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# Researchers track down protein responsible for chronic rhinosinusitis with polyps

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A protein known to stimulate blood vessel growth has now been found to be responsible for the cell overgrowth in the development of polyps that characterize one of the most severe forms of sinusitis, a study by Johns Hopkins researchers suggests. The finding gives scientists a new target for developing novel therapies to treat this form of the disease, which typically resists all current treatments.

Chronic sinusitis, a constant irritation and swelling of the nasal passages, is a common condition thought to affect about one out of every six people. This problem has several forms with a range of severities. One of the most severe forms produces polyps, overgrowths of unhealthy sinus tissue that can block the nose and sinus passages and make breathing through the nose difficult or impossible. This often results in pain, swelling, and an increase in infections. Though researchers aren't sure how many people have this subtype, it's estimated to affect between 15 and 30 percent of sinusitis patients.

"This type of sinusitis isn't subtle—you can spot the patients with polyps from across the room. They're breathing through their mouths, they talk with nasal voices, they're constantly sniffling, and their faces are swollen," says Jean Kim, M.D., Ph.D., assistant professor in the Departments of Otolaryngology and Allergy and Clinical Immunology at the Johns Hopkins University School of Medicine, and a researcher at the Johns Hopkins Allergy and Asthma Center at the Johns Hopkins Bayview Medical Center.

Kim explains that surgery to remove the polyps is one of the most common treatments for this disease. However, nasal and sinus polyps in these patients almost always regrow. "Once the patient has entered the cycle of growing polyps, it's very hard to get out," she says. Another common treatment is oral steroids, but these drugs are fraught with many harmful side effects and also only temporarily treat the disease.

She and her Johns Hopkins colleagues have long studied sinusitis, often growing sinus cells isolated from patients in petri dishes. After noticing that cells from patients with polyps typically multiplied faster than cells from normal patients, the researchers speculated that cells from polyp patients might be producing extra amounts of some type of growth factor, a protein that encourages cell growth.

To identify which growth factor might be to blame, the researchers had sinusitis patients with and without polyps rinse their sinus passages with a wash solution, then tested the runoff for the presence of various growth factors. They found that solution from patients with polyps contained high amounts of a substance called vascular endothelial growth factor, or VEGF, a protein important for normal blood vessel growth that also seems to play a key role in a variety of diseases, including cancer. The more VEGF they found in a cell culture, the faster those cells grew.

To further examine whether this protein is present not only in the sinus passages but also in the sinus tissue, Kim and her colleagues used a stain that highlights VEGF on sinus tissue removed from polyp-producing patients and those with other types of sinusitis. The stained tissue from polyp patients "lit up very dramatically, like a city skyline," Kim says, while the tissue from other patients showed little to no staining.

Though these results confirmed that the sinuses of patients with polyps were overproducing VEGF, the researchers still weren't sure that VEGF

was instigating cell overgrowth seen in polyps. Looking for a cause-and-effect relationship, Kim and her team treated cells isolated from sinusitis patients with agents that inhibit VEGF production and action. The cells from polyp-producing patients slowed their growth rate to match that of normal patients.

"It's a strong indicator that VEGF is indeed responsible for the over-exuberant cell growth that contributes to polyp development," Kim says.

Her findings, published in the Dec. 1 *American Journal of Respiratory and Critical Care Medicine*, suggest that doctors may eventually treat sinusitis in patients with polyps using therapies that reduce VEGF in sinus tissues. "In the future, we might have a nasal spray with an anti-VEGF agent in it," she proposes.

The results also suggest a new way of predicting which patients will go on to develop polyps. They might also simplify tracking the progression of the disease, a process which now relies on repeated CT-scans, which expose patients to radiation. Since many patients with polyps already use sinus washes to ease their symptoms, doctors may be able to use any VEGF present in the runoff from these washes as a marker for the disease and its severity.

Source: Johns Hopkins Medical Institutions

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