Results Summary

4 Clinically Significant Variants Detected

- NRAS Q61R; TERT c.-146C>T; TP53 c.375+2T>G, F109Sfs*14

Pertinent Negatives

NO abnormalities detected in the following genes: BRAF, RET

Interpretation

- Dependent on tumor type, TERT mutations are often associated with a poor prognosis and aggressive disease. Clinicopathologic correlation recommended.

See full list of genes tested in Biomarkers Evaluated section at end of report.

Profile Results Detail

Molecular Testing Detail

<table>
<thead>
<tr>
<th>Gene name</th>
<th>Variant</th>
<th>Amino Acid Change</th>
<th>Nucleotide Change</th>
<th>Consequence</th>
<th>Mutant Allele Frequency (%)</th>
<th>Read Depth</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRAS</td>
<td>Q61R</td>
<td>p.Q61R</td>
<td>NM_002524.4: c.182A&gt;G</td>
<td>nonsynonymous</td>
<td>58.1</td>
<td>1028</td>
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<tr>
<td>TERT</td>
<td>c.-146C&gt;T</td>
<td>c.-146C&gt;T</td>
<td>NM_198253.2: c.-146C&gt;T</td>
<td>promoter</td>
<td>33.8</td>
<td>231</td>
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<tr>
<td>TP53</td>
<td>c.375+2T&gt;G</td>
<td>c.375+2T&gt;G</td>
<td>NM_000546.5: c.375+2T&gt;G</td>
<td>splice site</td>
<td>34.5</td>
<td>1168</td>
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<tr>
<td></td>
<td>F109Sfs*14</td>
<td>p.F109Sfs*14</td>
<td>NM_000546.5: c.326delT</td>
<td>frameshift</td>
<td>21.2</td>
<td>2108</td>
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</table>

FISH Testing Detail

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>ISCN Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>RET FISH - STP</td>
<td>Not Detected (Atypical)</td>
<td>nuc ish(RET x1)[16/50]</td>
</tr>
</tbody>
</table>

Test Description & Methodology

The NGS Thyroid Profile non-MTC uses next-generation sequencing (NGS) and FISH as listed below. Test orders include summary interpretation of all results to help guide treatment decisions.
Clinical Significance

The NGS Thyroid Profile non-MTC is useful to classify fine needle aspirates of thyroid nodules that are indeterminate or suspicious on cytology. Presence of mutations or gene rearrangements as detected by FISH predicts malignancy with varying degrees of specificity depending on the gene mutated and histological subtype. BRAF mutation V600E is associated with poor prognosis in papillary thyroid carcinoma (PTC).

Methodology

Nucleic acid is isolated from paraffin-embedded tissue (FFPE) or fresh cells. Testing for NGS Thyroid Profile non-MTC is performed using Next-Generation Sequencing (NGS) of the coding DNA of the listed genes. This includes sequencing of all the exons. An additional 50 nucleotides at the 5’ and 3’ ends of each coding exon are also sequenced to detect important splicing abnormalities. The NGS method has a typical sensitivity of 3% for detecting common specific mutations and 5% for other mutations. If TERT Gene Promoter is ordered, PCR product is purified and sequenced in both forward and reverse directions and analyzed using GenBank Acc# NG_009265.1. Both -146 C>T or -124 C>T hotspot mutations are reported. This assay has a typical sensitivity of 10-15% for detecting mutated TERT Promoter DNA in a wild-type background. Various factors including quantity and quality of nucleic acid, sample preparation, and sample age can affect assay performance. If FISH or IHC testing is ordered, please see individual reports for description of testing.

Biomarkers Evaluated (by molecular analysis unless otherwise noted)

AKT1, ALK, ARID1A, ATM, BRAF, CDKN2A, CTNNB1, ERBB2, ERBB4, HRAS, KRAS, MEN1, MET, NF1, NF2, NRAS, PIK3CA, PTEN, RET, RET FISH, SMAD4, SMO, SRC, TERT Promoter, TP53, TSC1, TSC2

Electronic Signature

Sample Doctor, M.D., Pathologist - NeoGenomics Laboratories

The Technical Component Processing, Analysis and Professional Component of this test was completed at NeoGenomics California, 31 Columbia, Aliso Viejo, CA / 92656 / CLIA #05D1021650 / Medical Director(s): Dr. Lawrence Weiss.

The performance characteristics of this test have been determined by the performing laboratory. This test has not been approved by the FDA. The FDA has determined such clearance or approval is not necessary. This laboratory is CLIA certified to perform high complexity clinical testing.

Images that may be included within this report are representative of the patient but not all testing in its entirety and should not be used to render a result.