

Scientists reveal 90 percent of skin-based viruses represent viral 'dark matter'

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Scientists in recent years have made great progress in characterizing the bacterial population that normally lives on human skin and contributes to health and disease. Now researchers from the Perelman School of Medicine at the University of Pennsylvania have used state-of-the-art techniques to survey the skin's virus population, or "virome." The study, published in the online journal *mBio* last month, reveals that most DNA viruses on healthy human skin are viral "dark matter" that have never been described before. The research also includes the development of a set of virome analysis tools that are now available to researchers for further investigations.

Researchers and the public are increasingly aware that microbes living on and inside us—our "microbiomes"—can be crucial in maintaining good health, or in causing disease. Skin-resident bacteria are no exception. Ideally they help ward off harmful infections, and maintain proper skin immunity and wound-healing, but under certain circumstances they can do the opposite.

"There has been a real need for a better understanding of these viruses, given their potential effects on our skin cells as well as on our resident bacteria," said senior author Elizabeth A. Grice, PhD, an assistant professor of Dermatology at Penn Medicine. "Until now, relatively little work has been done in this area, in part because of the technical challenges involved. For example, a skin swab taken for analysis will contain mostly human and bacterial DNA, and only a tiny amount of viral [genetic material](#)—the proverbial needles in the haystack."

Previous mapping attempts used databases of known [viral genes](#) to recognize some of this viral genetic material amid all of the bacteria and human DNA. But such an approach tends to overlook the many viruses not already catalogued in databases. Using optimized techniques for isolating virus-like particles (VLPs) from skin swabs, and for analyzing very small amounts of genetic material, the research team was able to focus their sequencing and analysis on viral DNA without entirely depending on databases.

Their analysis of samples from 16 healthy individuals revealed some results that were expected. The most abundant skin-cell infecting virus was human papilloma virus, which causes common warts and has been linked to skin cancers. However, most of the detected DNA from the VLPs did not match viral genes in existing databases. "More than 90 percent was what we call viral dark matter—it had features of viral genetic material but no taxonomic classification," Grice said. That came as a surprise, although of course it highlighted the importance of mapping this unexplored territory.

The findings also clearly linked the skin virome to the skin microbiome: Most of the detected viral DNA appeared to belong to phage viruses, which infect and often take up long-term residence within bacteria. And when Grice and colleagues sequenced skin bacterial DNA from the same 16 subjects, they found that it often contained tell-tale marks—called CRISPR spacers—of prior invasion by the same phage viruses.

Although the results suggest that most of our normal skin-resident viruses are in fact resident in our skin bacteria, such viruses can still affect our health via their influence on the microbiome. The Penn researchers found evidence in the phage DNA of genes that could make host bacteria more resistant to antibiotics, for example, or more likely to cause a harmful infection.

The results also showed that the skin virome varies considerably depending on the body site. Grice's team took swabs from the palm, the forehead, the armpit, the navel, and other sites, and found, for example, that the virome was most diverse in the crook of the arm, a site that is intermittently exposed and occluded.

The research establishes a baseline for future investigations of the normal, healthy skin virome and its alteration during disease. In addition, it gives other researchers a ready-made toolkit for such investigations—Grice and her colleagues even made available, with the paper's supplemental information, the algorithms they devised for the DNA sequence analysis. "It's all freely available so that people can do their own studies, or even reproduce our results," she said.

Grice and her team are now using those methods to study the genomic variability of skin viruses, as well as changes in the [skin](#) virome in response to common factors such as ultraviolet radiation exposure and antibiotic use.

Provided by University of Pennsylvania School of Medicine

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