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DNA-Repairing Sunscreen: Legit or Not?

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HAVING GROWN UP in Tucson, Arizona, one of the sunniest cities in the world, I consider myself well-versed in the carcinogenic threat of UV exposure, the skin-sparing sanctity of shade, and the redeeming qualities of the sartorial atrocity that is the broad-brimmed hat. I am also a compulsive sunscreensplainer. "Well, actually, SPF 30 lotions block about 97 percent of UVB rays—4 percent more

than SPF 15 and just 2 percent less than SPF 50" is the kind of #sunscreenfact I've been rattling off, insufferably, since the age of 7.

So I was surprised, on a recent trip to Florida, to learn something new about sunscreen: Recently, several products have become available that claim to repair DNA damage inflicted by UVB rays. That's ... a bold assertion. To protect your genetic code from the structural harm that can lead to skin cancer is one thing—to actively correct that harm is another challenge entirely.

I was skeptical. So was biologist Errol Friedberg, professor emeritus at the University of Texas Southwestern Medical Center and an expert on DNA damage and gene-repairing enzymes. But when I called him, he told me he'd never heard of any of those enzymes being applied via lotions or sunscreens. "And even if they were, enzymes are fragile," he said. "And rubbing them into the skin, which is a multi-layered organ, doesn't necessarily ensure they're getting into cells. So I would have to see data to be convinced of that."

When I hung up, I was prepared to find no such data. Then I did some digging. Turns out it *does* exist: DNA repair enzymes can not only be applied topically, but there's compelling evidence that they could augment your body's natural gene-repairing machinery. So why aren't those enzymes in *all* sunscreens?

The short answer? Money. The long answer is a little more complicated, but it's easily the most fascinating thing about sunscreen I've ever heard.

Probably the best place to start is with some of the DNA repair sunscreens currently on offer. There's Neova's "DNA Damage Control" sunscreen, three ounces of which will set you back $45; Eryfotona Actinica, from Spanish dermatology company ISDIN, which runs $50 per 3.4-ounce bottle; and DNARenewal's 50+ SPF "DNA Defense" sunscreen, 4 ounces of which costs $75.

That's expensive, and prohibitively so for most people. (By comparison, an 8 ounce bottle of Coppertone—the top sunscreen pick from *Wirecutter*, the *New York Times*' product-reviewing offshoot—costs just 10 bucks.) Here's another #sunscreenfact: The stuff works best when applied often and in copious amounts; the rule of thumb is to apply one ounce every two hours, or after swimming or sweating. At that rate, none of the aforementioned DNA-repairing sunscreens would last you more than 8 hours at the beach.

What you're paying for are molecules like UV endonuclease and photolyase. When you name them out loud it sounds like you're talking about an interstellar cargo vessel and its fuel source. In actuality,

they're DNA-repairing enzymes that sniff out and repair genetic damage caused by exposure to UV light—damage which, when it accumulates, can lead to skin cancers.

Decades of research have shown these molecules and several of their cousins to be legitimately weird and wonderful enzymes. Take photolyases: They're activated by light from visible wavelengths through a process called photoreactivation. I say again: Photolyases are powered by light. As in: They can repair DNA damage caused by sunlight … when they're exposed to sunlight. Nicely done, evolution!

But evolution giveth, and evolution taketh away; humans, it turns out, don't produce photolyases. Almost all organisms on Earth do, from animals and plants to bacteria and fungi, but at some point in their history, placental mammals like us stopped producing enzymes that heal DNA with light. (Instead, we get by with a genetic patch-up called nucleotide excision repair, which is not only less efficient, but, let's be honest, a lot less cool-sounding than photoreactivation.)

Humans don't make UV endonuclease, either; researchers found it in a bacterium called *Micrococcus luteus*. Neither do we produce the DNA repair enzyme T4 Endonuclease V, aka "T4N5"—an imposingly-named cousin of UV endonuclease that scientists first extracted from parasitized *E. coli*. (Friedberg, the DNA-repair expert, developed a technique for doing just that in the early '70s.) Photolyases were derived from sources like plankton and algae.

Once they'd been isolated, some scientists began to wonder whether these enzymes could survive in topical treatments and delivered into human skin cells. The idea was tantalizing, and potentially very lucrative. The founder of Revlon famously characterized cosmetics as hope in a jar—but why would anyone settle for hope when they could actively rebuild their DNA?

One of the first people to recognize this opportunity was a molecular biologist named Daniel B. Yarosh. In the 1980s he came up with a way to purify T4N5 that was faster, cheaper, and simpler than the techniques developed by Friedberg and his contemporaries. Then he found a way to package it and other DNA-repair enzymes inside tiny spherical pockets of phospholipids called liposomes. Along the way, he founded a company to produce it all at scale: Applied Genetics Incorporated. And in 1988, he patented his methods.

In the three decades since, researchers have repeatedly demonstrated that liposomes can transport DNA repair enzymes into skin cells. Yarosh pulled it off in cultured dishes of UV-irradiated human cells first. Then he did it in live mice. Results were promising: Cells treated with Yarosh's enzyme-loaded liposomes removed more irradiated DNA, mended faster, and survived longer.

Soon, researchers were using liposomes to smuggle DNA repair enzymes into the skin cells of human test subjects. In one 2000 study, scientists blasted participants' buttocks with UVB radiation and treated the DNA damage with photolyases, showing significant repair. Around the same time, Yarosh led a phase III clinical trial in which test subjects prone to skin cancer applied a T4N5 liposome lotion for one year. The results, which appeared in *The Lancet* in 2001, showed that patients who applied the T4N5 developed significantly fewer cancerous and precancerous lesions than the placebo group.

After reviewing the research, I found myself feeling less skeptical about the ability to deliver DNA repair enzymes into skin cells and see a real benefit. I emailed Friedberg, the DNA damage expert, the aforementioned studies along with a handful of others and asked him to look them over. His reply arrived the next day: "Well there you have it. The experimental data in at least two labs suggest that it can be done!"

But I still had questions. What became of the lotion from the phase III trial? Why are DNA-repairing sunscreens still so expensive and difficult to come by? It was time to reach out to Yarosh.

WHEN I REACH him on his cell phone, Yarosh is waiting to board a plane home from an off-grid vacation. "I've been at this so long, most of the patents have expired," I hear him say over the sound of an airport PA announcement.

I'm asking him about patents because I want to know where companies like Neova, ISDIN, and DNARenewal get their DNA repair enzymes. If the patents are expired, I ask, then these companies … are they producing their enzymes in-house?

"I know all those brands, I know their products" Yarosh says. "And all of their ingredients are coming from the same place: Esteé Lauder."

Wait. What?

After his phase III trial, Yarosh spent several years trying to raise money to conduct still more studies, to bolster the evidence supporting the effectiveness of DNA-repair enzymes. That was partly to woo prospective clients—cosmetic companies, to whom his company, Advanced Genetics Inc., sold enzymes and other ingredients—but mostly to appease the Food and Drug Administration. An entire arm of AGI was devoted to getting DNA-repair enzymes approved not as cosmetic ingredients, but as drugs. "But the T4N5 cream from the *Lancet* study got bogged down with FDA objections, and they demanded additional trials," Yarosh says.

Easier said than done. The FDA's approval process is known for interacting with the patent system in ways that incentivize the funding of trials in search of cures, rather than prophylactic measures; a pill that might squeeze a few more months of life from a terminally ill cancer patient is more likely to receive funding for clinical trials than, say, a cream that prevents skin cancer—and more likely to receive FDA approval. The numbers bear this out: In 2015, MIT economist Heidi Williams examined cancer clinical trial data between 1973 and 2011 and found that some 29,000 studies had centered on treatments for patients with late-stage and recurring cancers. In the same time period, just 500 had focused on cancer prevention.

Yarosh's efforts to raise the money he needed were ultimately in vain. "But in the process, AGI got an offer from Estée Lauder to sell, and that's the business decision that we made. So the company I founded is now a subsidiary of Estée Lauder, and it continues to supply these repair enzymes and liposomes."

Estée Lauder controls the market, and enough of its customers are willing to pay for DNA repair enzymes that it can charge high prices for them. "Everything comes down to money," says dermatological surgeon Ronald Moy, founder of DNARenewal. A past president of the American Academy of Dermatology and the American Society for Dermatologic Surgery, Moy says he created his own skin care line with DNA repair enzymes because he was compelled by the evidence of their efficacy, "but putting them in sunscreens is expensive."

In light of all of this, you'll probably be surprised to learn that Yarosh doesn't even think DNA repair enzymes belong in sunscreens. "Sunscreen is supposed to stay on the surface of the skin. DNA repair enzymes are supposed to penetrate the skin's surface. It's hard to create a formula that delivers one thing to the top and another to the subsurface," he says. "What I'd really prefer to see is a DNA repair serum you apply first, and apply your sunscreen on top."

Maybe cosmetic companies can develop a clever way to deliver both at once, Yarosh says. And who knows; perhaps they already have. But in the absence of more research, it's difficult if not impossible to say which formula is best—let alone which is most worth the several-hundred-percent premium over the affordable stuff.

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