Cellular Therapy for the Treatment of Alzheimer’s Disease
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Abstract

- Alzheimer’s Disease (AD) is one of the most common forms of dementia and neurodegenerative disease from nowadays. It was first described more than 100 years ago by Dr. Alois Alzheimer and it still hasn’t got a cure.
- It is molecular characterized by progressive accumulation of misfolded proteins with the formation of toxic oligomers.
- AD has three manifestations, going from mild (preclinical), mild cognitive impaired (MCI) and finally to severe (dementia). Once reached this last stage, patients are disabled: work and daily activity, such as getting dressed, is impaired.

Involved Molecules

- Amyloid Precursor Protein (APP):
  - Transmembran protein encoded at chromosome 21.
  - Depending on splicing processes, it might form a normal peptide or toxic peptide (Aβ1-42).
  - Toxic peptides generate amylogenic plaques and cause neuronal death.
- Presenilines 1 and 2 (PSEN1, PSEN2):
  - Both presenilines encode the γ-secretase catalytic centre, so mutations on these genes might increase the proportion of Aβ1-42.
- Tau Protein: when hyperphosphorylated it induces formation of neurofibrillary tangles.
- Apolipoprotein E (apoE):
  - Cholesterol transporter, responsible for the neuronal membrane’s repair and modification.
  - Different alleles: ε3 (most common), ε2 (protective for AD) and ε4 (risk factor for AD).

How Alzheimer’s Disease is generated

- Based on the utilization of monoclonal antibodies: high specificity antigen-antibody
- Three possible action mechanisms of monoclonal antibodies:
  1. Anti-Aβ cross the hemathoencephalic barrier, recognize the amyloid plaques and eliminate them.
  2. Anti-Aβ activate the microglia and phagocytosis of Aβ, mediated by Fc receptors.
  3. Descent of peripheral Aβ by altering the flux from brain to plasma.
- Bapineuzumab (didn’t report significant effect) and Solanezumab (ongoing research).

Passive Immune Therapy

- Body generates it’s own antibodies: vaccination strategy.
- CAD106 (Novartis®), ABVac40 and ABVac42 (Aracron Biotech®) vaccines.

Active Immune Therapy

- Body generates it’s own antibodies: vaccination strategy.

Conclusions

Alzheimer’s disease is a complex pathology. Nowadays, the only effective strategy consists on premature detection, and administration of cholinesterase inhibitory treatment in order to slow down the apparition of the memory loss.

Most of the actual ongoing clinical trials are based on active and passive immune therapy, where patients require a periodic vaccination. Some of these trials will have results soon, such as those performed by Aracron Biotech® or based on Solanezumab.

The worldwide spread of Alzheimer’s and the increased life-expectancy in developed countries turns this pathology into one of the most important epidemics of the 21st century, promoting companies to investigate it. Alzheimer’s disease treatments have a promising pipeline, with a wide range of clinical trials and research ongoing that might give hope to those patients who otherwise would have no choice.

References