

Children's Mercy Kansas City

## SHARE @ Children's Mercy

---

Research Days

GME Research Days 2020

---

May 11th, 11:30 AM - 1:30 PM

### Two Cases of Severe Combined Immunodeficiency Disease with No Known Variants Identified in Genes Associated with Immunodeficiencies

Megan H. Tucker  
mtucker1@cmh.edu

Follow this and additional works at: <https://scholarlyexchange.childrensmercy.org/researchdays>



Part of the Allergy and Immunology Commons, Congenital, Hereditary, and Neonatal Diseases and Abnormalities Commons, and the Immune System Diseases Commons

---

Tucker, Megan H., "Two Cases of Severe Combined Immunodeficiency Disease with No Known Variants Identified in Genes Associated with Immunodeficiencies" (2020). *Research Days*. 8.  
[https://scholarlyexchange.childrensmercy.org/researchdays/GME\\_Research\\_Days\\_2020/researchday1/8](https://scholarlyexchange.childrensmercy.org/researchdays/GME_Research_Days_2020/researchday1/8)

This Poster Presentation is brought to you for free and open access by the CONFERENCES, EVENTS, GRAND ROUNDS at SHARE @ Children's Mercy. It has been accepted for inclusion in Research Days by an authorized administrator of SHARE @ Children's Mercy. For more information, please contact [library@cmh.edu](mailto:library@cmh.edu).

## Research Abstract Title

**Submitting/Presenting Author (must be a trainee):** Megan H Tucker

**Primary Email Address:** mtucker1@cmh.edu

**Resident/Psychology Intern ( $\leq$  1 month of dedicated research time)**

**Resident/Ph.D/post graduate ( $>$  1 month of dedicated research time)**

**Fellow**

**Primary Mentor (one name only):** Jotishna Sharma, MD

**Other authors/contributors involved in project:** Rakesh K Goyal, MD; Nikita Raje, MD; Carol Saunders, PhD; Emily Farrow, PhD; Isabelle Thiffault PhD.

**IRB Number:** N/A, consent obtained from families

**Describe role of Submitting/Presenting Trainee in this project (limit 150 words):**

I was directly involved in the patient care of Case 2 and indirectly in the care of Case 1. I composed the abstract below in collaboration with my mentors, and I presented the work at the North American Immuno-Hematology Clinical Education and Research Symposium in Columbus Ohio.

**Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words**

**Background:**

Traditionally, cases of severe combined immunodeficiency (SCID) are classified immunophenotypically based on the lymphocyte subsets affected. More recently, there has been an increasing effort to classify SCID by its genetic etiology as genotype influences treatment options and predicts prognosis. However, in approximately 10-15% of SCID cases no genetic defect is identified.

**Objectives/Goal:**

We report two challenging cases of SCID with novel findings without identifiable genetic defects.

**Methods/Design:**

Case 1: An intrauterine growth restricted (IUGR), 34-week male infant presented with multiple congenital anomalies (severe micrognathia requiring tracheostomy, cleft palate, agenesis of the corpus callosum, sensorineural hearing loss, intestinal malrotation, nephrotic syndrome, pulmonary valve stenosis and skeletal dysplasia). He was severely lymphopenic, and immune workup led to a phenotypic diagnosis of T-B+NK+ SCID. He underwent a matched-sibling donor bone marrow transplant without conditioning which led to donor T-cell engraftment. At 6 months of life, he presented with respiratory failure due to staphylococcal tracheitis and died. Case 2: A term female IUGR infant presented at birth with thrombocytopenia and severe lymphopenia. Immune workup led to a phenotypic diagnosis of leaky T-B-NK+ SCID. She developed progressive hypoxic respiratory failure secondary to pulmonary

arterial hypertension (PAH) and required cannulation to extracorporeal membrane oxygenation (ECMO). After ECMO decannulation, she died at 5 weeks of age from refractory PAH.

**Results:**

On exome sequencing, no reportable variants were identified in genes associated with SCID in either case. In Case 1, exome sequencing identified 10 variants of unknown significance (VUS) (Table 1), one of which, a hemizygous variant in *SEPT6*, c.44G>A (p.Arg15Gln), is particularly intriguing as this gene is involved in neural tube development and lymphocyte migration. In case 2, exome sequencing identified 3 VUS (Table 1), one of which, a heterozygous variant in *PSMB8*, c.265G>T (p.Asp89Tyr), is of interest as it was found to be a *de novo* mutation in a highly evolutionarily conserved amino acid residue and was located within a gene involved in immunoproteasome formation.

**Conclusions:**

Despite advancements in the classification of SCID through identification of genetic defects, these cases with non-diagnostic genetic work up highlight the limitation of presently available clinical genomic testing.