



Brain Chemistry Labs

ANNUAL REPORT

2023

Letter From the Chair

It is indeed a great honor and responsibility to chair the Board of Directors of the Brain Chemistry Labs (BCL). While acknowledging it is a daunting task to succeed Bill Egan, our past chair and great leader, I deeply appreciate the trust and support of all.

I would like to thank my colleagues on the Board for their ongoing passion, dedication, and commitment to increase their involvement on Board committees. The multi-talented board members' skills, wisdom, and experience have added a great deal of value to BCL's continued success. I applaud all for helping formulate the strategy that will allow the achievement of not only our vision, mission, and purpose, but also meet the needs and expectations of all those individuals and groups that are impacted by what we do.

The Brain Chemistry Labs is an innovative not-for-profit research institute with the unique mission of discovering novel ways to prevent, diagnose, and treat brain diseases such as ALS, Alzheimer's, and Parkinson's, some of the most vexing health challenges facing our world today.

I first met the co-founder and Executive Director Dr. Paul Alan Cox when he was invited to join the Miller Institute for Basic Research in Science at the University of California, Berkeley after he received his Ph.D. in biology at Harvard. I think his experience at the Miller Institute, which fosters groundbreaking scientific research by granting unfettered access to cutting-edge scientists, deeply influenced Paul's design and foundation for BCL today, allowing a new approach to an understanding of progressive neurodegenerative illnesses. Paul is truly a one-of-a-kind valued leader and brilliant scientist.

BCL's diligent staff and highly capable scientific team cannot be sufficiently acknowledged or thanked enough for their insights and amazing discoveries into disease

processes that have the potential to significantly improve the outcome of patients and impact the world for good. Their willingness to collaborate with an international consortium of multi-disciplinary scientists toward major achievements and advances, despite a modest budget, is inspiring.

Let us not forget to express our gratitude to all our valued donors, advisors, and partners who allow this important work to continue.

I am grateful to serve as Chair of this remarkable enterprise and invite you to join me in helping BCL move forward to the next level of success.



Sue Severson
Chair
Brain Chemistry Labs



Our Research on Alzheimer's, ALS, and Parkinson's Disease

Our research began in two small villages in Guam where 25% of the adults died of an unusual illness with aspects of Alzheimer's, ALS, and Parkinson's disease. We discovered that villagers who died had in their brains a toxin, BMAA, which is produced by cyanobacteria in the environment. This toxin contaminated traditional foodstuffs.

Together with our consortium members in Australia, we found that the naturally occurring amino acid L-serine reduces protein misfolding.

Prevention

We have monitored BMAA in cyanobacterial blooms throughout the world, helping individuals to avoid exposure.



We seek to discover ways to prevent, diagnose, and treat progressive neurodegenerative diseases.

Diagnosis

We have invented a microRNA blood test to help neurologists diagnose ALS at an early stage. We have also invented a blood test for early-stage Alzheimer's disease.



Treatment

We have conducted extensive studies on L-serine finding that it reduces neurodegeneration in the brain. Our most recent study is an advanced clinical trial of L-serine for the treatment of Mild Cognitive Impairment, a precursor to Alzheimer's disease.





The Reporter from *Fortune* Told Us That We Were Disruptive to the Pharmaceutical Industry. He Said It Was a Good Thing.

With 50 scientists in our research consortium, we explore approaches not considered by Big Pharma.

“It’s hard not to see in [Brain Chemistry Labs] grassroots international consortium a research model that’s more flexible, responsive, curious, and humbly collaborative than the siloed, conservative approach of the pharmaceutical industry.” – *Fortune*



“Convening world-class scientists in a not-for-profit research institute in Jackson Hole, we have come up with new research paradigms for ALS, Alzheimer’s, Parkinson’s, and other brain diseases.”

– Paul Alan Cox, Ph.D.



Dr. Paul Alan Cox



Dr. Rachael Dunlop



Dr. James Metcalf



Dr. Sandra Banack

Discovery: ALS Diagnostics



With patient samples from our clinical trials and the Centers for Disease Control, we have validated a microRNA fingerprint for ALS. Based on a single small blood sample, we can rapidly identify an individual at risk of ALS. This discovery will improve patient outcomes by allowing therapy to be more quickly initiated.

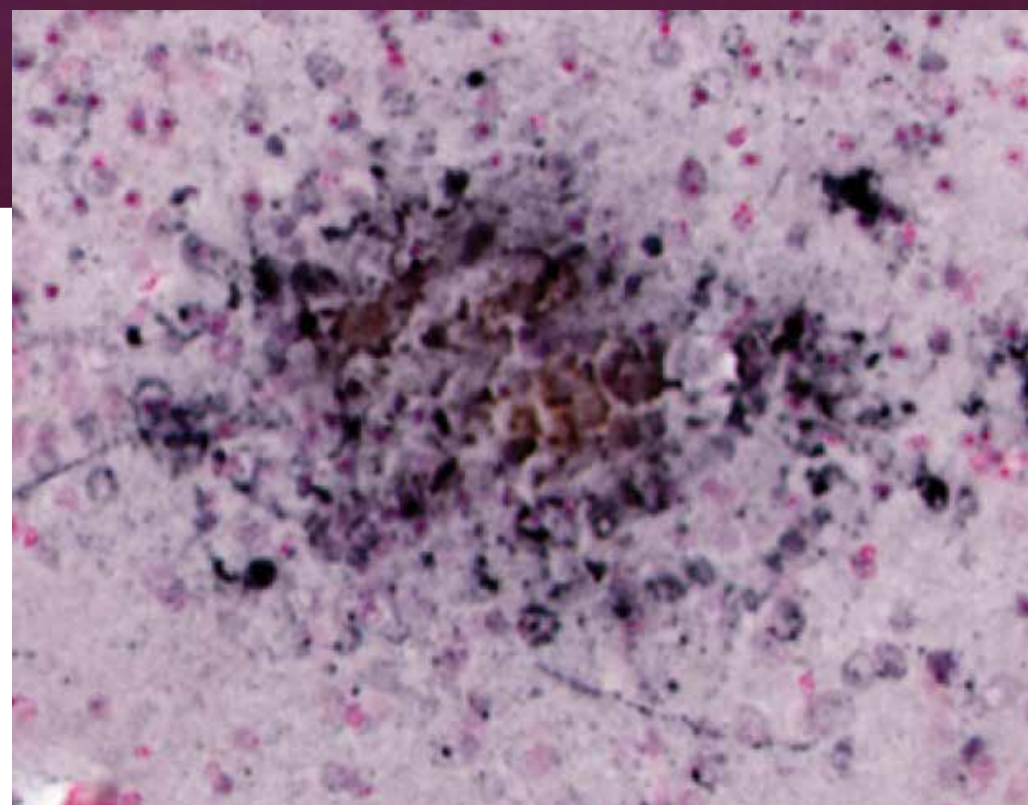
Discovery: ALS Therapy



Based on neuronal cell culture, research on animals in St. Kitts, and two clinical trials, we discovered that L-serine significantly slows disease progression. We seek a pharmaceutical partner to move this naturally occurring amino acid into Phase III clinical trials necessary for FDA approval.

Discovery: Alzheimer's Diagnostic & Therapy

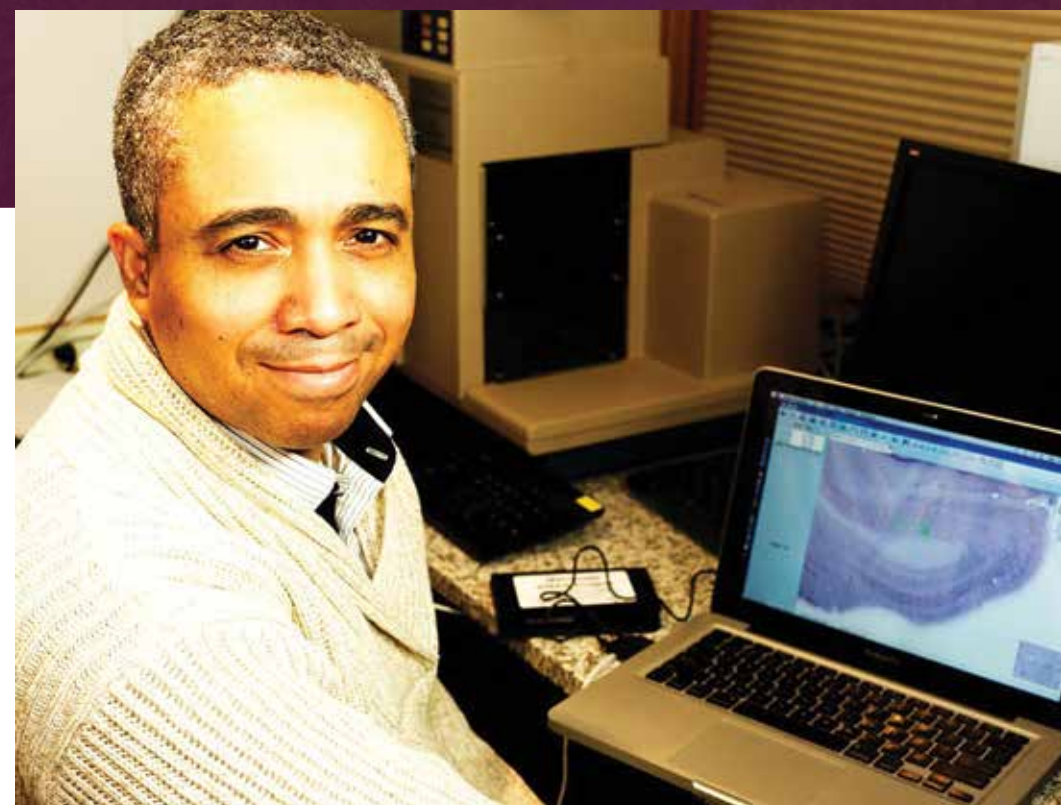
We have discovered a unique metabolite for Alzheimer's that does not rely on fragments of misfolded proteins in the bloodstream, and which identifies Alzheimer's disease at the earliest possible stage. We have also found that L-serine slows the formation of A β 42 fragments and misfolded tau tangles in the brain. We are sponsoring a Phase IIa clinical trial of Mild Cognitive Impairment, which is often a precursor to Alzheimer's disease.



A brain tangle containing misfolded tau proteins

Discovery: Treatment of Advanced Parkinson's Disease

We have identified a different natural compound that shows promise as a treatment for patients in advanced stages of Parkinson's disease. Our research indicates that it is possible to prevent cognitive decline experienced by some patients. We hope to rapidly initiate an FDA-approved clinical trial for this compound.



Neuropathologist Dr. David Davis

Discovery: Detection of Neurotoxins in Air and Water



Drs. Paul Alan Cox & James Metcalf

We discovered that a bacterial toxin in traditional foods of Chamorro villagers in Guam triggers a disease with brain pathology and symptoms of ALS, Parkinson's, or Alzheimer's. We have since found this toxin to be present in water and air near polluted lakes and rivers. Current detection techniques are expensive. We have developed an immunoassay—similar to a COVID-19 test—that is cost effective and can be used by lay people.

Discovery: Glioblastoma



Dr. Samantha Gerlach

We discovered that small circular proteins extracted from violets are effective in killing cells of glioblastoma, a lethal form of brain cancer. Patients with glioblastoma usually survive less than a year after diagnosis. Synthetic forms of violet cyclotides increase the potency of the current chemotherapy Temozolomide (TMZ) eight-fold *in vitro*. These discoveries bring new hope to adults and children who suffer from glioblastoma.

Scientific and Public Engagement

Brain Chemistry Labs scientists presented our discovery of a microRNA ALS blood diagnostic test at the International Symposium on ALS/MND in Switzerland. Our discovery of cyanobacterial neurotoxins in dust from the Great Salt Lake was presented at a press conference in the Utah State Capitol, an advance reported by *Newsweek*, *Science Magazine*, and *ALS News Today*. Other press articles profiled our discovery of a new test for neurotoxins in air and water.



Scientific Articles Published in 2023

Dunlop RA, Banack SA, Cox PA. LICAM immunocapture generates a unique extracellular vesicle population with a reproducible miRNA fingerprint. *RNA Biology*. 2023 Dec 31;20(1):140-8.

Garamszegi SP, Banack SA, Duque LL, Metcalf JS, Stommel EW, Cox PA, Davis DA. Detection of β -N-methylamino-L-alanine in postmortem olfactory bulbs of Alzheimer's disease patients using UHPLC-MS/MS: An autopsy case-series study. *Toxicology Reports*. 2023 Jan 6;10:87-96.

Li A, Yan Y, Qiu J, Yan G, Zhao P, Li M, Ji Y, Wang G, Meng F, Li Y, Metcalf JS. Putative biosynthesis mechanism of the neurotoxin β -N-methylamino-L-alanine in marine diatoms based on a transcriptomics approach. *Journal of Hazardous Materials*. 2023 Jan 5;441:129953.

Metcalf JS, Banack SA, Cox PA. Cyanotoxin analysis of air samples from the Great Salt Lake. *Toxins*. 2023 Nov 15;15(11):659.

Metcalf JS, Banack SA, Wyatt PB, Nunn PB, Cox PA. A direct analysis of β -N-methylamino-L-alanine enantiomers and isomers and its application to cyanobacteria and marine mollusks. *Toxins*. 2023 Nov 1;15(11):639.

Weeks RD, Banack SA, Howell S, Thunga P, Metcalf JS, Green AJ, Cox PA, Planchart A. The effects of long-term, low-dose β -N-methylamino-L-alanine (BMAA) exposures in adult SOD^{G93R} transgenic zebrafish. *Neurotoxicity Research*. 2023 Aug 8:1-5.

Whitaker MR, Banack SA, Mescher MC, Cox PA, De Moraes CM. BMAA in cycad-feeding Lepidoptera: defensive sequestration or bioaccumulation? *Frontiers in Ecology and Evolution*. 2023 May 2;11:1114636.

Zhang F, Icyuz M, Tollefsbol T, Cox PA, Banack SA, Sun LY. L-Serine influences epigenetic modifications to improve cognition and behaviors in growth hormone-releasing hormone knockout mice. *Biomedicines*. 2022 Dec 30;11(1):104.

Board of Directors

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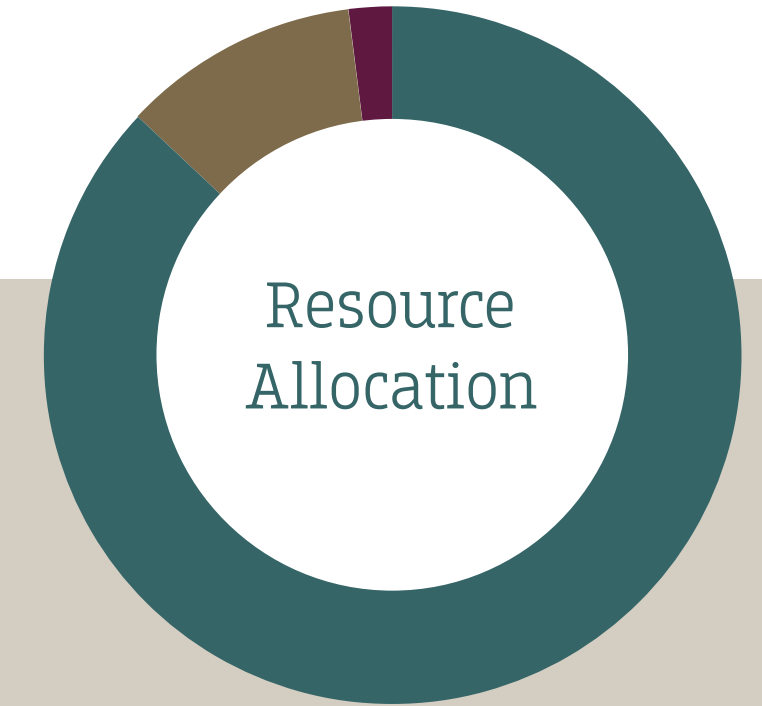
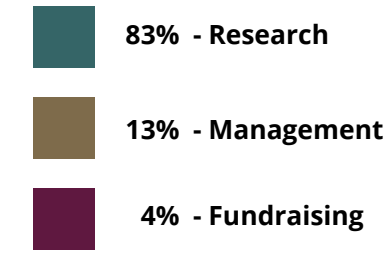
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Directors Emeritus

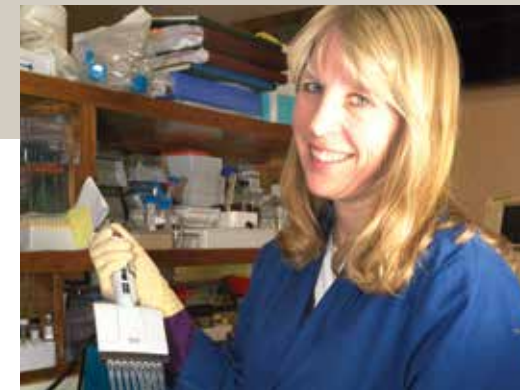
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Jackson, Wyoming

James Gorter
Jupiter Island, Florida

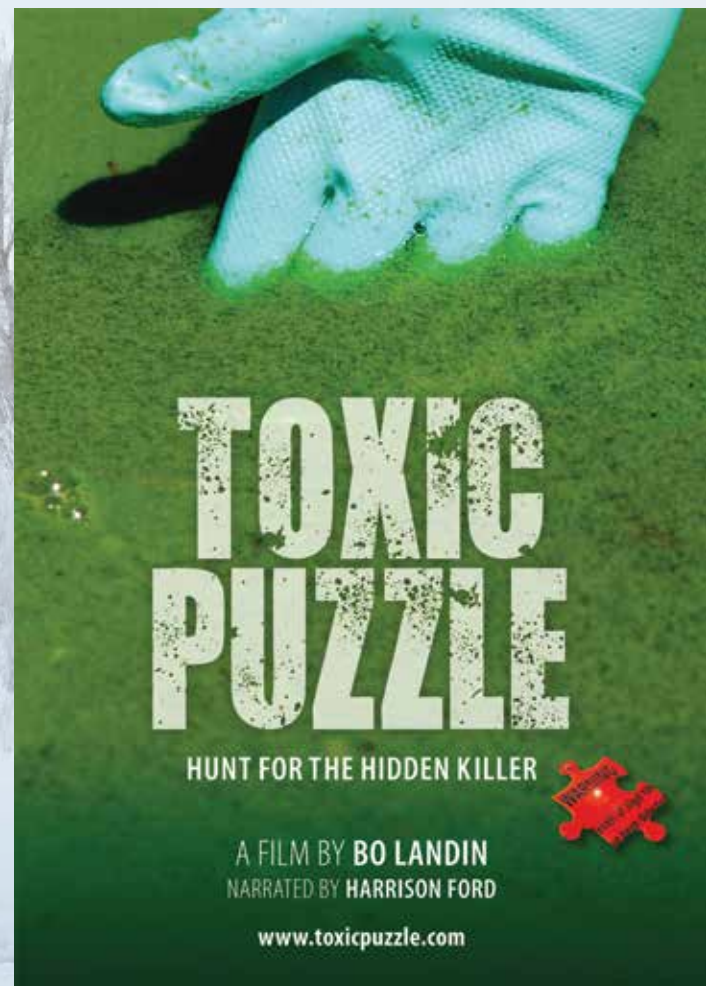
Finances



Operating on an annual budget of \$2.8 million, the Brain Chemistry Labs ensures that each donated dollar is carefully used. Based on our 2022 audit—which continued the string of “clean” audits since we began our laboratory—Brain Chemistry Labs devotes 83% of all gifts to medical research, with only 13% used for administrative and legal costs, and a scarce 4% for fundraising. This is why Charity Navigator gives us their top four-star rating.

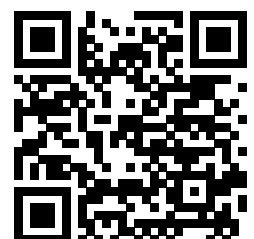


Complimentary Viewing of *Toxic Puzzle* Available



Swedish filmmaker Bo Landin followed our scientists from Jackson Hole to Guam—where neurodegenerative diseases had the highest incidence rate—to Ogimi, Japan where ALS and Alzheimer’s are unknown. You can view *Toxic Puzzle* at www.brainchemistrylabs.org or use the QR code.

SCAN ME



Harrison Ford, with Director Bo Landin, narrates *Toxic Puzzle*.

How You Can Help

Your gift can have a significant impact on preventing, diagnosing, and treating brain diseases. Innovative research leading to novel scientific discoveries, combined with tight financial management, means that your gift will have maximum value.

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organization.

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