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PHYSIOLOGICAL ECOLOGY - ORIGINAL RESEARCH

Telomere length and antioxidant defense associate with parasite-induced retarded growth in wild brown trout

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Abstract Early growth conditions can have profound impacts on individuals' development, growth and physiology, with subsequent long-term consequences for individuals' fitness and life expectancy. Telomere length (TL) has been suggested to indicate both individual fitness and life expectancy in wide range of species, as the telomere attrition rate at early age can be accelerated due to exposure to various stressors, including parasites and inflammatory diseases, which increase production of reactive oxygen species (ROS) and influence antioxidant (AO) levels. We investigated impacts of *Tetracapsuloides bryosalmonae* infection, a causative agent of proliferative kidney disease (PKD), on AO status and TL in a natural population of juvenile brown trout (*Salmo trutta*). The fish with higher parasite load showed more severe kidney hyperplasia, anemia and smaller body size compared to less parasitized fish. Furthermore, fish with severe PKD symptoms had lower SOD-, CAT- and GST activity than fish with milder kidney hyperplasia. However, parasite load was not directly correlated either with AOs or with TL. Smaller fish showed shorter TLs, potentially reflecting lower individual quality. The fish, which were less sensitive to parasite-induced impaired growth, quantified as parasite load-adjusted fork length, showed also longer TLs, lower GR- and GST activity and less GSH_{tot} compared to more sensitive fish. These results provide novel knowledge about the impacts of the PKD in brown trout at the molecular level and support the idea that TL may reflect individual quality and ability to cope with parasitic infections.

Keywords Infectious disease · Myxozoan endoparasite · Oxidative stress · PKD · Salmonids

Introduction

Myxozoan *T. bryosalmonae* is a causative agent for economically important proliferative kidney disease (PKD) in both farmed and wild salmonids (Burkhardt-Holm et al. 2005; Sterud et al. 2007). PKD causes renal swelling, impaired excretion and anemia, and infected fishes are highly sensitive to secondary infections (Chilmonczyk et al. 2002; Clifton-Hadley et al. 1987; Hedrick et al. 1993). Surviving fish can restore normal kidney function, although spore-forming stages of *T. bryosalmonae* may remain within kidney tubules (Okamura et al. 2011). PKD severity is temperature dependent, and global warming has raised serious concerns about the effects of PKD on brown trout, and other salmonids that are dependent on cool water (Borsuk et al. 2006; Bruneaux et al. 2016; Debes et al. 2017).

Host–parasite research has traditionally focused mainly on host resistance, i.e., ability to limit parasite load, whereas more recent studies underline the importance of considering also the hosts ability to minimize the fitness costs of

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increasing parasite load (Gomez et al. 2014; Medzhitov et al. 2012; Råberg et al. 2009; Schneider and Ayres 2008). *T. bryosalmonae* parasite load in brown trout is associated with large range of kidney hyperplasia, and physiopathological symptoms strongly correlate with hyperplasia, but less with parasite load (Bettge et al. 2009; Bruneaux et al. 2016; Gomez et al. 2014; Grabner and El-Matbouli 2009). This suggests that brown trout shows high among-individual variation in both resistance and tolerance to *T. bryosalmonae*-induced disease symptoms (Debes et al. 2017). Tolerance has often been measured as the rate of decline in body weight in different parasite–host systems (Adelman et al. 2013; Hayward et al. 2014; Råberg et al. 2007). Exposure to myxosporean parasites has shown to cause weight loss and delayed growth in fish (Golomazou et al. 2009; Minchella 1985; Sitja-Bobadilla et al. 2008). Therefore, in this study, we included both the original fork length and the parasite load-adjusted fork length (ability to grow despite the parasite load) as a measure of sensitivity to parasitism, to investigate the relationships between telomere length (TL), antioxidants (AOs), parasite load, and disease symptoms.

Pathogenic infections and chronic inflammatory diseases are stressors, which can cause telomere attrition (Blackburn et al. 2015; Cawthon et al. 2003). Telomeres, the repetitive DNA sequences $(TTAGGG)_n$ at the end of eukaryotic chromosomes, protect the genome during cell division, and become shorter with increasing number of cell divisions and thus with advancing age (e.g., Blackburn 2005). Previous studies have shown that TL is a promising biomarker for individual quality (Houben et al. 2008; Monaghan 2010) and life expectancy (Bakaysa et al. 2007; Bize et al. 2009; Cawthon et al. 2003; Haussmann et al. 2005; Heidinger et al. 2012; Salomons et al. 2009). Exposure to different stressors is expected to accelerate telomere loss: Firstly, because the high GC content of telomeric sequences makes them vulnerable to oxidative damage (Henle et al. 1999; von Zglinicki 2002). Secondly, oxidative stress can accelerate TL attrition also indirectly, by interfering with telomere repair by the telomerase enzyme (Kurz et al. 2004). Thirdly, high cellular proliferation rate increases telomere loss due to end-replication problem (Allsopp et al. 1995). Due to fast growth and high cell proliferation rate, telomere shortening is faster in early-life (Bhattacharyya and Lustig 2006; Foote et al. 2011; Heidinger et al. 2012). Short TL is often thought to be a cost of attaining a large body size (Monaghan 2010). However, it is likely that the interaction between early growth and TL is more complex, and affected by several environmental stressors (Beaulieu et al. 2011; Debes et al. 2016; Hall et al. 2004; McLennan et al. 2016; Mizutani et al. 2013; Parolini et al. 2015), which might cause oxidative stress, and thus take part in telomere shortening.

Previous knowledge of infection–telomere interactions is mainly based on correlative human studies (reviewed in Monaghan 2014) and rather limited experimental work in mammals (Cohen et al. 2013; Ilmonen et al. 2008; Raymond et al. 2014), and birds (Asghar et al. 2015, 2016; Hau et al. 2015). Experiments with rodents have shown bacterial infection-induced telomere attrition: *Salmonella* sp.-infected wild house mice (*Mus musculus musculus*) (Ilmonen et al. 2008) and *Staphylococcus aureus*-infected laboratory rats (Raymond et al. 2014) had higher telomere attrition rate and shorter TLs compared to sham-infected controls. An experimental study with Eurasian blackbirds (*Turdus merula*) has also shown that birds exposed to repeated immune and disturbance stressors have accelerated telomere loss and more oxidative damage than control birds (Hau et al. 2015). Furthermore, studies from malaria-bird systems have shown long-term costs of malaria infection on aging via telomere loss in multiple tissues (Asghar et al. 2015, 2016). On the other hand, short telomeres might expose individuals to higher infection risk and poor disease tolerance. Ilmonen et al. (2008) found, in addition to infection-induced telomere attrition, that short white blood cell (WBC) TL at early age was associated with decreased resistance to infection at older age in wild house mice. Cohen et al. (2013) found similar results in an experiment in humans, in which individuals with short WBC TLs were more susceptible to experimentally induced upper respiratory viral infection and clinical illness. Observed effects have been explained by the fact that effective immune response and resistance to pathogenic infections requires sufficient leukocyte proliferation capacity, which seems to be limited with short WBC TLs (Goronzy et al. 2006; Herrera et al. 1999; Vallejo et al. 2004; Weng et al. 1995). However, despite the growing interest in infection–telomere interactions, there is considerable lack of knowledge on host–parasite interactions from telomere biology's perspective, and in particular from native host–parasite systems in the wild.

Parasitic infections have been shown to cause oxidative damage in fish host–parasite systems (Kurtz et al. 2006; Stumbo et al. 2012), and in other vertebrate hosts (Sorci and Faivre 2009). However, knowledge about the role of AO responses on parasite resistance and tolerance in fish is still scarce and the results have been rather contradictory. For example, some of the studies have found that parasitic infection reduces AOs (Elia et al. 2009; Hursky and Pietrock 2015) or down-regulates expression of AO-related gene transcripts (Sitja-Bobadilla et al. 2008; Wynne et al. 2008), whereas others have found increased AO activities (Dautremepuits et al. 2003; Radovanovic et al. 2010, 2015) and up-regulated expression of AO genes as a response to infection (Davey et al. 2011). These inconsistent findings could be due to various reasons. Firstly, AO responses most likely vary depending on host–parasite system. Secondly, AO response may change depending on the phase of the infection (Tancredo et al. 2015). Finally, AO responses may also interact

with other environmental stressors, such as water quality (Garcia et al. 2011) or contaminants (reviewed in Martinez-Alvarez et al. 2005).

In the present study, we investigated the potential roles of TL and AO defense, and their relationships with parasite load and disease severity in *T. bryosalmonae*-infected fish. Our a priori hypothesis was that *T. bryosalmonae* infection results in higher production of reactive oxygen species (ROS), which in turn could lead to increased telomere damage (von Zglinicki 2002). Furthermore, we predicted that effective AO defense could prevent telomere attrition, reduce severity of PKD symptoms due to *T. bryosalmonae* infection, and thus provide higher tolerance to parasitism. Moreover, we predicted that fish with longer TLs would have higher tolerance and less severe infection-induced disease symptoms. To our knowledge, this study is the first to investigate the relationship between TL and AO defenses in wild host–parasite system in fish.

Materials and methods

This work is based on a subset of individuals ($N = 52$) that were earlier analyzed by (Bruneaux et al. 2016) in different context. In short, anadromous juvenile young-of-the-year brown trout were caught by electrofishing in Vainupea river (Estonia) at the end of September 2011. Hatching in the wild is relatively synchronized in brown trout (Elliott 1984), and therefore that is reasonable to assume that all the fish were exposed contemporary to the *T.bryosalmonae* in the same environment. Fishes were measured for fork length (FL), from snout to the end of the middle caudal fin, after euthanasia. In addition, relative parasite load (PL) (quantification of *T. bryosalmonae* using qPCR) and various physiological and disease-related traits (e.g., kidney hyperplasia, haematocrit, leucocyte formula) were measured (see Bruneaux et al. 2016 for more details). Kidney hyperplasia, which reflects the severity and the phase of infection, was quantified from a cross section photograph, where the kidney-to-body thickness ratio (K/B) was calculated. For the statistical analysis, we used the count of thrombocytes *per* 10,000 RBCs, and the percentage of each leucocyte category *per* all counted leucocytes to track relative changes in the WBC formula, independently of variation in haematocrit levels. Due to the small size of juvenile fish all the measurements could not be done from kidney tissue, and thus liver was chosen for TL and AO measurements.

Genomic DNA for TL measurement was extracted from liver samples using a salt extraction method (Aljanabi and Martinez 1997). We used a qPCR method developed by (Cawthon 2002) for relative TL estimation. This method allows estimating the total amount of telomere sequence in a sample relative to the amount of a nuclear control gene. This method has also been previously adopted for our study species (Debes et al. 2016; Näslund et al. 2015). Using primers developed by (Epel et al. 2004) for telomeric DNA and by (Maeda et al. 2002) for 18S rRNA (nuclear control gene), we performed qPCR amplifications on a 7900HT FAST Real-Time (Life Technologies). Baseline fluorescence, PCR efficiencies of each reaction and quantification cycle (Cq) values were estimated using LinRegPCR version 2012.0 (Ruijter et al. 2009).

All of the AO defense measurements were performed with an EnVision plate reader (Perkin-Elmer, Turku, Finland) and the protocols were adjusted to be more suitable for small sample volumes. Activities are expressed per protein content, which was determined using the Bradford method (Bradford 1976). The protocol from Glutathione Fluorescent Detection Kit (K006-F1, Arbor Assays) was used to measure the ratio between reduced and oxidized glutathione species (GSH/GSSG) and total glutathione (GSH_{tot}). Sigma kits (Sigma Chemicals, St. Louis, USA) were used to measure catalase (CAT), glutathione peroxidase (GP), glutathione reductase (GR) and glutathione *S*-transferase (GST) activities, and a Fluka kit (Fluka, Buchs, Germany) to measure superoxide dismutase (SOD) activity. Glucose-6-phosphate dehydrogenase (G6PDH) activity was measured according to (Noltmann et al. 1961). Sample preparations and method for TL and AO defense measurements are described in more detail in Online Resource (ESM 1).

Statistical analyses were conducted with IBM SPSS Statistic software 22 (IBM SPSS Statistics 22. New York: IBM Corporation). Spearman correlations were used to evaluate relationships among variables. To quantify the relative costs of infection, parasite load-adjusted fork length (PLadj.FL, unstandardized residuals) was calculated from linear regression between the square-root-transformed parasite load and fork length of the fish (Fig. 1a). In other words, higher residuals indicate that fish are of relatively large size despite the amount of parasites, and thus have been able to sustain high growth rate despite the parasite burden. On the other hand, low residuals indicate retarded growth in relation to parasite load, most likely reflecting elevated physiological costs of the PKD.

Results

Tetracapsuloides bryosalmonae DNA was detected from all of the fish with a qPCR method (100% prevalence). Associations among disease symptoms, TL and AO variables are presented in Table 1 and visualized in the correlation network graph in Online Resource (ESM 2). As expected, fish with high parasite load showed more severe kidney hyperplasia and anemia, and were of smaller size than fish with less *T. bryosalmonae*, indicating that the parasite has a

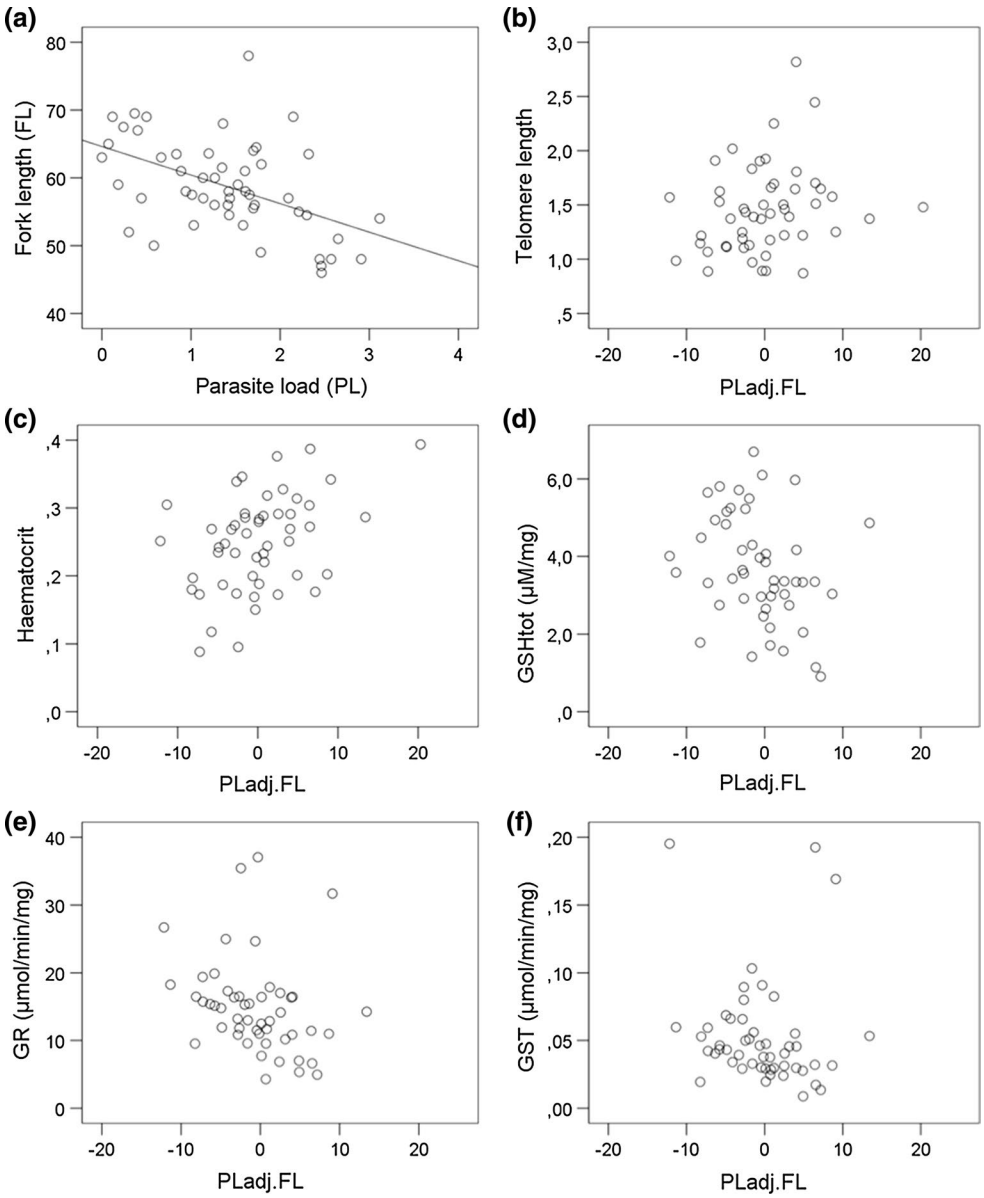

Fig. 1 Differences in brown trout ability to grow despite the parasite load, and its associations with TL, AOs and disease traits. Unstandardized residuals were calculated from **a** linear regression between the sq-transformed parasite load (PL) and fork length (FL) ($R^2 = 0.235$, $F = 15.33$, $N = 52$, $P < 0.001$) and used to reflect physiological sensitivity to parasites (PLadj.FL). Brown trout with higher PLadj.FL exhibited. **b** Longer TL (Spearman correlation, $r_s = 0.291$, $N = 51$, $p = 0.038$), **c** higher hematocrit ($r_s = 0.386$, $N = 51$, $p = 0.005$), **d** less GSH_{tot} ($r_s = -0.369$, $N = 49$, $p = 0.009$), **e** lower GR- ($r_s = -0.408$, $N = 50$, $p = 0.003$) and **f** GST activity ($r_s = -0.298$, $N = 51$, $p = 0.034$)

strong physiological effect on host. In addition, as presumed, AO variables formed a clear cluster due to strong intercorrelations among them. Parasite load was not directly associated with AO defense, but fish with severe kidney hyperplasia showed reduced AO activities (GST, SOD, CAT), and increased amount of thrombocytes per 10,000 RBCs, compared to fish with more normal kidneys. In addition, trout with low haematocrit and higher number of thrombocytes per 10,000 RBCs exhibited higher GR activity (Table 1). TL was not associated with parasite load, AO defense or kidney hyperplasia. However, TL was positively correlated with the size of the fish (Table 1) and the fish that were able to sustain higher growth rate despite the parasite load possessed longer TLs (Fig. 1b), higher hematocrit (Fig. 1c), less GSH_{tot} (Fig. 1d) and lower GR- (Fig. 1e) and GST activity (Fig. 1f) than fish showing retarded growth in relation to parasite load.

Discussion

Our study provides first glance into complex relationships among TL, AO defense, parasite load and disease symptoms in native brown trout/*T. bryosalmonae* host–parasite system. *T. bryosalmonae* infection caused severe kidney hyperplasia and anemia, as reported earlier in brow trout (Bruneaux et al. 2016), and in other salmonids (Chilmonczyk et al. 2002; Hedrick et al. 1993). Furthermore, both the parasite load and the PKD symptoms were associated with impaired growth, indicating strong physiological cost of the disease.

Table 1 Spearman correlation coefficients for studied variables

	PLadj.FL	K/B	Haematocrit	Lympho cytes	Monocy tes	Granulo cytes	Thrombo -cytes	PL	TL	GST	SOD	CAT	GSH/G SSG	GSH_{tot}	GP	GR	G6PDH
FL	**0.868**	**−0.337**	**0.609**	0.297	0.279	−0.314	−0.327	**−0.484**	**0.341**	−0.232	0.069	−0.041	0.063	**−0.319**	**−0.312**	**−0.531**	−0.217
	<0.001	**0.014**	**<0.001**	0.079	0.100	0.062	0.051	**<0.001**	**0.014**	0.102	0.672	0.794	0.672	**0.025**	**0.029**	**<0.001**	0.148
	***N* = 52**	***N* = 52**	***N* = 51**	*N* = 36	*N* = 36	*N* = 36	*N* = 36	***N* = 52**	***N* = 51**	*N* = 51	*N* = 47	*N* = 44	*N* = 47	***N* = 49**	***N* = 49**	***N* = 50**	*N* = 46
	PLadj.FL	−0.119	**0.386**	0.180	0.246	−0.186	−0.078	−0.050	**0.291**	**−0.298**	0.071	−0.022	0.097	**−0.369**	−0.228	**−0.408**	−0.145
		0.401	**0.005**	0.293	0.148	0.278	0.652	0.727	**0.038**	**0.034**	0.618	0.888	0.515	**0.009**	0.115	**0.003**	0.337
		N = 52	***N* = 51**	*N* = 36	*N* = 36	*N* = 36	*N* = 36	*N* = 52	***N* = 51**	***N* = 51**	*N* = 51	*N* = 44	*N* = 47	***N* = 49**	*N* = 49	***N* = 50**	*N* = 46
		K/B	**−0.501**	−0.115	−0.160	0.178	**0.539**	**0.541**	0.113	**−0.350**	**−0.340**	**−0.373**	0.276	−0.233	−0.051	0.055	0.079
			<0.001	0.505	0.352	0.299	**0.001**	**<0.001**	0.428	**0.012**	**0.015**	**0.013**	0.061	0.107	0.728	0.706	0.602
			***N* = 51**	*N* = 36	*N* = 36	*N* = 36	***N* = 36**	***N* = 52**	*N* = 51	***N* = 51**	***N* = 51**	***N* = 44**	*N* = 47	*N* = 49	*N* = 49	*N* = 50	*N* = 46
			Haematocrit	0.012	**0.336**	−0.063	**−0.462**	**−0.566**	0.254	−0.032	0.126	−0.077	−0.058	−0.083	−0.143	**−0.337**	−0.245
				0.947	**0.045**	0.716	**0.005**	**<0.001**	0.075	0.825	0.385	0.620	0.702	0.574	0.331	**0.018**	0.105
				N = 36	***N* = 36**	*N* = 36	***N* = 36**	***N* = 51**	*N* = 50	*N* = 50	*N* = 50	*N* = 44	*N* = 46	*N* = 48	*N* = 48	***N* = 49**	*N* = 45
				Lympho cytes	−0.023	**−0.991**	−0.138	−0.066	−0.126	−0.089	−0.071	−0.068	−0.238	−0.033	0.083	−0.211	−0.197
					0.896	**<0.001**	0.423	0.700	0.471	0.604	0.681	0.706	0.681	0.849	0.640	0.217	0.273
					N = 36	***N* = 36**	*N* = 36	*N* = 36	*N* = 35	*N* = 36	*N* = 36	*N* = 33	*N* = 36	*N* = 35	*N* = 34	*N* = 36	*N* = 33
					Monocy tes	−0.047	**−0.330**	−0.020	0.271	−0.202	0.006	−0.068	−0.171	−0.248	−0.136	−0.254	−0.051
						0.786	**0.049**	0.910	0.115	0.238	0.973	0.706	0.349	0.151	0.444	0.134	0.778
						N = 36	***N* = 36**	*N* = 36	*N* = 35	*N* = 36	*N* = 36	*N* = 33	*N* = 32	*N* = 35	*N* = 34	*N* = 36	*N* = 33
						Granulo cytes	0.172	0.089	0.101	0.071	0.036	−0.088	0.287	0.020	−0.074	0.192	0.170
							0.317	0.604	0.563	0.679	0.836	0.628	0.112	0.908	0.677	0.263	0.345
							N = 36	*N* = 36	*N* = 35	*N* = 36	*N* = 36	*N* = 33	*N* = 32	*N* = 35	*N* = 34	*N* = 36	*N* = 33
							Thrombo cytes	0.304	−0.123	0.095	−0.011	−0.004	0.336	−0.024	0.175	**0.357**	0.182
								0.071	0.481	0.581	0.948	0.984	0.060	0.893	0.322	**0.032**	0.311
								N = 36	*N* = 35	*N* = 36	*N* = 36	*N* = 33	*N* = 32	*N* = 35	*N* = 34	***N* = 36**	*N* = 33
								PL	−0.196	−0.088	−0.080	0.025	0.005	−0.013	0.162	0.240	0.054
									0.168	0.540	0.578	0.874	0.972	0.930	0.265	0.093	0.721
									N = 51	*N* = 51	*N* = 51	*N* = 44	*N* = 47	*N* = 49	*N* = 49	*N* = 50	*N* = 46
									TL	−0.084	−0.004	−0.087	0.114	−0.115	−0.030	−0.047	0.223
										0.563	0.977	0.573	0.452	0.436	0.841	0.750	0.140
										N = 50	*N* = 50	*N* = 44	*N* = 46	*N* = 48	*N* = 48	*N* = 49	*N* = 45
										GST	**0.612**	**0.429**	−0.019	**0.537**	**0.307**	**0.667**	**0.313**
											<0.001	**0.004**	0.898	**<0.001**	**0.034**	**<0.001**	**0.034**
											***N* = 50**	***N* = 44**	*N* = 46	***N* = 49**	***N* = 48**	***N* = 50**	***N* = 46**
											SOD	**0.568**	0.078	**0.633**	**0.325**	**0.649**	**0.539**
												<0.001	0.605	**<0.001**	**0.024**	**<0.001**	**<0.001**
												***N* = 43**	*N* = 46	***N* = 48**	***N* = 48**	***N* = 49**	***N* = 45**
												CAT	−0.138	**0.373**	0.099	**0.338**	0.237
													0.401	**0.014**	0.532	**0.025**	0.142
													N = 39	***N* = 43**	*N* = 42	***N* = 44**	*N* = 40
													GSH/G SSG	−0.239	0.085	0.209	0.164
														0.118	0.585	0.168	0.307
														N = 44	*N* = 44	*N* = 45	*N* = 41
														GSH_{tot}	**0.373**	**0.659**	**0.490**
															0.010	**<0.001**	**0.001**
															***N* = 47**	***N* = 49**	***N* = 46**
															GP	**0.484**	0.263
																<0.001	0.085
																***N* = 48**	*N* = 44
																GR	**0.785**
																	<0.001
																	***N* = 46**
																	G6PDH

Table 1 (continued)

The statistically significant correlations ($p < 0.05$) are with black bold font

Visualization as a correlation network (Epskamp et al. 2012) is provided in Online Resource (ESM 2)

FL fork length, *PL* parasite load, *PLadj.FL* parasite load-adjusted fork length, *K/B* kidney-to-body thickness ratio

Somewhat surprisingly, we did not find direct associations between parasite load and either TL or AOs. Instead, our results suggest that TL might reflect quality in terms of individuals' ability to grow despite the parasitic infection, and that the different components of the AO responses are associated with kidney hyperplasia and growth.

Despite the lack of associations between parasite load and measured AO variables, AO defense correlated with PKD symptoms. Fishes that were able to maintain their GST-, SOD- and CAT activities at sufficient level, likely suffered less from infection-induced ROS, and thus experienced less severe kidney hyperplasia compared to those with lower GST, SOD and CAT. GST has an important role in biotransformation, and its activity has been shown to decrease due to host immune response during parasitic infection (Skalova et al. 2007). Our results corroborate with a previous study, which found that PKD decreases SOD- and CAT activity in the liver of farmed rainbow trout (*Oncorhynchus mykiss*) compared to the healthy fish (Elia et al. 2009). This consistency was not self-evident, since only the brown trout and the brook trout (*Salvelinus fontinalis*) have been identified as permissive hosts for *T. bryosalmonae* (Grabner and El-Matbouli 2008; Morris and Adams 2006) and previous studies have found interspecific differences in expression of immune response related genes in *T. bryosalmonae*-infected brown trout and rainbow trout (Kumar et al. 2015). Low haematocrit and increased amount of thrombocytes, which are also typical symptoms of PKD, were both correlated with increased GR activity. These results indicate that GR activity plays an important role in *T. bryosalmonae*-induced immune response in brown trout, as higher GR activity and lower NADPH/NADP+ ratio are known to speed up the pentose phosphate pathway to replace NADPH used in immune response after phagocytosis (Halliwell and Gutteridge 2007).

We found that larger fish possessed longer TLs compared to smaller fish. Large body size has many advantages, e.g., higher survival and reproductive success (Blanckenhorn 2000; Dmitriew 2011), and thus likely reflects good individual quality. Our result corroborate with recent avian studies, which have shown that birds with longer TLs exhibit faster growth rate (Caprioli et al. 2013; Kim and Velando 2015; Mizutani et al. 2016; Parolini et al. 2015). It is, therefore, likely that individuals with long TLs are of superior physiological quality, which enables simultaneous investment both into maintenance of long TLs and attaining a large body size. However growth, and especially rapid growth rate after period of food shortage, i.e., catch-up growth, is expected to be traded-off with investment to TL maintenance (reviewed in Monaghan 2014), and several studies have found negative associations between size and TL. For example, negative correlation between size and TL has been reported in juvenile salmonids (Debes et al. 2016; McLennan et al. 2016; Näslund et al. 2015; Pauliny et al. 2015), and in house sparrow (*Passer domesticus*) fledglings (Ringsby et al. 2015). These contradictory results suggest that the link between early growth and telomere dynamics is complex, and potentially affected by additional extrinsic stressors that can override the impacts of intrinsic growth *per se*. This view is in good agreement with our results, and with studies where accelerated telomere attrition has not found to be associated with the growth rate, but merely with the degree of exposure to environmental stressors, such as harshness of the environment of Atlantic salmon (*Salmo salar*) (McLennan et al. 2016), or nestling growth conditions, like within brood competition and food shortage (Nettle et al. 2015; Parolini et al. 2015; Reichert et al. 2015; Stauffer et al. 2017), or elevation gradient (Stier et al. 2016). Furthermore, Mizutani et al. (2016) found in a longitudinal study in black-tailed gull chicks (*Larus crassirostris*) that the relationship between TL and growth rate was positive, and changed depending on the presence or lack of sibling competition. Therefore, it seems that TL and telomere attrition rate depend on additional environmental factors during the early growth, and also on individual quality and ability to deal with environmental stress.

Some individuals were able to manage the higher *T. bryosalmonae*-load with less severe physiological consequences in terms of parasite-induced impaired growth, and thus appeared to be more tolerant than others. The positive correlation between TL and parasite load-adjusted fork length suggests that the fish with longer TLs were able to sustain higher growth rate despite the parasite burden compared to those with shorter TLs. Thus, our results indicate that TL might be a useful biomarker for assessing individual quality and ability to tolerate parasitism. However, a potential caveat that we cannot fully exclude by studying natural population is the possibility that there might be among-individual variation in exposure to the *T. bryosalmonae*, which could, at least partly, explain the association between the parasite load-adjusted size and TL. Nevertheless, high heritability estimates of *T. bryosalmonae* resistance in wild brown trout populations (Debes et al. 2017) suggest that genetic, rather than environmental variation explains large part of among-individual variation. We also found that fish, which were less sensitive to parasite-induced retarded growth, exhibited lower GR- and

GST activity and less GSH_{tot}. Since higher GR activity is expected to be advantageous for immune response to speed up the pentose phosphate pathway (Halliwell and Gutteridge 2007), lower GR activity in brown trout is most likely indicative of good physiological condition. Usually parasitic infections have shown to decrease GST activity in fish hosts (Frank et al. 2011), and the decrease in GSH_{tot} is considered to indicate high oxidative stress due to parasite infection (Giri and Roy 2016; Gismondi et al. 2012). We suggest that compromised AO defense, due to low GST activity and low amount of GSH_{tot}, may be related with a cost for attaining a large body size despite the parasite load.

To best of our knowledge, this is the first attempt to disentangle the relationships in AO response, disease symptoms and TL in native brown trout/*T. bryosalmonae* host–parasite system in a natural environment. Neither parasite load, nor the PKD symptoms were correlated with TL, indicating lack of direct, strong effects of parasite abundance on TL, or vice versa. However, our results suggest that TL might reflect quality in terms of individual's ability to grow under parasitic infection, since juvenile trout with longer TLs was of larger size, and sustained higher growth rate despite the parasite load compared to fish with shorter TLs. Interestingly, we also found that different AOs were associated with kidney hyperplasia and parasite-induced retarded growth, which highlights the complexity of AO defense. Yet, a cross-sectional study, such as ours, provides only a limited snapshot view into complex inter-relationships among TL, AO defense, parasite load and disease symptoms, which makes it challenging to draw any strong causal conclusions for dynamic relationships in this system. Therefore, longitudinal studies, and preferably experimental ones, are needed to further confirm the causative relationships of oxidative stress and telomere dynamics during different stages of *T. bryosalmonae* infection and PKD.

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Author contribution statement AV and PI conceived the ideas and designed the study. MB, MV and AV conducted fieldwork, JS, BP and MV executed the laboratory measurements and JS analyzed the data. JS and PI wrote the manuscript; other authors provided editorial advice.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical approval All applicable institutional and national guidelines for the care and use of animals were followed. All experiments were performed according to the animal experimentation permit no. 53 issued by the Estonian Ministry of Agriculture (issued on 17.11.2010, valid from 17.11.2010 until 31.12.2014).

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