

Scientists discover how a bacterial pathogen breaks down barriers to enter and infect cells

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Scientists from the Schepens Eye Research Institute, a subsidiary of Mass. Eye and Ear and affiliate of Harvard Medical School, have found for the first time that a bacterial pathogen can literally mow down protective molecules, known as mucins, on mucus membranes to enter and infect a part of the body. Their landmark study, published in the March 7, 2012 *PLoS ONE*, describes how they discovered that an "epidemic" strain of the bacterium *Streptococcus pneumoniae*, which causes conjunctivitis, secretes an enzyme to damage mucins and breach the mucosal membrane to infect and inflame the eye.

"We are excited about this finding," says Ilene Gipson, Ph.D., the study's principal investigator and a senior scientist at the Schepens. "Our discovery may ultimately lead to new ways of diagnosing, treating and preventing bacterial infections originating not only in the eye but in other parts of the body as well."

More than 80 percent of infections are contracted through the body's mucus membranes, which are the wet epithelial surfaces of the eye and the urogenital, respiratory, and gastrointestinal tracts of the body. The outer surface of all [mucus membranes](#) are protected by two types of mucin molecules – one that is secreted and is in constant motion to sweep away trapped foreign material from the membrane surface, and the other that remains rooted in the membrane surface. The latter type of mucin molecules constitutes a physical shield that keeps potentially harmful substances from penetrating the membrane.

These membranes often encounter two types of bacterial pathogens. Some are "opportunistic." They sit on the [membrane surface](#) and only enter the tissue when there is trauma or injury that leaves a gap in the mucus membrane layer. An example of an opportunistic [bacterium](#) is *Staphylococcus aureus* that is often the cause of surgery related infections.

The other type of pathogen is non-opportunistic or "epidemic" and causes more invasive and aggressive infections such as occur in epidemic conjunctivitis caused by the strain of *Streptococcus pneumoniae* used in this study. These disease-causing bacteria enter the body even when there is no apparent injury to the protective layer. And, they can cause rapidly expanding and contagious diseases.

Until the current *PLoS ONE* study, little has been known about how epidemic infection causing bacteria are able to cross through the mucin barrier. Experts in the study of mucins and determined to find a piece of this puzzle, the Schepens scientists hypothesized that "epidemic" bacteria must somehow remove the mucins themselves.

To test their hypothesis, the team grew "epidemic" [conjunctivitis](#) bacteria (a strain of [Streptococcus pneumoniae](#)) in a culture. This bacteria causes an inflammation of the conjunctiva, the mucous membrane covering the white of the eyes and the inner side of the eyelids.

They then applied the fluid that the bacteria were cultured in to cell lines that mimicked the eye's surface, including presence of intact mucins, and found that the membrane-anchored mucins were cut off and released from the surface of the cells. Removal of the mucins allowed the bacteria to enter the cells.

Using mass spectrometry, the researchers were then able to identify the

enzyme, ZmpC, as the culprit. They confirmed their findings by knocking out the gene in the bacteria that produced this enzyme and demonstrated that the bacterium could no longer remove the mucins from the membrane.

According to Dr. Gipson, "This discovery is a major breakthrough in this long unsolved puzzle about how "epidemic" bacteria enter the body and has given us a new target for drugs that could even be used preventatively."

The next step in the research, according to Dr. Gipson, will be to determine if the method of enzymatically removing the surface mucins to gain entrance is used by other disease causing [bacteria](#).

More information: To view the entire study, titled "A Metalloproteinase Secreted by *Streptococcus pneumoniae* Removes Membrane Mucin MUC16 from the Epithelial Glycocalyx Barrier, go to [dx.plos.org/10.1371/journal.pone.0032418](https://doi.org/10.1371/journal.pone.0032418)

Provided by Schepens Eye Research Institute

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