Prolyl oligopeptidase (POP, E.C. 3.4.21.26) cleaves short peptides, of less than 30 amino acid long, at the C-side of an internal proline. It has been associated with many pathophysiological processes, such as neurodegeneration and inflammation. At the moment there are no studies that have been focused on POP function in multiple sclerosis (MS). A preliminary study in a Spanish cohort reported altered POP activity in plasma samples of patients with relapsing-remitting multiple sclerosis (RR-MS) compared with healthy controls. Also they observed increased levels of the endogenous POP inhibitor in plasma samples of patients with RR-MS.

The first objective of this study was to evaluate the POP activity levels in serum and cerebrospinal fluid (CSF) samples from RR-MS patients and healthy controls in a Finnish population using a kinetic fluorescence assay. The seral levels of the endogenous POP inhibitor were also investigated by preincubating recombinant porcine POP (rPOP) with serum and determining the percentual decrease of POP activity compared to basal rPOP values (inhibitory capacity %). The second objective of this study was to purify and characterize the endogenous POP inhibitor in serum. In order to accomplish this goal, different biochemical and biophysical features, such as temperature resistance and filtering cut-off were tested. Also a combination of chromatographic approaches (affinity/anion exchange/hydrophobic interaction chromatography) with polyacrylamide gel electrophoresis and protein staining was used.

All the differences observed in POP activity/inhibitor levels (serum, serum with DTT, CSF) between healthy controls and patients with RR-MS in this study did not reach statistical significance due to low values in all the samples. However, the trends in all the measured parameters were similar to the preliminary study in a Spanish cohort. Thus, the data supports further, more comprehensive, studies on the role of POP in MS.

After series of chromatographic runs, a mass spectrometry analysis revealed the endogenous POP inhibitor to be α₂-macroglobulin, a panprotease inhibitor in serum. α₂-Macroglobulin has also been associated with MS, thus this finding substantiate the relationship between POP and MS.