Multiple Sclerosis (MS) is a debilitating demyelinating autoimmune disease affecting mainly young adults. Next to genetics, environmental factors including Epstein-Barr Virus (EBV) infection have been implicated. MS-specific oligoclonal IgG bands in the cerebrospinal fluid have been identified as EBV-specific and autoantibodies against myelin basic protein, oligodendrocyte specific protein and myelin have been identified. Our group has additionally proven anti-EBV nuclear antigen-1 (EBNA-1,398-413) antibodies as an independent risk factor for MS. This epitope is of particular interest, as it shares high amino acid sequence homology with human crystallin alpha-B which has already been implicated in cross-reactivity.

**Objectives:**
- Identify cross-reactive targets for anti-EBNA-1,398-413, IgG antibodies.
- Compare cross-reactive immune responses between MS and healthy controls and serum/plasma against human brain-derived proteins.

**Methods:**
Selecting MS (n=8) and healthy controls (n=10), based on clinical subtype, gender and genetic typing (Human Leukocyte Antigen; HLA; Table 1):
1. Isolate anti-EBNA-1,398-413, IgG antibodies using pull down columns.
2. Test these selective antibodies and antibodies from whole serum/plasma on a HexSelect macroarray containing recombinant human brain proteins to identify any new potential self-reactive targets of antibodies.

**Results:**
Anti-EBNA-1,398-413 IgG from MS patients identified two new potentially cross-reactive targets. Both MS patient and healthy control antibodies from serum/plasma reacted against multiple proteins of the array. A total of 18 different protein targets were identified, with some overlap between groups (Table 2). Functionally, proteins were mainly involved in growth control, cell metabolism, autophagy, endocytosis and microtubule destabilization (Figure 3).

**Discussion, Conclusions, Future Aims:**
- Multiple targets were identified for both specific anti-EBNA-1,398-413 IgG antibodies and whole serum or plasma for both cohorts.
- Different targets were identified for the same cohort (Acute MS) anti-EBNA-1,398-413 IgG and whole serum, suggesting antibody cross-reactivity could be masked by other stronger binding antibodies.
- Identified targets will be confirmed by western blot, with addition of the protein crystallin alpha-B which was not included on the protein array and previously shown to share homology with the EBNA-1,398-413 peptide, and myelin based proteins.
- Obtaining a more comprehensive understanding of the potential of cross-reactive antibodies will aid in understanding the underlying MS pathomechanism.