

FRAXA
Research Foundation

IMPACT REPORT

October 2022



Dr. Tranfaglia

RESEARCH UPDATE

Michael Tranfaglia, MD, Medical Director and Co-founder

Things are moving fast in Fragile X research. It's back to business on all fronts, post-pandemic.

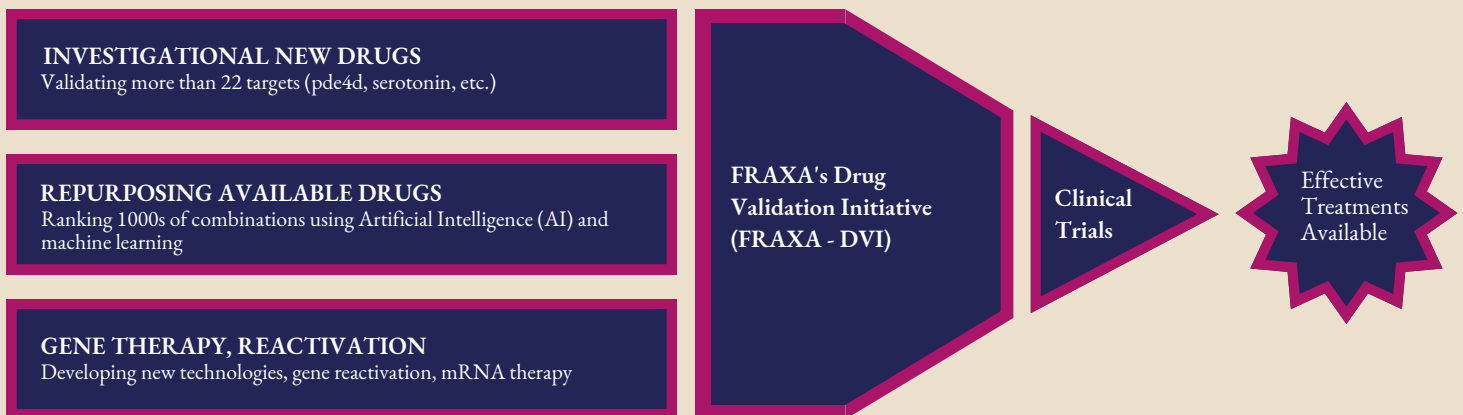
The recent unparalleled success of a FRAXA-funded phase 2 clinical trial has led to much larger pivotal clinical trials launching now. If this new round of trials is also successful, Tetra Therapeutics' PDE4D inhibitor will become the first officially approved treatment for Fragile X.

The promise of this approach, which evolved from much FRAXA funding over many years, has sparked renewed interest from other pharmaceutical companies. Not surprisingly, any company with a PDE4 inhibitor is suddenly interested in Fragile X. This surge of interest and investment extends to other drug classes as well, and so we are forging ahead, working diligently with many partners to advance multiple treatment options.

Getting new drugs to the market will always take longer than we would like. This is the rationale for repurposing available drugs, which has already led to 2 ongoing clinical trials in Fragile X, with more coming soon!

Efforts to reactivate the Fragile X gene have advanced markedly, thanks to FRAXA-funded research teams. We expect one or two companies to form around these discoveries in the coming year. Additionally, several companies are developing gene therapy approaches based on previous FRAXA-funded research, and we are now studying the possible use of mRNA vaccine technology to replace the Fragile X protein.

CURRENT STRATEGIES AT WORK TO TREAT OR CURE FRAGILE X



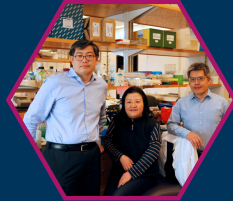
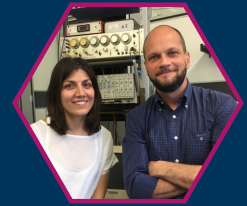
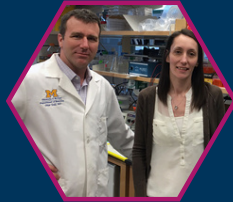
Dr. Snape

"I have interacted with FRAXA since 2006, as a researcher working in development of new medicines for Fragile X Syndrome. What attracted me to FRAXA in the first instance, and continues to be true today, is the role FRAXA has played in putting Fragile X syndrome on the radar of the pharmaceutical industry. Now there is an industry-wide pipeline of programs in development across many companies. I think it is a simple truth that without FRAXA this would not be the case. The initiatives FRAXA has in place have -- and continue to be -- crucial to this critical mass of effort to find new options for people with lives touched by Fragile X syndrome."

- Mike Snape, PhD, AMO Therapeutics

Current Projects Funded by FRAXA Research Foundation

<u>Principal Investigator</u>	<u>Institution</u>	<u>Project Total (over 2-3 years)</u>
Charles A. Nelson PhD <i>Neural Markers of Fragile X: a Powerful New Tool for Clinical Trials</i>	Boston Children's Hospital	\$90,000
Kathryn A. Whitehead PhD <i>mRNA Therapy for FX Syndrome</i>	Carnegie Mellon University	\$103,000
Ernest Pedapati PhD <i>Translational Studies of Fmr1 Gene Therapy for Fragile X Syndrome</i>	Cincinnati Children's Hospital	\$90,000
Craig Erickson MD <i>Use of FNIRS to Measure Treatment Response in Young Children With FXS</i>	Cincinnati Children's Hospital	\$90,000
Antonella Borreca PhD <i>Characterization of Microglia Transcriptional Profile in the FXS Mice Model</i>	CNR Institute of Neuroscience, Italy	\$90,000
Barbara Bardoni PhD <i>Characterization of Interneurons in the FXS Mouse Brain: Paving the Way for Cell-Replacement Therapy</i>	CNRS Valbonne, France	\$100,000
Gary Bassell PhD <i>Characterization and Modulation of MicroRNAs in Human Fragile X Syndrome</i>	Emory University School of Medicine	\$100,000
Peng Jin PhD <i>Towards Understanding FMRP-Mediated Gene Regulation in Human Brain Development</i>	Emory University School of Medicine	\$90,000
Tue Banke PhD <i>Developmental Profile of Glutamatergic Synapses and their Properties in a Model of FXS</i>	Emory University School of Medicine	\$90,000
Hirofumi Morishita MD, PhD <i>Pharmacological Modulation of Nicotinic Signaling to Ameliorate Cognitive Deficits in Fragile X Mice</i>	Icahn School of Medicine at Mt Sinai	\$100,000
Stephane Martin PhD <i>Exploring Drug Repurposing to Restore the Hippocampal Function in FXS Mouse Models</i>	IPMC Valbonne, France	\$90,000
Alberto Martire PhD <i>Exosomes as a Source of Therapeutic Biomarkers in Experimental Models of Fragile X</i>	Istituto Superiore di Sanità, Italy	\$100,000
Jeannie T. Lee MD, PhD <i>Reactivating the Fmr1 Gene to Reverse Fragile X Syndrome</i>	Massachusetts General Hospital	\$140,000
Clinton Canal PhD <i>Targeting Serotonin 1a Receptors to Treat Neuronal Hyperexcitability and Neuroanatomical Perturbations in FXS Mice</i>	Mercer University	\$100,000
Daniele Di Marino PhD <i>A Novel CYFIP1-Derived Peptidomimetic Restoring Dysregulated mRNAs Translation: An Innovative Therapeutic Strategy</i>	Polytechnic University of Marche, Italy	\$90,000
Sean McBride MD, PhD <i>Translating Novel Treatments for Fragile X Syndrome from the Fly to the Mouse Model</i>	Rowan University	\$45,000
Elizabeth Berry-Kravis MD, PhD <i>Trial of Ergoloid Mesylates, 5-Hydroxytryptophan, and the Combination in Adult Males with Fragile X</i>	Rush University Medical Center	\$106,600
Nicola Allen PhD <i>Screening Combinatorial Pharmacological Therapies for Fragile X Syndrome</i>	Salk Institute for Biological Studies	\$90,000
Philippe Jacques Mourrain PhD <i>Screening Combinatorial Pharmacological Therapies for Fragile X Syndrome</i>	Stanford University	\$90,000
Yongjie Yang PhD <i>Human Fmr1 Isoform-Specific Regulation of Translation and Behavior</i>	Tufts University School of Medicine	\$100,000
Andres Ozaita PhD <i>Assessing Transcriptional Signatures Sensitive to Cognition-Improving Pharmacological Treatments in FXS</i>	Universitat Pompeu Fabra, Spain	\$100,000
Artuela Caku MD <i>Investigation of the Link Between Lipid Profile, ECbome System and Gut Microbiota in Fragile X</i>	Université de Sherbrooke, Canada	\$90,000



<u>Principal Investigator</u>	<u>Institution</u>	<u>Project Total (over 2-3 years)</u>
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Frank Kooy PhD	University of Antwerp, Belgium	\$100,000
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Combining Multi-Electrode Array (MEA) and Live Mouse Tracker (LMT) to Screen Drugs for Fragile X

Mahmoud A. Pouladi PhD	University of British Columbia	\$100,000
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Evaluating the Sigma-1 Receptor as a Therapeutic Target in Human Pluripotent Stem Cell Models of Fragile X

Ning Cheng PhD	University of Calgary, Canada	\$90,000
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Screen and Validate Novel Inhibitors of ERK Signalling to Treat Fragile X Syndrome

Iryna Ethell PhD	University of California, Riverside	\$100,000
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Combining Gene Reactivation with Controlled Sound Exposure to Treat FXS

Khaleel Abdulrazak PhD	University of California, Riverside	\$100,000
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Targeting Serotonin 1a Receptors During Development to Reverse Neurobehavioral Phenotypes in FXS Mice

Devin Binder MD, PhD	University of California, Riverside	\$100,000
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Cannabinoids As a Treatment for Fragile X Syndrome

Oswald Steward PhD	University of California at Irvine	\$100,000
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Modulation of Inhibitory Circuits and Translation-Dependent Pathways to Amend Cognitive Function

Carlos Portera-Cailliau PhD	University of California at Los Angeles	\$45,000
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Correcting Sensory Processing in Fragile X Mice by Modulating Kv3.1

Patricia Cogram PhD	University of Chile	\$120,000
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FRAXA-DVI: Drug Validation Initiative for Fragile X Syndrome

Maija Castren MD, PhD	University of Helsinki, Finland	\$45,000
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Contribution of Astrocytes to Beneficial Responses of Lovastatin in Fragile X Syndrome

Joel Richter PhD	University of Massachusetts	\$187,000
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Alternative Splicing in White Blood Cells: a Biomarker for Fragile X Syndrome

Anna Dunaevsky PhD	University of Nebraska	\$100,000
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Astrocyte Contribution to Sensory Hypersensitivity in FXS

Alessandra Murgia MD PhD	University of Padova, Italy	\$100,000
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Fragile X Developmental Motor Phenotype: Assessing Motor Control Through Innovative Gait Analysis and Defining Biomarkers

Nicola Elvassore PhD	University of Padova, Italy	\$90,000
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FMR1 Silencing & Stability During Human Brain Development; From Early Stage of Pluripotency to 3d Cortical Organoids of Patients

Lynne Maquat PhD	University of Rochester	\$90,000
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Using FXS Mice to Assess the Therapeutic Value of Inhibiting Nonsense - Mediated mRNA Decay as a Function of Development

Jay Gibson PhD	University of Texas at Southwestern	\$90,000
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Circuit Mechanisms for Auditory System Dysfunction and Drug Tolerance in the Inferior Colliculus of FXS Mice

Brian Christie PhD	University of Victoria, Canada	\$90,000
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Adiponectin As a Potential Therapy in Fragile X Syndrome

Xinyu Zhao PhD	University of Wisconsin-Madison	\$90,000
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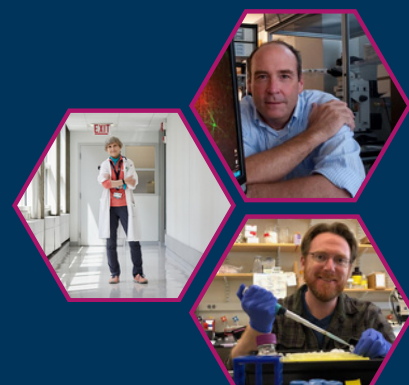
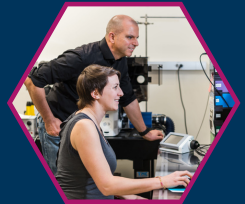
Identifying Cellular and Molecular Signatures in Human Neurons That Distinguish FXS Patients with Divergent EEG Profiles

Cara Westmark PhD	University of Wisconsin-Madison	\$90,000
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Preclinical Testing of High Fat/Low Carb Diets in Fragile X Mice and Cells

Kimberly F. Raab-Graham PhD	Wake Forest University Health Sciences	\$90,000
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Repurposing FDA-Approved Drugs to Treat Major Depressive Disorder in Fragile X Syndrome





World
FRAGILE X
Day

383
Landmarks

18
Countries

5
Continents

13
Sponsors

19
Partners

World Fragile X Day (WFXD) celebrates families impacted by Fragile X and highlights advancements of research to find effective treatments and ultimately a cure.

The world shone bright on July 22, 2022 for World Fragile X Day, with an impressive 383 locations on 5 continents illuminated. While it is difficult to pick a favorite lighting, Chicago's Blue Cross Blue Shield building sparked the most excitement by displaying "Fragile X" in big bright letters.

Many new countries joined our efforts this year. First-time illuminations were seen in Austria, Denmark, Indonesia, Italy, Portugal, Uruguay, and the United Kingdom! There were illuminations in 18 countries on 5 continents! Online, we broadcast "*Fragile X Syndrome: Innovative Approaches to Finding a Cure*" which showcased 30+ scientists each presenting a unique approach to finding a cure.

World Fragile X Day is an initiative of FRAXA Research Foundation launched in 2021 with communities around the globe. WFXD is bringing more and more new research teams into the race to find a cure.

Visit worldfragilexday.com to get involved and make 2023 the most successful awareness day ever!



FUNDRAISING HIGHLIGHTS

FRAXA relies on contributions from thousands of individuals who want to be part of building better lives for families everywhere. We receive no government funding. An investment in FRAXA is an investment in the future of those living with Fragile X. Become a partner in our life-changing work by hosting an event or donating to FRAXA today.



FRAXA's ANNUAL APPEAL Everywhere - Our largest fundraiser happens each fall through our annual appeal. Thousands of contributors provide over 60% of FRAXA's income by mailing in donations or giving online. The annual appeal brings in around \$1 million dollars each year, enabling us to fund new Fragile X research.

PATRICK'S PALS TOURNAMENT Cambridge MA - This remarkable 3 on 3 basketball tournament has run for almost 25 years thanks to Fragile X parents James & Pamela Vershow and their incredible team of volunteers!



CALLUM CUP Millburn, NJ - This annual intra-club charity match is the marquee event of the Millburn FC soccer calendar. The game honors Callum Murphy, son of goalkeeper Andrew Murphy.

HALL GOLF TOURNAMENT Haverhill, MA - Brothers Pete and Dave Hall host an Annual Charity Golf Tournament. For the fifteenth consecutive year the money raised has gone to FRAXA, raising over \$262,000 for Fragile X research!



POKER RUN Sparta, NC - For over 15 years the Charlton Family has hosted their annual Poker Run. Over 100 motorcycles travel through 4 states along the Blue Ridge Parkway raising money for FRAXA.

WALK FOR FRAGILE X Derry, NH - Fragile X grandparents Darlene and Pat Donovan host an annual Fragile X 5K in honor of Elias. With the support of family, friends, and the community, raffles top off this great event.





SARDINA ICE CREAM EVENT Lititz, PA - The sweetest of all fundraisers is hosted by the Sardina family who matches all donations from ice cream sales each fall in honor of their son, JT.

SWIRL WINE TASTING Naples, FL - Debra and Kevin Fennessey and Ginna & Pidge Goodrich hosted family and friends for a Wine Tasting and Silent Auction, raising over \$65,000 for Fragile X research.



3 PEAKS CHALLENGE North Wales, UK - To raise money for FRAXA research, Fragile X father Michael Leonard climbed 3 peaks: Ben Nevis in Scotland, Scafell Pike in England, and Snowdon in Wales.

COMPANY MATCH WEEK New York, NY - Fragile X father Lou Barbera and his partners at VLM Commodities challenged staff and clients to donate their earnings to Fragile X research, raising \$10,000 in one week!



FLATBREAD PIZZA FUNDRAISER Amesbury, MA - This family-friendly fundraiser brought one family over 3 hours to meet others with Fragile X (and enjoy delicious pizza!) It was a tasty event filled with laughter and new friendships.

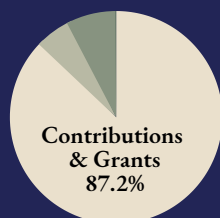
BOSTON BRUINS 50/50 NIGHT Boston, MA - Each year the Boston Bruins Foundation invites FRAXA to host a 50/50 raffle with all proceeds going to fund Fragile X research. FRAXA is proud to partner with the Bruins!



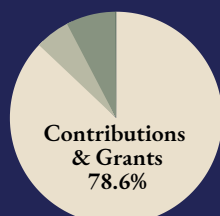
WORLD FRAGILE X DAY CELEBRATIONS Everywhere - World Fragile X Day inspired families and friends throughout the world. This Boston gathering was one of many events celebrating landmarks illuminated for Fragile X.



2021 Income

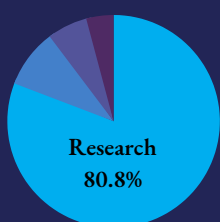


2022 Income *through 9/30/22

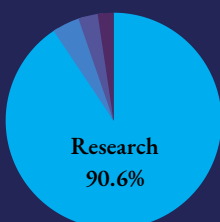


FRAXA's funding comes from individuals and organizations who believe in our mission. We receive no government funding.

2021 Expenses



2022 Expenses *through 9/30/22



FRAXA's priority is research, with over 80% of our budget supporting research grants and clinical trials. 90% of FRAXA's funding goes directly to our programs!

FINANCIAL HIGHLIGHTS

FRAXA recognizes the responsibility that comes with your contribution and is proud to be continually recognized as one of the most reliable stewards of donor gifts. We earn the highest marks possible from major nonprofit rating agencies.

INCOME	2021*	2022**
Contributions and Grants	1,915,294	727,282
Fundraising Events	116,223	196,238
Interest & Investment Income	<u>165,723</u>	
Total Revenue and Support	2,197,240	925,940
EXPENSES	2021*	2022**
Research Program	1,126,798	1,363,443
Education Program	124,390	61,579
Fundraising	85,498	43,829
Administration	<u>57,958</u>	<u>35,634</u>
Total Expenses	1,394,644	1,504,485
ASSETS	2021*	2022**
Change in Net Assets	802,596	[578,545]
Net Assets - Start of Period	<u>3,092,475</u>	<u>3,902,071</u>
Net Assets - End of Period	3,902,071	3,323,526



*2021 Audited financial statements and 990s can be found at fraxa.org/about

**2022 numbers through 9/30/22 are unaudited and preliminary

I have no doubt that we will see effective treatments and, ultimately, a cure for Fragile X. Many preclinical research studies and a successful clinical trial have demonstrated that Fragile X symptoms can be reduced - at least partially - even for adults.

Much work remains to be done to close the knowledge gaps. Talented, dedicated university-based research teams and pharmaceutical and biotechnology experts are joining the Fragile X field, coming up with new approaches and solutions.

The biggest roadblock is lack of funds. Funds are the key to shorten the timeline to our goal.

Your support has enabled the progress made so far! Thanks to your donations, we have overcome daunting roadblocks that looked insurmountable. With your continuing support, we are certain that we can push beyond the remaining obstacles to deliver effective treatments and a cure for Fragile X syndrome.

Katie Aggs

President and Co-founder



Thank you

to all our donors and volunteers for joining this life-changing journey!

"FRAXA lives and breathes its mission to help the Fragile X community through funding cutting-edge research. I know when I support and donate to FRAXA, they will be excellent stewards of my contributions. The research they are funding will ensure a bright future for my son."
- Sara Hamilton



"FRAXA has given our family so much hope. We've reached out to their leadership for advice about medications and research trials. We are enrolling our teenage son in one and really excited about its potential. FRAXA helped designed this trial and funded its early phases. If they hadn't built relationships and expertise like they have, we wouldn't have access to groundbreaking studies like this. We are so excited."
- Jennifer Frobish

One of our company founders has a grandchild who has Fragile X. As a result we have engaged the company to support FRAXA's efforts and have found them to be a wealth of information. We have had numerous interactions with the founders and have experienced a high level of commitment and integrity."
- Ken Steinberg



FRAXA
Research Foundation

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fraxa.org