



Seminar of Prof. Dr. Tetsumori Yamashima

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“Toxicity of Cooking Oil-Derived Hydroxynonenal”

November 20, 2025, 12.00 AM, at the Dept. of Sense Organ,
Policlinico Umberto I, Rome,
Clinica Oculistica, Aula B.

Professor Yamashima is a renowned expert in nutrition and neuroscience
with implications for aging.

4-Hydroxynonenal is a derivative of linoleic acid found in most vegetable oils (peanut, sunflower, olive) that is toxic to the nervous system.

It is formed during high-temperature cooking, such as frying, and is believed to be a major cause of neuronal death, with implications for neurodegeneration and Alzheimer's disease.

Abstract

Currently, lifestyle-related diseases such as Alzheimer's disease, type 2 diabetes, chronic heart, liver, and kidney diseases, etc., constitute increasingly prevalent life-threatening diseases, but the causal relation and cross-talks among these diseases remain poorly understood. The pathophysiology of each disease is complex, multifaceted, and multi-angled. The oxidative stress due to prolonged generation of reactive oxygen species (ROS) induces lysosomal membrane rupture/permeabilization, mitochondrial dysfunction, endoplasmic reticulum stress, impaired autophagy, etc., in human organs. The characteristics of lifestyle-related diseases include progressive loss of function due to cell degeneration/death in various tissues and organs. ROS-induced lipid and protein oxidation synergistically exerts a crucial role in the development of cell degeneration and death. The lipid-peroxidation product, 4-hydroxy-2-nonenal (HNE), is generated exogenously via deep-frying of linoleic acid-rich cooking oils and/or endogenously via oxidation of fatty acids involved in the mitochondrial inner membranes. Although its toxicity for human health is widely accepted, the underlying mechanism long remained unknown. In 1998, we formulated the “calpain–cathepsin hypothesis” as a molecular mechanism of ischemic neuronal death, using the ischemic monkey experimental paradigm. Exogenous and intrinsic HNE may synergistically oxidize the representative cell stress protein Hsp70.1, which has dual functions as a ‘chaperone protein’ and ‘lysosomal stabilizer’. We found that activated calpain due to chronic ischemia cleaves Hsp70.1, which becomes vulnerable after the HNE-induced carbonylation at the key site Arg469. Since diverse cell death-degeneration in the brain, liver and pancreas similarly occurs by chronic ischemia via the calpain–cathepsin cascade triggered by HNE, excessive consumption of deep-fried foods is thought to be one of the most critical epidemiological factors common to lifestyle-related diseases.

Host Researcher: Marco Fiore

Biography

Tetsumori Yamashita MD, PhD is a consultant neurosurgeon specialized in neuroscience. In 1975, he graduated from Kanazawa University Faculty of Medicine. In 1979, he completed his research diploma in the Kanazawa University Graduate School Medical Research Course (Doctor of Medicine). He then studied abroad in Germany and Sweden, including neuropathology and brain science. He became Chief of Medical Staff at Kanazawa University Hospital, Associate Professor of Kanazawa University Medical Faculty, and Director of Restorative Neurosurgery at Kanazawa University Graduate School of Medical Science. At present, he is CEO of the Arimatsu Medical and Dental Clinic in Kanazawa city, works at this clinic (Tuesday to Saturday), and at Minami-gaoka Hospital (consultant neurosurgeon: Monday mornings). At Kanazawa University Hospital (part-time lecturer: Monday afternoons), he heads a special "higher brain dysfunction" outpatient clinic. He is acknowledged for using the RBANS (Repeatable Battery for the Assessment of Neuropsychological Status), MRI and PET scans for early detection of Alzheimer's disease, even a few years before dementia appears, allowing preventive treatment to be carried out. In 1998, he proposed the "calpain-cathepsin hypothesis" as a mechanism of neuronal cell death. He also discovered that the causative agent responsible for Alzheimer's disease is not amyloid β , but hydroxynonenal derived from "cooking oil". He is the author of 200 published scientific papers in English, and 75 papers and 15 books in Japanese.