

SUMMARY

Toll-like receptors and their associated molecules like CD14 are the most important pattern recognition receptors of the innate immune system. They support the elimination of invading microorganisms, furthermore have an important role in the initiation of the adaptive immune response and even can participate in the development of autoimmune disorders. In our studies we analyzed the expression and functions of the CD14 system and certain TLRs in autoimmune disorders (systemic lupus erythematosus – SLE, poly/dermatomyositis – PM/DM) and in atopic dermatitis (AD) characterized by frequent bacterial skin infections. A novel flow cytometric assay was developed to measure serum sCD14 concentrations, the receptor expression and ligand binding was quantitated by cytofluorometry, ligand induced cellular activation was evaluated by measuring TNF α secretion, sCD14 isoforms were identified by Western-blotting and the C(-159)T polymorphism of the CD14 gene was characterized using a PCR+RFLP assay. In the intrinsic form of AD we observed an upregulation of CD14, TLR2, TLR4, CD180, and the CD14 mediated LPS- and bacteria-binding was not altered. Based on these data, the presence of frequent infections in AD are probably not attributable to the diminished functions of these molecules. It is more likely that bacterial components are able to translocate through the altered barrier of the skin and can induce the systemic activation of the immune system and upregulation of certain receptors. The T/T genotype of the C(-159)T polymorphism showed association with high sCD14 concentrations and with the chronic disease course in myositis. In this way the T/T genotype might mean susceptibility for the development of chronic disease course by maintaining elevated sCD14 levels that can induce the mild but constant activation of CD14-negative endothelial and muscle cells. Pulse steroid treatment significantly reduced CD14-expression, CD14-mediated LPS-binding and LPS-induced cellular activation in monocytes of SLE patients that can mean a new biochemical pathway of steroid action.