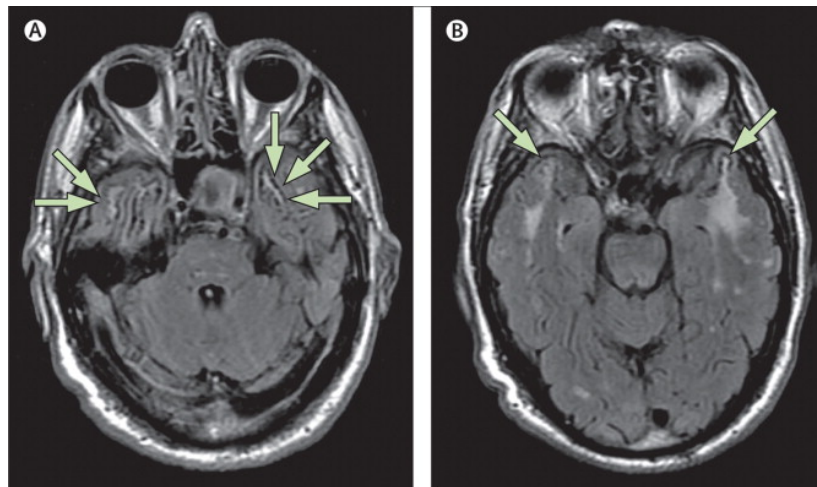


## *The development of therapeutics for CADASIL patients*

**Market Sector: Central Nervous System, CADASIL. Gene therapy**



*Fig. 1 Specific MRI features of CADASIL MRI scans (A and B) showing multiple hypointense lesions (lacunes related to dilated perivascular spaces) at the cortico-subcortical junction (arrows).*  
(Chabriat, H. *et al.*, CADASIL, *The Lancet Neurology*, Volume 8, Issue 7, July 2009, Pages 643-653)

**Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a condition causing ischemic brain lesions, which gradually leads to cognitive decline and eventually to dementia. The disease is caused by mutations in the NOTCH3 gene, which is exclusively expressed in vascular smooth muscle cells (VSMC), and which encodes the NOTCH3 protein. In CADASIL patients there is accumulation of the extracellular domain of the NOTCH3 protein and granular osmiophilic material on the surface of degenerating VSMC, which leads to impaired vascular reactivity and decreased cerebral blood flow. Currently, there is no treatment for CADASIL patients available yet.**

**Although the pathogenesis of the disease is still poorly understood, it has been shown that, due to the characteristic mutations, misfolding of the protein occurs resulting in an unequal number of cysteine residues.**

**Scientists at the Leiden University Medical Center succeeded in re-establishing an equal number of cysteine residues in the NOTCH3 protein by the exclusion of specific exons from the mRNA. They demonstrated that this reduces or even delays the accumulation of NOTCH3 on the surface of VSMC. This novel finding could eventually lead to the development of gene therapeutic strategies for CADASIL patients.**

**Keywords**

CNS, CADASIL, Gene Therapy

**Applications**

Gene therapeutic strategies for CADASIL patients

**Commercial Partner Sought**

Biotechnology and pharmaceutical companies with expertise in the field of the central nervous system and/or gene therapy

**Key Benefits**

- New gene therapeutic strategies
- Unmet need
- Benefits related to orphan disease status
- New insights for other autosomal dominant diseases

**Patent / IP Status**

Premier depot filed in 2009

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Leiden University Medical Center (LUMC) is strongly committed to the advancement of health care, through research and innovation. In particular, the focus is on translational research, with the overall aim to accelerate transfer of findings from the laboratory to clinical application, and to the market.

LUMC has a reputation as a pioneering institute in its field, both nationally and internationally.