

18th February 2020

Dear Editor

We would like to submit the manuscript “**Extensive genomic and transcriptomic variation defines the chromosome-scale assembly of *Haemonchus contortus*, a model gastrointestinal worm**” for publication as a research article in *Genome Biology*. In our study, we report a highly resolved chromosomal genome assembly for *Haemonchus contortus*, a major gastrointestinal pathogen responsible for significant animal health and economic burdens worldwide. We describe chromosome-scale structural variation, patterns of transcriptional change and putative co-regulation throughout its life cycle using a comprehensive genome annotation derived from short- and long-read cDNA sequencing, and within- and between-population genetic diversity from a globally sampled cohort.

Our work represents a step-change in the genetic resources for *H. contortus*. A 370 Mbp highly fragmented and haplotypic draft assembly [ $n = 23,860$ ;  $N50 = 0.083$  Mbp] for this parasite strain was published in *Genome Biology* in 2013 (Laing et al.; gb-2013-14-8-r88). The utility and impact of this resource is highlighted by the fact that the publication describing the draft genome has been accessed over 20,000 times and cited at least 160 times in the last 7 years. Since completion in early 2019, we have made our chromosomal assembly [283 Mbp;  $n = 7$ ;  $N50 = 47.4$  Mbp] and all associated resources publicly available before publication via the main community portal for nematode research, WormBase Parasite, and since that time, has been used and referred to in at least 14 publications.

We believe that this work will be of great interest to communities that work on parasitic nematodes. *H. contortus* is the key model representing a group of parasites that includes most of the nematode species of relevance to veterinary health and the hookworms, which are important and neglected human pathogens that infect more than a billion people worldwide. However, we feel our work is particularly suited to *Genome Biology*, rather than a more specialised parasitology journal, as this assembly represents the most complete and accurate reference genome for any nematode species outside *Caenorhabditis*. Our analysis of resolved chromosomes reveals a remarkable pattern of almost complete conservation of chromosome content between the evolutionarily related *H. contortus* and *C. elegans*, but almost no conservation of gene order, and yet, important contrasts with this model, for example, in the patterns of *cis*- and *trans*-splicing, and chromosome dosage compensation components. Further, this work will be broadly applicable to readers of *Genome Biology* with an interest in chromosome-scale biology and potential insights gained from genetic and transcriptomic analyses derived from long molecule sequencing, especially for species with high genetic diversity.

We look forward to hearing from you.

Yours faithfully,

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