

JUNE 23, 2016 | THE PULSE

## Scientists discover new pathway for darkening and lightening skin



Researchers are looking into using synthetic estrogen and progesterone as a potentially safer alternative to today's skin lightening and darkening methods. (AP Photo/Alexandre Meneghini)



BY IRINA ZHOOROV

Researchers at a University of Pennsylvania dermatology lab were running a cancer study when they noticed that sex hormones were affecting pigment production in normal cells. They'd add estrogen to their culture and the skin cells would make more pigment. They'd add progesterone, and they'd see less pigment.

"And after we saw that, that's when we decided to narrow it down on figuring out this pigmentation story instead of pursuing the cancer bit," said Chris Natale, a Penn graduate student who led the work.

Scientists have known for a while how skin becomes darker from the sun. The sun damages DNA and in the process of repairing it, proteins trigger pigment production in skin cells. Other pathways for changing skin pigmentation were largely unknown. But the team found (<https://elifesciences.org/content/5/e15104v1>) that that pigment machinery, like a series of latches and gears that generate darker skin tone, was the same with the hormones as with the sun.

“So it wasn’t as if estrogen was creating some brand new way of making pigment. It was just accessing pathways that we already knew about, but accessing them in a different way,” said Todd Ridky, who runs the lab that performed the research.

In other words, there was just a different door – called a receptor – that led to the pigment machine room of a skin cell, but once the hormones unlocked the door, the process happened in the same way. All the same latches and gears doing the same work.

The problem then became figuring out what kind of receptor it was. Estrogen and progesterone are like keys, and the type of receptor they usually fit wasn’t on the pigment producing skin cells, called melanocytes. “It was sort of like a wild goose chase to figure out what other thing it could be,” Natale said.

The team eventually figured out what receptor activated the pigment production. Hippocrates described a darkening of the skin on the face of pregnant women more than 2,000 years ago and finally scientists understood how it happened.

The team developed synthetic estrogen and progesterone derivatives shaped to exclusively fit the new receptors discovered on melanocytes. They used synthetic hormones because they didn’t want the natural hormones to accidentally trigger receptors on other kinds of cells and set off unintended processes. Natural hormones could attach to receptors in the reproductive system, for example, in bones.

The hormone derivatives were incorporated into a gel and applied to lab-grown skin, on mice, and then on pigmented guinea pigs, which can have different colors of skin on one animal.

Ridky pulled up a picture of the backside of a guinea pig on his computer, it’s haunches shaved on either side. The researches had applied gel with the estrogen derivative to one of the shaved areas and a gel with no hormones or derivatives to the other side.

“After a couple of weeks the side with the drug is noticeably quite a bit darker than the other side,” Ridky said, pointing.

The estrogen darkens skin. Progesterone lightens it. The process works just as well on cells from men's skin as women's skin.

## Big deal

"This is going to be a big deal in dermatology," said Thomas Leung, another dermatologist at Penn. He was not involved in the research. "You're going to be able to modulate something in the field that hasn't been able to be done."

Leung said he sees patients all the time who, for one reason or another – a rash, scarring, vitiligo, want to either darken or lighten their skin and he has no effective medication to offer them. Ridky added to the list of medical issues that could be addressed by changing skin pigment: darkening very fair or otherwise cancer-prone people's skin to protect them from skin cancers, or to ease rare disorders, like porphyria, that make people extremely sensitive to the sun.

But Ridky also sees non-medical potential in the discovery.

Worldwide, people try to lighten their skin for cosmetic purposes. Global Industry Analysts calculated the international cosmetic skin lightening market will reach \$23 billion by 2020, lead by Asian countries. Many of those products contain mercury, a neurotoxin that can damage the kidney and cause psychosis.

There's also a ubiquitous reverse industry in the form of tanning salons. IbisWorld Industry Research estimates the tanning industry in the U.S. alone to be worth more than \$2 billion.

SunMyst Tanning Spa, in Philadelphia, has a UV bed, and manager Frances DiStefano said it was the first in the city to offer spray tanning. Today, she said, its three spray-tanning rooms can be triple booked on any given night.

DiStefano said as more and more people reckon with the cancer risk of UV tanning, whether in beds or in the sun, they're turning to other options. "Basically if people come in as new clients and don't know what they want to do, we're going to right off offer them spray tanning. It's a lot healthier than UV tanning," she said. That's an industry-wide trend. The salon offers several color levels, which last about a week.

DiStefano says what hasn't changed is her clients' desire to look tanned. She held up a stack of papers about half an inch thick showing me just the new clients' paperwork from the previous week. I told her about the skin lightening market.

“That’s so crazy. I mean, no one’s satisfied with what they have, they always want to be the opposite, the grass is always greener. But for our clients, they like to be tanned.”

## Long road ahead

Ridky and Natale say they didn’t set out to study skin pigmentation or to find a product for skin lightening and darkening. But if they can prove that using synthetic estrogen and progesterone can be a safer alternative in a booming and at times unsafe cosmetic industry, Ridky said, why not?

“If there’s a safer alternative to that, it would meet a need,” Ridky said.

Leung, the doctor not involved in the research, said he’d prescribe something like this, if it becomes available on the market, to his patients for medical conditions. “This is something we would be very attracted to once this theoretical cream comes about. For the cosmetic things, I leave that to cosmetic dermatologists and for people to make their own decision whether to use that medication or not,” he said.

The cream itself is a long ways off. Before it can be available on the market, the team will need to figure out a cream formula people like to use, run tests to make sure there aren’t bad side effects, and perform human trials to get FDA approval. They’ve formed a start-up company to woo investors to help pay for the expensive development process. But if the researchers can pull it off, the discovery could be big news in both medical and cosmetic dermatology worlds.

*Listen to The Pulse Fridays at 9 a.m. and Sundays at noon on WHYY-FM, listen live at [whyy.org/thepulse](http://www.whyy.org/thepulse)*

*(<http://www.newsworks.org/thepulse>) or download our podcast on iTunes*

*(<https://itunes.apple.com/us/podcast/the-pulse/id772127662?mt=2>).*

THE PULSE IS SPONSORED BY

A generous gift from

**THE SUTHERLAND FAMILY  
CHARITABLE FUND**

**Independence** 

(<http://www.ibx.com>)



Robert Wood Johnson  
Foundation

(<http://www.rwjf.org/>)

SUPPORT PROVIDED BY

SUPPORT PROVIDED BY

