



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

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**Dr. Alzheimer's First Patient**



*(She 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**

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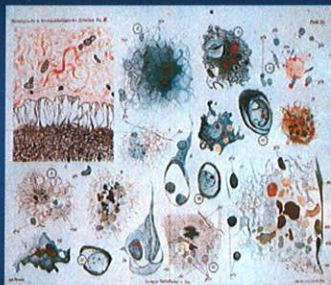
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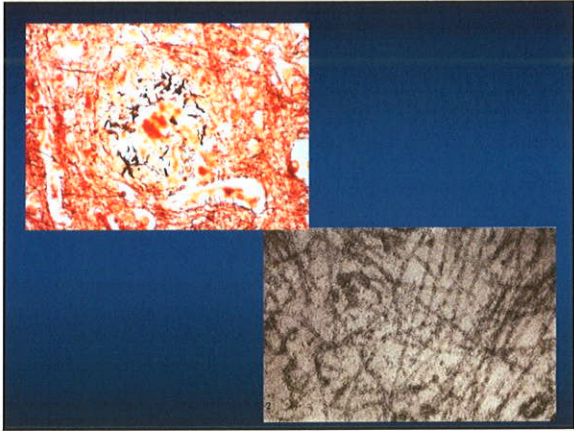
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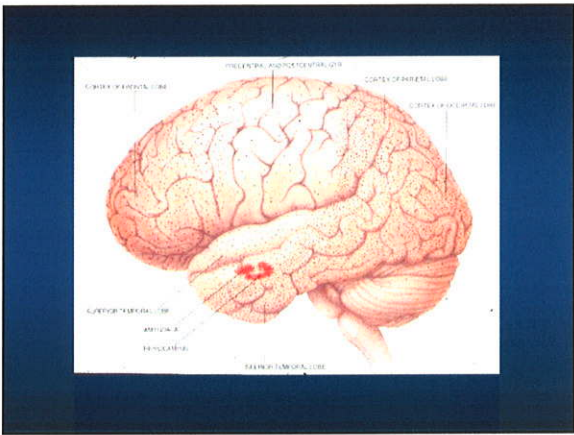
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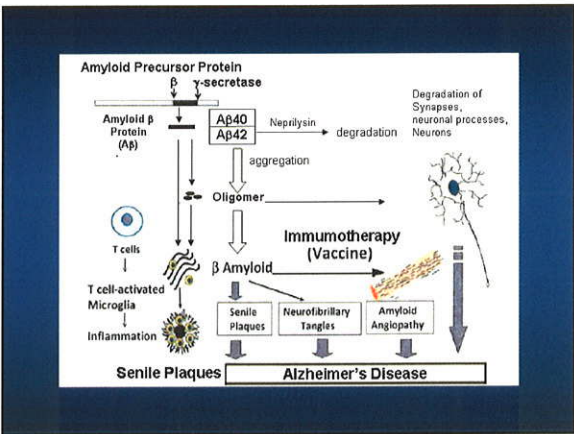
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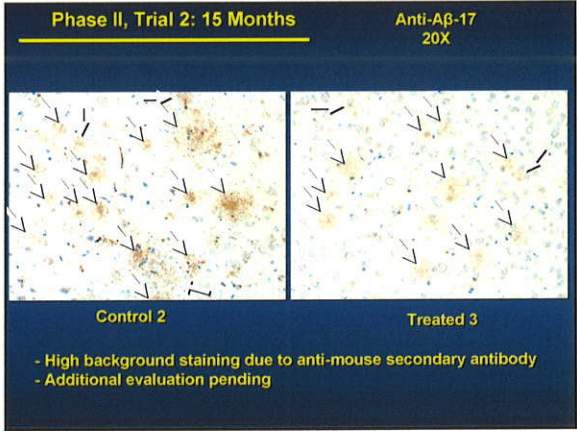
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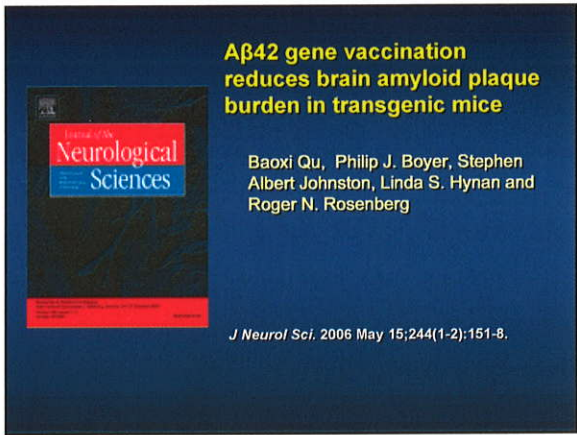
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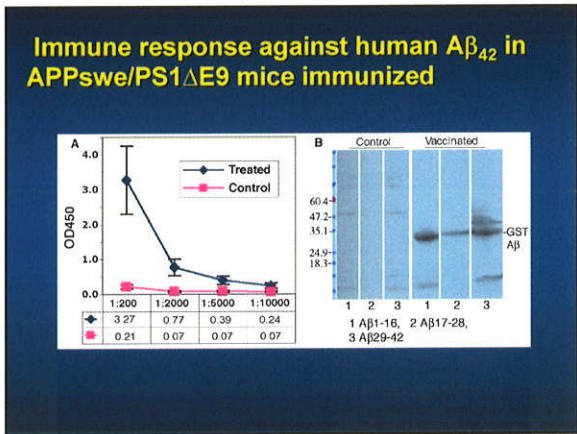
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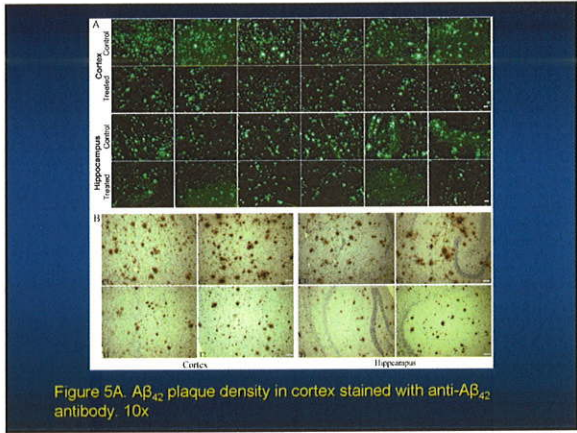
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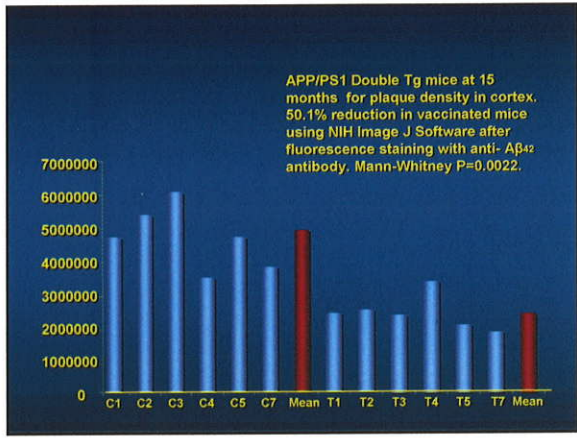
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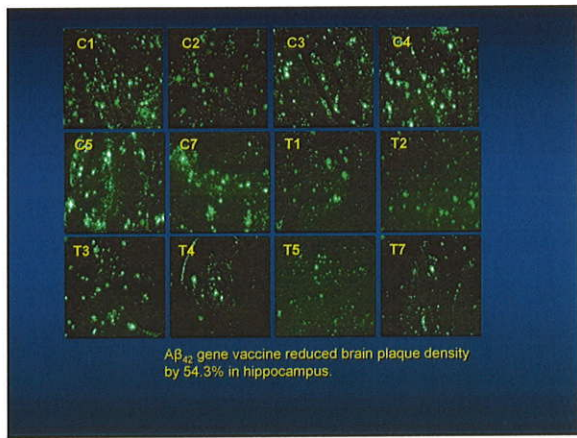
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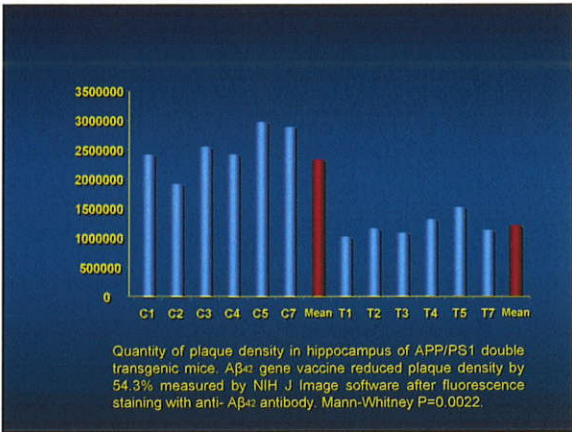
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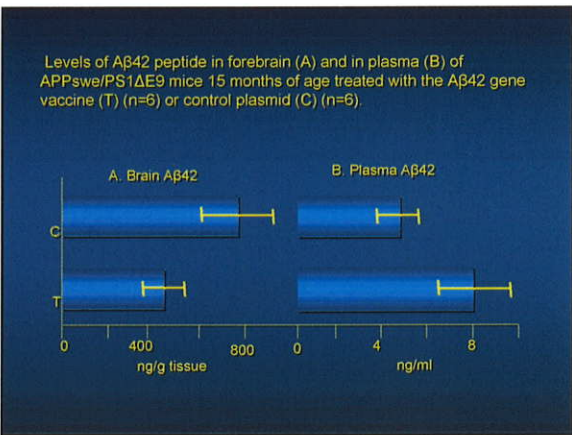
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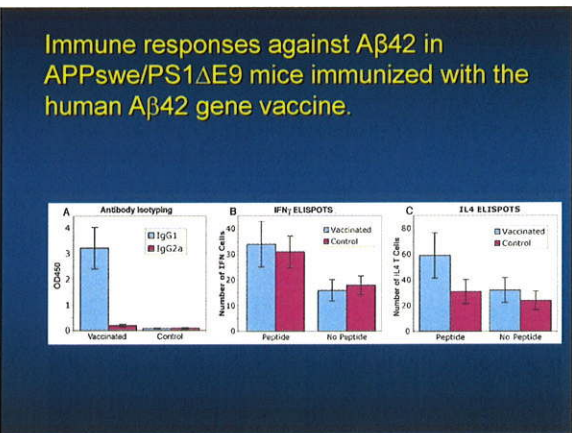
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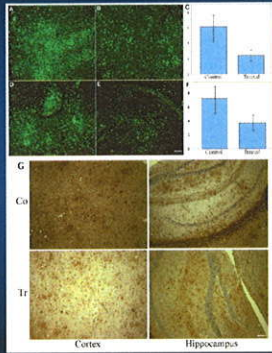
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Fluorescence immunolabeling of glial fibrillary acidic protein in AD Tg mice.




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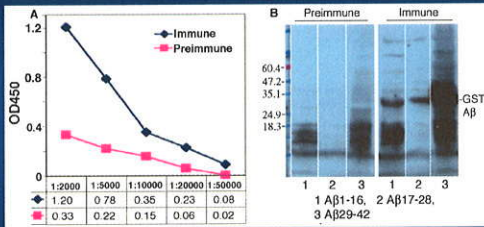
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**Anti A $\beta_{42}$  Antibody Produced By DNA Gene Vaccine In Monkey**



ELISA analysis showed that the specific titer against A $\beta_{42}$  was 1:20,000 in comparison to the preimmune serum. Western blot of serum from a Rhesus monkey (n=1) before and after gene immunization identifies anti-A $\beta_{42}$  antibody (arrow).

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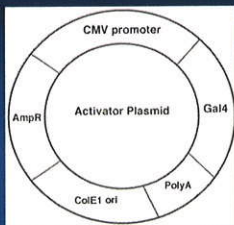
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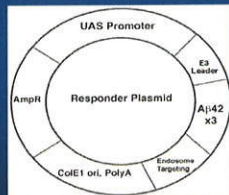
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**DNA –Amyloid  $\beta$ 1-42 Trimer Immunization for Alzheimer Disease in Wild-Type Mouse Model**



JAMA, 2009, 302(16):1796-1802

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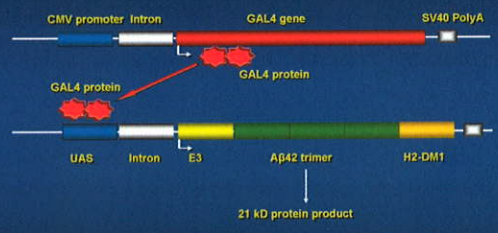
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**Double Plasmid System: Activator – and Responder Plasmid  
GAL4/UAS A $\beta$ 42 Trimer DNA Vaccine**



DNA –Amyloid  $\beta$ 1-42 Trimer Immunization for Alzheimer Disease in Wild-Type Mouse Model  
JAMA, 2009; 302((16):1796-1802

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**A Activator Plasmid**

**Responder Plasmid**

**B**

**C**

**D**

JAMA, 2009; 302((16):1796-1802

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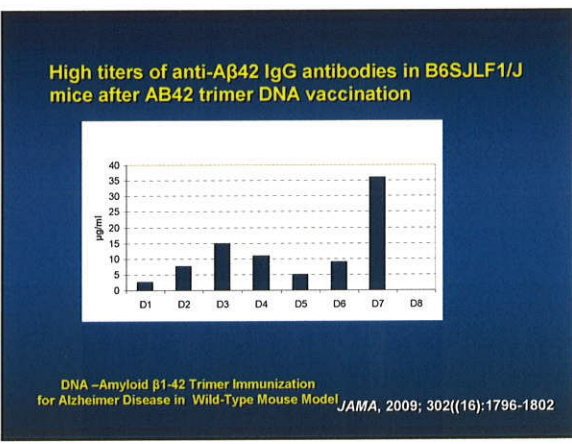
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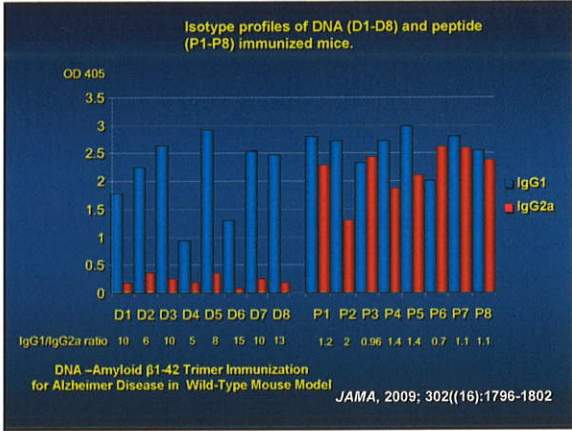
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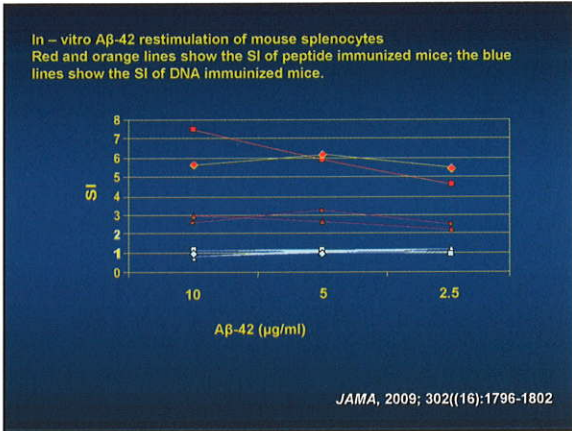
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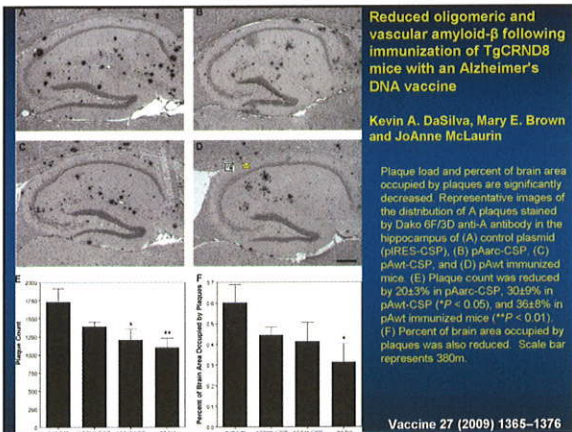
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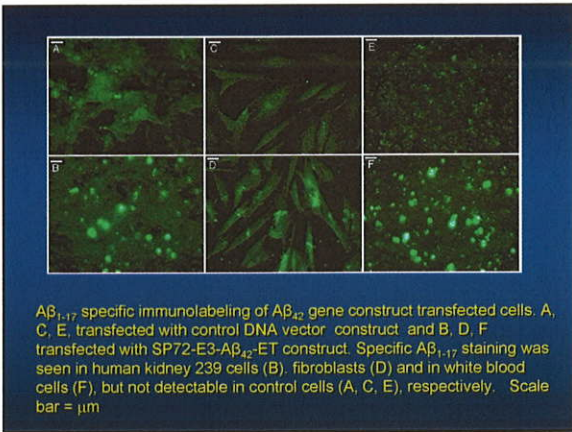
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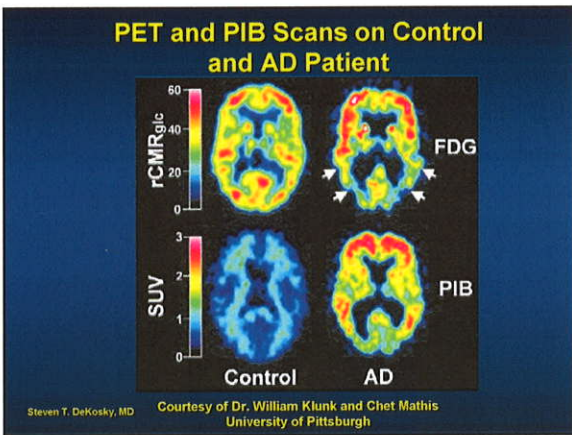
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### Conclusions: DNA Aβ<sub>42</sub> Vaccine Prevents Aβ<sub>42</sub> Peptide Deposition in Brain of Double Transgenic Mice

- 50% reduction in Aβ<sub>42</sub> peptide levels in cerebral cortex and hippocampus.
- 1:10,000 titer of anti- Aβ<sub>42</sub> antibody in all 6 treated transgenic mice.
- Isotyping of anti-Aβ<sub>42</sub> antibody is Th2 (IgG<sub>1</sub>) type; 30μg/ml of mouse serum IgG<sub>1</sub> with the Gal4/UAS Aβ<sub>42</sub> trimer constructs.
- T cells synthesize increased interleukin 4 and not gamma globulin in presence of Aβ<sub>42</sub> peptide.

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**Conclusions: DNA A $\beta$ 42 Vaccine Prevents A $\beta$ 42 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 (IgG<sub>1</sub>) type of anti-A $\beta$ <sub>42</sub> antibody in Rhesus monkey.
7. Human WBC, fibroblasts and kidney cells are positively transfected with the DNA A $\beta$ 42 vaccine and produce A $\beta$ <sub>42</sub> peptide.
8. DNA A $\beta$  42 vaccination produces an IgG, anti-A $\beta$  42 antibody that has a low probability to cause inflammation and is effective to lower A $\beta$ 42 peptide in the transgenic mouse brain.

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**DNA A $\beta$ 42 vaccination delivered by the gene-gun may be an effective immunization method as therapy for Alzheimer's disease.**

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**A Clinical Trial of DNA A $\beta$ 42 vaccination with Alzheimer's disease patients is the next objective!!!**

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**Research Collaborations:**  
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Todd Eagar, PhD  
Olaf Stuve, MD, PhD  
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**Supported by:**  
NIH, NIA, Alzheimer's Disease Center P30AG12300  
University of Texas Southwestern Medical Center at Dallas  
Rudman Foundation - Texas  
Luttrell Foundation - California  
Alzheimer's Association Research Grant IIRG-06-24428

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