Abstract

CADASIL is a hereditary late-onset disease which is caused by a mutation in *NOTCH3* gene. This gene belongs to the *notch* gene family that is conserved among Metazoa. The *notch* genes code transmembrane receptors which play role in Notch signal pathway during organism development. CADASIL is characterized by the impairing of small and medium vessels, especially cerebral arteries. The first symptoms appear in the middle age and the main symptoms are migraines with aura, recurrent strokes, cognitive impairment and dementia. The causes of this disease are mostly missense mutations altering the number of conserved cysteine residues in EGF-like domains of Notch3 protein. This thesis is focused on molecular genetic basis of CADASIL disease, it describes causative mutations and compares hypothesis about pathogenic mechanism of mutations. The penetration of the disease is not clarified yet but the thesis summarizes all current findings about genotype-phenotype correlations which can help to elucidate it. The phenotype differs between families and also between members of the same family. There is described the difference between men and women and the environmental influence too. There are also characterized the most common diagnostic techniques with their sensitivity and specificity in this thesis. In addition, the opinions to optimize the diagnostic protocols are interpreted as well.