Alzheimer's Disease: The Medical Challenge for the 21st Century
A Dreadful Disease Requires Drastic Measures
DNA Vaccine as immunotherapy to prevent Alzheimer's Disease

Dr. Alzheimer's First Patient

(He sat on her bed with a helpless expression.)

"What is your name?"

"Auguste."

"Last name?"

"Auguste."

What is your husband's name?

"Auguste, I think.

This 1902 photo shows Auguste D's helplessness.
Gene Vaccination to Bias the Immune Response to Amyloid-β Peptide as Therapy for Alzheimer's Disease

Gene gun-mediated vaccination

The gene gun was used to deliver the gene-coated bead through the epidermis, where DNA is taken up by epidermal (Langerhan) cells (Fig A). The epidermal cells further migrate to the draining lymph node, and the Foreign DNA is transcribed. The expressed polyepitope antigen binds to the major histocompatibility complex and elicits an immune response (Fig B). The expanded CD8+ T cells then are prevented by CD28.

Gene Vaccination to Bias the Immune Response to Amyloid-β Peptide as Therapy for Alzheimer's Disease

Aβ-specific immune responses in BALB/c wild-type mice immunized with mouse Aβ42 dimer gene vaccine.

Archives of Neurology, 2004;61:1858-1864
Phase II, Trial 2: 15 Months

Anti-Aβ-17
20x

- High background staining due to anti-mouse secondary antibody
- Additional evaluation pending

Aβ42 gene vaccination reduces brain amyloid plaque burden in transgenic mice

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Roger N, Rosenberg


Immune response against human Aβ42 in APPswe/PS1ΔE9 mice immunized
Figure 5A: Aβ plaques density in cortex stained with anti-Aβ42 antibody, 10x.

APP/PS1 double Tg mice at 15 months for plaque density in cortex. 50.1% reduction in vaccinated mice using NIH Image J Software after fluorescence staining with anti-Aβ42 antibody. Mann-Whitney P=0.0022.

Aβ42 gene vaccine reduced brain plaque density by 54.3% in hippocampus.
Quantity of plaque density in hippocampus of APP/PS1 double transgenic mice. Aβ42 gene vaccine reduced plaque density by 54.3% measured by NIH Image J image software area fluorescence staining with anti-Aβ42 antibody. Mann-Whitney P=0.0022.

Levels of Aβ42 peptide in forebrain (A) and in plasma (B) of APPswe/PS1ΔE9 mice 15 months of age treated with the Aβ42 gene vaccine (T1) (n=8) or control plasma (C) (n=8).

Immune responses against Aβ42 in APPswe/PS1ΔE9 mice immunized with the human Aβ42 gene vaccine.
Fluorescence immunolabelling of glial fibrillary acidic protein in AD Tg mice.

Anti Aβ1-42 Antibody Produced By DNA Gene Vaccine In Monkey

ELISA analysis showed that the specific titer against Aβ1-42 was 1:20,000 in comparison to the preimmune serum.

Western blot of serum from a Rhesus monkey (m1) before and after gene immunization identifies anti-Aβ1-42 antibody (arrow).

DNA–Amyloid β1-42 Trimer Immunization for Alzheimer Disease in Wild-Type Mouse Model

JAMA, 2009; 302(16):1796-1802
Conclusions: DNA Aβ42 Vaccine Prevents Aβ42 Peptide Deposition in Brain of Double Transgenic Mice

1. 50% reduction in Aβ42 peptide levels in cerebral cortex and hippocampus.
2. 1:10,000 titer of anti- Aβ42 antibody in all 6 treated transgenic mice.
3. Isotyping of anti-Aβ42 antibody is Th2 (IgG1) type; 30μg/ml of mouse serum IgG1 with the Ga4/UAS Aβ42 trimer constructs.
4. T cells synthesize increased interleukin 4 and not gamma globulin in presence of Aβ42 peptide.
Conclusions: DNA Aβ42 Vaccine Prevents Aβ42 Peptide Deposition in Brain of Double Transgenic Mice

5. 64% reduction in cortex and 51% reduction in hippocampus of GFAP immunostaining. Reduced reactive glia.
6. 1:20,000 titer of Th2 (IgG1) type of anti-Aβ42 antibody in Rhesus monkey.
7. Human WBC, fibroblasts and kidney cells are positively transfected with the DNA Aβ42 vaccine and produce Aβ42 peptide.
8. DNA Aβ 42 vaccination produces an IgG, anti-Aβ 42 antibody that has a low probability to cause inflammation and is effective to lower Aβ42 peptide in the transgenic mouse brain.

DNA Aβ42 vaccination delivered by the gene-gun may be an effective immunization method as therapy for Alzheimer’s disease.

A Clinical Trial of DNA Aβ42 vaccination with Alzheimer’s disease patients is the next objective!!!
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