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ANTIBODY PROTEASES AS A NOVEL BIOMARKER AND A UNIQUE TARGET TO SUIT TRANSLATIONAL TOOLS TO BE APPLIED FOR BIOENGINEERING AND BIOPHARMA

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Catalytic Abs (catAbs) are multivalent im-munoglobulins (Igs) with a capacity to hy-drolyze the antigenic (Ag) substrate. In this sense, proteolytic Abs (Ab-proteases) rep-resent Abs to provide proteolytic effects. Abs against myelin basic protein/MBP with proteolytic activity exhibiting sequence-specific cleavage of MBP is of great value to monitor demyelination whilst in multiple sclerosis (MS). The activity of Ab-proteases was first registered at the subclinical stages 1-2 years prior to the clinical illness. And the activity of the Ab-proteases revealed significant correlation with scales of demy-elination and the disability of the patients as well. So, the activity of Ab-proteases and its dynamics tested would confirm a high subclinical and predictive (translational) value of the tools as applica-ble for personalized monitoring protocols. Of tremendous value are Ab-proteases di-rectly affecting remodeling of tissues with multilevel architectonics (for instance, my-elin). By changing sequence specificity one may reach reduction of a density of the negative proteolytic effects within the mye-lin sheath and thus minimizing scales of demyelination. Ab-proteases can be pro-grammed and re-programmed to suit the needs of the body metabolism or could be designed for the development of new cata-lysts with no natural counterparts. Further studies are needed to secure artificial or edited Ab-proteases as translational tools of the newest generation to diagnose, to moni-tor, to control and to treat and rehabilitate MS patients at clinical stages and to prevent the disorder at subclinical stages in persons-at-risks to secure the efficacy of regenerative manipulations.

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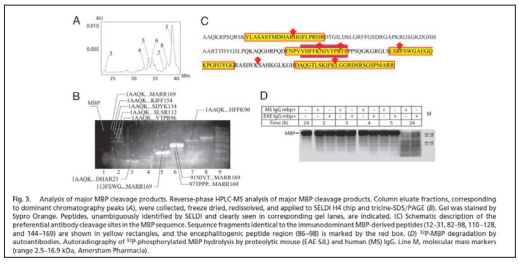

Fig. 3. Analysis of major MBP cleavage products. Reverse-phase HPLC-MS analysis of major MBP cleavage products. Column eluate fractions, corresponding to dominant chromatography peaks (A), were collected, freeze dried, redissolved, and applied to SELDI H4 chip and tricine-SDS-PAGE (B). Gel was stained by Sypro Orange. Peptides, unambiguously identified by SELDI and clearly seen in corresponding gel lanes, are indicated. (C) Schematic description of the preferential antibody cleavage sites in the MBP sequence. Sequence fragments identical to the immunodominant MBP-derived peptides (12–31, 82–98, 110–128, and 144–169) are shown in yellow rectangles, and the encephalitogenic peptide region (86–98) is marked by the red box. (D) ^{32}P-MBP degradation by autoantibodies. Autoradiography of ^{32}P-phosphorylated MBP hydrolysis by proteolytic mouse (EAE SJL) and human (MS) IgG. Line M, molecular mass markers (range 2.5–16.9 kDa; Amersham Pharmacia).