Pacific Center for Emerging Infectious Diseases Research

University of Hawai'i Mānoa

Department of Tropical Medicine, Medical Microbiology & Pharmacology

JOHN A BURNS SCHOOL OF MEDICINE, UNIVERSITY OF HAWAI'I AT MANOA

Peripheral Challenge with Alpha-synuclein Fibrils Results in Parkinson's Disease-like Signs in Mice

Alpha-synuclein is a soluble cytoplasmic protein that in some neurodegenerative diseases forms pathological deposits, such as Lewy bodies and Lewy neurites in neurons of patients with Parkinson's disease. After intracerebral inoculation in transgenic and wild-type mice, pathological alpha-synuclein propagates in a prion-like manner causing neurodegeneration. We investigated the ability of misfolded alpha-synuclein to invade the CNS and induce disease after peripheral inoculation. For inoculation experiments, we used Tg(M83$^{+/-}$:Gfap-luc$^{+/-}$) mice hemizygously expressing luciferase and human alpha-synuclein with the familial A53T mutation. Mice inoculated with phosphate-buffered saline or bovine serum albumin remained healthy, whereas intraperitoneal, intravenous, and oral inoculation with alpha-synuclein fibrils led to CNS disease with signs of kyphosis and paralysis. Biochemical analysis showed that sick mice had accumulated aggregates of sarkosyl-insoluble and phosphorylated α-synuclein in their brains and spinal cords. Neuropathological analysis revealed that CNS deposits of misfolded alpha-synuclein co-localized with ubiquitin and p62. Neurologic illness was accompanied by neuroinflammation, which was confirmed by immunofluorescence staining for GFAP and IBA-1 and by bioluminescence imaging. We show that peripheral inoculation with alpha-synuclein fibrils induces neurodegeneration in Tg(M83$^{+/-}$:Gfap-luc$^{+/-}$) mice.

Dr. Gültekin Tamgüney

Research Group Leader
German Center for Neurodegenerative Diseases (DZNE)
Bonn, Germany

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John A. Burns School of Medicine, Kaka'ako Campus
Medical Education Building Auditorium (Room 315)
For further information, contact (808) 692-1654

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