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Neuropathology

Papillomavirus-like particle A β vaccine induces specific antibody response, and prevents behavioral impairment in APP/PS1 transgenic mice.

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Non-infectious virus-like particles (VLP) composed of the L1 capsid protein of papillomaviruses are successfully being tested in humans as vaccines to prevent papillomavirus infection and cervical cancer. In the present study, we have used the baculovirus system to generate a chimeric bovine papillomavirus type 1 (BPV1) L1 incorporating 9 N-terminal amino-acid of A β (A β -VLP). This recombinant protein was used to immunize APP^{swe}/PS1^{dE9} mice (APP/PS1), a transgenic model of Alzheimer's disease. The aims of the study are to evaluate the specific antibody response, toxicity, reduction of A β deposits in the brain, and to prevent the behavioral deficits shown by these transgenic mice.

Six APP/PS1 mice, starting at 3 months of age, received monthly intramuscular injections of 10 μ g VLP-A β . Six control mice received LI-L2 VLP and one received PBS on the same schedule as the experimental group. Animals were euthanized at 12 months of age. Neither the experimental nor the control mice showed signs of toxicity. A β antibody titers measured by ELISA were elevated in mice immunized with VLP-A β (IgG 1/5000 to 1/10000), but not in controls. The sera of immunized mice recognized amyloid plaques in postmortem tissue sections of Alzheimer's disease.

In the open field test conducted at 12 months of age, mice immunized with VLP-A β displayed a number of central crossings similar to non-transgenic mice, whereas mice injected with BPV-L1/L2 or PBS showed significant less number of central crossings, indicative of higher levels of anxiety. This behavioral effect may reflect the diminished burden of soluble and/or aggregated A β in the brain of mice immunized with VLP-A β .

Measurements by ELISA demonstrate a trend for elevation of A β -40 and A β -42 in plasma and decreased levels in brain tissues. Assessment of A β load (plaque counting) in the brain is in progress.

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