CURE LBSL

Disease	• LBSL
Full name	• Leukoencephalopathy with Brain Stem and Spinal Cord Involvement and Lactate Elevation
Alternate	• Mitochondrial Aspartyl-tRNA Synthetase Deficiency
Nickname	• "Awesome Disease"
Disease Description	• Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) is a rare leukodystrophy caused by biallelic mutations in the DARS2 gene and characterized by progressive ataxia and spasticity with proprioceptive deficits. Deterioration of motor skills starts in childhood and often progresses to loss of independent walking by adulthood. (KKI) • LBSL is an ultra-rare, progressive, genetic condition that is both a mitochondrial disorder (affecting energy to the cells), and a form of leukodystrophy (affecting the brain, spinal cord, and nerves). • First identified in 2004, LBSL is caused by mutations in the DARS2 gene, which provides the body with instructions for making an enzyme called mitochondrial aspartyl-tRNA synthetase. This enzyme is important for production of proteins in the mitochondria – the energy factories of our cells, which turn nutrients into energy. As a result of mutations in DARS2, certain parts of nervous system do not have sufficient energy to function properly affecting their function and the production of myelin. • LBSL can manifest as infantile onset, early childhood onset, late childhood onset, and adult onset.

Genetics	• Gene: DARS2
	• Chromosome 1q25
	• Inheritance: autosomal recessive
	• Variants:
	  • LOVD open database
	  • ClinVar Miner
	  • dbVar
	  • NIH Variation Viewer
	  • dbSNP

Classification	• OMIM: 611105
	• Gene/locus: 610956
	• ORPHA: 137898
	• ICD-10:
	  • E88.8 - Other specified metabolic disorders
	  • E75.2 - Other sphingolipidosis
	• GARD: 12652
	• UMLS: C1970180
	• PHAROS
	• MONDO:0012622
	• UniProt: Q6PI48
	• NCBI: 55157
	• SNOMED CT: 703537008
	• HGNC: 25538

Disease categories	• Leukodystrophy/leukoencephalopathy • Mitochondrial disorder • Rare disease
Comprehensive Reviews	• Orphanet • GeneReviews • MedlinePlus • GARD • MalaCards

Umbrella disease organizations	Leukodystrophy • United Leukodystrophy Foundation Mitochondrial Disorders • United Mitochondrial Disease Foundation • MitoAction Rare Disorders • NORD – National Organization for Rare Disorders • EURORDIS – Rare Diseases Europe
Referral centers	• Kennedy Krieger Institute – Moser Center for Leukodystrophies (Baltimore, US) • Childrens Hospital of Philadelphia – Leukodystrophy Center of Excellence (Philadelphia, US) • Massachusetts General Hospital – Leukodystrophy Clinic (Boston, US) • University of Utah – Leukodystrophy Clinic (Salt Lake City, US) • Amsterdam University Medical Center - Center for Children with White Matter Disorders (Amsterdam, NL) • GLIA Network Leukodystrophy Centers
Clinical Care Team	• United Leukodystrophy – find a physician • Mitochondrial Care Network
Patient connection forums	Forums moderated by CureLBSL staff • LBSL Families (private Facebook group) • Rare Connect – LBSL Community
Patient apps	• MitoAction mobile app
Patient registry	• International LBSL Patient Registry (2022/2023)
Biobank	• North American Mitochondrial Disease Consortium (NAMDC) Patient Registry and Biorepository
Research Consortium	• www.lbslresearch.com

Patient Advocacy Group	Cure LBSL (formerly A Cure For Ellie) • www.curelbsl.org • www.acureforellie.org
Social Media	Instagram Facebook Twitter YouTube LinkedIn
Patient connection forums	Forums moderated by CureLBSL staff • LBSL Families (private Facebook group) • Rare Connect – LBSL Community (13 world languages)
Non-profit status	A Cure For Ellie (doing business as "Cure LBSL") is a 501(c)(3) organization, with an IRS ruling year of 2013, and donations are tax-deductible. • Charity Navigator • Guidestar • CauseIQ
Leadership & Staff	• Beth McGinn – Executive Director and Founder • Mike McGinn – Executive Director and Founder • Melody Kisor – Director of Patient Engagement
Board	• https://acureforellie.org/board-of-directors/
Media	• In the news
Professional Affiliations	• Chan Zuckerberg Inititiative - RAO Network • NORD – 2022 Platinum Member • Kennedy Krieger Institute Board of Directors • GLIA – Global Leukodystrophy Initiative
Fundraising	• Network for Good donation site • Giving Tuesday • Silent Auction • Fairlington 5K

Research links	• PubMed • Google Scholar • Researchgate
Research updates	• 2022 • 2021 • 2020 • 2019
Clinical trials	• United States • Europe
LBSL Natural History Study	https://clinicaltrials.gov/ct2/show/NCT03624374 • USA – Dr. Amena Smith Fine - Kennedy Krieger Institute (JHU) • Netherlands – Dr. Marc Engelen - Amsterdam University Medical Center • Finland – Dr. Emil Ylikallio - University of Helsinki • Brazil – To Be Determined (expected in early 2023)
Current therapies	• Mito cocktail • Rehabilitation medicine and physical therapy • Nutrition • Supportive Care
Potential/ emerging therapies	• ASO • AAV9 • Drug Repurposing • Ethylmethylhydroxypyridine Succinate (EMHS)
LBSL Patient Protocols	• LBSL Patient Protocol Coversheet • Head injury (coming soon)

2022 LBSL International Patient Conference (Hybrid)	"Information is Power" • English summary and slides • Russian interpreter recording • Portuguese interpreter recording •
2020 LBSL Conference (Virtual)	"Connection, Collaboration, Cures" • Agenda • Videos
2018 LBSL Conference (In-person)	• Summary • Video: Clinical Discussion of LBSL & trials • Video: Management of Mitochondrial disease and role of supplements and emergency protocols • Video: LBSL Research Update • Video: Genetics 101: LBSL-Specific Mutations • Video: Nutrition • Video: Clinical Studies Update • Video: Overcoming social challenges • Video: Fundraising to find a cure • Video: Function and Malfunction of Mitochondria and tRNA Synthetases • Video: Advocating for yourself or your child • Video #6: One Man's Perspective on Living with LBSL
2022 GLIA Scientific Meeting	• LBSL & HBSL Workgroup
Conference travel stipends	• Thisbe and Noah • Cure LBSL foundation: info@curelbsl.org
Medical transportation	• Angel Flight • PALS SkyHope