SEMINAIRE du 21 Février, 2020

Salle des Thèses, de 11h à 12h30

Faculté de Pharmacie de Chatenay-Malabry, 5 Rue Jean-Baptiste Clément, 92290 Châtenay-Malabry

Anti-inflammatory and anti-neurodegenerative therapeutic activity of human-derived 5-MER peptide, recognizing Serum Amyloid A (SAA) : a new potential peptide drug (MTADV) and a new target (SAA)

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Invité par le Prof. Elias Fattal

Background and Aims

Synthetic 5-MER peptide (or "the peptide") MTADV (methionine, threonine, alanine, aspartic acid, valine), derived from the sequence of a human pro-inflammatory CD44 variant, alleviates pathological inflammation in mouse models of Rheumatoid Arthritis (RA),Inflammatory Bowel diseases (IBD), Multiple (MS) and Alzheimer disease (AD). The study aim: elucidation the peptide mechanism of action.

Methods

Daily administration of the peptide by injections or oral delivery Histopathological staining of tissue sections ; Bio-luminescence analysis of the peptide therapeutic effect ; Mass Spectrometry to identify the peptide targets, evaluation of clinical symptoms ; Gene Set Enrichment Analysis (GSEA) and qRT-PCR of mRNA.

Results

The peptide displayed a specific therapeutic effect. Mass Spectrometry and gel analyses revealed that amyloid proteins, including serum amyloid A (SAA) and Amyloid β (Aβ), are potential targets of the peptide. SAA attracted a special attention, because its involvement in RA, IBD and MS pathology and it's hallmarks of chronic inflammation. Muscle paralysis of C. elegans worms, expressing the human Aβ transgene, was inhibited by the peptide. The peptide restored the learning potential of 5-FAD AD mice, expressing mutated Aβ human transgenes. The peptide prevents aggregation/fibrillation or polymer formation of SAA and it targets Aβ, presenting pathological versions of these proteins. The peptide (but not the scrambled peptide) inhibits the release of the pro-inflammatory cytokines IL-6 and IL-1β from SAA-stimulated human RA fibroblasts by blocking the polymer formation of this protein.

Conclusions

We predict the peptide can target wide spectrum of diseases, including cancer, in which amyloidogenic proteins are involved (e.g., SAA, Aβ, amylin, α-synuclein, prions).