Lymphoid Mutation Panel for testing relevant genes in chronic lymphocytic leukemia, hairy cell leukemia, and lymphoplasmacytic lymphoma

This panel targets selected genes to facilitate diagnosis, classification, and prognostic stratification in patients with chronic lymphocytic leukemia (CLL), hairy cell leukemia (HCL), or lymphoplasmacytic lymphoma (LPL). Mutation hotspots in 5 genes are examined using massive parallel sequencing (next-generation sequencing). Results inform diagnosis and management as below:

1) **Chronic Lymphocytic Leukemia**: In patients with CLL, mutations in *NOTCH1, SF3B1, and TP53* may help select patients with inferior prognosis and increased risk of Richter’s transformation, who may merit more aggressive intervention.

2) **Hairy Cell Leukemia**: *BRAF* codon 600 mutations are present in nearly all cases of hairy cell leukemia. The presence of a *BRAF* mutation may assist diagnosis and classification by distinguishing this leukemia from cases of hairy cell-variant and splenic lymphomas which lack *BRAF* mutation.

3) **Lymphoplasmacytic Lymphoma**: *MYD88* p.L265P (also known as *MYD88* p.L273P) distinguishes cases of LPL from histologically and immunophenotypically similar cases of marginal zone lymphoma.

**Specimen Requirements for the Lymphoid Mutation Panel:**
Bone marrow aspirate (1 mL, EDTA) and peripheral blood (3 mL, EDTA) are preferred. However, Wright-stained or unstained cytologic slides (e.g. bone marrow aspirate smears, lymph node touch preparation) are also accepted. Unacceptable sample types include: fresh or frozen solid tissue or paraffin embedded tissue. The assay is generally sensitive to variants above 5% allele frequency (10% clonal cells). Therefore, a minimum percentage of 10% neoplastic cells is required. This test is NOT appropriate for monitoring minimal residual disease.

**Gene Regions Tested** – DNA is sequenced using Illumina TruSight reagents on a MiSeq instrument:

<table>
<thead>
<tr>
<th>Gene</th>
<th>Targeted exons</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>BRAF</em></td>
<td>15</td>
</tr>
<tr>
<td><em>MYD88</em></td>
<td>3-5</td>
</tr>
<tr>
<td><em>NOTCH1</em></td>
<td>26-28, 34</td>
</tr>
<tr>
<td><em>SF3B1</em></td>
<td>13-16</td>
</tr>
<tr>
<td><em>TP53</em></td>
<td>2-11</td>
</tr>
</tbody>
</table>

**Limitations:**
Gene amplifications, translocations, and insertions or deletions over 25 bases in length are not detectable by this assay. Variants predicted to be non-deleterious (such as synonymous coding changes and population variants) are not reported. Normal tissue is not tested to determine whether a gene variant is somatic (acquired) or germline (heritable). If the patient has evidence of a heritable cancer syndrome (e.g. different tumor types, early age of onset, family history), genetic counseling is recommended.

**References:**

To consult a pathologist about indications for testing or the significance of a result, call the Molecular Genetics Lab at (984) 974-1825.