Conclusion

The diagnostic potentialities in RA are limited by the absence of reliable serologic markers. Especially for the differentiation of early manifestations of RA from other forms of arthritis the available autoimmune parameters provide only a low sensitivity and specificity. In this context, they are also detectable to a considerable degree in other rheumatic and/or non-rheumatic diseases. Thus, in accordance to the therapeutical concept of an early and effective administration of disease modifying drugs, new and reliable screening systems need to be established.

This thesis evaluated the diagnostic significance of six relevant parameters in patients with RA in comparison to other rheumatic diseases. A panel of relevant autoantigens was analyzed for a respective B and T cell response including rheumatoid factor, citrulline, calreticuline, calpastatine, BiP and RA33. The frequencies of all potential multiparameter patterns consisting of 3, 4, 5 and 6 autoreactivities were determined from sera and SF samples. As a result, disease specific autoreactivity patterns were determined in 60% of the RA patients including cases of early RA. This analysis revealed for the first time that a combined interpretation of autoreactivities provides a high predictive value for the diagnosis of RA. Importantly, these profiles were apparently also expressed in early disease. For routine clinical diagnostic practice it is feasible to test a rheumatic patient for a pattern of autoreactivities and to assess the immunological heterogeneity.

Moreover, in this thesis, specific autoreactivities against calreticuline, calpastatine, BiP and p205/IgG were analysed for a better understanding of the pathogenesis of RA. It was demonstrated that RA patients are distinguishable for each autoreactivity by antigen-specific T cells. These T cells are HLA-restricted. Supressiv immunreaction implied regulatory T cells.

Il-15 was found in high concentrations. It seems to play an importend role in the pathogenesis as an activating factor of T cells. Proliferating T cells shown a cytokine pattern, which differs from the pattern of TH1 and TH2 cells. Overexpressed antigens were present in the lining of synovia tissue made of fibroblasts and macrophages. However, a co-localization with immunological cells or follicular structures was not detectable. Interestingly, a peptid of the p205/IgG antigen stimulated the production of rheumatoid factor in cell cultures of RA patients.

The presence of reactive T cells and the secretion of proinflammatory cytokines were involved in the complex pathogenesis of RA. The heterogeneity of clinical aspects in RA is apparently also reflected on the immunological level and requires an intensive future research.

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Eidesstattliche Erklärung

Hiermit erkläre ich, Frank Schumann, eidesstattlich, daß diese Dissertation von mir persönlich und ohne die unzulässige Hilfe Dritter verfaßt wurde und auch in Teilen keine Kopien anderer Arbeiten darstellt. Desweiteren versichere ich, alle benutzten Hilfsmittel und Literatur vollständig angegeben zu haben.

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Datum Frank Schumann

Veröffentlichungen

Teile der Arbeit wurden bereits veröffentlicht.

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