Physiochemical 'fingerprint' of parasitic 'American murderer' uncovered

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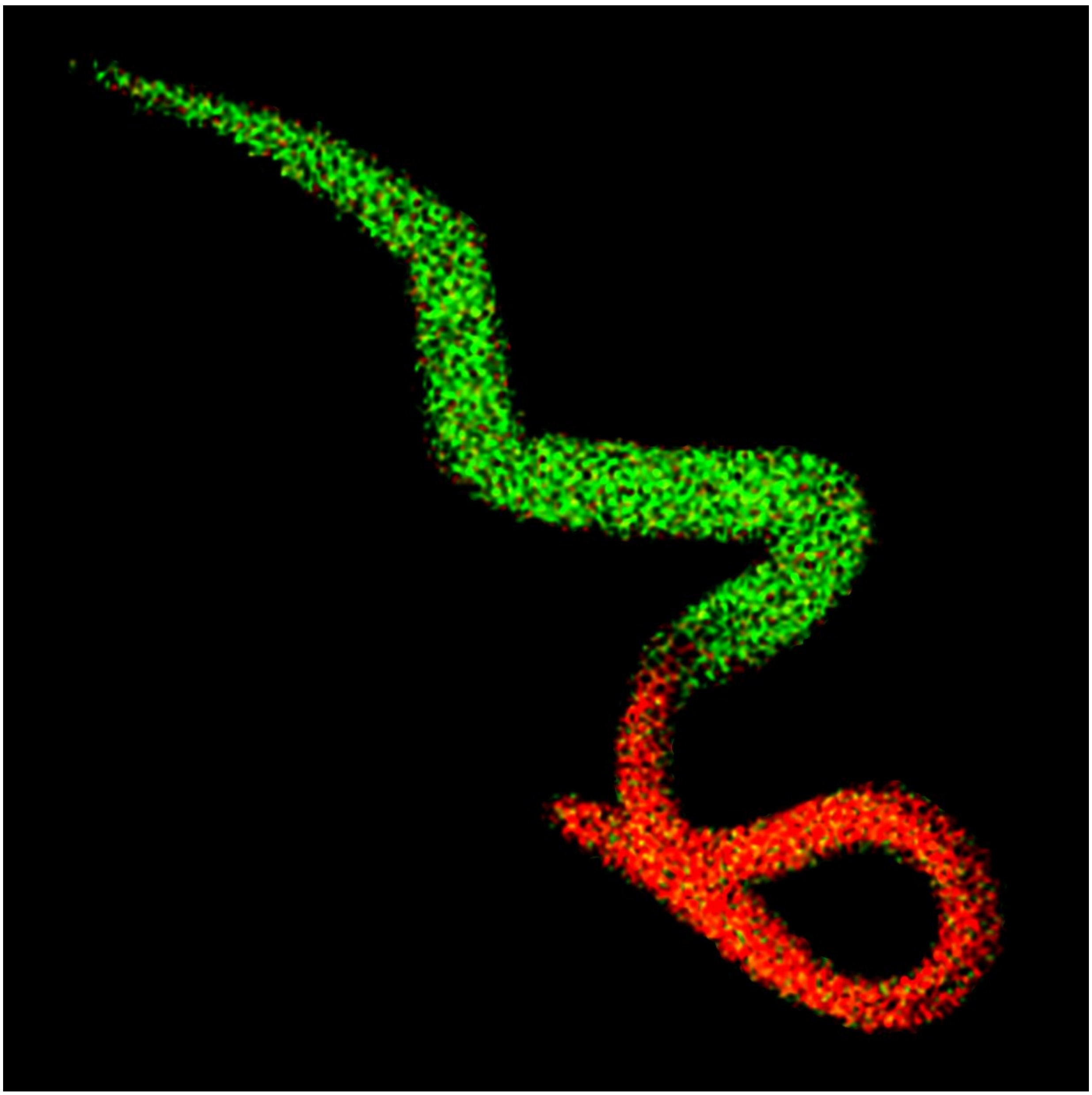


Researchers interrogate the worm surface and its sheath in unprecedented detail using Atomic Force Microscopy and Time-of-Flight Secondary Ion Mass Spectrometry. Credit: The University of Nottingham

The physical and chemical 'fingerprint' profile of a parasitic worm, dubbed the 'American murderer,' which infects hundreds of millions of people worldwide, has been uncovered for the first time by researchers at the University of Nottingham - a discovery that could allow for more effective and earlier treatment.

They have captured detailed movies reproducing the process the worm goes through as it enters the body and sheds its skin, or sheath, in a process called exsheathment. This has enabled the researchers to interrogate the worm surface and its sheath in unprecedented detail using Atomic Force Microscopy (AFM) and Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS).

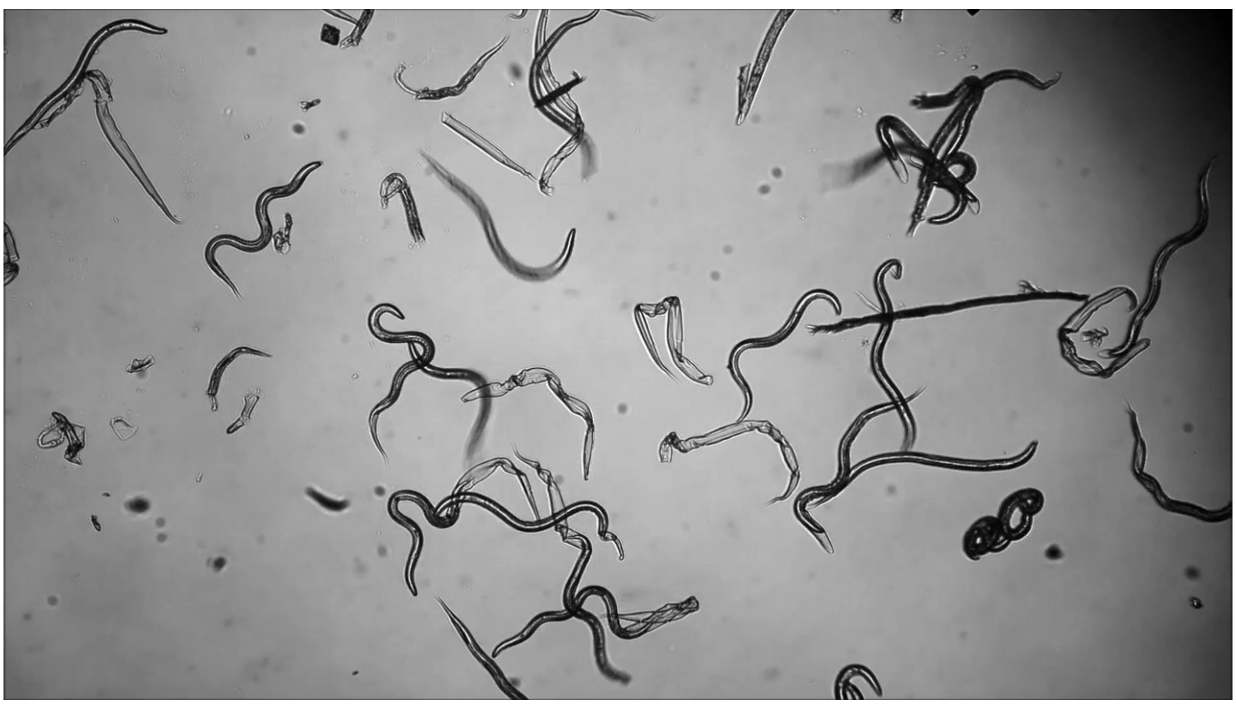
It is the first time the physicochemical make-up of the infective stage of N. americanus has been studied in this detail and the results provide a vital insight into its extremely successful infection mechanism. The research - 'The Physiochemical Fingerprint of Necator Americanus' - has been published in *PLOS Neglected Tropical Diseases*.

The hookworm *Necator americanus* is found in tropical climates and gets into the body through the skin, usually when trodden on barefoot. The worm then sheds its own skin, which is thought to trigger an immune response. If left untreated heavy infections result in anaemia and long-term discomfort and disability. These immunological observations inspired the team to explore the chemistry of the two surfaces in greater detail.

Lifecycle insight

The work was carried out by the University of Nottingham's School of Pharmacy and was led by Dr Veeren Chauhan and Professor David Pritchard, working with Dr David Scurr, Thomas Christie, Dr Gary Telford and Dr Jonathan Aylott.

In a precursor to this study, in research due to be published separately by PhD student Asha Hassan, Professors David Pritchard and Amir Ghaemmaghami, it has been shown that infection fighting cells gravitate toward the sheath the worm has left behind, creating a diversion to allow the worm to freely enter the body and travel to the guts, where it reproduces.



Researchers interrogate the worm surface and its sheath in unprecedented detail using Atomic Force Microscopy and Time-of-Flight Secondary Ion Mass Spectrometry. Credit: The University of Nottingham

Original parasite

The worms studied in this research originate from a parasite isolate brought back in 2001 by Professor David Pritchard's team from Papua New Guinea, where it was shown how effective this worm is in its mission to get into, then stay in, the body.

The findings showed that at body temperature (37 °C) the worm is at its most active and is able to escape from its sheath, which has a 'sticky' sugar-like-coating, when compared to the migratory worm's surface, which is much more slippery.

Blue-sky thinking led to latest results

Professor Pritchard said: "The present study originated from some blue-sky thinking from the team, who wanted to find out more about the initial infection stage. Much research exists on the adult stage of this parasitic worm, which is found in the guts, but comparatively little work has been done to follow the worm at the start of its journey into the body. With a detailed understanding of its fingerprint at this point, we can think of treatments to stop the parasite in its tracks before it gets to the lungs and gut, where it causes damage to the body."

The research team was able to control the exsheathment process of the worm and examine the physical surface and chemical structure using the complementary analytical techniques of AFM and ToF-SIMS, respectively.

AFM uses a nanometre sized tip that bounces along surfaces to provide a detailed map of height and topographical forces, whereas ToF-SIMS bombards surfaces with ionic atoms to release fragments of secondary molecules. The fragments are analysed using a mass spectrometer to determine their chemical identities.

Dr Chauhan added: "Directly observing the physical and chemical properties of this globally important pathogen in this amount of detail is extremely significant and paves the way for an in-depth biological study to develop early interception methods, such as vaccines, not only for Necator americanus but for other infective organisms."

More information: *PLOS Neglected Tropical Diseases* (2017). journals.plos.org/plosntds/art … journal.pntd.0005971

Provided by University of Nottingham

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