Clinic *for* Special Children
535 Bunker Hill Road, PO Box 128, Strasburg, PA 17579 **T** 717.687.9407 **F** 717.687.9237

Contact: Kelly Cullen
P | 717-687-9407
E | kcullen@clinicforspecialchildren.org

FOR IMMEDIATE RELEASE

CLINIC FOR SPECIAL CHILDREN RESEARCHERS CONTRIBUTE TO NOVEL DISCOVERY OF *DE NOVO* AND INHERITED VARIANTS IN *GBF1*

STRASBURG, PA- A new study details the identification of pathogenic variants in the gene *GBF1* in four unrelated families with individuals affected by Charcot-Marie-Tooth neuropathy (CMT2) or hereditary motor neuropathies (HMNs). The study includes a long-term patient of the Clinic for Special Children (CSC) and details an example of gene discovery work at CSC. The project was a broad, international collaborative effort with contributions from clinicians and researchers at CSC and appears in *The American Journal of Human Genetics* in September 2020.

The study included genomic sequencing analyses in seven affected individuals of German, Belgian, and Old Order Amish descent and uncovered four distinct heterozygous *GBF1* variants, two of which occurred *de novo*. The common presenting symptoms of the affected individuals were motor neuropathy that mostly affected the foot muscles resulting in foot abnormalities or deformities with gait disturbance. Electrophysiological studies showed damage to nerve axons and chronic neurogenic changes. While the study's participants exhibited similar symptoms, through next generation sequencing (NGS) it was discovered that they had distinct and novel changes in the same *GBF1* gene.

The researchers also conducted functional work in the lab to show how the specific variants in the *GBF1* gene exhibited disease in a murine (mouse) model. The results shown in the study demonstrate that pathogenic variants in *GBF1* are associated with CMT2 and HMNs and reinforce the existing link between neurodegeneration and Golgi fragmentation.

###

The research was conducted by a team including the study's first authors Natalia Mendoza-Ferreira and Mert Karakaya from the Institute of Human Genetics, Center for Molecular Medicine Cologne, Center for Rare Diseases Cologne, and Institute for Genetics, University of Cologne, Cologne, Germany; senior author Brunhilde Wirth from the Institute of Human Genetics, Center for Molecular Medicine Cologne, Center for Rare Diseases Cologne, and Institute for Genetics, University of Cologne, Cologne, Germany; Nur Cengiz, Nico Fuhrmann, Irmgard Holker, Maximilian P. Thelen, Sebastian Zetzsche, and Roman Rombo from the Institute of Human Genetics, Center for Molecular Medicine Cologne, Center for Rare Diseases Cologne, and Institute for Genetics, University of Cologne, Cologne, Germany, Danique Beijer and Tine Deconinck from Translational Neurosciences, Faculty of Medicine, University of Antwerp, B-2610 Wilrijk, Belgium and Laboratory of Neuromuscular Pathology, Institute Born-Bunge, University of Antwerp, B-2610 Wilrijk, Belgium, Karlla W. Brigatti, Erik G. Puffenberger, Kevin A. Strauss, and Vincent Carson from the Clinic for Special Children, Strasburg, PA 17579 USA, Claudia Gonzaga-Jauregui from Regeneron Genetics Center, Regeneron Pharmaceuticals Inc., Tarrytown, NY 10591 USA, Peter De Jonghe and Jonathan Baets from Translational Neurosciences, Faculty of Medicine, University of Antwerp, B-2610 Wilrijk, Belgium and Laboratory of Neuromuscular Pathology, Institute Born-Bunge, University of Antwerp, B-2610 Wilrijk, Belgium, and Neuromuscular Reference Centre, Department of Neurology, Antwerpen University Hospital, B-2650 Edegem, Belgium, Stephan Zuchner from Dr. John T. Macdonald Foundation Department of Human Genetics and Hussman Institute for Human Genomics, Miller School of Medicine, University of Miami, Miami, 33136 FL, USA, Bertold Schrank from DKD Helios Klinik, Department of Neurology, 65191, Wiesbaden, Germany, and Gilbert Wunderlich from Department of Neurology and Center for Rare Diseases, University Hospital Cologne, 50931 Cologne, Germany.

About the Clinic for Special Children

The Clinic for Special Children (CSC) is a non-profit organization located in Strasburg, PA, which provides primary pediatric care and advanced laboratory services to those who suffer from genetic or other complex medical disorders. Founded in 1989, the organization provides services to over 1,050 active patients and is recognized as a world-leader in translational and precision medicine. The organization is primarily supported through community fundraising events and donations. For more information, please visit www.ClinicforSpecialChildren.org