SIU Southern Illinois University
CARBONDALE

TRIS project online module Trisomy 9 mosaic: Overview, care and resources

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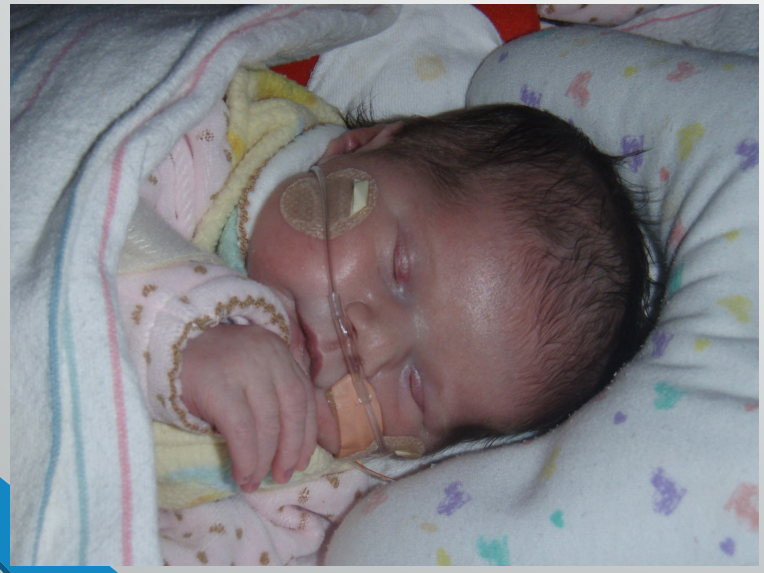
TRIS project
Mission statement

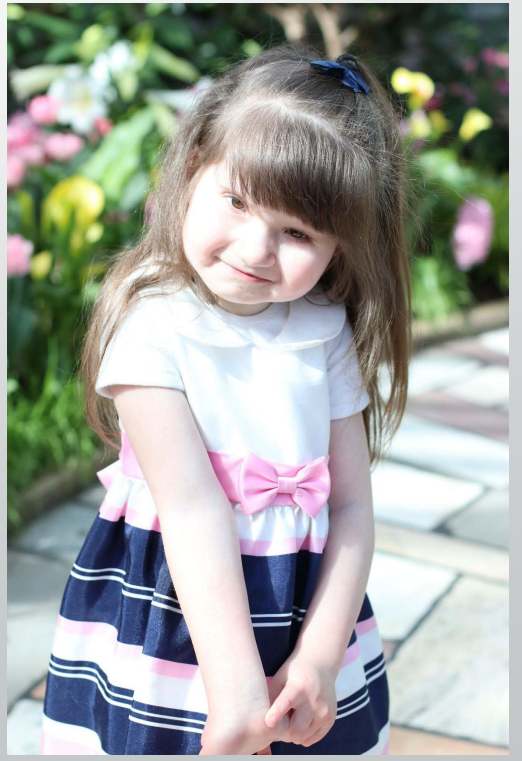
The Tracking Rare Incidence Syndromes (TRIS) project seeks to increase the knowledge base on rare incidence trisomy conditions, and to make this information available to families and interested educational, medical and therapeutic professionals. Related outcomes will be the development of appropriate services, advance treatment options, and supports during the prenatal, newborn and subsequent developmental periods. Children affected by trisomy 18, trisomy 13, and other rare syndromes, including trisomy 9 mosaicism, possess unique needs requiring education of those involved in their daily, educational and medical care.

Continuing Education (CE) information

This module will provide a historical review and current perspective on cases diagnosed with trisomy 9 mosaicism. Information includes prevalence and incidence, overview of the literature, phenotypic characteristics, common medical issues and their treatment as well as ongoing management and care. Developmental outcomes will also be shared. A list of resources and a glossary of terms are also provided.



Mackenzie
DOB 11/14/09

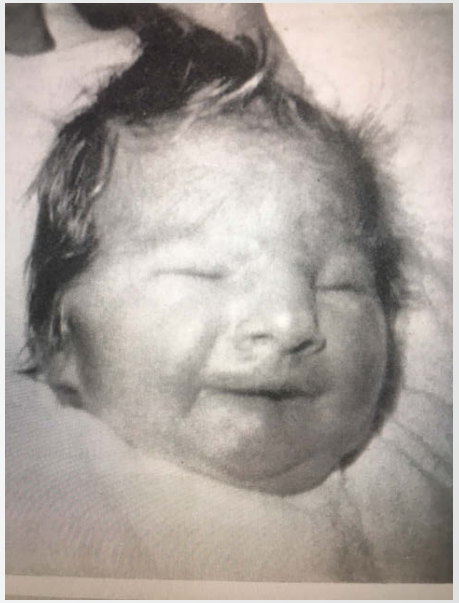


Module overview

This module will provide results from the medical literature along with findings from the TRIS project, materials from rare trisomy focused organizations such as the Support Organization for Trisomy 18, 13 and related disorders (SOFT), media reports (e.g., newspaper articles) and parent experiences. Photos are also provided to illustrate phenotypic features and highlight long-term survivors with this genetic condition.

Taken together, this module offers a synthesis of care and management for cases diagnosed with trisomy 9 mosaicism within a context of professional recommendations and those involved in day-to-day care.

Trisomy 9 mosaic



The first published account was by Feingold and Atkins in 1973.

The authors described the infant as follows:

"Physical examination on admission showed a weight of 3180 g, a head circumference of 32.5 cm, and a height of 50-8 cm. His face was distinctive with small palpebral fissures, enophthalmos, bulbous nose, marked micrognathia, and low-set malformed ears… Cardiac anomalies included a double outlet right ventricle with a patent foramen ovale, ventricular septal defect, hypertrophy of both ventricles, dilated pulmonary artery, and a patent ductus arteriosus." Infant passed at approximately one month of age.

Feingold M, & Atkins L. (1973). A case of trisomy 9. J Med Genet 10, 184–187.

Additional information on this initial case can be found in Kurnick et al. (1974)

Historical view:
Case studies focusing on trisomy 9 mosaicism

An infant was described as follows, "…referred to us for genetic evaluation at 52 days of age. Physical examination showed: weight 2800 g, height 46 cm, and head circumference 335 cm. The patient was hypotonic and had difficulty in sucking…hypertelorism, enophthalmus, and small and slightly upward slanting palpebral fissures. The nose was broad and prominent with a bulbous tip, and carp-shaped mouth, high palate, and marked micrograthia…bilateral hip and right knee dislocation were observed."

Based on literature at the time, the authors also note, "For early diagnosis of trisomy 9 [mosaic] syndrome, the examination of joints is of great importance, since seven patients had hip dislocation and four had fixed or dislocated knees and elbows."

Sanchez JM, Fijtman N, & Migliorini M. (1982). Report of a new case and clinical delineation of mosaic trisomy 9 syndrome. J Med Genet 19, 384–387.

Historical view:
Case studies focusing on trisomy 9 mosaicism continued

Confirmation of the phenotype in an older child (nine years at time of death) is documented in an early publication.

Haslam RHA, Broske SP, Moore CM, Thomas GH, Neill CA. (1973) Trisomy 9 mosaicism with multiple congenital anomalies. J Med Genet, 10, 180-183.

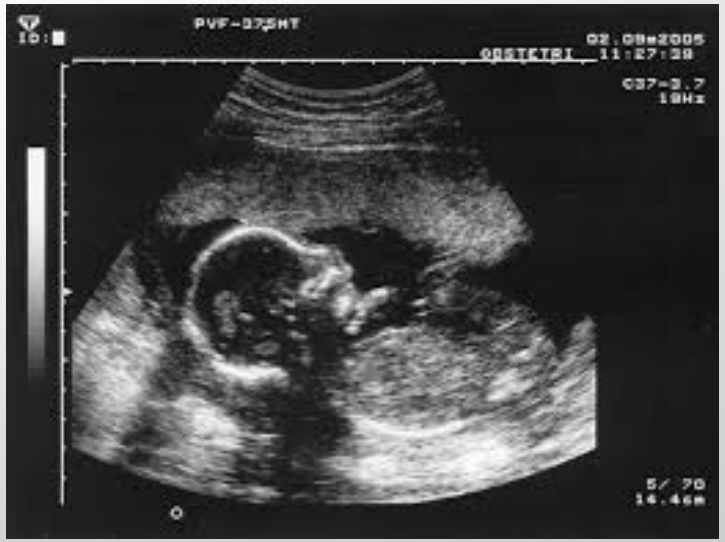
Two cases are described. One lived to 15 years of age and experienced many urinary tract complications even with medication. Discussion of the second case focused on phenotypic characteristics including "low-set malformed ears, micrognathia, bulbous nose…[and] joint limitations". Respiratory tract infections and failure to thrive were also noted.

Okumura A, Hayakawa F, Kat, T, Kuno K, & Watanabe K. (2000). Two patients with trisomy 9 mosaicism. Pediatr Int, 42(1), 89-91.

Prenatal markers

Although some conditions may resolve prior to birth, the following are considered "**major**" prenatal markers for trisomy 9 mosaicism:

- One or more cardiac defects including VSD and ASD and possible identification of aortic stenosis, double outlet right ventricle and/or valvular pulmonary stenosis
- Cystic hygroma
- Dandy-Walker malformation
- Renal hypoplasia
- Hydronephrosis
- Horseshoe-shaped kidney
- Skeletal malformation such as bone dysplasia or vertebral defects
- Two or one vessel umbilical cord
- Intrauterine growth restriction (small for gestational age)



Prenatal markers continued

The following are considered "**minor**" prenatal markers for trisomy 9 mosaicism and primarily related to phenotype (physical characteristics):

- Hypertelorism (space between eyes)
- Microphthalmia
- Low-set ears
- Cleft lip and/or palate
- Bulbous nose; often with broad nasal bridge
- Small palpebral fissures
- Micrognathia
- Overlapped finger(s)
- Rocker-bottom feet

Prenatal testing and diagnostics

- It is critical to fully explain results of non-invasive prenatal testing (NIPT; also termed Cell Free DNA Screening) to prospective parents including the occurrence of false positives and results are not definitive as this testing only screens for possible genetic issues.
- Parents with NIPT results can use the Predictive Value Calculator to view the risk of trisomy chromosome conditions by maternal age at https://www.perinatalquality.org/Vendors/NSGC/NIPT/
  This is one option for measuring risk of a chromosomal condition, there are others. Important to note that prevalence defaults may not be the best estimates of an individual patient's prior risk for a chromosome condition. Also, sensitivity of the screening test contributes to determining the risk percentile.

Prenatal testing and diagnostics continued

- Diagnostic testing is required for a definitive diagnosis. These tests are more invasive than NIPT and there is a nominal risk to the fetus.
- Termination of the pregnancy may be recommended after a prenatal diagnosis. Conversely, prospective parents should also be assisted to plan for a live birth including development of a birth plan and active care options. Many hospitals offer a perinatal palliative care program for this purpose. An end of life plan may also be developed.
- AND parents and family members are increasingly turning to social media including Facebook groups and blogs to ask questions and gather recommendations (e.g., "trisomy friendly" hospitals and physicians, details about identified anomalies, care options at birth, perinatal course).

Incidence of trisomy 9 mosaicism

- Due to limited data, difficult to estimate incidence of this condition
- Limited data on prevalence by sex but appears to be more female survivors
- Majority of cases in recent studies (e.g., Bruns & Campbell, 2015) are reported as over one year of age

Grace
DOB 4/27/12

Phenotype

Facial features including

- Microphthalmia
- Broad, bulbous nose
- High arched or cleft palate
- Low-set ears
- Hypertelorism
- Short palprebral fissures

Jones KL, Jones MC, & Del Campo M. (2013). *Smith's recognizable patterns of human malformation*. Elsevier Health Sciences.

UNIQUE:
http://www.rarechromo.org/information/Chromosome%20%209/Trisomy%209%20mosaicism%20FTNP.pdf

Alana
DOB 12/9/09

Phenotype continued

Other features including

- Clenched or overlapping fingers and/or toes
- Nail hypoplasia
- Joint anomalies including dislocation of hips, knees and/or fingers
- Cryptorchridism in males
- Rocker bottom feet

Jones KL, Jones MC, & Del Campo M. (2013). *Smith's recognizable patterns of human malformation*. Elsevier Health Sciences.

UNIQUE: http://www.rarechromo.org/information/Chromosome%20%209/Trisomy%209%20mosaicism%20FTNP.pdf

Key medical information

- Common cardiac conditions include ventricular septal defect, patent ductus arteriosus, and atrial septal defect. Other valve defects are possible but less frequent. Surgery is recommended to correct cardiac anomalies.
- Reports of central and obstructive apnea. Some children may require use of continuous positive airway pressure (CPAP) or a tracheotomy, may be needed long-term.

Bruns DA, & Campbell, E. (2015). Twenty-five additional cases of trisomy 9 mosaic: Birth information, medical conditions, and developmental status. Amer J Med Genet Part A, 167(5), 997-1007.

Key medical information continued

- Variety of feeding difficulties due to anatomical anomalies such as cleft palate, low muscle tone and/or impaired ability to coordinate suck, swallow and breathing in neonates and infants.
- Concerns about aspiration and reflux affecting oral intake, weight gain and overall health. Often need supplemental nutrition or fully tube fed to intake concerns and address medical or anatomical conditions. Should have a feeding team including a dietitian.
- Dislocation of joints is possible including hips, knees and elbows and should be monitored.

Key medical information continued

- May be enlarged ventricles in the brain and some cases may also be diagnosed with Dandy Walker syndrome. Hydrocephalus is also possible.
- Seizures are possible as well as infantile spasms in neonates.
- Potential for vision and/or hearing issues with greater likelihood of the former due to eye defects (e.g., strabismus, amblyopia). Optic nerve may also be affected. Tubes may be needed for ears. Treatment will depend on type of defect and presence of additional conditions that may impact interventions.
- Renal conditions may include hydronephrosis, and (poly)cystic kidney.
- Defects to male and female genitalia is possible.

Needs to be noted some individuals with this diagnosis show few of the conditions described here and may only have minimal developmental delay.

Developmental milestones

Recent articles (Bruns, 2011; Bruns & Campbell, 2015) described developmental milestones; some key findings:

- Ability to imitate gestures, signs and/or words to communicate needs
- Explores objects with hands; demonstrates pincer grasp; scribbles
- Shows preference for main caregiver
- Some walk with devices (e.g., gait trainer), others independently (may need orthotics)

Hebe
DOB 6/15/12

Care and management

- Monitor cardiac conditions and determine treatment with medical team (e.g., surgical intervention).
- Work with medical team to provide proactive such as a sleep study and/or ongoing treatment for respiratory difficulties to reduce likelihood of more serious issues (e.g., pneumonia).
- Monitor for airborne allergies and other irritants affecting respiratory functioning.

Jasmijn
DOB 8/23/14

Care and management continued

- Ongoing monitoring of growth; efforts are moving forward on development of height and weight charts across childhood years.
- Monitor feeding for aspiration and reflux. There are several tests to determine these conditions such as a videoflouroscopy or upper GI series. Testing may need to be repeated.
- Work with feeding team to monitor and adjust intake (e.g., textured foods, thickened liquids).

Care and management continued

- If present, monitor kidney conditions and treat when determined necessary.
- In males, cryptorchidism (undescended testicle[s]) is possible. Treatment decided by child's medical team including parents.
- Monitor vision for changes glasses may be needed.
- Audiological testing may be warranted to determine hearing range and acuity as both can, potentially, change over time.
- Monitor neurological status; report all suspected seizure activity.

Care and management continued

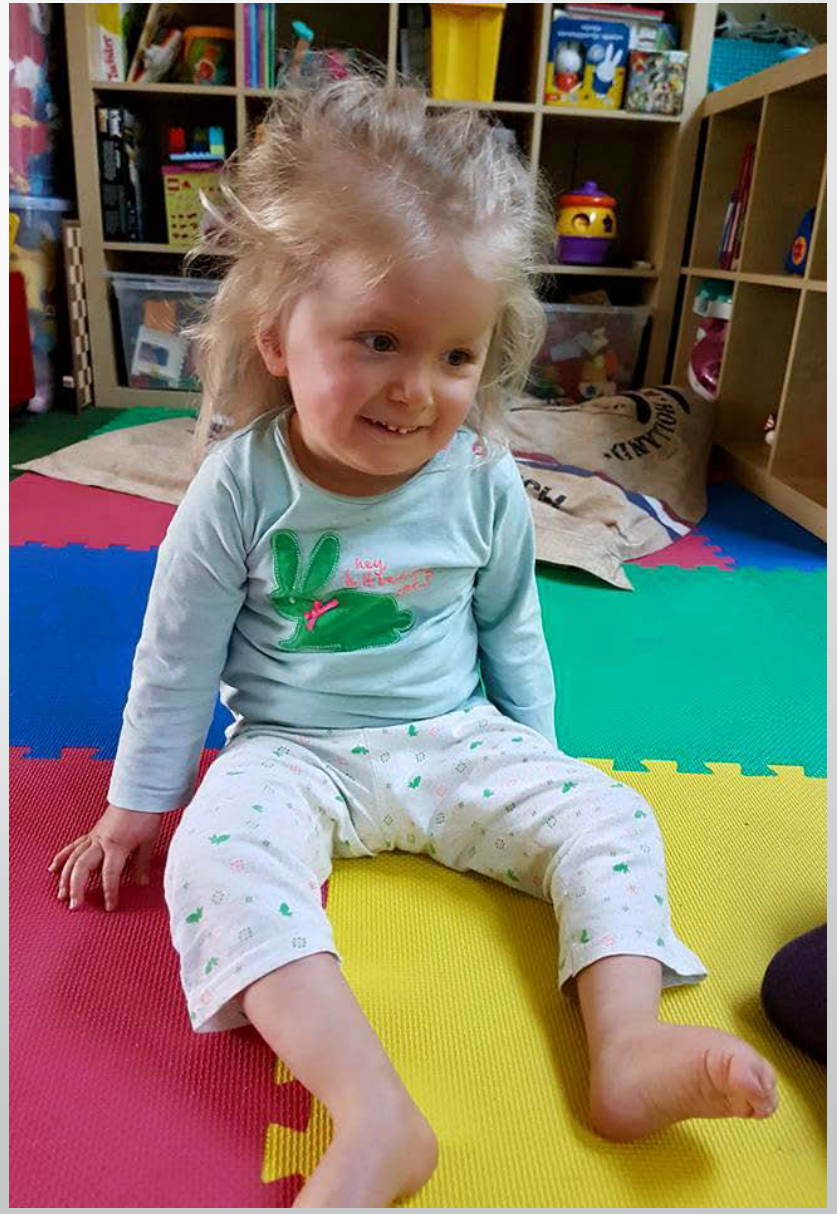
Overall, the following medical tests and procedures are recommended; consult with medical team for optimal timing and follow-up (e.g., shortly after birth, two years of age, puberty) including an electrocardiogram/echocardiogram, brain scan, kidney and or hip ultrasound, functional vision test, swallow study, and sleep study.

An additional area is dental care. An article by Moskovitz and colleagues describes dental management of a 13-year-old girl with trisomy 9 mosaicism. Initial treatment was provided under general anesthesia. Later treatments used conscious sedation. The authors explain the need for adjustments to treatment to address the case's respiratory issues and skeletal malformations including ability to sit in the dental chair in an upright position.

Moskovitz M, Brener D, & Annick RR. (2006). Dental management of a child with trisomy 9 mosaicism: A case report. Pediatr Dent, 28, 265–268.

Care and management continued

- Early intervention services for infants and toddlers to encourage gains in developmental areas (in home, clinic, child care setting).
- Preschool-aged children should attend school as tolerated (e.g., one hour session, half day) for developmental activities and socialization.
- Schooling continues for children age five and older. Focus on functional skills such as choice making, sensory stimulation, and developing age appropriate interests. Some may work on functional academics (e.g., reading "survival words", basic math).



Special considerations: Medically related

- Confer with medical team regarding adjustments to immunization schedule.
- Use of growth hormone therapy must be tempered with possible side effects and expected long-term outcomes.
- Feeding concerns require ongoing collaboration among parents, caregivers and child's team to meet caloric and nutritional needs such as quality and quantity of oral feeds weighed against aspiration risk and importance of repeated evaluation of intake amount, swallowing, reflux etc.

Special considerations: Non-medical needs

- Changes at puberty (may be early onset) including seizure activity (necessary to reevaluate all medications) and other symptoms including irritability.
- May be at-risk for cardiac myopathy; monitor and follow-up existing and/or new cardiac issues.
- May be affected by hemihyperplasia (also termed hemihypertrophy), which is overgrowth of one side of the body or body part(s) on one side of the body; possible link with liver or kidney cancer.

Special considerations: Non-medical needs

- Therapy and educational goals including short and long-term outcomes related to parent and caregiver preferences and covering a range of functional skills
- Long-term survivors may need planning in the following areas: guardianship, community and regional adult services, and application to state and national programs for adults with disabilities

Aidan
12/31/97

Parent and family experiences

Phillip
DOB 9/23/07

Parent and family experiences

- We work as a team to balance Julia's needs and our normal household duties.
- He [husband] is my right hand and so helpful with physically/emotionally taking care of Lucy.
- He [husband] has been there through everything. We talk regularly and make decisions together. He has supported my part time work so that I can care for our daughter.
- He [husband] and I have been in this together since day one. We rely on one another to share the joys of Anemarie's progress, the heartaches of her set backs and illnesses and the never ending work of daily life.
- She [wife; two mom family] helps me with Peyton and well as the emotional support that I need.
- We share all the joys and sorrows together. We celebrate the accomplishments and cry when things go wrong.

Parent and family experiences continued

- She [maternal grandmother] has been involved in the child's care since the minute he was born. She is supportive and has helped to regain normalcy in our lives.
- They [maternal and paternal grandmothers] help a lot, support us and take care of our other two children with us.
- She [aunt] helps with watching Aidan and other needs.
- My mother-in-law is a nurse and despite living 1.5 hours away often comes to help care for our son when we don't have a nurse or other care provider. My in-laws have also helped us financially.
- She [mother's sister] is wonderful with my kids and has taken the time to understand and help with Skylar as well as be an emotional support to me.
- They [maternal brothers] are always available & will do anything for our daughter. They love her like she was their own.

Parent and family experiences: Parent descriptions of unmet needs

- I have no help with Courtney's care and no one who understands her needs.
- State has cut back on my nursing hours my daughter with t9m is very complex now I will need to do more hours of care myself.
- Financial cost of medical supplies and equipment are very difficult to manage
- Fears about being able to work full-time, financial issues as child gets older.
- We're isolated geographically, and socially because of Kieran's behaviors.
- Aside from the T9M Family group on FB, I feel that my social needs are not met.

Parent and family experiences: Parent descriptions of unmet needs

- Not enough qualified child care out there for special needs.
- We need more help to be able to spend time without other children and together.
- We feel we have to work very hard to get the doctors to listen. We know more about t9m than they do. We feel there should be more possibilities to improve her chances of developing at her best.
- Emotional support to accept diagnosis and grieve, help with caring for child so that my husband and I can have time for ourselves (both together and alone). Our child does not sleep. We are terribly sleep deprived…We are emotionally exhausted, support from doctors has been crappy - not at all proactive and do not take my concerns seriously. It is extremely difficult with both of us working, but we don't feel we can afford to give up our jobs.

Trisomy 9 mosaic in the news

"Lily-Grace was born several weeks early, was light, at 1.7kg, and had malformed airways which required life-saving surgery at 4 weeks. She has had five bouts of pneumonia requiring hospital admission, four procedures requiring general anesthesia and she may need spinal surgery. Her joints, heart, and eyesight are also affected and she suffers extreme anxiety, seizures and low immunity. But mum Amanda Davies says Lily-Grace is progressing, against the odds…She can walk, she can now spell 10 words, she can look at letters and read them. What I have proven is she can learn…Her first word was Elmo and then months with nothing else. Then came that beautiful call I longed to hear - 'Mummy'." (*Kiwi toddler's extremely rare disorder, The New Zealand Herald, March 6, 2017*)

"Meg has had a fantastic year, she has been very healthy and the surgery she is having on Sunday will replace the feeding tube in her nose with one that goes directly into her stomach, reducing the risk of pneumonia from aspirated feeds. She will also have grommets [ear tubes] in her ears to help improve her hearing. We are seeing her meet milestones one step at a time, albeit at a much slower pace." (*Brothers to take part in mini run to raise funds for charity which supports their younger sister, The Shuttle, Kidderminster, UK, October 11, 2016)*

Trisomy 9 mosaic in the news continued

"Because there is so much unknown about trisomy 9, Carole admits the future for Grace is also an unknown…Everybody [with the diagnosis] is different…that's why these meetings [with other families] are so important. We try to teach the doctors about her condition because we're the ones doing the research…" (*Strongville patrolman offers Vitamix to family in need, Strongsville Post, Medina, OH, July 3, 2016*)

"Little Holly as not predicted to live beyond two [due to trisomy 9 mosaicism], but at six years old, she has been an 'inspiration' to strangers…No matter what she's going through that kid always has a smile on her face. She has the most contagious laugh…she inspires me [fundraiser]." *('Brave' battle of six year old fighting rare disease captures hearts of strangers over 200 miles away, East London and West Essex Guardian, UK, December 2, 2015*)

Trisomy 9 mosaic in the news continued

"A little girl who was so ill when she was born doctors warned she wouldn't reach her first birthday has celebrated turning four…We appreciate her every day and planning for the future…She doesn't talk with words, but she likes being around people and she's a joy to be around. Audrey has trisomy 9 mosaic…she's doing really well. She's a little star." (*Tot who doctors said wouldn't reach one celebrates fourth birthday, Telegraph & Argus, Bradford, UK, April 2, 2015*)

Triton will have multiple surgeries…the family also relies on different therapy appointments several times a week…Heather is also dedicated to raising awareness of trisomy 9. There's only one institute in the country she's found that actively researches the condition – Southern Illinois University Carbondale – and there are no foundations raising funds for research in the United States." (*Rock Hill baby battles rare genetic condition, The Herald, Rock Hill, NC, March 21, 2015*)

Additional information: SOFT and UNIQUE

Support Organization for Trisomy 18, 13 and Related Disorders (SOFT) provides information, support and opportunities for face-to-face meetings.

The following are links to some active SOFT groups around the world:

- SOFT USA: http://trisomy.org
- SOFT UK: http://www.soft.org.uk
- SOFT Australia: http://www.trisomyaustralia.com
- SOFT Italy: http://www.trisomia.org

UNIQUE runs helplines for new and existing member families and professionals to find out more information about the group and about specific rare chromosome disorders. We have developed and maintain a comprehensive offline computerized database. Online at http://www.rarechromo.org/html/home.asp and contact by email to info@rarechromo.org

TRIS project links

TRIS project website links:

Homepage: http://tris.siu.edu

Enrolling in the project: http://tris.siu.edu/survey/form/PreEnroll.php

Publications and presentations list:
http://tris.siu.edu/publications-presentations/index.php

Case studies: http://tris.siu.edu/case-studies/index.php

TRIS project Facebook page:

https://www.facebook.com/TRIS.Trisomy.project