New research points to novel approach to tackling Ascaris roundworm

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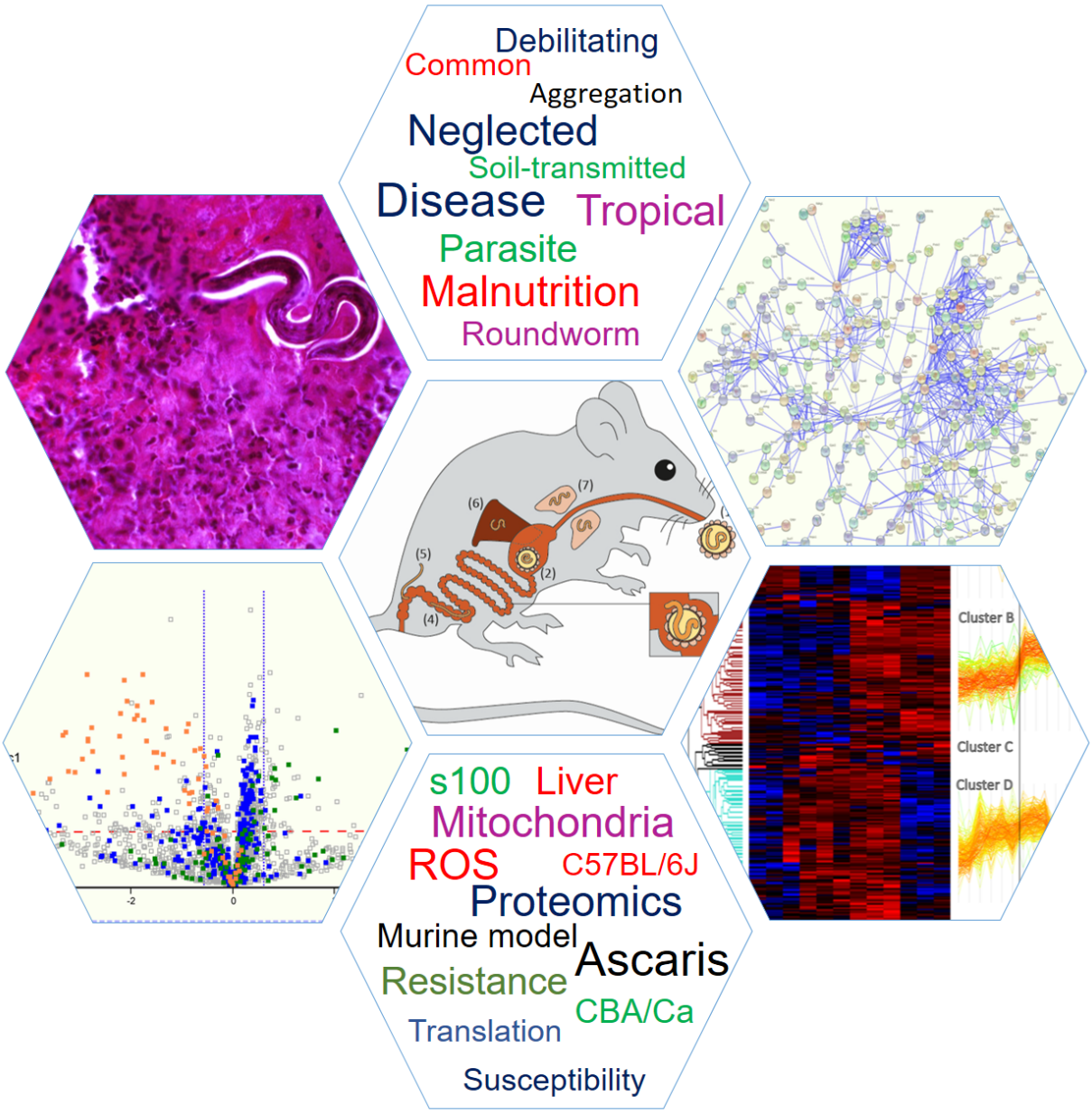

Infographic/cartoon showing the various research strands and components involved in the work. Credit: Dr Christina Dold, Professor Celia Holland and Dr Jim Carolan.

Scientists working out of Trinity College Dublin, Maynooth University, and Queen Mary University of London have unearthed a potential new preventative option to combat *Ascaris* roundworm infection. *Ascaris lumbricoides* is an intestinal parasite that results in severe health consequences, including growth retardation and impaired cognitive development. The infection, which affects an estimated one billion people worldwide, is particularly common in Third World countries and is estimated to be responsible for 60,000 deaths per annum.

Susceptibility to *Ascaris* infection differs between individuals, and heavily infected individuals have more severe symptoms and higher morbidity. Building on previous studies, which showed a difference in susceptibility to *Ascaris* between two different strains of mice, the researchers identified a clear distinction between the two strains and published their findings in the internationally regarded peer reviewed journal *PLoS Neglected Tropical Diseases*. It is thought that these new insights could lead to the development of better ways to prevent and treat Ascaris infection.

The lifecycle of the *Ascaris* roundworm in humans sees the infection progress from the stomach, following ingestion of viable eggs which hatch as larvae, to the liver before moving on to the lungs and then returning to the stomach. In mice, the roundworms do not progress beyond the lungs. Professor of Zoology at Trinity College, Celia Holland, has spent over a decade developing a mouse model to study Ascaris infection and has previously demonstrated that susceptible mice

have more than ten-fold higher larval numbers in the lungs than resistant ones. This difference in susceptibility between the two strains, however, is first visible in the liver of infected mice.

Following infection with identical numbers of Ascaris eggs, mice from the resistant strain show an earlier inflammatory immune response coupled with more rapid tissue repair in the liver compared with susceptible mice. The researchers therefore set out to investigate the differences in the liver proteomes (via a broad analysis of liver proteins) of both uninfected control mice and infected mice, for each strain.

Professor Holland said: "By focusing on the liver we aimed to target the metaphorical front line in this particular host-parasite interaction."

The researchers identified and quantified thousands of proteins and found that hundreds of liver proteins differed substantially between the two strains, even without *Ascaris* infections. The resistant strain showed generally higher levels of mitochondrial proteins and proteins associated with the generation of reactive oxygen species (ROS). *Ascaris* infection increased the level of these proteins in both strains, supporting the evidence of their role in the response to the parasite.

Other proteins were seen only in infected mice; these included proteins involved in a part of the immune response. Two of these proteins were absent from both strains before infection, but were among the highest expressed proteins in both strains following infection. Proteins involved in translation were of lower abundance in all infected mice livers, which suggests either a broad response in the host to the presence of Ascaris or a specific targeting of the protein synthesis machinery by the parasite itself.

Lead author Gwendoline Deslyper said: "Given our findings and the central role of the liver in the *Ascaris* migratory pathway, we suggest a

potentially novel research direction to develop alternative preventative control strategies for Ascaris. It seems that the key determinant in resistance to *Ascaris* in mice may lie in highly oxidative conditions that presumably restricts and arrests successful larval migration within the hepatic environment - at least of the resistant strain. By manipulating the hepatic ROS levels in the susceptible mouse strain we hope to determine the importance of the mitochondria and intrinsic ROS in conferring resistance to Ascaris."

The proteomic study, which mapped the proteins of the affected organs, was led by Dr Jim Carolan, Maynooth University Department of Biology in conjunction with Dr Joe Colgan of Queen Mary University London. Discussing the findings, Dr Carolan said: "There is still a long way to go and much research to be done, but these findings point to new options in our efforts to control a disease that affects around one eighth of our planet's population."

Provided by Trinity College Dublin