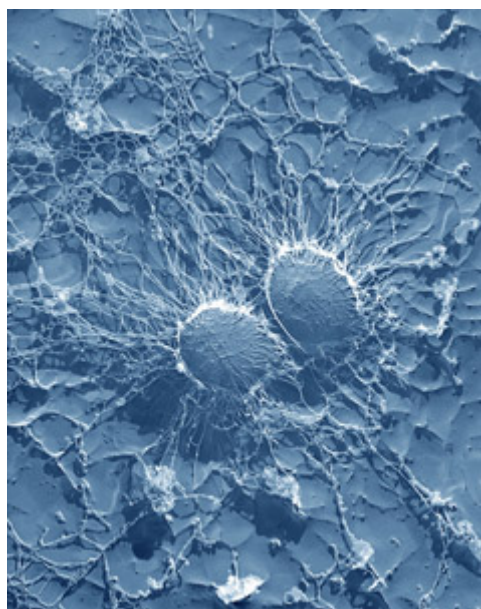


Hormone Plays Surprise Role in Fighting Skin Infections

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Boosts immune response when vitamin D levels are low

Antimicrobial peptides (AMPs) are molecules produced in the skin to fend off infection-causing microbes. Vitamin D has been credited with a role in their production and in the body's overall immune response, but scientists at the University of California, San Diego School of Medicine say a hormone previously associated only with maintaining calcium homeostasis and bone health is also critical, boosting AMP expression when dietary vitamin D levels are inadequate.



Staphylococcus aureus, magnified 50 thousand times.

The finding, published in the May 23, 2012 online issue of *Science Translational Medicine*, more fully explains how the immune system functions in different situations and presents a new avenue for treating infections, perhaps as an alternative to current antibiotic therapies.

The immunological benefits of vitamin D are controversial. In cultured cell studies, the fat-soluble vitamin provides strong immunological benefits, but in repeated studies with humans and animal models, results have been inconsistent: People with low levels of dietary vitamin D *do not* suffer more infections. For reasons unknown, their immune response generally remains strong, undermining the touted immunological strength of vitamin D.

Working with a mouse model and cultured human cells, Gallo and colleagues discovered why: When levels of dietary vitamin D are low (it's naturally present in very few foods), production of parathyroid hormone (PTH), which normally helps modulate calcium levels in blood, is ramped up. More PTH or a related peptide called PTHrP spurs increased expression of AMPs, such as cathelicidin, which kill a broad spectrum of harmful bacteria, fungi and viruses.

“No one suspected a role for PTH or the PTH-related peptide in immunity,” said Richard L. Gallo, MD, PhD, professor of medicine and chief of UCSD’s Division of Dermatology and the Dermatology section of the Veterans Affairs San Diego Healthcare System. “This may help resolve some of the controversy surrounding vitamin D. It fills in the blanks.”

For example, the findings relate to the on-going debate over sun exposure. Sunlight triggers the production of vitamin D. Low levels of vitamin D have been claimed in some studies to increase the risk of cardiovascular disease and cancer, but other studies have failed to confirm this. On the other hand, high levels of solar exposure that could increase vitamin D have been shown to increase the risk of skin cancer.

“Since sunlight is a carcinogen, it’s a bad idea to get too much of it,” said Gallo. “PTH goes up when levels of vitamin D from diet and sun exposure are low. PTH may be what permits us to have low D in the diet and not kill ourselves with too much UV radiation.”

Gallo said PTH’s newly revealed immunological role provides a new connection between the body’s endocrine system (a system of glands secreting different regulatory hormones into the bloodstream) and its ability to fight invasive, health-harming pathogens.

While much more work remains to be done, including human studies, it’s possible that PTH or PTHrP might eventually become an effective antibiotic treatment without the risk of antibiotic resistance in targeted microbes. One challenge would be how to specifically limit treatment to the targeted infection. “Maybe that could be done by developing the therapy as a cream,” Gallo said.

Co-authors of the study are Beda Muehleisen, Carolos Aguilera and George Sen, Division of Dermatology, UC San Diego; Daniel D. Bikle, Department of Medicine and Dermatology, UC San Francisco; Douglas W. Burton, Veterans Administration San Diego Healthcare System; Leonard J. Deftos, Veterans Administration San Diego Healthcare System and Department of Medicine, UC San Diego.

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