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Genome size evolution in macroparasites

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ABSTRACT

Reduction in genome size has been associated not only with a parasitic lifestyle in intracellular microparasites but also in some macroparasitic insects and nematodes. We collected the available data on genome size for flatworms, annelids, nematodes and arthropods, compared those with available data for the phylogenetically closest free-living taxa and found evidence of smaller genome sizes for parasites in six of nine comparisons. Our results suggest that despite great differences in evolutionary history and life cycles, parasitism as a lifestyle promotes convergent genome size reduction in macroparasites. We discuss factors that could be associated with small genome size in parasites which require further exploration in the future.

Reduction in genome size has been reported to be a common feature of intracellular parasitic/pathogenic and symbiotic bacteria (Toft and Andersson, 2010) as well as in fungal microparasites such as several microsporidians (see e.g. Corradi et al., 2010). Recently, an association between small genome size and parasitic lifestyle has also been suggested for metazoan parasites such as insects and nematodes (Kirkness et al., 2010; Visser et al., 2010; Ellers et al., 2012; Poulin and Randhawa, 2013). To date, linking genomic changes with particular features in lifestyles common to all parasites (Poulin and Randhawa, 2013), or to specific genes or sets of genes defining a parasitic lifestyle (Rödelsperger et al., 2013), have been unsuccessful.

In contrast to intracellular (micro)parasites, many extracellular (macro)parasites have complex life cycles with different transmission stages between different host species, which would intuitively suggest genomic reduction to be unlikely. Extracellular and/or metazoan parasites could even be expected to possess more genes than free-living organisms due to the need to recognize and transmit to new hosts, find mates and to survive in both cold- and warm-blooded animals with different immunological strategies. Thus exploring the association between lifestyle and genome size in macroparasites is essential in understanding the evolution of host-parasite interactions.

To explore the genomic effects of parasitism in macroparasites, we collected the available data on genomic reduction in groups of macroparasitic organisms and their phylogenetically closest free-living taxa (see Supplementary Table S1 for data sources and phylogeny used in these analyses). Because whole genome sequence data is available only for some species, genome size was used as a proxy for genomic reduction. Genome sizes given in megabases (Mb) were converted to *C*-values i.e. to picogram (pg) of DNA (978 Mb equals to 1 pg) according to Dolezel et al. (2003).

Paired comparisons were made between Hirudinea and Oligochaeta within Annelida, between parasitic and free-living Hymenoptera (Arthropoda 1), between Strepsiptera and Coleoptera (Arthropoda 2), Phthiraptera and Hemiptera (Arthropoda 2) within arthropod insects, and between parasitic and free-living Acariformes within arthropod arachnids (Arthropoda 4). For Arthropoda 5, parasitic Parasitiformes (Arachnida) were compared with free-living Araneae (Arachnida). Within Platyhelminthes, Neodermata (cestodes and trematodes) were compared with Adiaphanida (including free-living Turbellaria in the orders Prolecithophora and Tricladida). Within nematodes, plant parasitic species (clades 12 and 10b/clade IV; see classification in Supplementary Table S1) were compared with free-living species (clade 11/clade IV) (Nematoda 1), and animal parasites (clades 8 and 9/clades III and V) with free-living species (clade 9/clade V) (Nematoda 2). The groups were compared using linear mixed models, with phylogenetic group and lifestyle (parasitic versus free-living) as grouping variables and $\log_{10}$ of the *C*-value (pg) as the dependent variable. Effect sizes (Hedges' g) were calculated as differences in means divided by pooled S.Ds.

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according to Durlak (2009). All of the analyses were performed with the IBM-SPSS statistics 20 package.

Despite their more complicated biology compared with microparasites, and the robustness of the data, the trend of genomic reduction was detected in our dataset for macroparasites in six of the nine comparisons made (Fig. 1). The genome sizes were significantly smaller for parasitic Annelida, Platyhelminthes, Arthropoda groups 1–3 and Nematoda group 1 compared with free-living groups (two-tailed sign-test, $P < 0.031$). No genome size differences between parasites and free-living species were detected in the two comparisons within Arachnida and Nematoda group 2. Due to a lack of data, these comparisons were, phylogenetically, perhaps not the most optimal ones. Arthropoda 4 (Acariformes) consisted of only five data points. For Parasitiformes, comparison within the order was not possible because genome size was available for only one free-living species. Therefore the comparison for parasitic Parasitiformes was made at a subclass level with free-living Araneae. For Nematoda 2, the species parasitic to animals belonged to two different, distantly related clades, however when the statistical tests were repeated only within one clade (9/V), the result did not change qualitatively. In Nematoda 2, the parasitic species have large genomes compared with free-living species. For example, *Parascaris univalens* has a *C*-value of 2.08, while all other nematodes have *C*-values $\leqslant$0.68 (see Supplementary Table S1). However, reasons for the differential genomic evolution are currently largely unknown. We also acknowledge that our dataset is limited due to low numbers of available genome size data on parasitic metazoans, as well as due to differences in the phylogenetic resolution between taxa. For example, within some taxa, the comparisons could be made within class and in most taxa between orders. For Platyhelminthes, the division into a parasitic lifestyle occurred so early in evolution that the comparison was made at a subphylum level and the possibility that the observed differences within this group are caused by ancient events not associated with parasitism should be taken into consideration.

Reduction in genome size can occur via compaction (loss of non-coding sequence) or by gene loss. In eukaryotes, the largest amount of genomic data has been obtained from microparasites, especially from microsporidians, in which both mechanisms, gene loss and compaction, are observed (Corradi et al., 2010). In macroparasites, genomic reduction has not been commonly acknowledged, despite detection in some taxa (Poulin and Randhawa, 2013). Here, we found that despite high taxonomic variation, genome size reduction seems to be a general trend associated with a parasitic lifestyle in several macroparasite groups. However, the importance of different mechanisms leading to evolution of a small genome size cannot be estimated until systematic comparative sequence data becomes available.

In intracellular parasitic/symbiotic bacteria, the genomic reduction has been suggested to result from the accumulation of deleterious mutations (Muller's ratchet) due to genetic drift in isolated populations with small effective population sizes (N_e), eventually leading to pseudogenization and gene erosion (Mira et al., 2001). In contrast, small N_e in multicellular organisms is suggested to lead to passive genome expansion due to the accumulation of non-functional DNA (Lynch, 2007). However, the metazoan parasites have generally smaller N_e than the free-living species (Criscione and Blouin, 2005), which could be expected to direct their genomic evolution towards larger genomes. On the other hand, it has been suggested that parasites (parasitic plants) have higher mutation rates than free-living organisms per se, possibly selected by the lifestyle itself and driven by shorter generation times but not affected by small N_e (Bromham et al., 2013). Furthermore, (hermaphroditic) mating systems in parasites can promote genomic reduction, as observed in nematodes (Wang et al., 2010; Thomas et al., 2012). Our observations on the small genome size in several macroparasitic groups suggest that a parasitic lifestyle imposes mechanisms or selection pressures which differ from those in free-living species, leading to differences in genome sizes.

Associations between small genome sizes and life history traits have been suggested in several systems. Replication of a small genome or transcription/translation of fewer genes requires less energy than that of a larger genome (Mira et al., 2001), releasing resources for other functions. In free-living plants and animals, a small genome size has been shown to be associated with small cell size and developmental complexity (Gregory, 2001, 2002), and in plants with short cell cycle phases (Simova and Herben, 2012), metabolic rate (Yang et al., 2013) and rapid vegetative growth rate

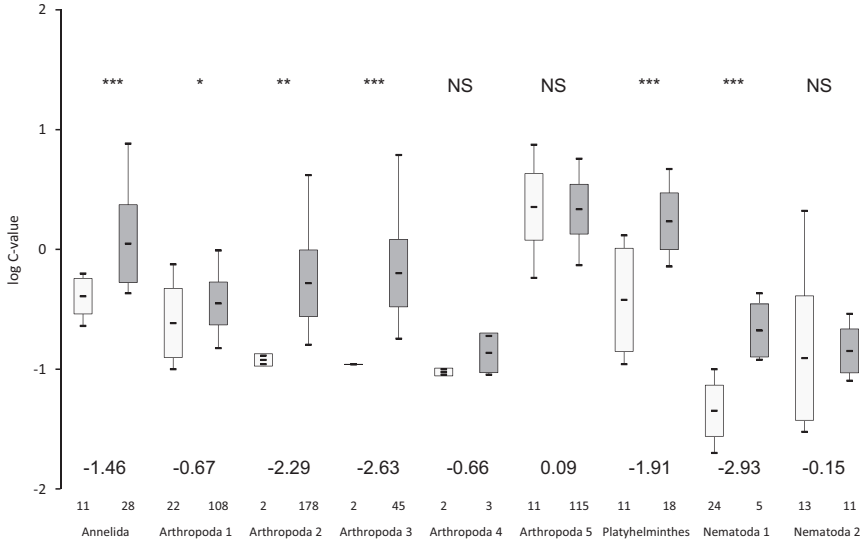

Fig. 1. Genome size variation in pairs of macroparasitic taxa (open boxes) and respective closest free-living taxa (shaded boxes), given in *C*-values (i.e. picograms of DNA where 978 megabases are equal to 1 pg). Mean values for log-transformed *C*-values for each group are given, surrounded by boxes denoting S.Ds. and whiskers showing minimum and maximum values. The number of species within each group is given along the base of the figure. The *P* values of pairwise comparisons with Bonferroni correction are given: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, NS $P > 0.05$, and numbers below the boxes are effect sizes measured as Hedges' g. Values >0.8 are considered large, indicating that there is little overlap between the two distributions, and negative values indicate smaller values for parasitic groups.

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