

### EDITORIAL



## Unique role of patient advocacy groups in clinical development of CGTx for rare diseases

Michelle Berg

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We’ve all heard those amazing stories where a tiny-framed mother channels her inner Hulk to lift a car off of her child, or the dad who stands between his children and a wild animal on the attack; each finding superhuman strength and ferocity in spite of incredible, if not impossible odds. These are examples of a phenomena called hysterical strength where, for a

brief moment in time, an ultra-surge of epinephrine and norepinephrine result in an immediate burst of oxygen to the muscles, an adrenaline rush resulting in the fight or flight response. It [hysterical strength] is the reaction that any parent imagines and believes that they could muster in that moment of need to protect or save their child.

Now, consider the level of strength that must be mustered and maintained in order to care for a child diagnosed with a rare and fatal disease. Such a disease, unheard of and therefore most likely without an approved therapy or drug, steals away precious skills built-up over the first years of life. The impact of this type of disease transforms a

once vivacious and full of potential child to an immobile, silent, and greatly redacted version until death carries them to eternal sleep. There are an estimated 7,000 rare diseases (defined as such in the USA if 200,000 or less are affected) of which half impact a pediatric population. The majority, an estimated 80%, of rare diseases, are genetic in origin of which half impact children – 30% of those children will not live to the age of 5 years old. The losses mourned by families are not only that of the out-of-order

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and early end to life, but also extend into what the majority of parents take for granted. Suddenly the tiny things become major and every remaining moment is a stingily doled out gift from TIME – the ultimate enemy who steals more with each passing moment. Every ‘I love you’ or call by name becomes a celebration, stacking a block atop another or identifying a color signifies a huge victory, and showing joy with a smirk or a flash of a smile is a significant day brightener. The normal that once was envisioned for a child, the family, for oneself, is swiftly and cruelly decimated with one passing moment of receiving the diagnosis and then being told that all you can do is take your child home, make him comfortable, and enjoy the remaining days to the fullest before he is gone.

Through this progressive march towards the inevitable, each parent or caregiver’s calling is put forth

along with the option to choose to respond in a multitude of ways, all acceptable and safe from judgment since it is each individual’s choice. These are a growing number of pioneering parents who have outright refused to accept the fate of a rare disease diagnosis for their child, bucking the trite recommendation to ‘take the child home and love him, keep him comfortable’ and swapping it for waging war on the disease and state of research. Others vow to create a legacy for their child who has lost the fight with a fatal rare disease, resolving to drive to a different future for other children who have yet to be diagnosed or even born with the same cruel rare disease. These unique power parents dig in, absorbing all they can on a significantly varied set of disciplines (genetics, molecular biology, healthcare coverage, educational plans, and medicine) that often leads them far from what their chosen vocation prepared them for. This means that in addition to caring for their ill child, advocating for his or her education and healthcare or mere recognition as a human life with worth, they become astute learners while staying on top of the everyday responsibilities of keeping a household on track and holding down a job. It is incredible what emerges when these parents choose to become citizen scientists, students of drug development, regulatory experts, rallying fundraisers, in some cases entrepreneurs.

A case in point where the coming of age for gene therapy research and rare disease advocacy align is held within one such rare disease called Sanfilippo syndrome. Sanfilippo syndrome, otherwise known as mucopolysaccharidosis (MPS) III, is a group of four genetic diseases,

referred to as MPS IIIA, MPS IIIB, MPS IIIC or MPS IIID, that are among 60 known lysosomal storage disorders. Children with MPS III are missing the enzyme needed to break down glycosaminoglycans or GAGs (long chains of sugar molecules), specifically, heparan sulfate (HS).

Without the missing enzyme, cells within the body are not functioning properly and as a result, to fully break down and replace heparan sulfate (HS), a material that is necessary for building connective tissues. The partially broken-down HS remains stored in cells of the body causing progressive damage. Infants and even toddlers may not show signs of the disease, but as more cells are damaged throughout the body, symptoms gradually appear. Children begin to show neurological and physical decline including loss of skills such as speaking, walking, eating, increased difficult behavior and sleep issues. This regression continues to full dependence, leading to a severely shortened lifespan. The combined incidence of Sanfilippo is estimated to be 1 in 70,000 births and, to date, there is no cure, meaningful intervention or method for slowing the disease progression. Additionally, no standard of care exists as symptom management through trial and error are all that families are left with.

While it would be exciting and expected that the scientific and medical communities be the ones to relentlessly drive forth the callout for research in this terrible disease, surprisingly, it was an entirely different group who did so. Let's step back to 1995; a time when the internet and immediate connectivity of social media as we know it did

not exist. Enter Sue and Brad Wilson from the suburbs of Chicago, and their youngest daughter, Kirby, who was 4 at the time and full of an energetic and curious zest for life. This little ray of sunshine and all of her energy was not due solely to an exuberant personality but also the beginning effects of Sanfilippo. The buildup of the sugar molecules was

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well underway in the cells of her body causing hints of the disease yet not enough for a swift diagnosis. She would often go around to adults asking ‘happy?’ as if to wonder aloud if they were pleased and feeling good about their day. Soon after the diagnosis of MPS IIIB was finally received, Brad spent hours in the University of Chicago library with an assigned medical librarian learning all he could about Sanfilippo syndrome. This self-directed layman's research led him to a series of scientists whose names kept appearing in the all too few publications. Continuing on their path of resistance, Brad and Sue raised the necessary funds to directly support up and coming researchers who would become dedicated scientists, driven to progressing the research and understanding for Sanfilippo.

A number of years after the Wilsons began their advocacy efforts and research drive, another couple, Randall and Elisabeth Linton from Toronto also became immersed unwillingly when their daughter, Elisa, was diagnosed also with MPS IIIB. Their family joined the

fight, learning all they could, sharing about Elisa and Sanfilippo with their community of friends, neighbors and supporters. The advocacy for advancing the understanding the disease and moving the science forward was well underway, incorporating other non-profit Patient Advocacy Groups focused on Sanfilippo research. This advocacy and drive led to a number of academic research programs including the pre-clinical gene therapy efforts taken on eventually by Abeona Therapeutics, a biotechnology company focused on rare diseases and named after the Roman goddess said to watch over children as they start on their journey. It is exciting to note that though the organization's collaboration with the Sanfilippo community started in March of 2013 it continues to grow and make progress with advancement into clinical trial for both MPS IIIA and MPS IIIB programs.

These parents are moving mountains in response to their call on behalf of what they hope will be meaningful for their children, realizing along the way that this may mean the vision for what is meaningful may need to adjust. They are also very intentional about the

mission of saving future families from walking the same devastating path that a rare and fatal disease diagnosis brings. The beauty of gratitude and selflessness that emanates and the bright light they so readily share demonstrates that superhuman strength can persist over time and that it is indeed exponential.

#### FINANCIAL & COMPETING INTERESTS DISCLOSURE

*The author is an employee of Abeona, who are currently conducting clinical research for Sanfilippo syndrome. No writing assistance was utilized in the production of this manuscript.*

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