**Pentapeptide, targeting Serum Amyloid A and Amyloid β suppresses /attenuates chronic inflammation, autoimmunity and neurodegeneration**

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Research Summary

5-mer peptide (MTADV-Methionine ,Threonine, Alanine , Aspartic acid, Valine) was derived from a pro-inflammatory CD44 variant that expressed mostly ,if not exclusively, in inflamed joints of a rheumatoid arthritis (RA) patient. The 5-MER MTADV is acetylated-N amidated-C to improve its stability. MTADV interacts with the amyloid proteins , Serum Amyloid A (SAA) and transthyretin and prevents their pathological aggregation or polymerization. In addition, a preliminary evidence revealed that it can also target Amyloid β. The MTADV peptide is polymerized in solution , displays β sheet configuration with alternating hydrophobic-hydrophilic amino acids, can cross cell membrane and its activity is lost when the amino acids are scrambled . The 5-MER peptide exhibits therapeutic activity in mouse models of inflammatory diseases associated with the stress acute phase protein SAA ,such as RA, inflammatory bowel disease (IBD) and multiple sclerosis (MS). For example , daily oral delivery of the MTADV peptide ,starting 5 days after induction Experimental Autoimmune Encephalomyelitis (EAE) by MOG, attenuated limb paralysis in this mouse model of MS. This finding further indicates that the peptide can tolerate the digestive system . The 5-MER peptide does not interfere with normal immune responses, such as delayed type hypersensitivity and does not generate ,as expected, neutralizing antibodies after IP injection. C. elegans worms , expressing human Amyloid β transgene , which induces muscle paralysis , restore their movement potential after exposure to MTADV. Finally , a preliminary experiment reveals that Alzheimer’s -like mice (5XFAD transgenic mice)-restored their learning potential after daily IP injection with MTADV peptide. To this end , Alzheimer’s 5x FAD-transgenic mice treated with MTADV showed the same learning potential as wild type mice, whereas the Alzheimer ‘s mice , that were not treated with the peptide display learning difficulties. Our next immediate goal is a medical translation of these academic findings.