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## From cancer research, smooth skin

Fox Chase scientists were looking to cure diabetes and cancer when they found a potentially lucrative bonus — an anti-aging cream.

By Susan FitzGerald

Annette Tobia made the rounds at last week's BIO 2005 convention carrying a backpack stocked with jars of secret anti-aging cream.

As she talked with potential investors and partners from as far away as Japan, India, Israel and Argentina, Tobia handed them each a jar.

"I tell them to try it where they have wrinkles," Tobia said between meetings at the Convention Center in Philadelphia. "I tell them to start at the neck."

Tobia could have been dismissed as just another huckster promising the next fountain of youth. But as head of Dynamis Therapeutics Inc., a biotech company in Elkins Park, she has some solid science in her portfolio.

The anti-aging cream grew from cancer research at Fox Chase Cancer Center in Northeast Philadelphia — a shift that shows how serendipitous science can be and how basic findings can have broad applications.

The same scientific rationale that led to the cream's development is now being used to find new drugs to prevent the devastating complications of diabetes, such as nerve damage and blindness.

The common thread is a highly reactive molecule called 3-deoxyglucosone, or 3DG, and the enzyme that makes it. The molecule causes inflammation and the formation of free radicals, which can damage cells. Elevated levels of 3DG have been found in the blood of diabetics.

Fox Chase scientists became focused on the molecular pathway by chance when they came across some unusual substances in tumors and other tissues while using high-resolution nuclear magnetic resonance.

"We found these strange compounds and we wondered where the devil they came from, and we realized there had to be an enzyme they came from," said Truman R. Brown, a former Fox Chase scientist now at Columbia University Medical Center. He is a stockholder and scientific adviser to Dynamis.

The enzyme in question turned out to be fructosamine 3-kinase. The scientists reasoned if they could block its action, they could inhibit production of 3DG and perhaps prevent the resulting cell damage. Dynamis was co-founded in 1997 by Fox Chase to translate that finding into treatments.

The leap to a skin care product also started by chance. The scientists had become interest-

ed in the role of 3DG in diabetic complications after finding the compound in the eyes and various tissue of diabetic rats.

Dynamis scientists were injecting an enzyme-blocking compound into rats to try to lower 3DG levels and prevent complications of diabetes when something interesting turned up.

"As they were handling the animals, they noticed that with the rats on the drug, their skin just felt different than the diabetic rats not on the drug. Their skin felt softer, it just didn't feel as stiff," said Frank Kappler, chief scientific officer at Dynamis and part of the earlier Fox Chase team.

As it turns out, human diabetics have skin problems, and the Dynamis scientists went on to find that the targeted enzyme and its toxic product, 3DG, were present in skin and sweat.

So began the pursuit of a skin cream — for people. Dynamis scientists, novices in the cosmetic field, concocted the lotion in the company's laboratory on the campus of the Pennsylvania College of Optometry.

Kappler was the master chemist. Over about a year, he tested out various combinations of ingredients, like a chef perfecting a recipe.

He and Tobia won't reveal the cream's formula because it is a company secret — though they will say there are 29 ingredients, all used in the cosmetic industry.

They do not know exactly how the cream works, but Kappler said that in a test tube, the active ingredients appear to inhibit the enzyme and lower 3DG levels.

Tobia, a scientist and lawyer by training, has "before and after" photos of the arms of women who tested the cream, and on a recent morning she pointed out what seemed to be a disappearance of fine aging lines.

Because the cream will be sold as a cosmetic, not a drug, it will not have to pass scientific review and scrutiny of the Food and Drug Administration.

There already are an abundance of products promising smoother, younger-looking skin. Kline & Co., a market research firm, estimates that sales of anti-aging skin care products total nearly \$2.5 billion annually in the United States.

"There are thousands of anti-aging products now and most of them are nothing more than hype," says Albert Kligman, professor emeritus of dermatology at the University of Pennsylvania and discoverer of Retin-A, the acne and anti-wrinkle drug.

Kligman's company, SKIN Inc., tests topical drugs and cosmetics, and will be involved in evaluating the Dynamis product. He says cosmetic firms can say what they want about their products "as long as you don't hurt anyone and you stay away from drug claims."

Gary Grove, vice president of research and development at CyberDERM Inc., a Media company where the Dynamis cream was tested, says he is frequently approached by companies claiming to have a "magic bullet." In Dynamis' case, he thinks the company is onto something.

"With their Fox Chase connection, this is a group of scientists first," he says. "I don't know how good business people they are, but they are good scientists."

Patricia Weeks, Fox Chase's vice president of planning and business development, says the cancer center would get 3 percent to 5 percent in royalties resulting from the skin product.

Tobia said the hope is to market the skin cream — both directly and by selling the formulation to cosmetic companies — and then use the revenue for research into more pressing problems, such as diabetes and skin cancer.

Dynamis, a privately held company with nine employees, already has a \$1.1 million grant from the National Institute of Diabetes and Digestive and Kidney Diseases to look for drugs that would prevent diabetic complications.

Tobia said that many of the ideas being promoted at the biotech conference last week were just getting to the point of being tried in rats and mice.

"Because we have the cosmetic application, we're showing we can have effects on people," she said. "It's the difference between having a concept and having a product."

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