What makes an infection dangerous?

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Amebiasis is a disease caused by an infection by a microorganism called *Entamoeba histolytica*. Thriving in warm areas such as the Philippines, *E. histolytica* can infect people who eat food or drink water that has been handled poorly and contaminated with the microorganism. Diarrhea and abdominal pains are symptoms of amebiasis, and the disease can progress to causing abscesses in the liver. If untreated, the infection can even result in death. According to estimates, the disease kills up to 70,000 people annually.

Research into amebiasis is extremely important to the Philippines. This is not only because the pathogen favors tropical climates but also because millions of poor Filipinos—who are more likely to come into contact with infected food or water and are less likely to receive proper medical care—are at risk of suffering and dying from the disease.

One peculiar thing about amebiasis infections is that only around 10% of people infected with *E. histolytica* exhibit amebiasis infections. There are different strains of this species, with some being harmful and others benign. The reasons for this are unclear, but research into them can give us insight into how the disease behaves and how to combat its spread. Understanding what exactly can make this disease so dangerous can help us treat it more effectively.

A team of Japanese researchers—as well as a Taiwanese researcher and a scientist from the University of the Philippines Mindanao—is trying to discover why some strains of *E. histolytica* are virulent, or harmful, and why some are not. The team's work is published in PLoS Pathogens.

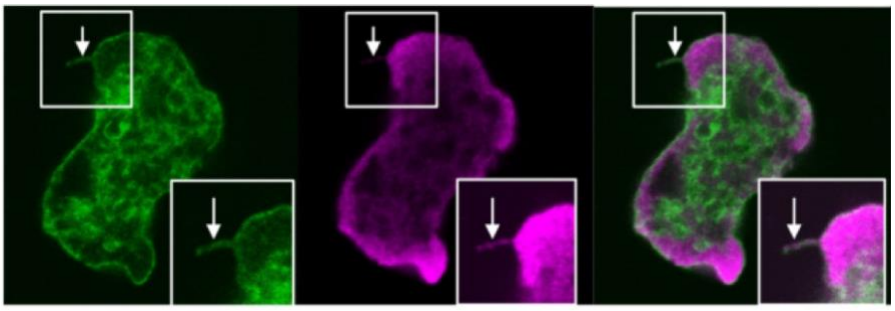
The team examined two strains of *E. histolytica*: KU27, which is less virulent (usually does not cause symptoms) and KU50, which is highly virulent. Specifically, the researchers sequenced the genomes of each, looking for significant differences. Their genetic analysis found that four genes were different between the two strains, but one gene was found to be active. This gene encoded a protein from the AIG1 family.

The researchers also examined stool samples of amebiasis patients. The gene was much more likely to be found in the stool of patients who did show symptoms than patients who did not. Given this evidence, the researchers hypothesized that this AIG1 protein played an important role in the virulence of *E. histolytica*.

The team then tried to determine methodically the function of this protein and how it might make the KU50 strain so dangerous.

Using genetic engineering techniques, the team created a strain of *E. histolytica* that produced a much greater amount of the AIG1 protein than usual; the team also observed how the protein interacted with human blood cells. The researchers observed that, with this increased amount of the AIG1 protein, the modified microorganisms were able to cling to red blood cells much more tightly than unmodified specimens.

The researchers then wanted to find out what exactly this AIG1 protein changed in *E. histolytica* to make this protein more able to attach to red blood cells. Using the same modified strain as the previous test, they used microscopes to look for any structural changes caused by the AIG1 protein and found that the modified microorganisms produced more filopodia, or protrusions that allow microorganisms to anchor themselves on surfaces.



Using microscopes and fluorescent imaging, the researchers were able to look at the structures created by the AIG1 protein

This is indicative of a link between the AIG1 protein, the filopodia it creates, and the ability of *E. histolytica* to cling to red blood cells and become more virulent. To come up with further proof, the researchers also modified specimens of the KU27 gene (the nonvirulent gene) to make them overexpress the AIG1 protein, similar to the other modified organisms. However, this change did not make the modified KU27 individuals more capable of clinging to red blood cells. This means that, while the AIG1 protein and its corresponding filopodia play a role in the virulent strain's capability to cause symptoms, there is still more to the puzzle.

This study yielded some very significant results. The identification of a genetic difference between a virulent and nonvirulent strain of *E. histolytica*, as well as how that difference manifests physically, and how that change affects the behavior of the microorganism is a big step toward identifying the probably many factors that can make this microorganism dangerous.

This research also opens up the possibility for further research into the matter. Now that there is a starting point, other studies can be done to study more closely the genetic difference, or to look more closely at the filopodia that the gene produces. A specialized study can also be done to determine really if the genetic difference is the cause of the virulence of the KU50 strain, as well as to look into other factors that could contribute to the difference.

REFERENCE

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