

## ALZHEIMER DISEASE

## Cancer immunotherapy drug reduces symptoms of Alzheimer disease in mice

“The treatment not only arrested disease progression, but partially reversed it”

Immune checkpoint blockade, a strategy used to treat certain cancers, might represent a novel therapeutic strategy against Alzheimer disease (AD), according to a recent mouse study published in *Nature Medicine*. The cancer immunotherapy drug, administered to AD model mice, evoked an immune response that reduced amyloid plaque burden and reversed cognitive impairment.

AD is accompanied by chronic neuroinflammation. Michal Schwartz and colleagues from the Weizmann Institute of Science, Rehovot, Israel, had previously put forward the hypothesis that neuroinflammation in AD is linked to

insufficient macrophage recruitment to the CNS. “Anti-inflammatory and immunosuppressive strategies have failed in the clinical trials,” explains Schwartz. “To drive an immune-dependent cascade needed for brain repair, systemic immunity should be boosted, rather than suppressed.”

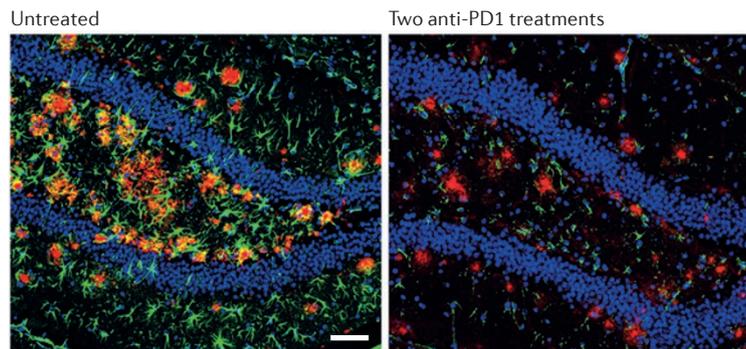
The researchers assessed the effect of an antibody against programmed cell death protein 1 (PD1; a molecule that restrains immune activation) on pathological and cognitive correlates of AD in 5xFAD and APP/PS1 mice. These mice are widely used AD models that carry several mutations associated with familial AD and develop cerebral amyloid pathology

similar to that seen in patients with AD. PD1 blockade evoked an IFN- $\gamma$ -dependent systemic immune response, which promoted clearance of existing amyloid- $\beta$  deposits, reduced neuroinflammation and gliosis, and improved memory performance.

In 12-month-old 5xFAD mice that received two PD1 blockade treatments, spaced 1 month apart, spatial navigation performance was comparable to that of wild-type mice. “The repeated treatment not only arrested disease progression, but partially reversed it,” Schwartz says.

PD1 blockers have been approved by the FDA for the treatment of metastatic melanoma and non-small-cell lung cancer, and are currently being investigated for the treatment of glioblastoma. “We believe this approach can be translated to clinical studies in Alzheimer disease in a relatively short time,” Schwartz contends.

Hemi Malkki



PD1 blockade reduces A $\beta$  deposition (red) and GFAP expression (marker of gliosis; green) in the hippocampus of 5xFAD mice. Scale bar 50  $\mu$ m. Adapted with permission from Macmillan Publishers Ltd.

**ORIGINAL ARTICLE** Baruch, K. PD-1 immune checkpoint blockade reduces pathology and improves memory in mouse models of Alzheimer's disease. *Nat. Med.* <http://dx.doi.org/10.1038/nm.4022>