# 'Infiltrin' protein discovery could help stop spread of deadly parasitic worm

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The discovery of a new 'infiltrin' protein on a parasitic egg that is responsible for spreading deadly infections amongst millions of people could lead to better prevention and treatment.

Schistosoma haematobium is a parasitic worm that lives in the blood vessels around the human bladder and causes genitourinal schistosomiasis. Found in Middle East, Africa and in Corsica (France), Schistosoma haematobium causes a range of devastating diseases ranging from haematuria (presence of blood in urine) to female genital schistosomiasis (FGS) and bladder cancer.

## Cause and spread of disease

Disease is caused by the eggs entrapped in the bladder and surrounding tissues, which cause a chronic inflammatory response. Infection is spread by the parasite's egg stage, which is passed through urine and when encountering fresh water, infects the intermediate host, a water snail. The parasite reproduces in the snails, shedding a larval stage called cercariae, which can infect humans in contact with soiled water. This puts the egg stage of this parasite at the centre of the cause and spread of disease.

The research published in *Infection and Immunity* was led by the School of Pharmacy at the University of Nottingham in collaboration with teams from George Washington University, the Biomedical Research

Institute in Rockville, Maryland and the School of Medicine of Stanford University.

The team has discovered a protein called H-IPSE, which occurs in several variants, but is only produced by the egg stage of the parasite. H-IPSE has unusual properties that allow it to enter host cells and pass through barriers and membranes causing weakening of tissues and promoting spread of disease. The discovery sheds light on the interaction of eggs with host tissues, ultimately resulting in translocation across the bladder wall and parasite transmission.

Such is the invasive nature of the protein it is being labelled an 'infiltrin', as it can enter host cells, crossing several barriers by passing at least two membranes, the cellular membrane and the nuclear membrane, finally entering the cell nuclei, where we the authors believe it will act as a transcription factor, causing weakening of the tissues and promoting passage of eggs into the bladder lumen. Thus, infiltrins may represent a previously unknown regulatory principle governing the host-parasite relationship at the molecular level.

## Vaccination and treatment

Dr Franco H. Falcone is Associate Professor in Allergy and Infectious Diseases at the University of Nottingham and led the research, he says: "The discovery of this protein is an important step in understanding the previously unknown process that allows the eggs to pass through the touch bladder wall into the bladder lumen. This discovery will now open the door for the targeted development of vaccinations and treatments."

This work was made possible by an R56 grant from the NIH, and will be continued through a brand new 5-year grant from the NIH awarded to the same collaborative transatlantic research team.

**More information:** Luke F. Pennington et al. H-IPSE is a pathogen-secreted host nucleus infiltrating protein (infiltrin) expressed exclusively by the Schistosoma haematobium egg stage, *Infection and Immunity* (2017). DOI: 10.1128/IAI.00301-17