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Targeting Trends

Reporting the latest news in Molecular Surgery

Cholinergic Immunolesioning Produced Tangle-like Inclusions in TgCRND8 Brain

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Today's Alzheimer's disease (AD) research lacks a "complete" model that would represent both plaque and tangle pathology together with correlative memory deficits. The currently available transgenic model that includes APP/PS1/tau mutations does not truly represent AD because tangles observed in AD brain are independent of tau mutations. Subtly increased β-amyloid (Aβ) levels either due to familial mutations or sporadic causes, primarily signals pre-tangle cytopathology and degeneration of basal forebrain cholinergic neurons (BFCN) via deranged signaling of glygogen

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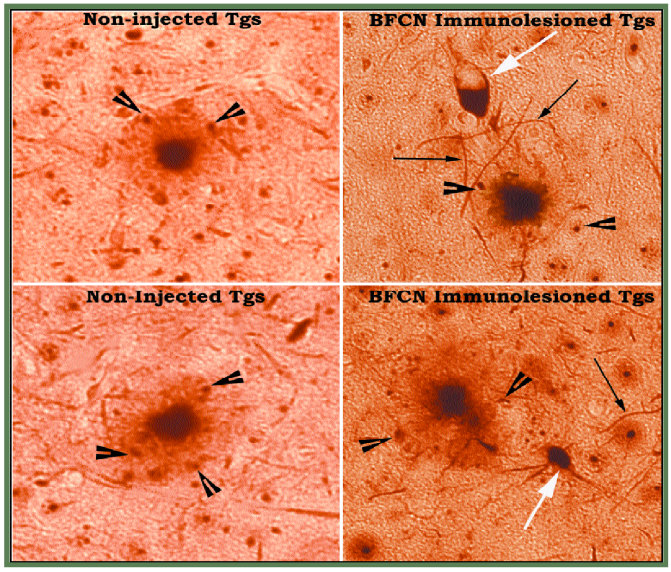
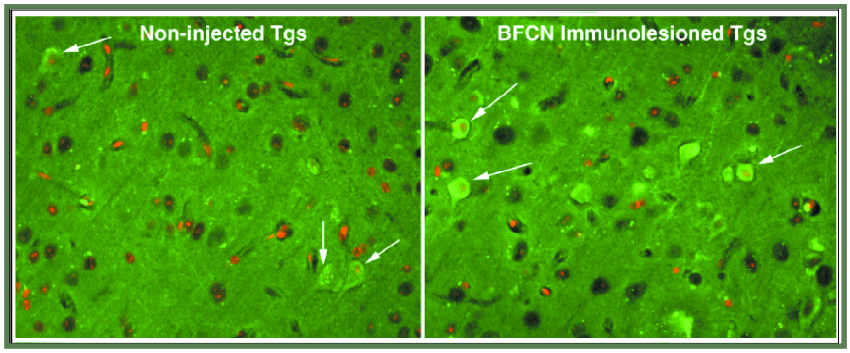


Development of a tangled neuron in plaque vicinity

Black arrowheads: plaque-associated hyperphosphorylated neurites; Black thin arrows: hyperphosphorylated neuropil threads in immunotoxin injected Tg brain (Right panel); White arrow: "Tangled" neuron in the vicinity of plaque showing intraneuronal phosphorylated tangle-like inclusion in immunotoxin injected Tg brain (Right panel). Note the absence of hyperphosphorylated neuropil threads and "Tangled" neuron in the vicinity of plaque in non-injected Tgs (Left panel).

Drastically increased AT8-positive neurons after BFCN immunolesioning



Left panel, white arrows: Cortical pyramidal neurons of non-injected Tg brain showing occasional punctate immunoreactivity for AT-8 (a marker protein for tangles) indicating "subtle" tau phosphorylation in untreated Tg brain.

Right panel, white arrows: Cortical pyramidal neurons of immunotoxin-injected Tg brain showing strong immunoreactivity for AT-8 (a marker protein for tangles) indicating the presence of "tangle-bearing" neurons in immunotoxin-injected Tg brain.

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Denise Higgins, Editor

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