fish_weight	1	0.552	0.5518	0.5115	0.0214	0.7128
	S. solidus	1	0.458	0.4578	0.4243	0.0177	0.4196
	Residuals	23	24.813	1.0788		0.9609	
	Total	25	25.823			1	
regulatory	fish_weight	1	1.179	1.1791	5.0028	0.1782	0.1847
	S. solidus	1	0.018	0.0182	0.0773	0.0028	0.9244
	Residuals	23	5.421	0.2357		0.8191	
	Total	25	6.618			1	

Table S52. Differences between gene expression profiles of infected and exposed Wolf stickleback. Fish were exposed to or infected with Wolf *S. solidus* (group).

Table S53. Differences between gene expression profiles of infected and exposed DE stickleback. Fish were exposed to or infected with Walby *S. solidus* (group). Bold numbers indicate significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	10.117	10.1166	3.5163	0.1242	0.2928	
	group	1	16.680	16.6799	5.7975	0.2048	0.0068	**
	Residuals	19	54.665	2.8771		0.6711		
	Total	21	81.461			1		
innate	fish_weight	1	3.910	3.9102	3.6167	0.1149	0.2160	
	group	1	9.567	9.5672	8.8490	0.2812	0.0026	**
	Residuals	19	20.542	1.0812		0.6038		
	Total	21	34.019			1		
adaptive	fish_weight	1	3.042	3.0419	3.3704	0.1224	0.1384	
	group	1	4.656	4.6563	5.1590	0.1874	0.0062	**
	Residuals	19	17.149	0.9026		0.6902		
	Total	21	24.847			1		
complement	fish_weight	1	2.464	2.4644	3.2348	0.1356	0.5945	
	group	1	1.239	1.2391	1.6265	0.0682	0.2300	
	Residuals	19	14.475	0.7618		0.7963		
	Total	21	18.178			1		
regulatory	fish_weight	1	0.709	0.7089	3.6038	0.1200	0.3331	
	group	1	1.462	1.4624	7.4342	0.2475	0.0177	*
	Residuals	19	3.738	0.1967		0.6325		
	Total	21	5.909			1		

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	1.826	1.8257	0.6563	0.0497	0.5833
	group	1	1.566	1.5658	0.5629	0.0426	0.1667
	Residuals	12	33.381	2.7818		0.9078	
	Total	14	36.773			1	
innate	fish_weight	1	0.667	0.6666	0.7761	0.0565	0.6944
	group	1	0.832	0.8319	0.9685	0.0705	0.1250
	Residuals	12	10.307	0.8589		0.8731	
	Total	14	11.805			1	
adaptive	fish_weight	1	0.348	0.3478	0.4759	0.0371	0.6389
	S. solidus	1	0.269	0.2692	0.3683	0.0287	0.7153
	Residuals	12	8.770	0.7309		0.9343	
	Total	14	9.387			1	
complement	fish_weight	1	0.811	0.8108	0.7222	0.0555	0.2500
	S. solidus	1	0.319	0.3190	0.2842	0.0219	0.2083
	Residuals	12	13.472	1.1227		0.9226	
	Total	14	14.602			1	
regulatory	fish_weight	1	0.009	0.0092	0.1091	0.0079	0.9097
	S. solidus	1	0.146	0.1458	1.7272	0.1248	0.2431
	Residuals	12	1.013	0.0844		0.8673	
	Total	14	1.168			1	

Table S54. Differences between gene expression profiles of infected and exposed DEstickleback. Fish were exposed to or infected with Wolf S. solidus (group).

Table S55. Differences between gene expression profiles of infected and exposed DE stickleback. Fish were exposed to or infected with NO *S. solidus* (group). Bold numbers indicate significance post FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	7.258	7.2580	2.8284	0.0963	0.5633	
	group	1	6.524	6.5235	2.5422	0.0866	0.0217	*
	Residuals	24	61.587	2.5661		0.8172		
	Total	26	75.369			1		
innate	fish_weight	1	2.115	2.1154	2.6651	0.0839	0.3165	
	group	1	4.052	4.0523	5.1053	0.1607	0.0007	***
	Residuals	24	19.050	0.7937		0.7554		
	Total	26	25.217			1		
adaptive	fish_weight	1	2.053	2.0529	5.0903	0.1523	0.0895	
	group	1	1.744	1.7442	4.3249	0.1294	0.0005	***
	Residuals	24	9.679	0.4033		0.7182		
	Total	26	13.476			1		
complement	fish_weight	1	2.952	2.9518	2.3082	0.0860	0.7866	
	group	1	0.694	0.6939	0.5426	0.0202	0.5132	
	Residuals	24	30.692	1.2788		0.8938		
	Total	26	34.337			1		
regulatory	fish_weight	1	0.163	0.1629	1.2720	0.0498	0.7509	
	group	1	0.035	0.0354	0.2761	0.0108	0.4619	
	Residuals	24	3.073	0.1280		0.9394		
	Total	26	3.271			1		

SI.4.7. Gene expression differences between control and exposed fish

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	8.943	8.9426	3.6914	0.0935	0.0625 .
	group	1	1.884	1.8845	0.7779	0.0197	0.4540
	Residuals	35	84.789	2.4225		0.8868	
	Total	37	95.616			1	
innate	fish_weight	1	0.523	0.5231	0.7056	0.0193	0.3698
	group	1	0.663	0.6631	0.8946	0.0244	0.4193
	Residuals	35	25.944	0.7412		0.9563	
	Total	37	27.130			1	
adaptive	fish_weight	1	0.184	0.1838	0.3773	0.0104	0.5651
	S. solidus	1	0.422	0.4218	0.8661	0.0239	0.3889
	Residuals	35	17.046	0.4870		0.9657	
	Total	37	17.652			1	
complement	fish_weight	1	8.225	8.2252	7.5143	0.1741	0.0582 .
	S. solidus	1	0.716	0.7163	0.6544	0.0152	0.5096
	Residuals	35	38.311	1.0946		0.8108	
	Total	37	47.253			1	
regulatory	fish_weight	1	0.013	0.0127	0.0879	0.0025	0.7743
	S. solidus	1	0.084	0.0837	0.5813	0.0163	0.4931
	Residuals	35	5.042	0.1440		0.9812	
	Total	37	5.138			1	

Table S56.	Differences	between	gene e	expression	profiles	of contro	and	exposed	Walby
stickleback	. Fish were sh	am-expose	ed or ex	kposed to W	alby S. so	<i>lidus</i> (grou	p).		

Table S57.	Differences between gene expression profiles of control and exposed Walby
stickleback	• Fish were sham-exposed or exposed to Wolf <i>S. solidus</i> (group).

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	3.332	3.3317	1.0784	0.0287	0.2441
	group	1	1.486	1.4859	0.4809	0.0128	0.6335
	Residuals	36	111.224	3.0896		0.9585	
	Total	38	116.041			1	
innate	fish_weight	1	0.119	0.1193	0.1351	0.0037	0.5872
	group	1	0.550	0.5497	0.6221	0.0169	0.0970 .
	Residuals	36	31.808	0.8836		0.9794	
	Total	38	32.477			1	
adaptive	fish_weight	1	0.126	0.1256	0.2257	0.0060	0.3809
	group	1	0.646	0.6461	1.1608	0.0311	0.0612 .
	Residuals	36	20.037	0.5566		0.9629	
	Total	38	20.808			1	
complement	fish_weight	1	3.047	3.0474	1.9603	0.0515	0.2428
	group	1	0.183	0.1827	0.1175	0.0031	0.8105
	Residuals	36	55.963	1.5545		0.9454	
	Total	38	59.193			1	
regulatory	fish_weight	1	0.049	0.0490	0.3410	0.0092	0.4785
	group	1	0.109	0.1086	0.7565	0.0204	0.0684 .
	Residuals	36	5.169	0.1436		0.9704	
	Total	38	5.326			1	

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	2.162	2.1619	0.7275	0.0166	0.2720
	group	1	0.617	0.6168	0.2075	0.0047	0.7854
	Residuals	43	127.788	2.9718		0.9787	
	Total	45	130.567			1	
innate	fish_weight	1	0.376	0.3760	0.4884	0.0111	0.1246
	group	1	0.477	0.4767	0.6192	0.0140	0.1292
	Residuals	43	33.104	0.7699		0.9749	
	Total	45	33.956			1	
adaptive	fish_weight	1	0.198	0.1984	0.4090	0.0094	0.5956
	S. solidus	1	0.040	0.0398	0.0821	0.0019	0.9221
	Residuals	43	20.858	0.4851		0.9887	
	Total	45	21.096			1	
complement	fish_weight	1	1.587	1.5867	0.9693	0.0220	0.2926
	S. solidus	1	0.074	0.0741	0.0452	0.0010	0.9156
	Residuals	43	70.388	1.6369		0.9770	
	Total	45	72.049			1	
regulatory	fish_weight	1	0.003	0.0029	0.0241	0.0006	0.9817
	S. solidus	1	0.051	0.0512	0.4307	0.0099	0.3043
	Residuals	43	5.110	0.1188		0.9895	
	Total	45	5.164			1	

Table S58. Differences between gene expression profiles of control and exposed Walbystickleback. Fish were sham-exposed or exposed to NO S. solidus (group).

Table S59. Differences between gene expression profiles of control and exposed Wolf stickleback. Fish were sham-exposed or exposed to Walby *S. solidus* (group). Differences were not significant after FDR correction

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	10.108	10.1080	2.5714	0.0778	0.1992	
	group	1	1.898	1.8979	0.4828	0.0146	0.6016	
	Residuals	30	117.928	3.9309		0.9076		
	Total	32	129.934			1		
innate	fish_weight	1	3.724	3.7242	4.3105	0.1236	0.0430	*
	group	1	0.486	0.4863	0.5628	0.0161	0.3203	
	Residuals	30	25.919	0.8640		0.8603		
	Total	32	30.130			1		
adaptive	fish_weight	1	5.536	5.5363	3.5848	0.1056	0.3281	
	group	1	0.583	0.5833	0.3777	0.0111	0.4375	
	Residuals	30	46.331	1.5444		0.8833		
	Total	32	52.451			1		
complement	fish_weight	1	0.351	0.3511	0.2504	0.0081	0.4219	
	group	1	0.814	0.8144	0.5808	0.0188	0.5625	
	Residuals	30	42.064	1.4021		0.9730		
	Total	32	43.229			1		
regulatory	fish_weight	1	0.758	0.7577	5.0093	0.1423	0.0117	*
	group	1	0.030	0.0295	0.1953	0.0056	0.7344	
	Residuals	30	4.538	0.1513		0.8522		
	Total	32	5.325			1		

Table S60. Differences between gene expression profiles of control and exposed Wolf stickleback. Fish were sham-exposed or exposed to Wolf *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	9.528	9.5279	2.6255	0.0750	0.0938	
	group	1	1.357	1.3570	0.3739	0.0107	0.5260	
	Residuals	32	116.125	3.6289		0.9143		
	Total	34	127.010			1		
innate	fish_weight	1	3.028	3.0280	2.9829	0.0846	0.1918	
	group	1	0.265	0.2654	0.2614	0.0074	0.6319	
	Residuals	32	32.483	1.0151		0.9080		
	Total	34	35.777			1		
adaptive	fish_weight	1	5.574	5.5744	4.2453	0.1163	0.0373	*
	S. solidus	1	0.327	0.3267	0.2488	0.0068	0.6849	
	Residuals	32	42.018	1.3131		0.8769		
	Total	34	47.919			1		
complement	fish_weight	1	0.224	0.2239	0.1996	0.0061	0.8498	
	S. solidus	1	0.731	0.7306	0.6512	0.0198	0.4149	
	Residuals	32	35.902	1.1219		0.9741		
	Total	34	36.856			1		
regulatory	fish_weight	1	0.986	0.9856	4.6553	0.1264	0.1875	
	S. solidus	1	0.035	0.0348	0.1644	0.0045	0.4913	
	Residuals	32	6.775	0.2117		0.8691		
	Total	34	7.795			1		

Table S61.	Differences	between	gene	expression	profiles	of	control	and	exposed	Wolf
stickleback	. Fish were sh	am-expose	ed or e	xposed to NO	S. solidu	<i>s</i> (g	group).			

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	6.662	6.6624	1.6774	0.0540	0.3281
	group	1	5.466	5.4661	1.3762	0.0443	0.3672
	Residuals	28	111.212	3.9719		0.9017	
	Total	30	123.341			1	
innate	fish_weight	1	2.290	2.2901	2.5767	0.0837	0.4766
	group	1	0.187	0.1870	0.2104	0.0068	0.9531
	Residuals	28	24.886	0.8888		0.9095	
	Total	30	27.363			1	
adaptive	fish_weight	1	3.462	3.4618	2.4024	0.0763	0.0938 .
	group	1	1.538	1.5382	1.0675	0.0339	0.7344
	Residuals	28	40.346	1.4409		0.8897	
	Total	30	45.346			1	
complement	fish_weight	1	0.729	0.7286	0.4798	0.0156	0.5859
	group	1	3.614	3.6140	2.3801	0.0771	0.1797
	Residuals	28	42.517	1.5185		0.9073	
	Total	30	46.860			1	
regulatory	fish_weight	1	0.446	0.4463	2.9607	0.0931	0.3359
	group	1	0.129	0.1292	0.8572	0.0269	0.2109
	Residuals	28	4.220	0.1507		0.8800	
	Total	30	4.796			1	

Table S62. Differences between gene expression profiles of control and exposed DE stickleback. Fish were sham-exposed or exposed to Walby *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	10.984	10.9838	3.5108	0.0768	0.1576	
	group	1	0.674	0.6737	0.2153	0.0047	0.7915	
	Residuals	42	131.401	3.1286		0.9185		
	Total	44	143.059			1		
innate	fish_weight	1	5.012	5.0119	4.4411	0.0950	0.0398	*
	group	1	0.369	0.3686	0.3266	0.0070	0.4246	
	Residuals	42	47.398	1.1285		0.8981		
	Total	44	52.779			1		
adaptive	fish_weight	1	2.293	2.2934	3.0985	0.0683	0.0714	
	S. solidus	1	0.211	0.2110	0.2851	0.0063	0.4110	
	Residuals	42	31.088	0.7402		0.9255		
	Total	44	33.592			1		
complement	fish_weight	1	2.942	2.9419	2.6135	0.0585	0.5571	
	S. solidus	1	0.065	0.0653	0.0580	0.0013	0.8963	
	Residuals	42	47.277	1.1256		0.9402		
	Total	44	50.284			1		
regulatory	fish_weight	1	0.740	0.7399	4.1399	0.0888	0.0864	
	S. solidus	1	0.085	0.0847	0.4739	0.0102	0.3566	
	Residuals	42	7.506	0.1787		0.9010		
	Total	44	8.331			1		

Table	S63.	Differences	between	gene	expression	n profiles	of	control	and	exposed	DE
stickle	back.	Fish were sha	am-expose	d or ex	posed to Wo	olf <i>S. solidu</i>	s (g	group).			

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	3.473	3.4725	1.0415	0.0251	0.6929
	group	1	5.064	5.0635	1.5187	0.0365	0.3650
	Residuals	39	130.026	3.3340		0.9384	
	Total	41	138.562			1	
innate	fish_weight	1	1.144	1.1440	1.0153	0.0244	0.8867
	group	1	1.728	1.7280	1.5336	0.0369	0.1793
	Residuals	39	43.943	1.1267		0.9387	
	Total	41	46.815			1	
adaptive	fish_weight	1	1.142	1.1416	1.4097	0.0338	0.1189
	group	1	1.027	1.0275	1.2688	0.0304	0.0734 .
	Residuals	39	31.583	0.8098		0.9357	
	Total	41	33.752			1	
complement	fish_weight	1	1.146	1.1463	0.8974	0.0217	0.6337
	group	1	1.971	1.9709	1.5430	0.0372	0.7036
	Residuals	39	49.816	1.2773		0.9411	
	Total	41	52.933			1	
regulatory	fish_weight	1	0.082	0.0816	0.5636	0.0131	0.9462
	group	1	0.496	0.4958	3.4241	0.0797	0.0532 .
	Residuals	39	5.647	0.1448		0.9072	
	Total	41	6.224			1	

Table S64. Differences between gene expression profiles of control and exposed DE stickleback. Fish were sham-exposed or exposed to NO *S. solidus* (group). Differences were not significant after FDR correction.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	10.947	10.9471	3.3859	0.0749	0.8677	
	group	1	2.653	2.6531	0.8206	0.0182	0.1188	
	Residuals	41	132.558	3.2331		0.9070		
	Total	43	146.158			1		
innate	fish_weight	1	4.962	4.9624	4.5008	0.0963	0.8774	
	group	1	1.367	1.3672	1.2400	0.0265	0.0506	
	Residuals	41	45.205	1.1026		0.8772		
	Total	43	51.535			1		
adaptive	fish_weight	1	1.970	1.9697	2.7663	0.0621	0.8853	
	S. solidus	1	0.576	0.5763	0.8094	0.0182	0.1616	
	Residuals	41	29.194	0.7121		0.9198		
	Total	43	31.740			1		
complement	fish_weight	1	3.513	3.5131	2.7265	0.0620	0.7778	
	S. solidus	1	0.291	0.2914	0.2262	0.0052	0.5052	
	Residuals	41	52.828	1.2885		0.9328		
	Total	43	56.633			1		
regulatory	fish_weight	1	0.502	0.5019	3.0768	0.0656	0.8784	
	S. solidus	1	0.460	0.4602	2.8212	0.0602	0.0495	*
	Residuals	41	6.688	0.1631		0.8742		
	Total	43	7.650			1		

SI.4.7. Sympatric versus allopatric combinations (Alaskan hosts and parasites)

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)	
total	fish_weight	1	8.681	8.6813	2.0897	0.0532	0.3447	
	combination	1	4.965	4.9647	1.1951	0.0304	0.1639	
	Residuals	36	149.556	4.1543		0.9164		
	Total	38	163.202			1		
innate	fish_weight	1	4.101	4.1014	4.4745	0.1080	0.5977	
	combination	1	0.862	0.8615	0.9399	0.0227	0.0493	*
	Residuals	36	32.998	0.9166		0.8693		
	Total	38	37.961			1		
adaptive	fish_weight	1	2.856	2.8557	2.4891	0.0635	0.4414	
	combination	1	0.816	0.8156	0.7109	0.0181	0.3717	
	Residuals	36	41.302	1.1473		0.9184		
	Total	38	44.973			1		
complement	fish_weight	1	0.945	0.9454	0.4904	0.0129	0.1126	
	combination	1	2.759	2.7589	1.4311	0.0377	0.2326	
	Residuals	36	69.400	1.9278		0.9493		
	Total	38	73.105			1		
regulatory	fish_weight	1	0.958	0.9576	4.7666	0.1085	0.4828	
	combination	1	0.635	0.6351	3.1613	0.0720	0.0172	*
	Residuals	36	7.232	0.2009		0.8195		
	Total	38	8.825			1		

Table S65. Differences between gene expression profiles of exposed sticklebacks. Alaskan sticklebacks were exposed in sympatric or allopatric combinations. Differences were not significant after FDR correction.

Table S66. Differences between gene expression profiles of infected sticklebacks. Alaska	n
sticklebacks were infected in sympatric or allopatric combinations.	

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
total	fish_weight	1	13.285	13.2854	4.2542	0.0895	0.1109
	combination	1	0.949	0.9489	0.3038	0.0064	0.8562
	Residuals	43	134.285	3.1229		0.9042	
	Total	45	148.519			1	
innate	fish_weight	1	4.639	4.6394	5.2143	0.1070	0.3272
	combination	1	0.470	0.4703	0.5286	0.0108	0.4752
	Residuals	43	38.259	0.8897		0.8822	
	Total	45	43.368			1	
adaptive	fish_weight	1	2.624	2.6238	2.4700	0.0542	0.2827
	combination	1	0.093	0.0933	0.0879	0.0019	0.9689
	Residuals	43	45.678	1.0623		0.9439	
	Total	45	48.395			1	
complement	fish_weight	1	5.116	5.1161	4.8983	0.1015	0.0599 .
	combination	1	0.372	0.3716	0.3558	0.0074	0.6151
	Residuals	43	44.912	1.0445		0.8911	
	Total	45	50.400			1	
regulatory	fish_weight	1	0.966	0.9655	5.9470	0.1212	0.1171
	combination	1	0.018	0.0180	0.1108	0.0023	0.8541
	Residuals	43	6.981	0.1624		0.8765	
	Total	45	7.965			1	

SI.5 Further information on gene expression targets

Table S67. Gene expression targets, function, references and primer sequences.

Gene	Function	References	Forward primer	Reverse primer
b2m	Beta-2-microglobulin, housekeeping	(Hibbeler et al., 2008)	GAAGATGTGTTGAATAGAAGCTGG	GAAGATGTGTTGAATAGAAGCTGG
ef1a	Elongation factor 1 a, housekeeping	(Hibbeler et al., 2008)	CCACCGTTGCCTTTGTCC	TGGGACTGTTCCAATACCTCC
rpl13a	L13A ribosomal binding protein, housekeeping	(Hibbeler et al., 2008)	CACCTTGGTCAACTTGAACAGTG	TCCCTCCGCCCTACGAC
ubc	Ubiquitin, housekeeping	(Hibbeler et al., 2008)	AGACGGGCATAGCACTTGC	CAGGACAAGGAAGGCATCC
cd97	Promotor of granulocyte and neutrophil migration, required for activation of the innate immune response	(Leemans et al., 2004; Brunner et al., 2017)	CTCGTGGCACTCTACGACATGAAG	CAGCCCTATCTTGGTGACCAGTTG
csf3r	Granulocyte colony- stimulating factor 3 receptor; role in differentiation and proliferation of granulocytes	(Tabbara, 1993; Brunner, 2016)	TCGGGATTCGTCCTCTTCTCAG	TGGGTCAAACTTGGCTGCAC
il-1β	Interleukin 1 β; cytokine with function in early response proinflammatory signalling	(Zhu et al., 2012; Brunner et al., 2017)	TGACGATGAAGCAGGTGGTCAAC	ACAGCGTCACGATCTCCTCTTC
marco, RON	Macrophage receptor with collagenous structure; mediates macrophage recognition and clearance of pathogens	(Kraal et al., 2000; Piecyk et al., 2019)	CCCTTTCGACCTTCACTGCC	TGTTTACCCCAACCCCTCCA
mif1	Macrophage migration inhibitory factor; stops random macrophage migration through tissue, proinflammatory mediator of the innate immune system	(Calandra & Roger, 2003; Brunner et al., 2017)	ATCAGCGGAGCTCACAACAAGC	TCAGGAGAGATGCTCAGGTGTTTG

mst1ra	Macrophage stimulating 1 receptor a; plays an important role in macrophage regulation	(Wang et al., 2002; Huang et al., 2016, Piecyk et al., 2019)	ATGGCCATCGAAAGCTTGCA	TGATGTCGTACGGGTCCACA
<i>nkef-b,</i> peroxiredoxin 1	Natural killer cell enhancing factor; enhances cytotoxicity of NK cells; protects against oxidative damage	(Shau et al., 1993; Stutz et al., 2015)	ACTTCTCCC ACTTTGCATGG	CAATGCCTTCATCCTCCTTC
p22phox	NADPH oxidase component p22phox; part of the reactive oxygen species production machinery	(Bedard & Krause, 2007; Piecyk et al., 2019)	GCCTCGGGACTCATTCTCCT	TGGCCCTCTTGCTTCTTGGA
saal1	Serum amyloid A; acute phase protein during inflammation response, mediates release of TNF-a and IL-1β	(Haarder et al., 2013; Brunner et al., 2017)	TCGCAGTGAGGCCAAAGATGAG	AAATCTGCCACCGTGTCCTTGG
sla1	Src-like-adaptor; necessary for maturation and activation of monocytic and dendritic cells, functions in T-cell signalling and B-cell development and function	(Marton et al., 2015; Brunner et al., 2017)	ACAGAGTCGGCTCCTTCATGATAC	TCACAGAGAGCGAATACAGACCTC
tnfr1	Tumour necrosis factor receptor 1; functions in regulation of inflammation, mediates cellular apoptosis and differentiation	(Zhu et al., 2012; Brunner et al., 2017)	AACTACTACAGAGCCAAGGGCAAG	ACGGCACTCAGCGGTACAATTC
tlr2	Toll-like-receptor 2, antigen recognition	(Wei et al., 2011; Brunner et al. 2017)	CGGAAGGTGATTTTCCTGACC	CTGACCAGGTACGAAGCCG
cd83	Marker for mature dendritic cells, expressed on activated B and T cells, costimulatory to activate naïve and memory T- cells	(Aerts-Toegaert et al., 2007; Stutz et al., 2015)	AGGACCCAGCGTATAAATGG	CCCTGGTGATTTTCCTCATC
<i>foxp3</i> ; forkhead box N2b	Transcription factor; regulates functions important for the establishment of the T-reg lineage, key mediator of T-cell activation	(Rao & Naqvi, 2011; Robertson et al., 2015)	GTTGACCCATGCAATTCCGA	CTGCTGTAGTTGTGGTCCTG

igm	Immunoglobulin heavy	(Zhu et al., 2012; Brunner et	AAGGCAGGAGAATGAAACCTTGG	CCGAGTGAGCAGACAGGGACTGG
-	constant mu (IgM); antibody molecule, part of the humoral	al. 2017)		
	immune response			
il-16	Interleukin 16; cytokine with function in T-cell migration and expansion, chemoattractant for	(Zhu et al., 2012; Brunner et al., 2017)	CTGGTCTGGGCTTCAGTATTGC	CTGGGAAACACTCTGTGGACTG
	monocytes and eosinophils			
mhcII	Major histocompatibility complex class IIb exon 2; pathogen recognizing protein of the adaptive immune	(Lenz et al., 2009; Brunner et al. 2017)	GTCTTTAACTCCACGGAGCTGAAGG	ACTCACCGGACTTAGTCAG
	response,			
stat4	Signal transducer and activator of transcription 4; required for TH1-cell	(Wang & Secombes, 2013; Robertson et al., 2015)	CTCTCAGTTTCGAGGCTTGCTT	GGCAGTTGGCTCACATTGG
	differentiation, opposes TH2			
	and TH17 like responses	(1)		
stat6	Signal transducer and activator of transcription 6; required for TH2-cell differentiation, regulates expression of TH2 relevant cytokine IL-4	(Wang & Secombes, 2013; Robertson et al., 2015)	CICAGCCACAGIICCAACCGIIC	GTCGGATGTTCTGGACCTCGAGT
tcr-β	T-cell receptor β -chain; function in binding of MHC- peptide ligands to initiate adaptive immune response	(Yanagi et al., 1984; Smith- Garvin et al., 2009; Stutz et al., 2015)	GAGGGCAAAAACTTCACCTG	TAGGAGAATCTGGCCGTTTG
tgf-β	Transforming growth factor β; cytokine with functions in cell growth, migration, differentiation and proliferation of T and B-cells	(Zhu et al., 2012; Robertson et al., 2015)	TCCCGCTTCGTCACCAACCA	ACGTCTGTCTGGCCACATTCAC
c7	Complement component 7; initializing function in the membrane attack complex of the complement system	(Zhu et al., 2012; Haase et al., 2014; Brunner et al., 2017)	TGGCTCAAGCTCAGCACAACAG	AGCGACACGTGTTTGTTTGATCG

с9	Complement component 9; structural part of the membrane attack complex of the complement system,	(Zhu et al., 2012; Haase et al., 2014; Brunner et al., 2017)	CCGTGACGAACAAAGACTCAGTTG	TCTGACCGATGTCAGCACCTTG
cfb	Complement factor B; activating complement component of the alternative pathway	(Zhu et al., 2012; Haase et al., 2014; Brunner, 2016)	GAGCGTCGCACAATACAGGTTG	TACCACCGGAAGCGCACAAATC
abtb1	Ankyrin Repeat and BTB Domain Containing 1; involved in translation elongation; gene regulation	Kindly provided by Jakob Gismann & Melanie Heckwolf (pers. comm.)	ACAACGTCCTGTACATGTGGAA	TCTTTGATGATCTCGGCGAACT
ascl1b	Achaete-scute homolog 1b; transcriptional regulator; transcription factor; gene regulation	Kindly provided by Jakob Gismann & Melanie Heckwolf (pers. comm.)	GTCAAGCAGGTCAACATGGGT	GCAAAGCCCTGATGTACTCCA
kat2a	Histone acetyltransferase involved in transcription activation; gene regulation	Kindly provided by Jakob Gismann & Melanie Heckwolf (pers. comm.)	AGATAAAGACTCACCCCGATGC	AAGGTCGGCAATGAAAAGCTTC
mapk13	Mitogen-activated protein kinase 13; gene regulation	Kindly provided by Jakob Gismann & Melanie Heckwolf (pers. comm.)	CCCTTCCAGTCAGAGATCTTCG	GGTAGAAGTCCTGCATGTCGTC

References

Aerts-Toegaert, C., Heirman, C., Tuyaerts, S., Corthals, J., Aerts, J.L., Bonehill, A., Thielemans, K., and Breckpot, K. (2007). CD83 expression on dendritic cells and T cells: Correlation with effective immune responses. Eur. J. Immunol. *37*, 686–695.

Anderson, M.J. (2001). A new method for non-parametric multivariate analysis of variance. Austral Ecol. 26, 32–46.

Bates, D., Mächler, M., Bolker, B., and Walker, S. (2014). Fitting Linear Mixed-Effects Models using Ime4. ArXiv14065823 Stat.

Bedard, K., and Krause, K.-H. (2007). The NOX Family of ROS-Generating NADPH Oxidases: Physiology and Pathophysiology. Physiol. Rev. *87*, 245–313.

Benjamini, Y., and Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. J. R. Stat. Soc. Ser. B Methodol. 57, 289–300.

Brunner, F. S. (2016). Parasitism along the speciation continuum - Variation of parasite effects across speciation stages of Gasterosteus aculeatus and their modification by environmental changes. University of London.

Brunner, F.S., Anaya-Rojas, J.M., Matthews, B., and Eizaguirre, C. (2017). Experimental evidence that parasites drive eco-evolutionary feedbacks. Proc. Natl. Acad. Sci. 201619147.

Calandra, T., & Roger, T. (2003). Macrophage migration inhibitory factor: a regulator of innate immunity. Nat. Rev. Immunol., 3(10), 791–800. http://doi.org/10.1038/nri1200

Haarder, S., Kania, P. W., Bahlool, Q. Z. M., & Buchmann, K. (2013). Expression of immune relevant genes in rainbow trout following exposure to live Anisakis simplex larvae. Exp. Parasitol. 135(3), 564–569. http://doi.org/10.1016/j.exppara.2013.09.011

Haase, D., Rieger, J. K., Witten, A., Stoll, M., Bornberg-Bauer, E., Kalbe, M., & Reusch, T. B. H. (2014). Specific Gene Expression Responses to Parasite Genotypes Reveal Redundancy of Innate Immunity in Vertebrates. PLoS ONE, 9(9), e108001. http://doi.org/10.1371/journal.pone.0108001

Hibbeler S, Scharsack JP, Becker S. 2008 Housekeeping genes for quantitative expression studies in the threespined stickleback Gasterosteus aculeatus. BMC Mol. Biol. 9, 18.

Hothorn, T., Bretz, F., and Westfall, P. (2008). Simultaneous inference in general parametric models. Biom. J. 50, 346–363.

Huang, Y., Chain, F.J.J., Panchal, M., Eizaguirre, C., Kalbe, M., Lenz, T.L., Samonte, I.E., Stoll, M., Bornberg-Bauer, E., Reusch, T.B.H., et al. (2016). Transcriptome profiling of immune tissues reveals habitat-specific gene expression between lake and river sticklebacks. Mol. Ecol. 943–958.

Johnson, P.C.D. (2014). Extension of Nakagawa & Schielzeth's R2GLMM to random slopes models. Methods Ecol. Evol. 5, 944–946.

Kraal, G., Van Der Laan, L. J. W., Elomaa, O., & Tryggvason, K. (2000). The macrophage receptor MARCO. Microbes and Infection, 2(3), 313–316. http://doi.org/10.1016/S1286- 4579(00)00296-3

Leemans, J.C., te Velde, A.A., Florquin, S., Bennink, R.J., de Bruin, K., van Lier, R.A.W., van der Poll, T., and Hamann, J. (2004). The Epidermal Growth Factor-Seven Transmembrane (EGF-TM7) Receptor CD97 Is Required for Neutrophil Migration and Host Defense. J. Immunol. *172*, 1125–1131.

Lefcheck, J.S. (2016). piecewiseSEM: Piecewise structural equation modelling in r for ecology, evolution, and systematics. Methods Ecol. Evol. 7, 573–579.

Lenz, T. L., Eizaguirre, C., Becker, S., & Reusch, T. B. H. (2009). RSCA genotyping of MHC for high-throughput evolutionary studies in the model organism three-spined stickleback Gasterosteus aculeatus. BMC Evo. Biol. 9, 57. http://doi.org/10.1186/1471- 2148-9-57

Marton, N., Baricza, E., Érsek, B., Buzás, E. I., & Nagy, G. (2015). The emerging and diverse roles of Src-like adaptor proteins in health and disease. Mediators Inflamm. http://doi.org/10.1155/2015/952536

Nakagawa, S., and Schielzeth, H. (2013). A general and simple method for obtaining R2 from generalized linear mixed-effects models. Methods Ecol. Evol. 4, 133–142.

Oksanen, J.F., Blanchet, G., Kindt, R., Legendre, P., Minchin, P.R., O'Hara, R.B., Simpson, G., Solymos, P., Stevens, M.H.H., and Wagner, H. (2015). vegan: community ecology package. 2.0-0. R package version 2.3-0.

Piecyk, A., Ritter, M., and Kalbe, M. (2019) The right response at the right time: Exploring helminth immune modulation in sticklebacks by experimental coinfection. Mol. Ecol. *28*, 2668–2680

Rao, D.N., and Naqvi, R.A. (2011). FoxP3: A Key Player in T Regulatory Biology. Indian J. Clin. Biochem. 26, 1–2.

Rhodes, L.D., Wallis, S., and Demlow, S.E. (2009). Genes associated with an effective host response by Chinook salmon to Renibacterium salmoninarum. Dev. Comp. Immunol. *33*, 176–186.

Robertson, S., Bradley, J. E., & MacColl, A. D. C. C. (2015). Measuring the immune system of the three-spined stickleback - investigating natural variation by quantifying immune expression in the laboratory and the wild. Mol. Ecol. Res., *16*(3), 701–713. http://doi.org/10.1111/1755-0998.12497

Shau, H., Gupta, R. K., & Golub, S. H. (1993). Identification of a natural killer enhancing factor (NKEF) from human erythroid cells. Cell. Immun. http://doi.org/10.1006/cimm.1993.1043

Smith-Garvin, J. E., Koretzky, G. A., & Jordan, M. S. (2009). T Cell Activation. Annual Review of Immunology, 27(1), 591–619. http://doi.org/10.1146/annurev.immunol.021908.132706

Stutz, W. E., Schmerer, M., Coates, J. L., & Bolnick, D. I. (2015). Among-lake reciprocal transplants induce convergent expression of immune genes in threespine stickleback. Mol. Ecol., *24*(18), n/a-n/a. http://doi.org/10.1111/mec.13295

Tabbara, I. A. (1993). Granulocyte colony-stimulating factor. Southern Med. J., 86(3), 350-5.

Wang, T., & Secombes, C. J. (2013). The cytokine networks of adaptive immunity in fish. Fish and Shellfish Immunology, 35(6), 1703–1718. http://doi.org/10.1016/j.fsi.2013.08.030

Wang, M. H., Zhou, Y. Q., & Chen, Y. Q. (2002). Macrophage-stimulating protein and RON receptor tyrosine kinase: Potential regulators of macrophage inflammatory activities. Scandinavian Journal of Immunology, *56*(6), 545–553. http://doi.org/10.1046/j.1365-3083.2002.01177.x

Wei, Y.C., Pan, T.S., Chang, M.X., Huang, B., Xu, Z., Luo, T.R., and Nie, P. (2011). Cloning and expression of Toll-like receptors 1 and 2 from a teleost fish, the orange-spotted grouper Epinephelus coioides. Vet. Immunol. Immunopathol. *141*, 173–182.

Yanagi, Y., Yoshikai, Y., Leggett, K., Clark, S. P., Aleksander, I., & Mak, T. W. (1984). A human T cell-specific cDNA clone encodes a protein having extensive homology to immunoglobulin chains. *Nature*, *308*(5955), 145–9. http://doi.org/10.1038/308145a0

Zhu, L., Nie, L., Zhu, G., Xiang, L., & Shao, J. (2012). Advances in research of fish immune-relevant genes: a comparative overview of innate and adaptive immunity in teleosts. Developmental and Comparative Immunology, 39(1–2), 39–62.