KLEINOVÁ, Pavlína. *Roztroušená skleróza mozkomíšní: korelace genové exprese a odpovědi na imunomodulační léčbu [Multiple sclerosis: correlation of gene expression and response to immunomodulatory therapy]*. Praha, 2023. 107 s., 3 přílohy. Disertační práce. 1. lékařská fakulta Univerzity Karlovy v Praze. Vedoucí práce Eva Kubala Havrdová.

Abstract

Multiple sclerosis is a chronic autoimmune disease of the central nervous system with a genetic component, modifiable with immunomodulatory therapy. It is assumed that genetic factors influence the course of the disease and the therapeutic response. The thesis presents the results of two studies investigating the genetic background of multiple sclerosis.

In the first study, the influence of the (GT)n polymorphism of the promoter of the HMOX1 gene for heme oxygenase 1 affecting its expression was investigated in people with multiple sclerosis. No effect of this polymorphism on the course of the disease was observed. We confirmed the effect of immunomodulatory therapy on delaying disease progression.

The second study, called the Genotype/Phenotype Project, is a multicentre international genome-wide association study aimed at detecting single nucleotide polymorphisms associated with severity of multiple sclerosis. It has been shown that common genetic variants with medium to large effect sizes do not contribute to the severity of multiple sclerosis. It has been demonstrated that machine learning using common clusters of single nucleotide polymorphisms together with clinical variables that are readily available at the time of diagnosis can improve prognostic ability at the time of diagnosis and, with further validation, has the potential to find use in clinical practice.

Keywords: multiple sclerosis, genetics, heme oxygenase 1, genome-wide association study, machine learning