Péter Reismann
Dr. med.

Toll-like receptor-4 and diabetic complications

Geboren am 26. 04.1979 in Budapest, Ungarn
Reifeprüfung am 17. 07. 1997 in Budapest, Ungarn
Studiengang der Fachrichtung Medizin vom WS 1997 bis SS 2004
Physikum am 1998 an der Semmelweis Universität, Budapest, Ungarn
Klinisches Studium in der Semmelweis Universität, Budapest, Ungarn
Praktisches Jahr in Semmelweis Universität, Budapest, Ungarn
Staatexamen am 2004 an der Universität Semmelweis, Budapest, Ungarn

Promotionfach: Endokrinologie
Doktorvater: Prof. Dr. med. P.P. Nawroth

Toll-like receptor-4, a central mediator of the innate immune response has been shown to play an important role not only in the defense mechanisms against microorganisms, but also other non-infectious, but inflammatory diseases such as atherosclerosis. Further, accumulating evidence suggest that acquired immunity as well as inflammation may take part in the pathogenesis of diabetic neuropathy. Therefore, we studied whether a modulated innate immune response, caused by the polymorphisms of TLR4 gene, have any association with diabetic neuropathy and nephropathy in type 1 and type 2 diabetes.

To evaluate the potential effect of TLR4 on diabetic complications we determined the common co-segregated alleles (Asp299Gly and Thr399Ile) of TLR4 in 776 patients with diabetes with restriction length analysis. The study was conducted in 246 patients with type 1 diabetes and 530 with type 2 diabetes. The alleles of both polymorphisms were detected using polymerase chain reaction (PCR) and subsequent cleavage by Nco I and Hinf I restriction endonucleases.

No difference was found for the prevalence of alleles of the Asp299Gly and Thr399Ile polymorphisms in patients with type 1 and type 2 diabetes. In most cases the alleles Gly299 and Ile399 occurred in a co-segregatory manner. The prevalence of the Asp299Gly and Thr399Ile haplotype was 10.6% and 12.1% in groups of patients with type 1 and type 2 diabetes, respectively ($p = 0.63$). No association with diabetic nephropathy or diabetic neuropathy was found in patients with type 1 diabetes. In patients with type 2 diabetes, however, heterozygote carriers of the Asp299Gly and Thr399Ile genotypes had a significantly reduced prevalence of diabetic neuropathy (odds ratio 0.34, 95%-confidence interval [0.19;0.61]; $p = 0.0002$), while there was no association with diabetic nephropathy.

Our data indicate that Asp299Gly and Thr399Ile genotypes of the TLR4 gene are associated with reduced risk of diabetic neuropathy in type 2, but not in type 1 diabetes. Thus different mechanisms may be involved in the pathophysiology of diabetic neuropathy in type 1 and type 2 diabetes.