MS characterization of apheresis samples from rheumatoid arthritis patients for the improvement of immunoadsorption therapy - a pilot study.

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Abstract

Identification of proteins from apheresis samples was performed by both SDS-PAGE and 2-D gel separation of eluted proteins from staphylococcal protein A-based immunoadsorption columns (Prosorba(®)) followed by MS peptide mass fingerprinting and MS/MS peptide sequencing on a MALDI QIT TOF mass spectrometer. MS/MS peptide sequencing was performed in conjunction with a micro reversed phase HPLC configured with an online MALDI plate-spotting device. Apheresis treatment had been performed in three patients with longstanding therapy refractory rheumatoid arthritis. 2-D gels displayed ca. 500 spots representing proteins that were eluted from the Prosorba(®) columns. From 54 gels, a total of 1256 protein spots had been picked and yielded in the identification of 56 non-redundant proteins without counting isoforms. Proteins from the eluates belong to five major groups comprising (i) immunoglobulins (IgG, IgA, IgM heavy and light chains; about 40% of the spots), (ii) proteins involved in coagulation, (iii) HDL/LDL-associated

proteins, (iv) proteins from the complement system, and (v) acute phase proteins. MS analysis showed that the full-length C3 complement protein had been cleaved upon complement activation, presumably on the column, such that the anaphylatoxin C3a was produced and released during therapy. Our results are consistent with clinical observations on both patient responses to therapy and reported adverse events. For the first time, direct molecular information has become available to support mechanistic reasoning for the principle of function of staphylococcal protein A-based immunoadsorption therapy and for the explanation of adverse events. According to our results, removal and/or modulation of immune complexes together with complement activation can be regarded as the major events that are taking place during Prosorba(®) therapy. In order to avoid complement activation and induction of an inflammatory cascade, we suggest the prevention of C3a anaphylatoxin-related reactions during immunoadsorption therapy.

Beteiligte Forschungseinheiten

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