

UCSD Researchers Discover Cause of Rosacea

August 7, 2007

Debra Kain

Doctors can describe the symptoms of rosacea, a common inflammatory skin disease that causes facial redness and affects nearly 14 million Americans. They can tell patients what triggers can worsen their condition: spicy foods, heat, alcohol, even embarrassment. But until now, they could not explain what caused rosacea.

A team of researchers, led by Richard L. Gallo, M.D., Ph.D., professor of medicine and chief of the Division of Dermatology at the University of California, San Diego (UCSD) School of Medicine and the Dermatology section of the Veterans Affairs San Diego Healthcare System, has determined that it is not one, but a combination of two abnormal factors, that result in rosacea.

"It's like having lots of gasoline...and a match," said Gallo, principal investigator of the study which will be published in the August 5 online edition of *Nature Medicine*. In essence, the researchers found that over-production of two interactive inflammatory proteins results in excessive levels of a third protein that causes rosacea symptoms, "a trifecta of unfortunate factors in people with rosacea," according to Gallo.

Rosacea, which has been called adult acne, usually affects people with fair skin, between the ages of 30 and 60. Unlike acne, rosacea isn't associated with a skin infection by one type of bacteria, although antibiotics are sometimes prescribed to treat its symptoms. A chronic condition, it gets worse over time and is generally cyclic, flaring up for a period of weeks to months, and then subsiding for a time. Current treatments are often not effective.

Gallo and his colleagues first observed in the laboratory that anti-microbial peptides - small proteins of the body's host defense system - caused the exact same symptoms in the skin that rosacea does, such as redness, an increase in visible blood vessels, bumps or pimples. The peptides also reacted to the same triggers.

"When we then looked at patients with the disease, every one of them had far more peptides than normal," said Gallo.

To learn why these patients have abnormal peptides, the researchers examined the source of these molecules. The precursor form of these peptides, called cathelicidin, is normally known for its function to protect the skin against infection. In other skin diseases, a deficiency of cathelicidin correlates with increased infection. In rosacea patients, researchers found the opposite was true; too much cathelicidin was present in their skin. They also observed that it was a different form than found in people without the skin disorder.

Patients with rosacea also had greatly elevated levels of enzymes called stratum corneum tryptic enzymes (SCTE). These enzymes turned the precursor into the disease-causing peptide. By injecting mice with the cathelicidin peptides found in rosacea, or adding SCTE, they increased inflammation in the mouse skin, thus proving that these abnormalities can cause the disease.

"Too much SCTE and too much cathelicidin leads to the abnormal peptides that cause the symptoms of this disease," said Gallo. "Antibiotics tend to alleviate the symptoms of rosacea in patients because some of them

work to inhibit these enzymes. Our findings may modify the therapeutic approach to treating rosacea, since bacteria aren't the right target."

Media Contact: Debra Kain, (619) 543-6163