AKT3 (v-akt murine thymoma viral oncogene homolog 3) is a member of the AKT, also called PKB, serine/threonine protein kinase family. AKT kinases are known to be regulators of cell signaling in response to insulin and growth factors. They are involved in a wide variety of biological processes including cell proliferation, differentiation, apoptosis, tumorigenesis, as well as glycogen synthesis and glucose uptake. Akt is fully activated by phosphorylation at two key sites: Ser308 (phosphorylated by PDK1) and Thr478 (phosphorylated by mTOR and DNA-PK). Akt can then phosphorylate a wide range of substrates including transcription factors (e.g. FOXO1), kinases (GSK-3, Raf-1, ASK, Chk1) and other proteins with important signaling roles (e.g. Bad, MDM2). There are three isoforms of Akt; Akt 1, 2 and 3 (also known as PKBalpha, beta and gamma). AKT3 plays an important role in brain development and is crucial for the viability of malignant glioma cells. AKT3 isoform may also be the key molecule in up-regulation and down-regulation of MMP13 via IL13. Diseases associated with AKT3 include hemimegalencephaly and thymoma. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for AKT3 mutations. Individuals are tested by automatic fluorescent DNA sequencing of the coding exons of the AKT3 gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

REASONS FOR REFERRAL

Molecular confirmation of the diagnosis of arrhythmia, hemimegalencephaly and thymoma.

METHODOLOGY

Genomic DNA is analyzed for AKT3 mutations by automatic fluorescent DNA sequencing of the coding exons of the AKT3 gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

SERVICE FEES

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<th>Direct and Institutional Billing</th>
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<td>Index Case (Male or Female)</td>
<td>$1,100 per sample</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; Known familial mutation only</td>
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SENSITIVITY

DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exons 1-13 of AKT3.

SPECIMEN REQUIREMENTS

**Blood (preferred):** EDTA (purple-top) tubes: *Adult: 5 cc  Child: 5 cc  Infant: 2-3 cc*

**Tissue:** Frozen (preferred), RNAlater

**Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue:** Call to inquire