How a natural antibiotic found in sweat affects microorganisms

The skin creates a barrier between the body and its environment. Natural antibiotics that can kill potential pathogens such as bacteria or fungi, represent an additional level of protection by the immune system. Dermcidin, one such antibiotic produced in human sweat glands, is active against a number of microorganisms on the skin. A team of scientists from the University Hospital Tübingen and the Max Planck Institute for Developmental Biology were part of a collaborative effort that has uncovered evidence for a novel mechanism of action of dermcidin in the harsh environment of sweat: dermcidin’s active component enters the bacterial outer membrane and produces tiny holes resulting in slow but certain death of the bacteria.

Many antibiotics on our skin kill microorganisms by creating pores in the bacterial envelope. They are electrostatically attracted to the overall negatively charged outer membrane of bacteria by their own positive charge and, after entering the membrane, build channels through the membrane. The subsequent destruction of the bacterial membrane potential leads to quick death of the microorganisms. Two previously published findings suggested that dermcidin acts in a fundamentally different way: First, DCD-1L, the active component produced by cleavage of dermcidin on the skin, is negatively charged. Second, bacteria affected by DCD-1L die slowly, with enough time to activate emergency rescue programs.

A team of scientists brought together by the Collaborative Research Center 766 “The Bacterial Cell Envelope” based at the University of Tübingen and funded by the German Research Organization, set out to take a new look at the old data. The team consisted of Maren Paulmann, Ines Wanke and Birgit Schittek from the Department of Dermatology of the University Hospital Tübingen, a group of scientists headed by Dirk Linke and Michael Habeck from the Max Planck Institute for Developmental Biology and colleagues from the Research Center Borstel and the Karlsruhe Institute of Technology.

The DCD-1L complex opens tiny channels through the bacterial outer membrane

While previous experiments based on electron microscopy and special labeling did not provide any evidence for pore formation by DCD-1L, novel highly sensitive measurements of electric currents through synthetic membranes treated with the antibiotic showed very slow leakage of charged particles. These data suggest that holes were indeed formed, but that they were very small. Based on the new results, the scientists have developed a new model of action for dermcidin: The positively charged terminus of overall negatively charged DCD-1L molecule binds to the bacterial membrane. Interactions with the bacterial membrane in the acidic and salty ambience of sweat cause the disordered DCD-1L molecules to adopt a helical structure and several molecules join to form a complex. The DCD-1L complex, stabilized by positively charged zinc ions present in high concentrations in sweat, opens tiny channels through the bacterial outer membrane. Individual charged particles pass through the narrow opening and, in time, charge gradients are equalized. The potential difference between the interior of the bacterial cell and its environment breaks down, destroying the basis for vital transport and metabolic processes. Finally, the bacterial cell dies.

Natural antibiotics produced by the human body, such as dermcidin-derived DCD-1L, may also play a role in the development of atopic dermatitis. Patients suffering from this skin disease show an increased susceptibility to skin infections. The observation that the sweat of these patients contains reduced quantities of DCD-1L and other dermcidin derivatives, suggests that in healthy people dermcidin significantly protects human skin against infections.

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Further Information:
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