



‘Cancer Protein’ Linked to Alzheimer’s

In a significant discovery, a group of proteins long associated with cancer research has been shown to have an important link to Alzheimer’s disease. Among other implications, this advance could fast-track Alzheimer’s drug development, as there are already relevant therapies in active cancer trials.

The protein family, protein kinase C, also known as PKC, helps cells throughout the body and brain respond to cues from their environment—it is an information processor, or “signal transducer.” Balancing the activities of these proteins so that they are active in just the right proportion is essential for cellular homeostasis—functional balance in all of our cells. In a first-of-its-kind study supported by Cure Alzheimer’s Fund (CAF), Dr. Alexandra Newton, Professor of Pharmacology at the University of California, San Diego (UCSD), was able to show that excessively active PKC is associated with Alzheimer’s, thus identifying PKC as a potential therapeutic target.

Dr. Newton has spent virtually her entire career studying the biochemistry and function of PKC. “Because PKCs can be affected by tumor-promoting molecules, the dogma over the past thirty-plus years has been that overly active PKC drives cancer progression,” explained Newton. But things didn’t add up—clinical trials with drugs to inhibit PKC have not only failed but, in some cases, worsened patient outcomes. To find out whether PKC suppresses or promotes cancer, Newton’s lab turned to the disease for an answer. Recent large-scale sequencing of tumors from thousands of cancer patients has identified hundreds of cancer-associated mutations that occur in PKC. Her lab posed the question: are these mutations activating or inactivating? To her surprise, the cancer mutations turned the protein off. “So having PKC is a good thing,” she said. “It protects against cancer. You take it away, and you give the cancer cell a huge survival advantage.”

When CAF Consortium member Dr. Roberto Malinow, a colleague of Newton’s at UCSD, discovered that mice lacking a certain type of PKC had brain differences relevant to Alzheimer’s, he asked Research Consortium Chairman Dr. Rudy Tanzi to look for genetic mutations in PKC in his genome sequencing of Alzheimer’s families. Dr. Tanzi subsequently found relevant mutations. Dr. Malinow then suggested that Dr. Newton examine how these mutations impact PKC function. “Imagine our excitement,” she said, “when we discovered that this mutant PKC, found in four unrelated Alzheimer’s families, had increased activity—the opposite of what occurs in cancer.”

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FEATURED RESEARCHER

Alexandra Newton, Ph.D.

*Professor of Pharmacology,
University of California, San Diego*



By the time she was 17, Alexandra Newton had lived in seven different countries and had mastered four different languages. But her family was not surprised when she chose to pursue a career in biochemistry instead of language arts. Newton had always had an intense curiosity about nature that has fueled her life-long passion for science. As a child she caught chameleons in Cape Town and butterflies on Corfu, and she collected rocks in the Sahara desert. Still, she didn't know that one day she would end up making some life-changing scientific discoveries in her very own lab.

Alexandra Newton was born in Cape Town, South Africa to an English father and a Cypriot Greek mother. Her father was a professor of classics at the University of Cape Town, and her mother was a stay-at-home mom who watched over her and her younger brother.

In 1965, when Newton was 7 years old, she and her family moved to Vancouver, Canada. Her father was one of the founding faculty members of Simon Fraser University and a self-taught linguistics professor who specialized in the phonology of Greek dialects. Every two years, the family would travel to Greece so her father could do field work. Before Newton graduated from high school, she had lived in South Africa, England, France, Greece, Germany, Cyprus and Canada and had learned to speak French, German and English along with her native tongue, Greek.

Despite her aptitude for the arts, science had always been her true passion. "I was a data fanatic from a young age," admits Newton, who refers to herself as a "total nerd" and even has earrings with amino acids of her favorite sequences. She kept hand-sewn lab notebooks, looked at pond water with her toy microscope, and even dissected frogs as a kid. Her first experiment at age 8 was an attempt to prove or disprove her parents' claim about the tooth-decaying qualities of Coca-Cola. Instead of putting her baby

tooth under her pillow for the tooth fairy, she measured her tooth's diameter with a piece of string and dunked it in Coca-Cola to see for herself whether or not the soda would really decay her tooth. After several days of recording tooth diameter, she was disappointed to realize that her parents had been right. Newton never drank soft drinks again.

In her youth she spent many idyllic summers on the Greek Islands, snorkeling in the Mediterranean, even catching octopuses with her bare hands. In fact, when she grew up and attended Simon Fraser University, she thought she wanted to be a marine biologist. But in her first semester there, she fell in love with chemistry. When she began learning about amino acids, she narrowed

her field to biochemistry and double-majored in French literature. After college, Newton earned a Ph.D. in chemistry from Stanford University.

Newton did her postdoctoral work at the University of California, Berkeley in the lab of renowned biochemist Dan Koshland, whose goal at the time was to better understand memory. Protein kinase C (PKC)—a critical enzyme that runs through our bodies and keeps our signaling pathways in check—had recently been discovered, and Koshland believed it to be a memory molecule, since it was abundant in the brain and made imprints on other proteins. Since then, Dr. Newton has studied PKC to understand its molecular mechanisms and how it goes wrong in diseases. Over the years she ultimately learned that PKC has to be exactly balanced in the body to be beneficial. "If your body has too much of it, it causes cells to die and leads to degenerative diseases such as Alzheimer's. If you don't have enough, it causes cancer," she says. In fact, Dr. Newton is so passionate about PKC she actually has had it displayed on her license plate for the past 20 years.

Personal Life

Dr. Newton grew up playing the piano and practicing ballet, both of which she's continued for her entire life. Chopin is her favorite composer, and she still dances ballet three times a week to "keep myself sane." She has two children, an 18-year-old daughter who is a trainee at Miami City Ballet, and a 16-year-old son whose passion is to one day engineer racecars. To find out more about Alexandra Newton's work, tune into our next Alzstream™ webinar in May. ■

Don't Miss Our Next Alzstream™ Webinar

The Cancer and Alzheimer's Connection

Tuesday, May 19, 2015 at 2:00 p.m. ET

Hear from University of California, San Diego biochemist Alexandra Newton, Ph.D., about her work on the enzyme protein kinase C and how it plays a role in both cancer and Alzheimer's disease. No registration is required—simply visit curealz.org/webinar on the 19th to join.

Research Consortium Recap

Every year the Cure Alzheimer's Fund (CAF) Research Consortium members get together with the Board of Directors to discuss their respective research projects, refine their strategy, and leave with a clear mission. This year was no exception.

On Feb. 5, 30 individuals gathered in San Diego for a full day of scientific discussions. The scientists presented their latest research to their peers, and followed up with an insightful discussion. "One of the things that often comes out of the presentations is that people in the room offer to work with the presenter on his or her project, or recommend someone who is working on something similar," said Tim Armour, President and CEO of CAF. "While researchers tend to work on individual projects, this type of forum gives them an opportunity to learn from and collaborate with each other."

After the presentation, the group participated in a general strategic discussion about what the Consortium should focus on going forward from a research perspective. The meeting also compiled a list of fellow scientists for potential recruitment to the "Genes to Therapies" (G2T) project, a highly focused initiative that targets all the genes in Alzheimer's pathology and pairs them with individual researchers for study. ■



Charles Glabe, Ph.D. shares his research findings.



Rudy Tanzi, Ph.D. presents at the Research Consortium meeting.



'Still Alice' Screenings

In an effort to bring people concerned about Alzheimer's disease together, Cure Alzheimer's Fund (CAF) held two private screenings of the film "Still Alice," based on the best-selling novel by Lisa Genova and starring Julianne Moore, who won an Oscar for her role in the film. Both events were held this past winter, one in New York City and the other in Newton, Mass.

The New York event served as a kickoff for the NYC Young Professionals Group, and more than 50 children and grandchildren of Alzheimer's disease sufferers from the group attended. Event organizers Lee Goldfarb and Allison Dorman, with help from Ellen McCance Pinschmidt and Emily Magid, spread the word and planned an inspiring evening. The viewing was followed by cocktails and a question-and-answer discussion with Sally Rosenfield, Senior Vice President, CAF, and David Shenk, author of *The Forgetting*.

The Newton event, which attracted 220 viewers and was completely sold out, helped to raise awareness and educate attendees about the disease. "Still Alice" author Genova, writer Greg O'Brien (who suffers from early onset Alzheimer's), CAF Research Consortium Chairman Rudy Tanzi and CAF Senior Vice President Mike Curren led a discussion after the film.

Copies of "Still Alice" were distributed at both events. Genova asks in her book for research donations, and she has raised over \$5,000 for CAF to date. To purchase your copy, visit <http://lisagenova.com>. ■

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"It's becoming apparent," Newton explained, "that PKC is a modulator that keeps signaling pathways in check so you don't overly signal. Its activity has to be perfectly balanced. If you don't have enough or if you have too much, you get pathologies."

Newton's study was funded as part of CAF's ambitious new "Genes to Therapies" (G2T) program. "Cure Alzheimer's Fund was instrumental," she said, "both in pointing out the mutations and in funding this study. They have changed the direction of our research."

She added: "This is just the tip of the iceberg. We've only looked at one of Dr. Tanzi's mutations. There's so much more to do."

"Collaboration is one of the founding principles of our innovative consortium," said CAF Chairman Jeffrey Morby. "This groundbreaking research is yet another example of what can be accomplished when you encourage fluid working relationships between the best scientists in the world." ■



SAVE THE DATE
October 14, 2015 for our next Symposium:
The State of Alzheimer's Research

Harvard Club of Boston
374 Commonwealth Avenue

Financial Update

| | This Quarter* | YTD* | Inception to Date |
|--|---------------|-------------|-------------------|
| Fundraising | \$2,578,000 | \$2,578,000 | \$50,853,000 |
| Expenses paid for by the founders | \$425,000 | \$425,000 | \$9,915,000 |
| Funded research | \$300,000 | \$300,000 | \$28,321,000 |

*Numbers shown are preliminary for the period and are rounded to the nearest \$1,000.

Research Update

Research funded during the first quarter of 2015

| Project | Researcher | Distribution Amount |
|---|---|---------------------|
| The Role of the KIBRA Gene in Aβ Regulation of AMPAR Trafficking | Richard L. Huganir, Ph.D., Johns Hopkins University School of Medicine | \$100,000 |
| Discovery of Alzheimer's Disease Blood Biomarkers Using Phage Display Technology, Year 2 | Yueming Li, Ph.D. Sloan-Kettering Institute | \$100,000 |
| Optimization of Pharmacologic Properties of Molecular Tweezers | Gal Bitan, Ph.D. David Geffen School of Medicine at the University of California, Los Angeles | \$100,000 |
| Total Distributed to Research for Q1 2015 | | \$300,000 |

Help us fund research with the highest probability of preventing, slowing or reversing Alzheimer's disease. Donations can be made through our website, curealz.org/donate, or sent directly to our office.

For gifts of securities or direct wire transfers, please contact Tim Armour at [877-CURE-ALZ \(287-3259\)](tel:877-CURE-ALZ) for further information.

CHARITY DESIGNATION

Cure Alzheimer's Fund® is a "doing business as" name for the Alzheimer's Disease Research Foundation, a 501(c)(3) public charity with federal tax ID #52-2396428.

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Mission

Fund research with the highest probability of preventing, slowing or reversing Alzheimer's disease.

Research Consortium

Develops and updates a "roadmap for research" for the most effective and efficient route to preventing, slowing or reversing Alzheimer's disease. Members research their own projects and recruit others whose work will hasten development of effective therapies for and prevention of Alzheimer's disease.

Rudolph E. Tanzi, Ph.D., Chairman, Research Consortium;
Harvard Medical School/Massachusetts General Hospital

Sam Gandy, M.D., Ph.D., Icahn School of Medicine at Mount Sinai
Charles Glabe, Ph.D., University of California, Irvine

David Michael Holtzman, M.D., Washington University, St. Louis

Richard L. Huganir, Ph.D., The Johns Hopkins University

Virginia M.-Y. Lee, Ph.D., M.B.A., University of Pennsylvania

Roberto Malinow, M.D., Ph.D., University of California, San Diego

Eric E. Schadt, Ph.D., Icahn School of Medicine at Mount Sinai

Sangram S. Sisodia, Ph.D., University of Chicago

Robert Vassar, Ph.D., Northwestern University

Steven L. Wagner, Ph.D., University of California, San Diego

Berislav Zlokovic, M.D., Ph.D., University of Southern California

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"Your donations make a big difference in our progress toward finding a cure for Alzheimer's disease. Your passion, your energy and your generosity are an inspiration to all of us to work even harder to end this terrible disease. Thank you all for your leadership and support."

—Tim Armour, president and CEO, Cure Alzheimer's Fund



Fifth-grade fundraisers

Fifth-Grade Fundraiser

Last February, a group of gifted fifth-graders at Martinez Elementary School in Evans, Ga. worked on a unit about the brain. As their final project, they created, entirely on their own, a fundraiser to raise money for Alzheimer's research. For a week each student in the school contributed a dollar a day to participate in different dress-up themes. Prior to the fundraiser, the students researched which charities used the most funds toward Alzheimer's research, and as a result chose to donate to Cure Alzheimer's Fund. "It's great to see how these students are learning at a young age the importance of research and how contributing can help," said their teacher, Britni Watts. "They raised more than \$1200. I am so proud of them." ■



CAF co-founders Jeff and Jacqui Morby and hosts Sheila and Milton Fine

Palm Beach Country Club Event

On March 9, a group interested in Alzheimer's research and several Cure Alzheimer's Fund board members joined hosts Sheila and Milton Fine, of Palm Beach, Fla., at the Palm Beach Country Club for an educational event about Alzheimer's disease. The Fines were encouraged by recent research advances and wanted to provide a forum to educate others. Presentations were made by Sheila Fine, CAF Chairman Jeff Morby and Research Consortium Chairman Rudy Tanzi, which was followed by a lively discussion about the progress CAF has made in getting closer to a cure. ■

PAR Golf Program

Golf tournaments are not only a great way to bring people together for an important cause, they are also some of the most successful ways to raise money for Alzheimer's research. However, there are steps planners can take to make an event even more successful. That's the idea behind the new PAR (Participating in Alzheimer's Research) golf program—to help those running golf fundraisers to be as successful as they can be. The PAR booklet offers tips from those who have run tournaments in the past for creating your own event—from managing your budget to choosing a format. To get your PAR brochure call Mike or Laurel at 781-237-3800 or email us at info@curealz.org. ■

Participating in Alzheimer's Research

A Website With a Conscience

A new e-commerce website based in California, called Beautykind, is aiming to change the way consumers shop for beauty products. The idea is for women worldwide to shop for their cosmetics online and donate 5 percent of their purchase to a cause of choice, ultimately making every user a philanthropist. "Beautykind.us is going to raise the bar in terms of the way people shop online," said Adil Wali, the company's co-founder and chief technology officer. To participate visit www.beautykind.us, create a login and search for Cure Alzheimer's Fund. ■



'Remember Me'

Music has a powerful connection to both memories and emotions. That's what inspired Dr. Rudy Tanzi, Cure Alzheimer's Fund (CAF) Research Consortium Chairman, to write the music and Chris Mann, a finalist on the hit show, *The Voice*, to write the lyrics to the song "Remember Me." This anthem of hope (now a music video) is about someone with Alzheimer's who doesn't want to be forgotten. Mann brings the song to life with his hauntingly beautiful voice. A portion of the proceeds of each song sold goes directly to CAF. Read more about the "Remember Me" campaign at curealz.org/remmemberme. ■





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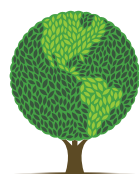
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Global Family
R E U N I O N



AJ Jacobs, Founder,
Global Family Reunion

AJ Jacobs, 47, lives in New York City and is a well-known journalist, author, editor and lecturer. He saw an opportunity to raise money for Alzheimer's research by creating the first-ever "Global Family Reunion," an initiative based on the notion that we are all connected in some way and all distant cousins. The event, to be held on June 6, 2015 at the site of the 1964 New York World's Fair, will be a fun-filled day of entertainment to support both the Alzheimer's Association's New York City Chapter and Cure Alzheimer's Fund (CAF).

Jacobs' grandfather suffered from Alzheimer's, and Jacobs saw first-hand how devastating the disease is. "Our stories and memories form the core of family relationships. If we lose those, we lose what's most important." That's why he wanted a portion of the proceeds from the event to go to CAF. "I was blown away by their approach. I love the idea of applying venture capital thinking to investing in research. And the list of scientists on their team is truly astounding."

The program will include several talks on the disease as well as an awards ceremony for the people who raise the most money for Alzheimer's research. Jonatha Brooke will perform excerpts from her one-woman show about Alzheimer's, *My Mother Has 4 Noses*. And CAF will have booths at the reunion to educate people about the disease.

"I'd encourage all my 'cousins' to come," said Jacobs. "There will be great speakers, including Henry Louis Gates Jr., Cass Sunstein and Morgan Spurlock, comedy from the New Yorker's Andy Borowitz, and Sister Sledge will perform 'We Are Family' live. There will be activities for all ages, including scavenger hunts, games, contests and food from around the world."

Early-bird tickets are already on sale for \$25 per person at **www.globalfamilyreunion.com**. Get your ticket today! ■