

Parasitic worm genome uncovers potential drug targets

August 28 2013



This is the front of the *Haemonchus contortus* (Barber Pole) worm. Credit: Moredun Research Institute

Researchers have identified five enzymes that are essential to the survival of a parasitic worm that infects livestock worldwide and is a great threat to global food security. Two of these proteins are already being studied as potential drug targets against other pathogens.

The team sequenced the [genome](#) of *Haemonchus contortus*, or the barber pole worm, a well-studied parasitic worm that resides in the gut of sheep and other livestock globally. This genome could provide a comprehensive understanding of how treatments against parasitic worms work and point to further new treatments and vaccines.

The barber pole worm or *H. contortus* is part of a family of gastrointestinal worms that are endemic on 100% of farms and are estimated to cost the UK sheep industry alone more than £80 million pounds each year. *H. contortus* has become resistant to all major treatments against parasitic worms, so its genome is a good model to understand how [drug resistance](#) develops in this complex group of closely related parasites and will also reveal further [potential drug](#) and [vaccine](#) targets.

"Our reference genome allows researchers to understand how *H. contortus* and other worms of this type acquire resistance to a wide range of anthelmintics – the drugs used to treat [worm infections](#)," says Dr James Cotton, senior author from the Wellcome Trust Sanger Institute. "Seeing a common theme of drug resistance in this well-characterised worm is extremely important because both people and animals are reliant on so few treatments against parasitic worms."



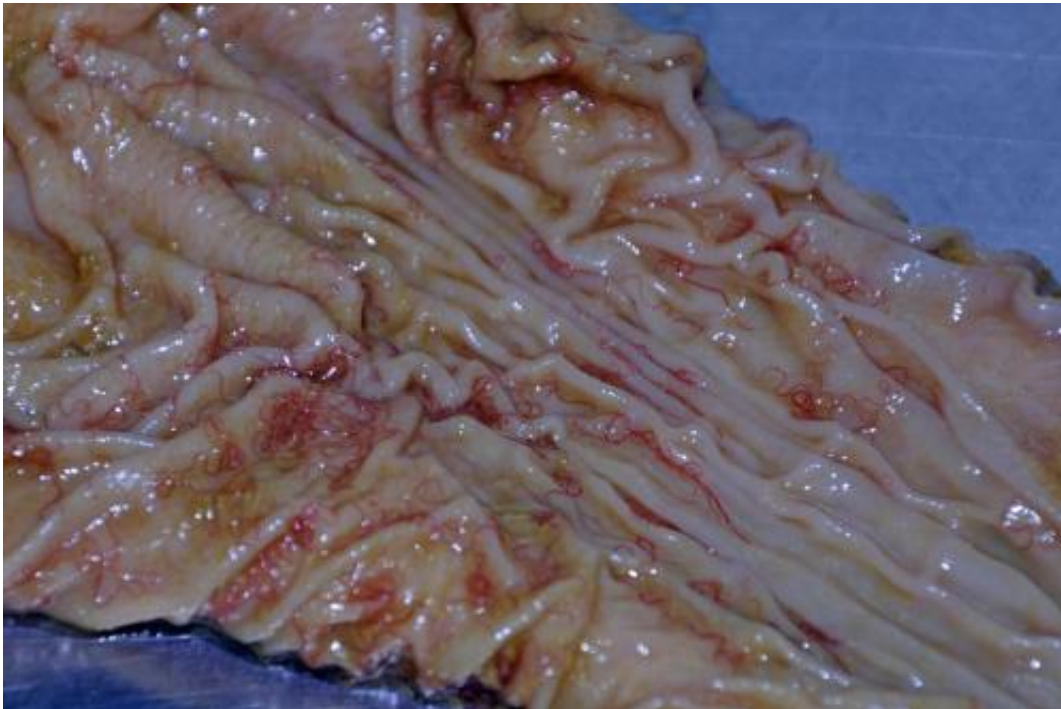
This is the back of the *Haemonchus contortus* (Barber Pole) worm. Credit: Moredun Research Institute

The team sequenced the genome of a strain of *H. contortus* that was susceptible to all major classes of drugs against parasitic worms. By comparing this sequence with that of worms that have acquired drug resistance, the researchers expect to reveal a wealth of information about how and why resistance has occurred.

"The *H. contortus* genome provides a rich and essential platform for future research in this and other types of parasitic worms," says Professor Neil Sargison, author from the University of Edinburgh, Royal (Dick) School of Veterinary Studies. "With the world population set to exceed nine billion by the year 2050, improving the security of our food supply is crucial. Getting to grips with genomes such as that of *H. contortus*, is our best option to tackle the issue of drug resistance and develop new drugs against parasitic worms to address this issue."

To generate a rich source of potential vaccine and drug target candidates, the team identified a set of genes that are more active in certain stages of the parasite life cycle and within the parasite's gut. They also identified five metabolic chokepoints – enzymes that are essential for a parasite's survival. Two of these enzymes are already being studied as potential [drug targets](#); one against *Mycobacterium tuberculosis* and another against another type of worm.

To discover these targets, the team determined when and where each gene is turned on or off in the cells and tissues of *H. contortus* to reveal new insights into the worm's lifecycle. The result is the most extensive dataset of its kind for any gastrointestinal worm and is expected to provide a valuable resource for future investigations.



These are *Haemonchus contortus* (Barber Pole) worms in situ in a sheep gut.
Credit: Moredun Research Institute

The researchers also described the full gene repertoires for known drug target families. This gives a comprehensive understanding of how several important treatments work against worms and begins to unravel why resistance has occurred in these genes.

"Not only is this worm closely related to many other parasites of livestock it is also similar to some species of worms in humans." Professor John Gilleard, joint senior author from the University of Calgary Faculty of Veterinary Medicine. "This makes it an extremely important model parasite species for experimental studies.

"Revealing new drug targets against *H. contortus* could provide much-needed new treatment opportunities against [parasitic worms](#) in both animals and humans."

More information: Roz Laing, Taisei Kikuchi, Axel Martinelli, Isheng J. Tsai, Robin N. Beech, Elizabeth Redman, Nancy Holroyd, David J. Bartley, Helen Beasley, Collette Britton, David Curran, Eileen Devaney, Aude Gilabert, Martin Hunt, Frank Jackson, Stephanie Johnston, Ivan Kryukov, Keyu Li, Alison A. Morrison, Adam J. Reid, Neil Sargison, Gary Saunders, James D. Wasmuth, Adrian Wolstenholme, Matthew Berriman, John S. Gilleard, James A. Cotton (2013) 'The genome and transcriptome of *Haemonchus contortus*, a key model parasite for drug and vaccine discovery' Advanced online publication in *Genome Biology*, 28 August 2013

Provided by Wellcome Trust Sanger Institute

Citation: Parasitic worm genome uncovers potential drug targets (2013, August 28) retrieved 19 April 2024 from <https://phys.org/news/2013-08-parasitic-worm-genome-uncovers-potential.html>

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