# Sequencing Analysis Report

## Patient

<table>
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<th>Name:</th>
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<tr>
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<td>Patient ID:</td>
<td>Weiz1</td>
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<tr>
<td>Accession #:</td>
<td>TTC37 Demo Patient</td>
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## Healthcare Provider

<table>
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<tr>
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<th>LifeMap Demo</th>
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## Main Specimen(s)

<table>
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<tr>
<th>Specimen Type:</th>
<th>GermLine</th>
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<tr>
<td>Accession Date:</td>
<td>1 Dec 2015</td>
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<td>Draw Date:</td>
<td>1 Nov 2015</td>
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<td>Report Date:</td>
<td>30 Sep 2019</td>
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## Clinical Information

A 4-year-old girl in a consanguineous family with no gastrointestinal history. Developed persistent secretory diarrhea at 18 days of age and has been completely dependent on total parenteral nutrition (TPN). Has minor dysmorphic features but no obvious developmental delay.

Phenotypes: diarrhea, "parenteral nutrition", ftt

## Main findings: variant(s) identified in TTC37

### Details about L761P (NM_014639.3) [Recessive HOM] - Relevance: High - Likely Pathogenic

The homozygote A→G substitution at chr5:94852859 is predicted to result in abnormal protein translation of the TTC37 protein at amino acid position 761.

Predicted effect(s) on the protein: Missense

The quality and reliability of the variant calling is High and the severity of the impact on the protein is Med.

This variant was not found in the available control databases (see methods).

**Variant Note:** Associated with Trichohepatoenteric syndrome 1, which matches phenotypes

## Clinical Significance of TTC37

### Indications

**TRICHOHEPATOENTERIC SYNDROME 1; THES1 [MIM:222470]**
Although the spectrum of phenotypic expression in trichohepatoenteric syndrome (THES) is broad, the characteristic features include intrauterine growth retardation, woolly hair, facial dysmorphism, intractable diarrhea in infancy requiring total parenteral nutrition, and immunodepression. Hepatic involvement contributes to the poor prognosis of affected patients (summary by Fabre et al., 2007).

**Genetic Heterogeneity of Trichohepatoenteric Syndrome**

Trichohepatoenteric syndrome-2 (THES2; 614602) is caused by mutation in the SKIV2L gene (600478) on chromosome 6p21.

Reference(s):

1. Intractable diarrhea with 'phenotypic anomalies' and tricho-hepato-enteric syndrome: two names for the same disorder. [PMID: 17318842]

**Evidence from GeneCards Suite Knowledgebase**

**Diseases directly associated with TTC37**

Trichohepatoenteric Syndrome 1  
[OMIM, ClinVar, Swiss-Prot and four more]

Aliases:

- diarrhea, syndromic; diarrhea, fatal infantile, with trichorrhexis nodosa; syndromic diarrhea; phenotypic diarrhea of infancy; syndromic diarrhea/tricho-hepato-enteric syndrome; phenotypic diarrhea; syndromatic diarrhea; intractable diarrhea with phenotypic anomalies; fatal infantile diarrhea with trichorrhexis nodosa

Symptoms:

- diarrhea, secretory, severe; infantile diarrhea; intractable diarrhea

Summaries:

- Tricho-hepato-enteric syndrome (THE), also known as syndromic or phenotypic diarrhea, is an extremely...
- Trichohepatoenteric syndrome is a condition that affects...the body. This condition is also known as syndromic diarrhea because chronic, difficult-to-treat diarrhea is one of its major features. Within the first few weeks of life, affected infants develop watery diarrhea that occurs multiple times per day. Even with nutritional...
- Trichohepatoenteric syndrome is a condition that affects...intestines. The condition is characterized by chronic diarrhea that begins during the first six months after birth. Continued diarrhea can lead to an inability to gain weight (failure to...
- Although the spectrum of phenotypic expression in trichohepatoenteric...retardation, woolly hair, facial dysmorphism, intractable diarrhea in infancy requiring total parenteral nutrition, and...
- Trichohepatoenteric syndrome 1: A syndrome characterized by intrauterine growth retardation, severe diarrhea in infancy requiring total parenteral nutrition, facial...

**Publications**

- Identifying Mutations of the Tetratricopeptide Repeat...Domain 37 (TTC37) Gene in Infants With Intractable Diarrhea and a Comparison of Asian and Non-Asian Phenotype... (PMID: 26945392)
  Abstract:
Syndromic diarrhea/tricho-hepato-enteric syndrome (SD/THE) is a rare...immunodeficiency diseases (PIDs). Neonates with intractable diarrhea underwent immunologic assessments including immunoglobulin...nonconsanguineous parents, suffered from intractable diarrhea.

Mesh Term: 
  *Diarrhea*, Infantile

- **Tricho-hepato-enteric syndrome (THE-S): two cases and review of the literature.** (PMID: 25976726)
  
  **Abstract:**
  Tricho-hepato-enteric syndrome (THE-S) is characterized by severe infantile diarrhea, failure to thrive, dysmorphism, woolly hair, and...sequencing (WES). Both cases presented with chronic diarrhea, failure to thrive, and recurrent infections. Case... • Tricho-Hepato-Enteric syndrome (THE-S) is characterized by severe infantile diarrhea, failure to thrive, dysmorphism, woolly hair, and...
  
  Mesh Term: 
  *Diarrhea*, Infantile

- **Novel mutations in SKIV2L and TTC37 genes in Malaysian children with trichohepatoenteric syndrome.** (PMID: 27050310)
  
  **Abstract:**
  Trichohepatoenteric syndrome (THES) is a rare autosomal...disorder that is classically associated with intractable diarrhea with an onset within the first few months of life...
  
  Mesh Term: 
  *Diarrhea*, Infantile
**Methods**

### Data sources used for variant annotation

<table>
<thead>
<tr>
<th>Version Set</th>
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### Protocol and genetic models

**Protocol**
- Germline - Single Sample

**Genetic Model**
- Recessive HOM, Recessive Compound HET, Dominant HET, Secondary Findings

### Summary of variants in the supplementary Excel

**Recessive HOM**
- 242 Locations in 228 Genes
  - Applied filters - Homo variants, Max AF Rec filter, Med-High Effect, Med-High Quality

**Recessive Compound HET**
- 237 Locations in 83 Genes
  - Applied filters - CompHet genes, Hetero variants, Max AF Rec filter, Med-High Effect, Med-High Quality

**Dominant HET**
- 571 Locations in 503 Genes
  - Applied filters - Hetero variants, Max AF Dom filter, Med-High Effect, Med-High Quality

**Secondary Findings**
- 216 Locations in 43 Genes
  - Applied filters - ACMG, Med-High Quality

* In cases where Max AF filter was applied the cut off used was 0.1%

### Gene panels and variant prioritization

**Keywords used for VarElect Scoring**
- diarrhea, "parenteral nutrition", ftt

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**Disclaimer:** We continually perform ongoing evaluations of variant classifications. In certain cases, healthcare providers may be contacted for more information or to arrange family testing to aid in variant classification. When new evidence about a variant is identified and determined to result in significance and management change, that information will automatically be made available to the healthcare provider through an amended report.