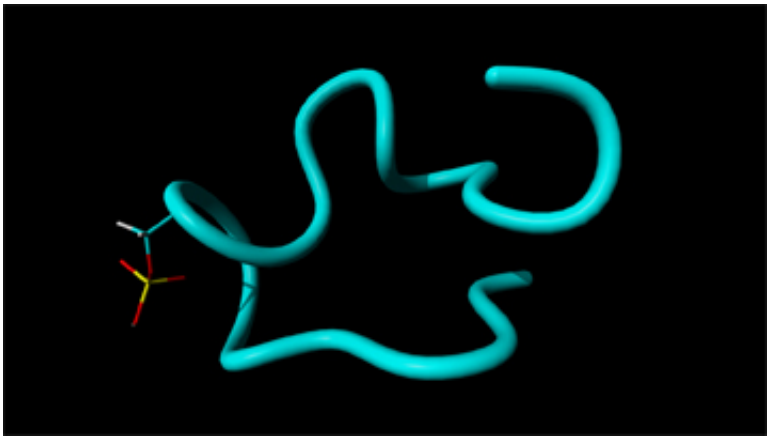
Treatment for lupus enters phase III

December 15 2015



Modeling of the 3D structure of the P140 peptide. The P140 peptide corresponds to the 131-151 sequence of the nuclear ribonucleoprotein U1-70K, whose residue 140 is a phosphoserine (visible on the left). Credit: Fanny Bonachera / IBMC / ICT / PDB

Lupuzor may become the first specific and non-immunosuppressant therapy for lupus, a disabling autoimmune disease that is currently incurable. Discovered by Sylviane Muller's team in the CNRS Immunopathologie et Chimie Thérapeutique laboratory, in Strasbourg, this peptide is the subject of a CNRS patent (granted in 2009) and has already successfully completed phases I and II of its regulatory clinical trials, supervised by ImmuPharma-France. An international phase III pivotal trial, also managed by this company, will begin in a few days' time in the US when the first patient starts the treatment, before the trial is extended to Europe. Phase III is the last stage in the testing of a

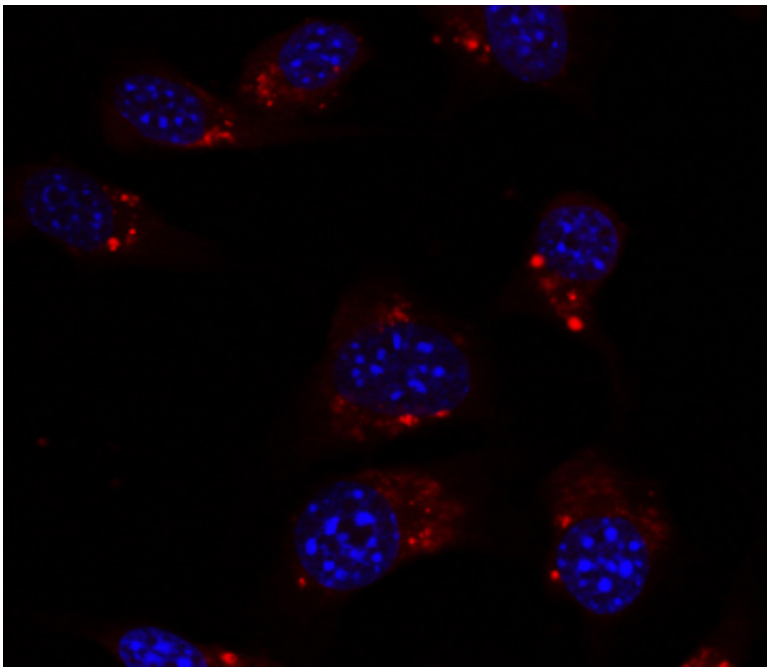
candidate drug, before it can be given market approval. The launch of phase III was the subject of a meeting involving around a hundred physicians on December 11-12, in Paris.

Lupus is a chronic autoimmune disease that affects more than five million people worldwide, 90% of whom are women. It is characterized by the production of autoantibodies that attack different organs (skin, joints, vascular system, brain, kidneys) and cause inflammation, hence the broad range of possible symptoms: skin lesions, joint pain, thromboses, psychotic episodes, etc. To alleviate this disease with many causes, only palliative treatments are available at present, most of which are non-specific: corticosteroids and immunosuppressants, but they also weaken the immune system. Although they can stop autoimmune attacks, they also render patients highly susceptible to multiple infections. It was therefore urgent to develop a more targeted therapy.

The team led by Sylviane Muller, who received the 2015 CNRS Medal of Innovation, developed a family of peptides (protein fragments) that can specifically correct dysfunction of the immune system. One of these peptides, called P140, proved capable of delaying the development of lupus in affected mice, while preserving their immune systems' ability to fight infective agents. Since then, phase I and II clinical trials have been carried out by the company ImmuPharma-France, which holds an exclusive license for the patents that protect this family of peptides, all owned by the CNRS or filed as joint property. During phase II trials, the disease regressed in 62% of patients after 3 months of treatment: this is the best result ever to have been achieved for this pathology.

Following these successes, ImmuPharma-France launched its pivotal phase III trial. In the same way as during the phase IIb trials, the candidate drug will be administered under double-blind conditions once a month by the subcutaneous route, at a rate of 200 µg per injection, but the duration of treatment will be extended to a year, as opposed to 3

months previously. Two hundred patients will be included in this trial, spread across 45 centers (10 in the US and 35 in Europe). The first patients will be recruited in the US by the end of 2015. In Europe, the trial should be starting in mid-January in the first centers, which include those in France. Recruitment should be completed by mid-2016 and the final results are anticipated at the end of 2017.



The P140 peptide acts by regulating excess autophagy of the immune cells in lupus. It thus corrects the production of auto-antigens, and consequently, downstream of the cascade of events, the production of autoantibodies. Credit: IBMC / ICT

The first Investigators' Meeting for the phase III trial took place on December 11 and 12 in Paris, and involved around a hundred American and European physicians.

Once this final phase of clinical trials is completed, and provided the

results confirm those of phase IIb, Lupuzor could be put on the market and subsequently play a central role in the treatment of patients with lupus.

According to preclinical findings, Lupuzor may also be effective in other chronic autoimmune pathologies, such as Sjögren's syndrome (dry eye syndrome) or Crohn's disease (an autoimmune disease that causes chronic intestinal inflammation). Fundamental studies on these promising leads are now underway in Sylviane Muller's laboratory.

Provided by CNRS