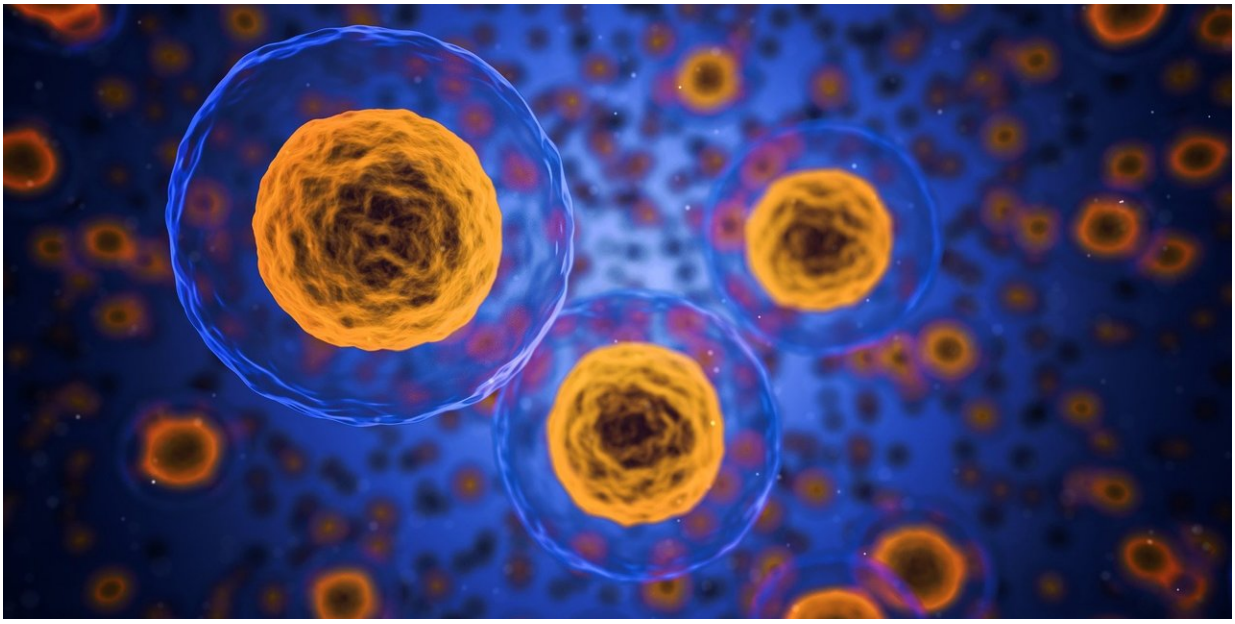
Mucus and mucins may become the medicine of the future

July 7 2021



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Many people instinctively associate mucus with something disgusting, but in fact, it has incredibly many valuable functions for our health. It keeps track of our important intestinal flora and feeds the bacteria. It covers all internal surfaces of our body, and, as a barrier to the outside world, it helps us protect ourselves from infectious diseases.

This is because mucus acts as a filter that keeps the bacteria in or out,

and the bacteria feed on the sugars in the mucus between meals. So, if we can produce the mucus that is already present in the body with the right sugars, it might be used in brand new medical treatments.

Now, researchers from the DNRF Centre of Excellence, Copenhagen Center for Glycomics, have discovered how to artificially produce the healthy mucus.

"We have developed a method for producing the important information found in human mucus, also called mucins, with their important sugars. Now, we show that it is possible to artificially produce it in the same way as we produce other therapeutic biologics today, such as antibodies and other biological medicine," says Professor Henrik Clausen, lead author of the study and Director of the Copenhagen Center for Glycomics.

The mucus, or mucins, consist mostly of sugars. In the study, the researchers show that it is actually special patterns of sugars on the mucins that the bacteria recognize.

"It is the body's way of selecting the good bacteria and deselecting those that cause diseases. And it is precisely the sugars in the mucus that we are now able to design as needed," says first author of the study, Ph.D. student Rebecca Nason.

The researchers are particularly interested in the mucus in the gastrointestinal tract. Like a giant fishing net, the mucus keeps track of all the bacteria, our microbiome, down there. So, if one could imitate the ability of bacteria to attach to the intestinal mucus, one could design oral medications that stick to the mucus, making them more effective.

"We have found a small molecule from bacteria—which we call X409—that binds to the intestine, and that is precisely one of the many possibilities we are now working on," says Nason.

It can be difficult to get medicine to be effective when it has to be ingested and absorbed into our intestinal system. So, when you design your drug as a pill that the patient swallows, it is not certain that it will be fully efficient.

There are many obstacles on the way down through the digestive system, and the medication needs time in the gastrointestinal tract to be dissolved and distributed in the body," explains Nason.

We swallow more than a liter of mucus in the form of saliva per day and more from the stomach, which together with the ever-changing fishing net of mucus in the intestine feed our intestinal microbiome. The microbiome of the intestine is absolutely crucial to our health and of great importance in relation to many diseases.

"An incredible number of diseases have a connection to the intestinal flora, but we still know very little about how we can control the intestinal flora in the treatment of diseases. This is where synthetic mucins could open up new treatment options," says Associate Professor Yoshiki Narimatsu, another of the lead authors of the study.

"Ultimately, one can imagine using mucins as a pre-biotic material, that is, as molecules that help the good bacteria in the body," says Narimatsu.

With artificial mucus, it will also be possible to alleviate infections in the body. Mucus in saliva flushes out bacteria and cleans the oral cavity, and mucus constantly runs down over our eyes and keeps them clean.

"We imagine that instead of using antibiotics, you might produce for example eye drops with the mucin that normally removes the bacteria in the treatment of eye infections. In concrete terms, this means that mucin can dissolve the so-called biofilm of bacteria, which is often pathogenic," says Narimatsu.

Biofilm is a film of bacteria on the surface of a material and is, among other things, what you can feel on your teeth if it has been a long time since you last brushed them.

It is not only bacteria that recognize mucins.

"We also show that mucins are very important for the way in which the common flu virus infects our mucous membranes in competition with mucins which inhibit the infection and flush out the virus," says Narimatsu.

Unlike the covid-19 virus, influenza virus binds to a sugar, which is found on all mucins, and a sugar has already been developed for treatment of the flu.

"We hope mucins may work even better," says Narimatsu.

More information: Rebecca Nason et al, Display of the human mucinome with defined O-glycans by gene engineered cells, *Nature Communications* (2021). DOI: 10.1038/s41467-021-24366-4

Provided by University of Copenhagen