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The therapeutic P140 peptide, a new immunomodulating tool for lupus may have applications in other chronic inflammatory conditions

P140 is a synthetic peptide issued from the U1-70K protein. It was chemically modified and contains a phosphoserine residue at position 140. P140/Lupuzor™ had no adverse safety signals and met its primary efficacy end points in a multicenter, randomized, placebo-controlled phase IIb study for lupus. A phase III-clinical trial is currently on-going for this indication. The mechanism of action of P140 has been recently elucidated in MRL/lpr lupus-prone mice. P140 binds HSPA8/HSC70 chaperone protein, decreases its expression and reduces autophagic flux in B-lymphocytes of peptide-treated MRL/lpr mice. P140 interferes with a selective form of autophagy called chaperone-mediated autophagy or CMA. It induces a lower expression class II-MHC molecules and alters the presentation of peptides to autoreactive T cells, leading to a reduction T and B cells activation and a drop of potentially pathogenic autoantibodies. This process does not affect the resistance of mice to an infectious agent. Based on this unique mechanism of action, we anticipated that the peptide could be efficient in other pathological conditions in which reduction of CMA activity would be beneficial. This was evaluated in several murine models of chronic inflammatory diseases.These models notably include a rat model of experimental autoimmune neuritis for chronic inflammatory demyelinating polyradiculoneuropathy, an autoimmune-mediated inflammatory disease of the peripheral nervous system. Our first results show that P140 peptide can curb the course of the disease and protect treated animals. These findings provide arguments to conclude that P140 peptide might efficiently work in indications other than lupus, most particularly in conditions of inflammatory, chronic diseases.

Biography

Sylviane Muller has received her Doctoral degrees in Molecular Biology (1978) and Science (1984) from the University of Strasbourg, France. She has worked as a Post-doctoral Fellow at the Max-Planck Institute for Immunobiology in Freiburg, Germany. She is currently a Distinguished class Research Director at the CNRS and Professor at the Institute of Advanced Studies of the Strasbourg University (Chair Therapeutic Immunology). She is a Deputy Director of the Molecular and Cellular Biology Institute, Director of the CNRS Unit Immunopathology and Therapeutic Chemistry and Head of the Drug Discovery Center for Cancer and Inflammation. Medal is awarded 'Laboratory of Excellence'. Her research interests focus on molecular and cellular events involved in autoimmunity, especially in the lupus disease. She has discovered the P140/Lupuzor peptide that is currently evaluated in a phase III clinical trial for lupus. She is the co-author of over 345 publications, Co-Inventor of ~30 patents and Co-Founder of NeoMPS (1986) and ImmuPharma (2002) companies. She has received the CNRS Silver Medal (2009) and the CNRS Innovation Award (2015). Her research interests include molecular and cellular events involved in autoimmunity, especially in the lupus disease.

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