# CADASIL

London Health Sciences Centre | St. Joseph's Health Care London

Pathology and Laboratory Medicine

# Orderable – E-order/Requisition

**Turnaround Time: 3 months**

## Alternate Name(s):

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

**Laboratory:**
Molecular Diagnostics Lab

**Requisition:**
MOLECULAR DIAGNOSTIC REQUISITION

**Method of Analysis:**
All coding exons and 20 bp of flanking intronic sequence are enriched using an LHSC custom targeted hybridization protocol (Roche Nimblegen), followed by high throughput sequencing (Illumina). Sequence variants and copy number changes are assessed and interpreted using clinically validated algorithms and commercial software (SoftGenetics: Nextgene, Geneticist Assistant, Mutation Surveyor; and Alamut Visual). All exons have >300x mean read depth coverage, with a minimum 100x coverage at a single nucleotide resolution. This assay meets the sensitivity and specificity of combined Sanger sequencing and

## Specimen:

Whole blood-2 x 4 mL Lavender EDTA top Vacutainer tube

## Collection Information:

Blood samples must be maintained at room temperature.

## Reference Ranges:

See month

## Interpretive Comments:

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL)(PMID:9388399) is a cause of stroke and vascular dementia. It is a condition of mid-adulthood that can result from mutations in the Notch 3 gene on chromosome 19. These mutations can be identified by direct sequence analysis of the Notch3 coding sequence (PMID:16009764). The CADASIL screen offered in this laboratory involves analysis of the entire Notch3 coding region by direct sequence analysis of PCR-amplified leukocyte-derived genomic DNA, of exons 1 through 33 of this gene.

## Comments:

For more information click on:
MOLECULAR DIAGNOSTIC LABORATORY

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## Critical Information Required:

Pedigree required.

## Storage and Shipment:

Must be received in testing laboratory within 5 days of collection, shipped at room temperature by courier/overnight delivery.

MLPA copy number analysis. All variants interpreted as either ACMG category 1, 2, or 3 (pathogenic, likely pathogenic, VUS; PMID: 25741868) are confirmed using Sanger sequencing, MLPA, or other assays. ACMG category 4 and 5 variants (likely benign, benign) are not reported, but are available upon request. This assay has been validated at a level of sensitivity equivalent to the Sanger sequencing and standard copy number analysis (>99%; PMID: 27376475).

**Test Schedule:**
As required,
Monday to Friday 0800-1600 hours