DPYD Validation

The Tempus DPYD test identifies certain alterations in the *DPYD* gene, which may be associated with a patient's potential toxicity to 5-FU/Capecitabine chemotherapy based on the associated drug labeling and guidelines from the Clinical Pharmacogenomics Implementation Consortium (CPIC). The assay reports on the presence of alterations detected within the *DPYD* gene through analysis of the patient's germline DNA by next generation sequencing (NGS). The Tempus DPYD assay may only be ordered in conjunction with the Tempus|xT Solid Tumor + Normal test and requires no additional tissue.

Validation of Tempus DPYD was performed in a CLIA-certified, CAP-accredited lab. The analytical validation cohort consisted of DPYD positive and negative blood and saliva patient samples and represented a range of DPYD genotypes. Using a germline genotyping pipeline, variations at each of the clinically reported positions were evaluated. Average depth of coverage was calculated at the 5 positions at approximately 200x. All reported genotypes were validated using an orthogonal technology.

Up to 15 samples of each category and position from the internal cohort were selected. Sample availability and rarity in the population affected the total number of samples represented for each category and position. The Tempus DPYD test has a sensitivity and specificity of >99%.

Samples were sequenced at each of the following loci:

rsID	Genomic coordinate for SNV of interest	Coding Change	Clinical Annotation	Enzyme Activity
rs55886062	g.97981343A>C	c.1679T>G	*13	Loss
rs3918290	g.97915614C>T	c.1905+1G>A	*2A	Loss
rs67376798	g.97547947T>A	c.2846A>T	c.2846A>T	Decreased
rs115232898	g.98165030T>C	c.557A>G	c.557A>G	Decreased
rs56038477	g.98039419C>T	c.1236G>A	HapB3	Decreased

*Genomic coordinates are based on genome build GRCh37/hg19, and cDNA (Coding change) coordinates are based off of accession NM_000110.3