Looking to saliva to gain insight on evolution

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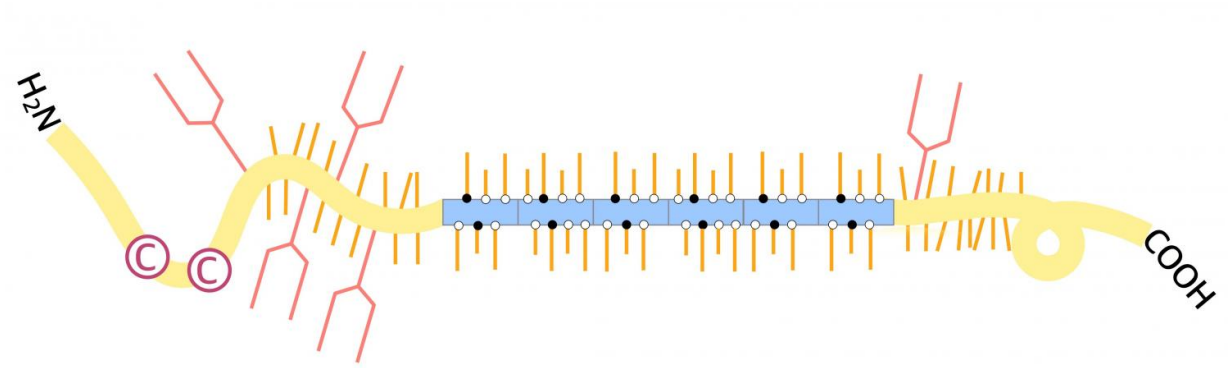

An illustration shows the MUC7 protein in humans. This bottlebrush-shaped protein, found in saliva, contains repeating units (shown in blue). Repeats of this kind may have conferred an evolutionary advantage to humans and other primates, possibly by enhancing traits of saliva such as its lubricity and its ability to bind to microbes (a capability that may help curb disease). Credit: Duo "Erica" Xu

There's no need to reinvent the genetic wheel.

That's one lesson of a new study that looks to the saliva of humans, gorillas, orangutans, macaques and African green monkeys for insights into evolution.

The research, published on Aug. 25 in *Scientific Reports*, examined a gene called MUC7 that tells the body how to create a salivary protein of

the same name. The protein, which is long and thin, forms the backbone of a bottlebrush-shaped molecule that helps to give spit its slimy, sticky consistency.

The study found that within the MUC7 gene, instructions for building important components of the bottlebrush were repeated multiple times in each of the five primate species studied. Gorillas had the fewest copies of this information (4-5), while African green monkeys had the most (11-12). Humans fell somewhere in between, with 5-6.

Through an in-depth analysis of MUC7's evolutionary history, the researchers concluded that having numerous copies of the repeated instructions likely conferred an evolutionary advantage to primates—possibly by enhancing important traits of saliva such as its lubricity and, perhaps even more importantly, its ability to bind to microbes (a capability that may help curb disease).

The takeaway lesson?

Evolution can favor the expansion of tried-and-true genetic tools, in addition to the development of totally new ones, says University at Buffalo biologist Omer Gokcumen, who led the study together with Stefan Ruhl, a salivary researcher in UB's oral biology department.

"You don't always have to invent a new tool," says Gokcumen, PhD, an assistant professor of biological sciences at UB. "Sometimes, you just need to amplify the tool you already have."

In the case of MUC7, repeating key genetic instructions over and over resulted in longer, denser proteins, which are likely better at performing two protective tasks: lubricating the mouth—which facilitates talking, chewing and other vital functions—and latching onto microbes, an action that's thought to expedite the removal of disease-causing pathogens from

the oral cavity.

The evolution of MUC7

The genetic instructions that are repeated within the MUC7 gene are what scientists call tandem repeats—short strings of DNA found multiple times inside the gene.

The new study shows that as primates evolved, the DNA in their MUC7 tandem repeats sometimes changed in places (a normal part of evolution).

But the genetic material stayed the same in one key way: Pieces of DNA that told the body how to make the amino acids serine and threonine, two vital building blocks of the bottlebrush backbone, persisted in all primates. The directions for creating serine and threonine were found in the same location in tandem repeats across humans, gorillas, orangutans, macaques and African green monkeys.

The likelihood of this happening at random is small, which hints that those genetic sequences provided an evolutionary advantage to their hosts, Gokcumen says.

This hypothesis is bolstered by the crucial role that serine and threonine play in the MUC7 protein's function. Within MUC7, the two compounds act as anchoring points for sugar molecules, which protrude from the protein backbone like the bristles of a brush. It's these bristles that carry out the important task of binding to microbes.

The research elucidates how tandem repeats may serve as modular building blocks for rapid evolutionary adaptation.

"Tandem repeats may be a major way that many different genes in the

genome quickly adapt to their environments," says Duo "Erica" Xu, the study's first author and a PhD student in biological sciences in the UB College of Arts and Sciences.

The research builds on the groundbreaking work of scientists in UB's oral biology department, who discovered the MUC7 protein more than 30 years ago and sequenced the MUC7 gene, says Ruhl, a professor in that same department, which is part of the UB School of Dental Medicine.

"Saliva is an important body fluid which has been for a long time underappreciated by mainstream biomedical science," Ruhl says. "It is amazing to see the research on MUC7 take off again with modern technology. In the next few years, we expect to learn a lot more about the importance of saliva for human health through such cross-disciplinary studies with evolutionary geneticists."

The research team also included scientists from the Foundation of Research and Technology in Greece and the University of Minnesota Twin Cities.

More information: Duo Xu et al, Recent evolution of the salivary mucin MUC7, *Scientific Reports* (2016). DOI: 10.1038/srep31791

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