

Transmembrane Activator and CAML  
 Interactor (TACI) Gene, Known Mutation Analysis

Patient ID <b>SA00055104</b>	Patient Name <b>SAMPLEREP, TACIG</b>	Birth Date <b>1966-06-10</b>	Gender <b>F</b>	Age <b>46</b>
Order Number <b>SA00055104</b>	Client Order Number <b>SA00055104</b>	Ordering Physician <b>UNKNOWN, PROVIDER</b>	Report Notes	
Account Information <b>C7028846 DLMP Rochester</b>		Collected <b>15 Mar 2013 03:44</b>		

## TACI Gene, Known Mutation

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#### Reason for Referral

CVID, splenomegaly

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described to be associated with TACI mutations (splenoemgaly, AITP). Recommend evaluation of B cell immunophenotyping analysis (test number 88800) to assist in classification of the CVID phenotype. Additional literature references for TACI mutations in CVID can be provided on request.

#### Method

Fluorescent DNA sequence analysis was used to test for the presence of mutations in the 5 exons, exon-intron boundaries, and the 5' and 3' UTR of the TACI gene.

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TACI mutations have been reported to account for 8–15% of CVID cases depending on the study population assessed. The majority of TACI mutations are sporadic though some familial mutations (autosomal dominant and autosomal recessive) have been reported. Present evidence seems to suggest that homozygous TACI mutations are associated with CVID and/or selective IgA deficiency, while the clinical significance of heterozygous mutations remains controversial, though these have also been reported in some CVID and IgA-deficient patients. It is possible that TACI may be a disease-associated gene rather than a disease-causing gene. The underlying genetic defect or molecular basis has not been identified in the majority (75–80%) of CVID patients. It may be reasonable to regard most cases of CVID as oligogenic, i.e., the phenotype results from the contribution of more than a single gene defect.

#### Result

This individual was shown to have one copy of the following mutation in the TACI gene: g. 24216, c.310T>TC, p.C104R in exon 3 of the TNFRSF13B (TACI) gene.

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#### Interpretation

This mutation is one of the most common TACI mutations reported in CVID patients. The mutation is within the extracellular (EC) domain of the TACI receptor in the second cysteine-rich domain (CRD). This residue is highly conserved and reported studies indicate that this mutation - C104R abolishes binding of the ligands -BAFF and APRIL to the TACI receptor. B cells from these patients have been shown to be unable to produce immunoglobulins in response to APRIL (ligand) stimulation. Further, the heterozygous C104R mutation has been shown to have a dominant-negative effect (Garibyan et al, JCI, 2007). The reported CVID phenotype of the patient matches what has been

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#### ADDITIONAL INFORMATION

Laboratory developed test.

#### Reviewed By

Yvonne Philo

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### TACI Known Mutation Sequencing

#### Sequencing

Performed

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**Received:** 15 Mar 2013 03:44

**Reported:** 13 Jun 2013 12:51

#### Performing Site Legend

Code	Laboratory	Address
MCR	Mayo Clinic Dept. of Lab Med and Pathology	200 First Street SW, Rochester, MN 55905