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Gut cells are gatekeepers of infectious brain diseases, study finds

Fresh insights into infectious brain conditions help to explain why some people – and animals – are more at risk than others.

The study reveals how prion diseases – which include variant Creutzfeldt-Jakob disease (vCJD) in people and bovine spongiform encephalopathy (BSE) in cows – can infect the gut if contaminated meat has been eaten.

Specialised cells called M cells are key to whether or not the infection can take hold, the research in mice has found.

Researchers say factors that affect the abundance of M cells in the lining of the gut – such as inflammation, infection or ageing – could influence a person's risk of contracting prion diseases after consuming infected food.

M cells are found in the lining of the gut and are part of the body's defences against infections. These specialised cells play a key role in transporting material across the lining of the gut where other cells of the immune system are waiting to respond.

The team – led by the University of Edinburgh's Roslin Institute – found that prions use M cells to enable them to infect the gut. Mice that do not have M cells are completely resistant to prion infections.

Those that have a greater number of M cells in the lining of their gut, however, were around ten times more susceptible.

The findings may part explain why most human cases have affected young people, who tend to have higher numbers of M cells in their guts than older people, the researchers say.

The research also suggests that the presence of other infections in the gut such as *Salmonella* may increase the chances of prions causing infection.

Prion diseases - also known as transmissible spongiform encephalopathies (TSEs) – are infectious brain conditions that affect people and animals. They are caused by abnormally shaped proteins which can be passed on by eating contaminated meat.

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Previous research revealed that the proteins must first build up in specialised structures in the lining of the small intestine called Peyer's patches before they are able to spread to the brain.

The diseases include vCJD in people, BSE in cows, scrapie in sheep and chronic wasting disease in deer. They cause extensive nerve and severe neurological symptoms including memory impairment, personality changes and difficulties with movement.

The research is published in the journal *PLOS Pathogens*. The Roslin Institute receives strategic funding from the Biotechnology and Biological Sciences Research Council.

Professor Neil Mabbott, who led the research at the University of Edinburgh's Roslin Institute, said: "Our next step is to understand how the prions exploit these cells to infect the gut. If we can design treatments to block the uptake of prions by M cells, this may provide a novel method to prevent prion infections in humans and animals."

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