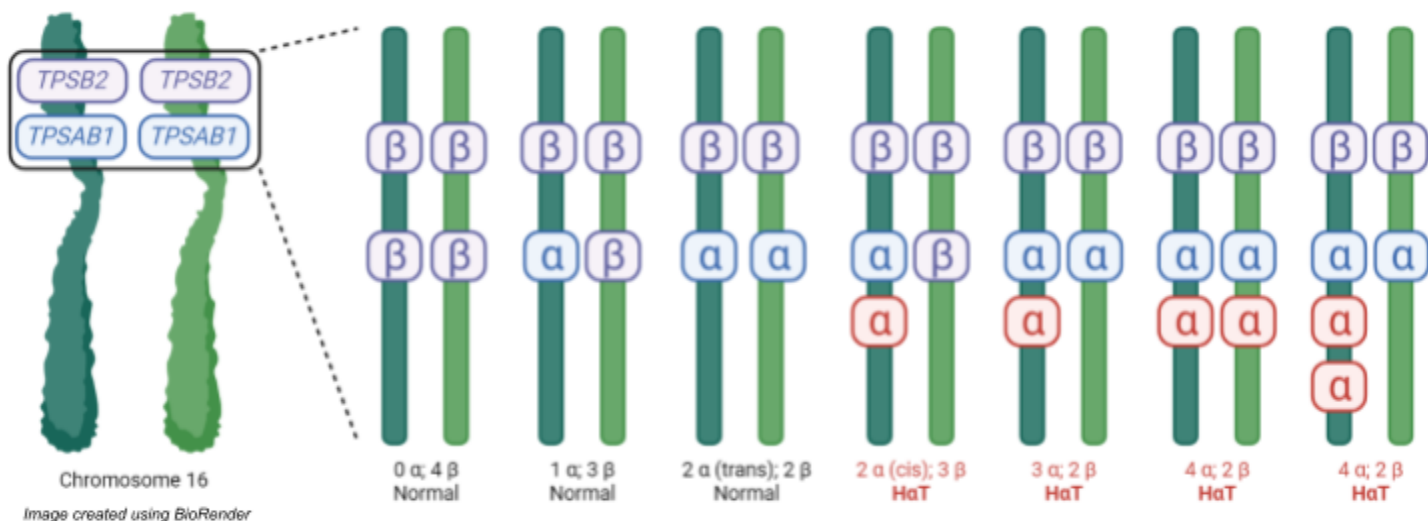


## MCD GENETIC TESTING RESULT INTERPRETATION

### For Healthcare Providers

#### Alpha-tryptasemia Copy Number Variation Result Interpretation

Your patient's result	Meaning	Clinical Significance
<b>Abnormal</b>	3 or more total copies of $\alpha$ -tryptase OR 2 or more copies of $\alpha$ -tryptase on the same allele (cis)	<b>The patient has the hereditary alpha-tryptasemia trait.</b> <b>Hereditary alpha-tryptasemia (HaT)</b> is when a patient has additional copies of the <i>TPSAB1</i> gene. The <i>TPSAB1</i> gene encodes both $\alpha$ -tryptase and $\beta$ -tryptase, which encode for the mast cell mediator <b>tryptase</b> . Additional copies of $\alpha$ -tryptase lead to elevated blood tryptase levels (it is unclear what additional copies of $\beta$ -tryptase mean and is considered benign). Increased tryptase levels cause HaT symptoms. Increased copies of $\alpha$ -tryptase are predictive of higher blood tryptase levels (i.e., a patient with 4 $\alpha$ -tryptase copies would have greater disease severity than a patient with 3 $\alpha$ -tryptase copies). Even if a patient carries the trait for hereditary alpha-tryptasemia, they may not experience symptoms; however, they are still capable of passing down the trait and having a symptomatic child.
<b>Normal</b>	No more than 2 copies of $\alpha$ -tryptase on opposite alleles (trans)	<b>The patient does not have the hereditary alpha-tryptasemia trait.</b> Patients with a negative report but high clinical suspicion of hereditary alpha-tryptasemia should be monitored closely.



#### High Sensitivity *KIT* D816V Mutation Hotspot Result Interpretation

Your patient's result	Meaning	Clinical Significance
<b>Positive</b>	<i>KIT</i> D816V mutated allele percentage is $\geq 0.015\%$	<b>The patient satisfies a minor criterion for the diagnosis of systemic mastocytosis.</b> <b>Systemic mastocytosis (SM)</b> is when a patient has abnormal proliferation and accumulation of mast cells in multiple, noncutaneous organ systems. The <i>KIT</i> gene produces a <b>receptor tyrosine kinase</b> that controls the growth and development of mast cells. A specific mutation in the <i>KIT</i> gene, <i>KIT</i> c.2447A>T p.D816V, known as <b><i>KIT</i> D816V</b> , produces a dysfunctional form of this receptor that causes increased mast cell growth, development, and mediator release. Increased levels of mast cell mediators, such as <b>histamine</b> and <b>tryptase</b> , cause SM symptoms. Detection of the <i>KIT</i> D816V mutation satisfies a minor criterion for the diagnosis of systemic mastocytosis. A higher percentage of mutated alleles indicates increased risk for disease. The <i>KIT</i> D816V mutation is a somatic mutation and cannot be passed down.
<b>Negative</b>	<i>KIT</i> D816V mutated allele percentage is 0%	<b>The patient does not satisfy a minor criterion for the diagnosis of systemic mastocytosis.</b> Patients with a negative report but high clinical suspicion of systemic mastocytosis should be monitored closely with consideration of repeat testing if their condition worsens.
<b>Inconclusive</b>	<i>KIT</i> D816V mutated allele percentage is 0.005-0.015%	<b>Repeat testing is necessary to determine if the patient satisfies a minor criterion for the diagnosis of systemic mastocytosis.</b> The presence of the <i>KIT</i> D816V mutation cannot be confirmed and repeat testing should be performed with a new sample.