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Antibodies with functionality as a new generation of translational tools designed to be pro-grammed via translational resources to predict and to prevent demyelination

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Abs against myelin basic protein/MBP present with the proteolytic-activity (Ab-proteases with functionality) of higher value to observe demyelination to show the evolution of multiple sclerosis (MS). Anti-MBP auto-Abs from MS patients and mice with EAE exhibited particular proteolytic cleavage of MBP which, in turn, markedly vary between: 1. MS patients and healthy controls; 2. Different clinical MS courses; 3. EDSS scales of demyelination to correspond with the disability of MS patients to predict the transformation prior to the changes of clinical course.

Ab-mediated proteolysis of MBP was shown to be sequence-specific while exhibiting 5 sites of preferential proteolysis to be located within the immunodominant regions of MBP and to fall inside into 5 sequences fixed. Some of the latter (with the highest encephalitogenic properties) were evident to act as a specific inducer of EAE and to be attacked by the MBP-targeted Ab-proteases in MS patients with the most severe (pro-gradient) clinical courses. The other ones whilst being less immunogenic happened to be EAE inducers very rare but were shown to be attacked by Ab-proteases in MS patients with moderate (remission-type) clinical courses.

The activity of Ab-proteases was initially registered at the subclinical stages 1-2 years prior to the clinical illness. About 24 percent of the direct MS-related relatives were sero-positive for low active Ab-proteases from which 22 percent of the seropositive relatives established were being monitored for 2 years while demonstrating a stable growth of Ab-associated proteolytic activity. Moreover, some of the low-active Ab-proteases in persons at MS-related risks (at subclinical stages of MS) and primary clinical and MRT manifestations observed were coincided with the activity to have its mid-level reached. Registration in the evolution of highly immunogenic Ab-proteases would illustrate either risks of transformation of subclinical stages into clinical ones, or risks of exacerbations to develop.

The activity of Ab-proteases in joining with particular sequence would confirm an increase subclinical and predictive (translational) value of the tools as applicable for personalized monitoring protocols. 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. Future studies on targeted Ab-mediated proteolysis could yield a translational tool for predicting demyelination and thus the disability of the MS patients.

Speaker Biography

Sergey Suchkov graduated from Astrakhan State Medical University and awarded with MD, then in 1985 maintained his PhD at the I M Sechenov Moscow Medical Academy and in 2001, maintained his doctorship degree at the Nat Inst of Immunology, Russia. From 1987 through 1989, he was a senior researcher at Koltzov Inst of Developmental Biology. From 1989 through 1995, he was a head of the lab of clinical immunology, Helmholtz Eye Research Institute in Moscow. From 1995 through 2004, as a chair of the dept for clinical immunology, Moscow Clinical Research Institute (MONIKI). He has been trained at NIH; Wills Eye Hospital, PA, USA; Univ of Florida in Gainesville; UCSF, S-F, CA, USA; Johns Hopkins University, Baltimore, MD, USA. He was an executive secretary-in-chief of the editorial board, biomedical science, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK. At present, he is a chair, dept for personalized and translational medicine, I M Sechenov First Moscow State Medical University. He is a member of the: New York Academy of Sciences, USA; American Chemical Society (ACS), USA; American Heart Association (AHA), USA; EPMA (European Association for Predictive, Preventive and Personalized Medicine), Brussels, EU; ARVO (American Association for Research in Vision and Ophthalmology); ISER (International Society for Eye Research) and PMC (Personalized Medicine Coalition), Washington, USA.

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