Natural signal holds promise for psoriasis, age-related skin damage

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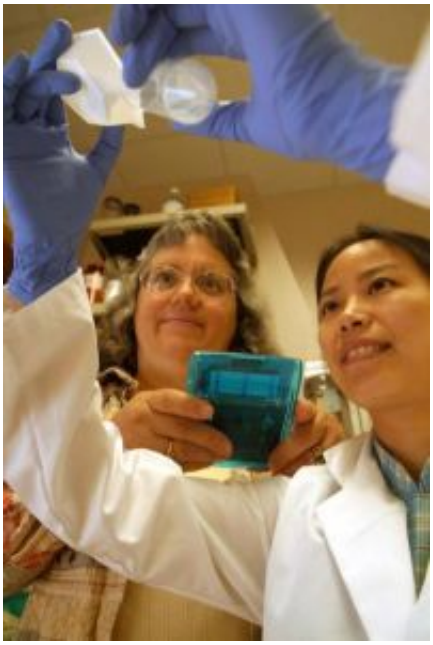

Phosphatidylglycerol, a natural body lipid or fat, may hold the secret to normalizing skin cell growth that is over zealous in psoriasis and non-melanoma skin cancers and too slow in aging and sun-damaged skin, says Dr. Wendy B. Bollag, cell physiologist at the Medical College of Georgia. Credit: Medical College of Georgia

The body may hold a secret to normalizing skin cell growth that is over zealous in psoriasis and non-melanoma skin cancers and too slow in aging and sun-damaged skin, researchers say.

Phosphatidylglycerol, a natural body lipid or fat, appears to signal cells to normalize growth and maturation or differentiation. “When we apply it to skin cells, we see the normalization ability,” says Dr. Wendy B. Bollag, cell physiologist at the Medical College of Georgia.

Her research, published online in *The Journal of Investigative Dermatology*, helps piece together the signaling pathway that prompts skin cells to stop multiplying and start differentiating.

Perhaps most importantly it shows that bypassing that pathway – one researchers suspect becomes dysfunctional in diseases like psoriasis – and giving the signal itself restores normal differentiation of skin cells or keratinocytes.

The findings prompted Dr. Bollag and John Edwards, CEO of Apeliotus Technologies of Atlanta, to seek National Institutes of Health funding for yearlong study in animal models of mild psoriasis to see if it works, with human trials as the goal. “Proof of principle is the first phase. If in vivo data looks promising, we’ll put together a study we can take into the clinic,” says Dr. Bollag. She and Apeliotus received an NIH Small Business Technology Transfer grant, which supports small businesses collaborating with U.S. research institutions to develop technologies and methodologies with commercial potential.

A Georgia Research Alliance Industry Partnership Grant will allow parallel studies in animal models of chronological aging and photoaging from too much sun exposure, Dr. Bollag says.

MCG and Apeliotus will work with Avanti® Polar Lipids, Inc., of Alabaster, Ala., which has a chicken-egg derived phosphatidylglycerol used primarily for lipid research. Avanti is developing different phosphatidylglycerol ointments or salves for the new studies. Dr. Bollag notes that the lipid, already used as drug-delivery mechanism in humans,

has been ingested at higher doses, so she believes lower doses applied externally will be safe.

Glycerol, a precursor of phosphatidylglycerol, also is available commercially and used in many skin care products because it's long been known to help skin retain moisture, so it looks and feels better. "We think that, yes, it's a water attractor, but we think it also has this additional role as a precursor for an important lipid signal in the skin," says Dr. Bollag. Naturally occurring glycerol is an important precursor for many things such as fat, phospholipids, various sugars and metabolic pathways in the body. "Glycerol levels go up when you exercise, because you are using fats as fuel."

She's shown that the channel, aquaporin-3, delivers glycerol to phospholipase D, resulting in the skin cell differentiation signal, phosphatidylglycerol. "This is serving as a signal, like an elevator operator who says, 'This way for normal keratinocyte differentiation,'" says Dr. Bollag. "That's good because without it, you get abnormal differentiation in skin diseases like psoriasis, non-melanoma skin cancer, some of the dermatitises; in a lot of these conditions, the cells proliferate too much and don't differentiate properly. We think maybe in psoriasis, the phospholipase D and aquaporin-3 become disconnected so now they can't produce phosphatidylglycerol. If you only put glycerol on it, it may not help."

But it looks as though the signal does.

Her newest research, done in mouse skin cells in culture, showed that aquaporin-3 manipulation impacted phosphatidylglycerol generation. "The glycerol was coming through aquaporin. If we blocked it, we stopped glycerol from coming through and we also blocked phosphatidylglycerol. Then we started manipulating the various players. We did some over expression of aquaporin and showed it promoted

differentiated status of the keratinocytes.

“Then we wondered what would happen if we actually gave phosphatidylglycerol itself, so we bypassed the whole aquaporin-phospholipase D system and we saw some interesting results.”

Phosphatidylglycerol inhibited growth of rapidly growing skin cells and increased growth in slow-growing cells. MCG has a patent pending on the ability of phosphatidylglycerol to normalize skin cell function.

“The key is cells are supposed to proliferate in this one layer,” she says of the basal layer, where a skin cell divides, with one staying to divide again and the other expressing different genes, proteins and functions as it moves toward the surface. Without phosphatidylglycerol, cells can proliferate too much and differentiate improperly, Dr. Bollag explains.

“Right before cells reach the layer that we actually see, called the cornified layer, they spit out lipids they synthesize to make the water permeability barrier then they basically die. But they leave behind these hard shells that give skin its mechanical strength. When you get older, you don’t turn it over as well,” Dr. Bollag says, explaining why despite ongoing cell turnover old skin looks, well, old.

Source: Medical College of Georgia