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Antibody-proteases as promising tools of novel generation to be translated into clinical practice for having multistep (subclinical and clinical) demyelination monitoring secured

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Among the best-validated proteome-related predictive biomarkers, antibodies (Abs) are the best known. A combination of different panels of auto-Abs in the diagnostic practice has become a great significance to predict risks of chronization of the autoimmune disorder since most of the latter are preceded by a long subclinical (symptom-free) phase when the patients or persons-at-risk could be identified via specific sets of auto Abs. Of particular interest would be algorithms which would em-ploy panels of targeted Abs for screening patients and their relatives at risks for the presence of pre-clinical (lab proof-based) signs and for thus having the data translated into the daily practice. Abs against myelin basic protein/MBP endowing with targeted and highly specific proteolytic activity (Ab-proteases) is appearing to be of great value to monitor demyelination at either of the stages. The activity of Ab-proteases identified and purified from MS blood samples markedly differed between: (i) MS patients and healthy controls; (ii) different MS courses; (iii) EDSS scales of demyelination to correlate with the disability of MS patients to predict transformations prior to changes of the clinical course. The sequence-specificity of Ab-proteases demonstrates five sites of preferential proteolysis to be located within the immunodominant region of MBP. The activity of Ab-proteases was first registered at the subclinical stages. About 24% of the direct MS-related relatives were seropositive for low-active Ab-proteases from which 50% of the seropositive relatives monitored for 2 years have been demonstrating stable growth of the proteolytic activity. And, finally, primary clinical manifestations observed were coincided with the activity to have its mid-level reached. The activity of Ab-proteases in combination with their sequence-specificity to attack well-defined epitopes to be released from MBP during epitope spreading, would confirm a practical value of Ab-proteases demonstrating their unique functionality. Meanwhile, Ab-proteases can be programmed and reprogrammed to suit complex cell biochemistry. And thus two logical questions would arise: (i) Would the original potential for the Ab-mediated proteolysis relate to natural Ab-related function? (ii) Could that potential be translated into the clinical practice to suit the need of clinicians? Canonical Abs play neither predictive nor discriminative role to affect the subclinical stage of MS. Meanwhile, sequence-specific Ab-proteases have proved to be greatly informative and thus valuable as translational biomarkers to monitor MS at both subclinical and clinical stages. So, the activity in combination with the sequence-specificity would confirm a high subclinical and predictive value of Ab-proteases as applicable for personalized monitoring protocols. Moreover, of tremendous value in this sense are Ab-proteases directly affecting the physiologic remodeling of tissues with multilevel architectonics (for instance, myelin). So, targeted Ab-mediated proteolysis could be also applied to isolate from Ig molecules catalytic domains directed against ence-phalitogenic epitopes or domains containing segments to exert proteolytic activity. And further stu-dies on Ab-mediated MBP degradation and other targeted Ab-mediated proteolysis may provide biomarkers of new generations and thus a supplementary tool for assessing the disease progression and predicting disability of the patients and persons-at-risks. The latter means that translation of the data collected on targeted Ab-mediated proteolysis may provide a supplementary tool for predicting demyelination and thus the disability of the MS patients.

Biography

Sergey Suchkov, a researcher-immunologist, a clinician, graduated from Astrakhan State Medical University, Russia, in 1980. He has been trained at the Institute for Medical Enzymology, The USSR Academy of Medical Sciences, National Center for Immunology (Russia), NIH, Bethesda, USA) and British Society for Immunology to cover 4 British university facilities. Since 2005, he has been working as Faculty Professor of I. M. Sechenov First Moscow State Medical University and of A. I. Evdokimov Moscow State Medical & Dental University. From 2007, he is the First Vice-President and Dean of the School of PPPM Politics and Management of the University of World Politics and Law. From 1991-1995, he was the Scientific Secretary-in-Chief of the Editorial Board of the International Journal "*Biomedical Science*" (Russian Academy of Sciences and Royal Society of Chemistry, UK) and The International Publishing Bureau at the Presidium of the Russian Academy of Sciences. From 1995-2005, he served as the Director of the Russian-American Program in Immunology of the Eye Diseases. He is a member of EPMA (European Association of Predictive, Preventive and Personalized Medicine, Brussels-Bonn), a member of the NY Academy of Sciences, a member of the Editorial Boards for Open Journal of Immunology and others. He is the author of the "Concept of post-infectious clinical and immunological syndrome", co-author of a "Concept of abzymes and their impact into the pathogenesis of auto immunity conditions", and as one of the pioneers in promoting the concept of PPPM into a practical branch of health services.

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