Deadly flatworm's skin rejuvenation may explain its long-term survival in humans

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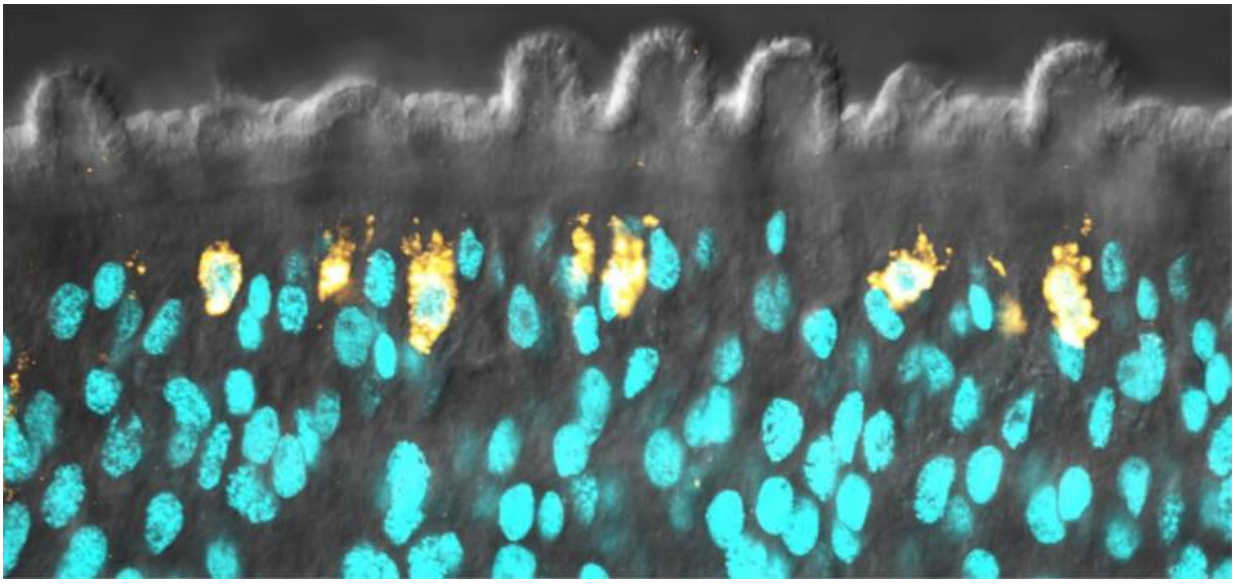

This is the tegument (skin) of a schistosome. Underneath the tegument are newly born cells (highlighted in orange) that will contribute to this tissue. Nuclei are show in cyan. Credit: James Collins and Phillip Newmark

A parasitic flatworm that infects hundreds of millions of people in the developing world is able to survive in the bloodstream for decades by constantly renewing its skin - a mechanism that could inform potential new treatments against infection.

Much like its free-living relatives, the flatworm Schistosoma mansoni

has a population of stem cells known as neoblasts that are capable of self-renewal, but the function of these cells was previously unknown.

Now, in a study to be published in the journal *eLife*, researchers have found that the neoblasts are destined to become cells that generate and regenerate the worm's outer layer of skin, a unique tissue called the tegument.

"The tegument serves as a barrier between *S. mansoni* and the bloodstream of its host, which would otherwise be an inhospitable environment for the parasite," says first author James Collins, Assistant Professor of Pharmacology at the UT Southwestern Medical Center.

"This tissue has long been considered an evolutionary innovation for parasitic flatworms to evade their host's immune defenses. Our current findings suggest that stem cells are playing a key role in perpetually renewing it, and we believe this is important for the parasite's ability to survive for decades inside their human host."

Schistosomes cause the disease schistosomiasis, the symptoms of which result from the worms' eggs becoming lodged in host tissues, such as the liver and bladder, evoking the immune system's response. People become infected with the parasites when they are exposed to larvae carried by freshwater snails in the water where they bathe, swim, fish, wash clothes or water their livestock.

Schistosomiasis is among the world's deadliest neglected tropical diseases, killing an estimated 280,000 people annually, around 90% of them in Africa. The chronic symptoms of infection deprive millions more of the chance to live healthy and productive lives, effectively condemning them to a life of poverty.

One of the first signs of infection is an itchy rash where larvae penetrate

the skin, followed by blood in the urine or faeces. Twenty million schistosomiasis sufferers develop painful, severe and sometimes disfiguring disabilities due to complications, including damage to the kidneys or liver and bladder cancer. Larvae can migrate to the heart and enter the lungs. Children can develop anaemia, malnutrition, and learning disabilities.

To discover the skin-reviving function of schistosome neoblasts, the researchers compared the short and long-term consequences of reducing the number of neoblasts in the parasites.

"Our experiments showed that the cells from which the tegument originates are short-lived and rapidly renewed, relying on a pool of stem cells for their continuous renewal," explains senior author Phillip Newmark, Howard Hughes Medical Institute Investigator and Professor of Cell and Developmental Biology at the University of Illinois at Urbana-Champaign.

"Within a week after reducing these stem cells with irradiation, nearly all the cells destined to contribute to the tegument had been depleted."

Neglected tropical diseases are among the most common afflictions of humankind and are so-called because they persist exclusively in the poorest communities. They thrive in places with unsafe water, poor sanitation, and limited access to basic healthcare.

The researchers believe it is now essential to determine whether disrupting the stem cells of schistosomes, and their ability to generate new tegumental cells, will have any effect on the parasites inside their human host. This could provide insights for potential new ways to break down the barrier with the immune system, allowing it to kill the worms.

More information: James J Collins et al. Stem cell progeny contribute

to the schistosome host-parasite interface, *eLife* (2016). DOI: 10.7554/eLife.12473