ARE SUPPRESSOR OF CYTOKINE SIGNALING (SOCS) PROTEINS INVOLVED IN ALZHEIMER´S DISEASE

D.G. Walker\textsuperscript{1}, J.C. Kruchowsky\textsuperscript{1}, L.-F. Lue\textsuperscript{2}

\textsuperscript{1}Laboratory of Neuroinflammation, \textsuperscript{2}Laboratory of Neuroregeneration, Banner Sun Health Research Institute, Sun City, AZ, USA

Introduction: Suppressors of cytokine signaling (SOCS) are a group of 8 proteins that can regulate cytokine signaling by repressing activation of JAK/STAT transcription factors. SOCS are rapidly induced in response to cytokine stimulation. As immunomodulatory proteins, they have potential for therapeutic applications.

Aims: Expression of SOCS in relation to Alzheimer´s disease (AD) pathology has not been explored. The aim of this study was to determine whether SOCS expression, particularly SOCS-1, SOCS-3 and SOCS-6, identified regions of active inflammation or pathology in brain.

Methods: This study utilized human brain tissue sections from non-demented (ND), mild cognitive impaired (MCI) and AD subjects to examine SOCS expression by immunohistochemistry. Regulation of SOCS expression in neural cells was analyzed by reverse transcription polymerase chain reaction and western blots using microglia, astrocytes and vascular endothelial cells isolated from postmortem brains and human hN2 neurons.

Results: Increased expression of SOCS-3, not SOCS-1 and SOCS-2, mRNA was detected in AD, but not in MCI and ND cortical samples, while all of these genes were significantly upregulated in amyloid beta peptide stimulated microglia. In tissue sections, strong expression of SOCS-1 was localized to the hippocampal formation; SOCS-3 protein was found in different classes of neurons, also astrocytes and endothelial cells but not microglia; while SOCS-6 was restricted to a subset of neurons with neurofibrillary tangles.

Conclusion: SOCS-1, SOCS-3 and SOCS-6 expression was present in brain tissue from elderly and AD cases, particularly in neurons, suggesting an ongoing response to cytokine activation (Supported by NIH R21 AG034409-01).