**Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts & Leukoencephalopathy (CADASIL)**

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts & Leukoencephalopathy (CADASIL) is a rare inherited condition that can lead to cerebral infarction & neurologic impairment, often resulting in dementia or mood disorders. It is the result of mutations in the NOTCH3 gene, ultimately leading to death of vascular smooth muscle cells. The resulting arteriopathy causes alteration of blood flow, particularly cerebral vessels within the brain, leading to parenchymal infarctions. The condition is often suggested by the presence of a strong family history of strokes, often in the absence of risk factors for arteriosclerosis. It can also be suggested in symptomatic patients by characteristic magnetic resonance imaging findings with genetic analysis of the NOTCH3 gene corroborating the diagnosis.

Electron microscopy can identify deposits of accumulating granular osmiophilic material (GOM’s) within degenerating vascular smooth muscle cells of arterioles.

**Specimen Requirements**

A full thickness punch or excision biopsy (3-4 mm) of skin of the upper arm fixed in EM fixative\*. Avoid sun-damaged areas. The tissue should contain deep dermis or upper subcutis containing medium-sized or small arterioles. On collection, the tissue may be hardened by a brief period of fixation (~15 minutes), then the full depth of the biopsy is cut into vertical slices (~1.0 mm thick) and placed back into fixative. This will help to ensure that all layers of skin architecture are present and that the tissue is small enough to adequately fix.

Alternatively, analysis can be attempted on formalin-fixed or paraffin-embedded tissue skin biopsies.

\*An appropriate EM Fixative contains 1.5 – 3.0% glutaraldehyde in a stable buffer (pH 6.8-7.3). It may also contain formalin up to 4%. Pieces should be no bigger than 3 mm in any one dimension. The fixative can be obtained free of charge by calling the UNMC Electron Microscopy Laboratory 402-559-6420.