DukeHealth

Department of Neurology

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Dear Friends of the Duke ALS Program,

How 2024 has flown by! Thanks to your generosity, we just had our most exciting and productive year ever.

All our education, advocacy, and research programs are built on a foundation of great patient care. In 2024, we welcomed a record number of diverse people living with ALS in our multi-disciplinary (https://alsclinic.duke.edu/our-team/) and telemedicine (https://alsclinic.duke.edu/telemedecine/) clinics.

Members of our team published 14 papers in peer-reviewed literature this year (https://pubmed.ncbi.nlm.nih.gov/?term=bedlack&sort=date) and gave dozens of lectures to people living with ALS, as well as students, clinicians and scientists all over the world. Many of these are available online, and the recordings have already been viewed over 30,000 times (ex. https://www.youtube.com/watch?v=I4WEXTmegi8, https://www.youtube.com/watch?v=vz44vdFEV-Q)

We led 5 more Clinical Research Learning Institutes, training people living with ALS to be even more powerful research advocates. There are now 800 graduates from these programs, and they are helping to change laws, raise funds, design more patient-centric studies, educate regulators and pressure payors toward optimizing ALS care and research (https://www.tandfonline.com/doi/10.1080/21678421.2019.1690519?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed). Thanks to a very generous supporter, we received a $1 million endowment in 2024 which will help ensure that these wonderful programs endure.

Dr Li and I again managed the unique, award-winning ALSUntangled program (www.alsuntangled.org) , which scientifically reviews alternative and off label treatments to help people living with ALS to make more informed decisions about them. We reviewed 5 new products this year, as well as updating and recording podcasts (https://www.spreaker.com/podcast/create-podcast--2845933) about older ones. We also published a detailed description of the 8 most promising products we have found in our 15-

year existence (https://onlinelibrary.wiley.com/doi/10.1002/ana.27126). ALSUntangled articles are now being translated into multiple languages and collectively have over 300,000 downloads.

We continued our innovative studies on people with ALS who progress to disability, then unexpectedly recover most or all of their lost motor function. While such "ALS reversals" have been reported since the 1960s, no one before had ever found an explanation. This year we published on a genetic finding in ALS reversals that might explain their recovery-a mutation in a gene controlling the expression of a protein called IGFBP7 (https://www.neurology.org/doi/10.1212/WNL.0000000000209696?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed). We collaborated with ALS TDI on a follow up study of IGFBP7 protein expression in the blood. While this underpowered study showed significantly higher IGFBP7 levels in people with ALS compared to healthy controls, it did not show a difference between the 11 ALS reversals that were studied and those who had not yet reversed (https://www.als.net/news/als-tdi-and-dr-rick-bedlack-igfbp7/). Of course, blood and brain levels may not be the same. We have very recent data from another collaborator confirming that IGFBP7 levels in the brain and spinal cord of people living with ALS are much higher than healthy controls. This appears to be true in other neurodegenerative diseases, too. In 2025, we plan to conduct a trial targeting IGFBP7 reduction in the brain with the hope of stopping or reversing ALS in all participants.

Far more common than ALS reversals are patients with very slow progression, including some who live with the disease for more than a decade. Over the past few years we have confirmed differences in the gut microbiome that might explain very slow (and very fast) ALS progression. Capitalizing on these learnings, we plan to launch trials of a probiotic called BL-001, and separately of fecal transplants, here in 2025. A major source of funding for these trials will come from our amazing friends at Hop On A Cure, who awarded me with their first ever "Accelerate a Miracle Project" this year (https://www.biospace.com/hop-on-a-cure-announces-grant-for-duke-university-als-clinic-study-on-efficacy-of-bl-001-in-people-with-als).

In addition to participating in the Combat ALS Phase 3 trial, the Healey Platform Trial, and expanded access programs for CNM-Au8, Pridopidine and Ibudilast, this year we also opened and rapidly filled our most outside-the-box trial to date: ROAR-DIGAP (https://clinicaltrials.gov/study/NCT06429059?cond=ALS&term=DIGAP&rank=1). Here we are using a new technology from GenieUS called Deep Integrated Genomics Analysis Platform (https://www.genieus.co/digap) to categorize each participant's ALS in terms of the molecular pathway most likely driving their progression. Each participant then gets a personalized treatment that was previously associated with at least 1 ALS reversal. Results are expected in mid-2025.

Beyond all this, we continue to build unique bridges, and to raise awareness and hope in our own creative ways. We had a blast traveling around the country to participate in events organized by people living with ALS, including golf tournaments, art shows, dinners, concerts and record release parties. Earlier this month we partnered with the NC State Fashion School to create new clothing lines that are both stylish and adaptive. And just last week we finished shooting a movie called "Stitching Strength" with Glassfire Studies. This documentary short will highlight my use of creativity, especially fashion, to generate positivity and hope. You can watch the trailer here https://www.youtube.com/watch?v=ZmMTqw1ch9w

None of this would be possible without partners like you who support our work. Margaret Meade once said: "never doubt that a small group of committed citizens can work together to make a difference. In fact, that is the only thing that ever does." Thanks for being part of a small group that cares about creating more options, more hope, and eventually a cure for people living with ALS. Can't wait to see where we go together in 2025!

Sincerely,

Richard Bedlack MD PhD

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