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# Antibody-proteases as a novel biomarker and a unique target to manage demyelination: A new way for drug design and drug discovery

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Catalytic Abs (catAbs) are multivalent immunoglobulins (Igs), endowed with a capacity to hydrolyze the antigenic substrate. In this sense, proteolytic Abs (or Ab-proteases) represents Abs endowed with a capacity to provide proteolytic effects. Ab-proteases were shown to occur at clinical courses and evidently correlate with the severity of the disease. A situation of much greater interest is occurred in multiple sclerosis (MS) which would demonstrate some new potential molecular targets to be selected for constructing newer diagnostic tools and setting up newer drug design as well. Anti-MBP autoAbs from MS patients exhibited sequence-specific proteolytic cleavage of MBP. The activity of Ab-proteases markedly differs: (1) between MS patients and healthy controls; (2) among MS patients with different types of the course to be the highest and thus dominate in a progradient course, progression phase in particular. The activity of the Ab-proteases revealed significant correlation with scales of demyelination and thus with the disability of the patients as well. Moreover, when bursts of the Ab-associated proteolytic activity are evident, the pre-early stages of the exacerbation could be predicted, even at no seeing any clinical manifestations. And when we saw a stable growth of the activity, we could predict changing of a remitting type (moderate one) into the progradient type (severe one) prior to changing of the clinical manifestations. Ab-mediated proteolysis of MBP results in generating a set of peptides. The final statistical data revealed six sites of preferential proteolysis. Most of those sites are located within the immunodominant regions of MBP. In contrast to canonical proteases, for Ab-proteases, there is an extra set of cleavage sites in the targeted autoantigens focused predominantly at the immunodominant sites of MBP. The activity of Ab-proteases was first registered at the subclinical stages 1-2 years prior to the clinical illness. About 24% of the direct MS-related relatives were seropositive for low-active Ab-proteases from which 38% of the seropositive relatives established were being demonstrating a stable growth of the activity for 2 years under the study. Moreover, low-active Ab-proteases in at-risk persons (at the subclinical stages) and primary clinical and MRT manifestations observed were coincided with the activity to have its mid-level reached. And registration in the evolution of highly immunogenic Ab-proteases to attack other sites predominantly would illustrate either risks of transformation of subclinical stages into clinical ones or risks of exacerbations to develop. Of tremendous value are Ab-proteases directly affecting remodeling of tissues with multilevel architectonics (for instance, myelin). By changing sequence specificity of the Ab-mediated proteolysis one may reach reduction of a density of points of the negative proteolytic effects within the myelin sheath and minimizing scales of demyelination. Moreover, Ab-proteases can be programmed and re-programmed to suit the needs of the body metabolism or could be designed for the development of principally new catalysts with no natural counterparts. So, further studies on Ab-mediated MBP degradation and other targeted Ab-mediated proteolysis may provide a supplementary (diagnostic, preventive and therapeutic) tool for assessing the disease progression, predicting disability of the patients and preventing the progression.

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