Research

The Ras/MAPK pathway brings growth regulating signals from outside the cell into the cell's nucleus. Within the cell, the information moves to the nucleus in a cascade. Our children's mutation is on the **HRAS gene**, which controls the *Hras function on the Ras/MAPK pathway in the cell*.

The HRAS gene instructs the Hras function in the cell, which acts like a gate that meters the flow of information as it cascades into the cell's nucleus. In our children, the gate gets stuck in the open position. This allows too much information into the nucleus.

The HRAS mutation is well-known to cancer researchers, so our children are able to benefit greatly from what is known so far about cancer with the same mutations. But unlike cancer tumors, our children have the mutation in every cell of their bodies ("germ line mutation").

The first benefit from cancer research was that we immediately had a gene test for it, which also made the cost for getting tested less expensive.

Researchers are working on how to translate what is known about cancer to help our children. For example, several medications already exist to make Hras close its gate. Might they help raise the quality of our children's life?

Stay tuned!

Please contact us

We'd like to help! Colin's website has a lot of information to share to share what we have gleaned, to help you and your doctors care for your child, as well as an international listserv. Our mission is to encourage and share information about Costello syndrome from home to hospital to school.

Joining through Colin's website also helps us keep you updated on the research efforts that may shed light on possible treatments – to allow you to choose to participate if you wish.

ICSSG
(International Costello Syndrome Support Group)
UK Registered Charity Number 1085605
Colin Stone, Webmaster and Founder, Helaina's Dad
http://costellokids.com
90, Parkfield Rd North, New Moston M/C40 3RQ
United Kingdom

CSFN
(Costello Syndrome Family Network)
a 501(c)(3) non-profit organization
1-(848) 228-CSFN (2736) – toll-free
PO Box 516
Woodinville, Washington 98072-0516
info@costellosyndromeusa.org
President: Sandra Taylor, Jill's Mom

RASopathies Network USA
a 501(c)(3) non-profit organization
Lisa Schoyer, Incorporator and Chair
Quin Johnson's Mom
244 Taos Road, Altadena CA 91001-3953
(626) 676-7694
http://rasopathies.org

012814

Costello Syndrome

A pamphlet for parents by parents

You are not alone!

We think there are about 300 people with Costello syndrome worldwide (most of whom are children), so what your child has is seriously rare, but we are here for you if you are seeking support and information. We are an active network of families who are willing to share and help. We understand much of what you're going through, because we've walked the same path.

Costello syndrome is a rare multiple congenital anomaly disorder in which individuals have characteristic craniofacial features, failure to thrive, ectodermal and musculoskeletal anomalies, cardiac abnormalities, endocrinopathy, developmental delay and a predisposition to neoplasia, both benign and malignant. [Estep et al, 2006]

A Spectrum of Issues

Since 2005, when the gene responsible for Costello syndrome – the HRAS gene – was identified, we continue to learn more about how an HRAS gene mutation affects our children's bodies ("genotype-phenotype correlations"). The most common mutation is known as G12S, which about 4/5 of all children who test positive for the Costello syndrome gene (HRAS) have. It appears that some mutations, though much rarer, may cause more or fewer issues.

The great news about our children is their sense of humor. Their charm and sheer resilience helps parents through the rough times. Our children are amazingly tough!

Here are some major issues our children can develop:

- Failure to thrive (FTT)
- Heart issues
- Cancer (about 15% chance)
- Orthopedic issues
- Endocrine issues
- Vision issues
- Global developmental delay

The first hurdle is usually the ***failure to thrive***, which can happen soon after birth, or several months later. As with colic, no one knows why. This is a stressful struggle that touches the core of parenting – being unable to nurture or console our child. Most children require a gastrostomy tube (g-tube) and extra calories. An enteral pump may be needed to provide formula at a slow enough rate that can be tolerated by your child's gut.

The low muscle tone that comes with Costello syndrome can affect peristalsis, which can easily be knocked off kilter by sudden changes like colds (with their extra mucus, causing (increased) vomiting and/or diarrhea), medical procedures (like ramping up the enteral feeding rate after surgery, etc.

Fortunately, families do learn how to nurture their child, and most children who get a gastrostomy tube (g-tube) outgrow the need of the g-tube (anywhere between ages 2-14).

Most of our children are born with or develop ***heart*** issues, but a number have also never developed anything for a cardiologist to follow. The mild end of the spectrum includes arrhythmias that respond to medication, and the severe end includes hypertrophic cardiomyopathy (HCM), also known as idiopathic hypertrophic subaortic stenosis (IHSS).

The risk of ***cancer*** is about 15%. The most common type is embryonal rhabdomyoscarcoma (eRMS), a childhood cancer. Regular ultrasounds are recommended to catch the cancer early for better treatment outcomes. Bladder carcinoma, the next most common, usually affects older adults, but has appeared in children w/Costello syndrome as young as 12 years old. Fortunately, this type of bladder cancer responds very well to treatment - no person with CS has been known to have died from this type. The third type of cancer that children can develop is neruoblastoma. The usual screening test, a urine test, is *NOT* recommended for our children because too many have tested false-positive!

Orthopedically, our children develop slowly. Most do learn walk but may need help with tight heelcords and/or vertical talus. Hypotonia and contractures challenge many of our families. Chiari 1 malformations may develop after early childhood, which is unusual in typical children (Gripp et al 2011).

Endocrine issues can include increased sweating, and may include osteopenia or osteoporosis, precocious or delayed puberty. A number of children have a documented growth hormone deficiency for which they receive growth hormone therapy under close observation by their doctor.

Vision issues are also common. Many of our children have nystagmus, and more children than the general population have strasbismus and myopia.