# Schinzel-Giedion Syndrome Patient Voice Publication

in collaboration with Nuala Summerfield of the Schinzel-Giedion Syndrome Foundation

## What is Schinzel-Giedion Syndrome (SGS)?

SGS is a severe, life-limiting condition caused by mutations in the *SETBP1* gene,[1–3] which plays a key role in the development of the brain and many other organs. Approximately 100 children worldwide have been diagnosed with SGS, but the true incidence is unknown.

Children with SGS have neurodevelopmental delay and uncontrollable seizures, and sadly many will die before their fourth birthday. Children with SGS also have gastrointestinal, urinary, and respiratory tract problems, as well as an increased risk of developing certain types of cancer.[2,3] There are no targeted treatments available.

**SGS symptoms can also include:**

- Cortical visual impairment
- Sleep disturbance
- Low muscle tone
- Feeding problems
- Characteristic facial features
- Cardiac defects


***"Ophelia attends a special needs school where she has 1:1 support from a highly trained teacher. The extensive daily therapies are crucial to help her interact with her environment and to maintain a comfortable range of movement. At home we need specialist medical equipment such as pumps (for oxygen, suction, and feeding), as well as home adaptations to install hoists and enable wheelchair accessibility."***

***"The impact of SGS is devastating, but a combination of early diagnosis and appropriate intervention and support can have a significant effect on quality of life and outcomes."***

***"My daughter Ophelia has recently celebrated her 10th birthday; although many children with SGS sadly do not survive as long as this, she is living proof that there is a spectrum of disease that is wider than may be first appreciated."***

## Burden of Therapy and Life Lost

SGS patients need high-level support and 24/7 care, which has a profound effect on the lives of both the affected child and their families. Children with SGS will have many hospital appointments and will be under the care of many different specialists for their entire lives.

There is a huge emotional impact on families, who often say they start the grieving process from the moment they receive the diagnosis of SGS, especially as the current prognosis and treatment options are so poor.

## Managing Symptoms

My daughter Ophelia is completely dependent on others for all of her care needs, and always will be. She has severe, medically refractory epilepsy, as well as difficulty sleeping, severe global developmental delay, and learning difficulties.

***"Due to visual and hearing impairment, interacting with her environment is challenging for my daughter. She is non-verbal, but she communicates with us through sounds and body language. She certainly knows what she likes and what she doesn't!***

***Ophelia cannot swallow properly, so she receives all nutrition and medications through a tube. She is also at risk of choking on her saliva so this needs to be suctioned frequently. Due to abnormalities with the structure and function of her urinary tract, she suffers from recurrent infections. She has low muscle tone and is unable to sit, stand, or walk, so she needs to use a wheelchair."***

## Trial Participation

Our research priority is targeting the severe epilepsy in our children. Existing research has suggested that the *SETBP1* gene may be a feasible treatment target at the post natal stage. We will also evaluate targets "downstream" of *SETBP1* to see if they may be implicated in the severe seizure phenotype.

Children born with SGS often spend time in neonatal intensive care due to significant breathing and feeding difficulties. So, by focussing on improving newborn genetic screening we can speed up the time to SGS diagnosis, which may improve outcomes.

We have a close-knit global community of families who realise the importance of research studies and are keen to collaborate. We are developing several different assets to facilitate research, including the first international SGS registry and natural history study, an SGS biorepository, and working to identify clinically relevant outcome measures and biomarkers.

## Hopes and Aspirations

- **In consultation with SGS parents and clinicians, the team at The Schinzel-Giedion Syndrome Foundation are targeting refractory seizures and proactively identifying academic and industry groups willing to work with us to accelerate this mission.**
- **There is just one Foundation representing the approx. 100 SGS patients currently identified around the world, and there is no cure for their extremely life-limiting condition. This is a global rescue mission.**

***"Our vision is for all children with SGS to receive a rapid genetic diagnosis and have access to effective therapies to ensure they live longer, healthier, and happier lives."***

Scan here to go to the SGS Foundation website for more information

Scan here to find out more about Patient Voice Publications

Schinzel-Giedion Syndrome Foundation


1. Banfi, F., Rubio, A., Zaghi, M. et al. SETBP1 accumulation induces P53 inhibition and genotoxic stress in neural progenitors underlying neurodegeneration in Schinzel-Giedion syndrome. Nat Commun 12, 4050 (2021). https://doi.org/10.1038/s41467-021-24391-3
2. Acuna-Hidalgo R, Deriziotis P, Steehouwer M, et al. Overlapping SETBP1 gain-of-function mutations in Schinzel-Giedion Syndrome and hematologic malignancies. PLOS Genetics 13(3) e1006683
3. Piazza R, Magistroni V, Redaelli S, et al. SETBP1 induces transcription of a network of development genes by acting as an epigenetic hub. Nat Comm 2018;9: 2192


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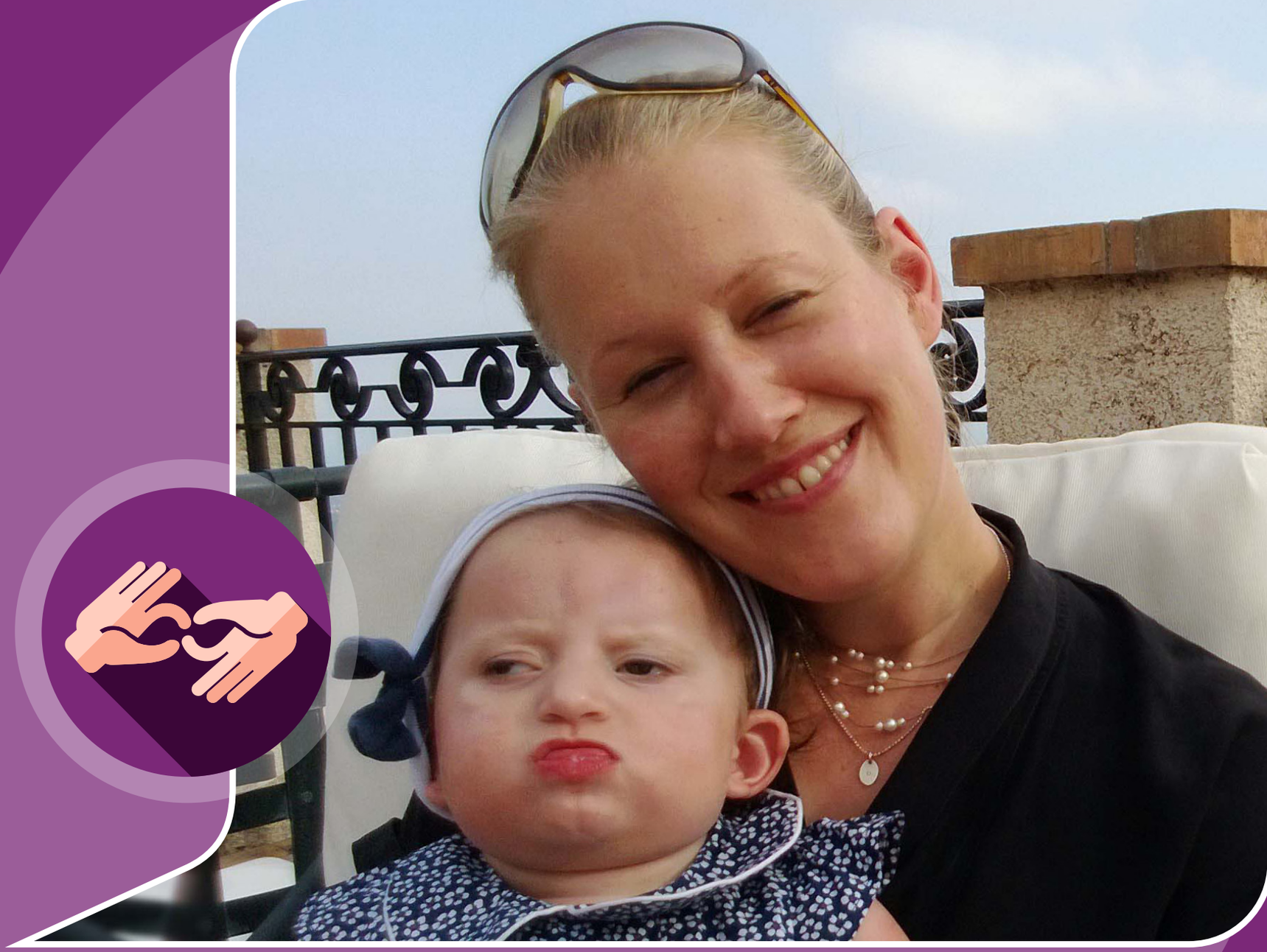

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