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Antibodies with functionality as a new generation of translational tools to monitor, to predict and to prevent demyelination

) iomarkers enable early diagnosis, guide targeted therapy and monitor the activity and therapeutic responses across B the diseases. So, identification and validation of biomarkers of newer generations to create a new strategy based upon subclinical recognition of the latter long before the disease clinically manifests itself is of great value. Among the best-validated predictive biomarkers are autoimmunity-related ones (including antibodies/Abs). Meanwhile, multiple sclerosis (MS)whilst being achronic autoimmune disorder would result in a destruction of myelin by different factors, including autoAbs. Along with canonical Abs, we have discovered a new family of Abs proven to be endowed with myelin basic protein (MBP)-targeted proteolytic activity (Ab-proteases). The proteolytic property mentioned is considered to serve a functional property of the biomolecule. Most (72-78%) of anti-MBP autoAbsharvested from MS patients and mice with EAE exhibited MBP-specific proteolytic cleavage of MBP. The activity of Ab-proteases markedly differed: (i) between MS patients and healthy controls and (ii) inpatients with different types of MS course. Moreover, the activity demonstrated a significant correlation with demyelination, neurological deficiency and thus with the disability of the patients. Of greater value is a sequencespecificity of Ab-proteasesto attack targeted sequences located in dominant fivesites of MBP. Most of those sites whilst being immuno dominant are concentrated within 43-170 of MBP.Two sites from the set would comprise 81-103and 82-98, which, in turn, whilst being sequence-specific, highly immunogeneic and encephalitogeneic both, proved to be major inducers of very aggressive EAE in SJL mice.In humans, both 81-103 and 82-98 have been proven to be major MBP targets to be attacked by Ab-proteases obtained from patients with secondary-progradient courses of MS, progression phase (SPPP), and with remittent course of MS, exacerbation phase (REP), both are with aggressive inflammation. Two extra sites from the same 43-170set are located within 43-68 and 146-170 that proved to be inducers of moderate EAE and thus targets to be attacked by Ab-proteases in MS patients with secondary-progradient courses, stabilization phase (SPSP), and with remittent course, remission phase (RRP), both are with inflammation quenched. So, the most immunogeneic and encephalitogeneic epitopes responsible for generating aggressive bursts are concentrated in three specific areas of MBP: (i) the strongest one is in the smallest 82-98; (ii) a weaker epitope is formed by a longer 81-103 subsequence; and (iii) an epitope with the lowest immunogeneic and encephalitogeneic properties is rooted in a rather long 143-170 sequence defined. The relatives being seropositive for Ab-proteases were being monitored for 3 years whilst demonstrating stable growth of the Ab-associated proteolytic activity when were being under the study.And when the activity reached its mid-level, we identified primary clinical and MRI manifestations to be coincided with the Ab-associated proteolytic activity. And then the proteolytic activity was being further escalated due to the time of progression, type of the disorder, and disability of the patient. Meanwhile, a substantial proportion (around 34%) of relatives demonstrating low-active Ab-proteases with no trends to grow had hadsubclinical evidence of autoimmunity without developing clinically overt dis-ease. The activity of Ab-proteases was first registered at the pre-early (subclinical) stages of the disorder, when Ab-proteases were still low-active whilst attacking presumably low-immunogeneicsequences, the inflammation is moderate, and the manifestations are thus scarcely visible. As the disorder progresses to transform from subclinical into clinical stages, the activity of Ab-proteases is being escalated to reach the indices to be typical for the clinical stage. And, when bursts of the proteolytic activity were evident, the pre-early stages of REP stage could be predicted, even at no seeing any clinical manifestations. And along with the evolution of the sequence specificity, when we saw an extensive growth of the activity, we could predict transformations in the clinical course, i.e., changing of RRP (moderate one) into SPP (severe one) prior to changing of the clinical manifestations.