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Involvement of normal prions in some human myelin diseases

We have experimentally demonstrated that cobalamin (Cbl) deficiency increases normal cellular prion (PrPC) levels in rat spinal cord (SC) and cerebrospinal fluid (CSF), and decreases PrPC-mRNA levels in rat SC. Repeated intracerebroventricular administrations of anti-octapeptide repeat-PrPC-region antibodies to Cbl-deficient (Cbl-D) rats prevent SC myelin lesions, and the administrations of PrPCs to otherwise normal rats cause SC white matter lesions similar to those induced by Cbl deficiency. Cbl positively regulates SC PrPC synthesis in rat by stimulating the local synthesis of epidermal growth factor (EGF), which also induces the local synthesis of PrPC-mRNAs, and down-regulating the local synthesis of tumor necrosis factor (TNF)- α , thus preventing local PrPC overproduction. We have clinically demonstrated that PrPC levels are increased in the CSF of patients with sub-acute combined degeneration (SCD), unchanged in the CSF of patients with Alzheimer's disease and amyotrophic lateral sclerosis, and decreased in the CSF and SC of patients with multiple sclerosis (MS), regardless of its clinical course. We conclude that SCD (human and experimental) is a neurological disease due to excess PrPC without conformational change and aggregation, that the increase in PrPC levels in SCD and Cbl-D polyneuropathy and their decrease in MS CNS make them antipodean myelin diseases in terms of quantitative PrPC abnormalities, and that these abnormalities are related to myelin damage in the former, and impede myelin repair in the latter.

Biography

Giuseppe Scalabrino Born in Milan, on July 4, 1944. He studied in Institute of General Pathology, University of Milan from 1965 to 1968 and at 1968 he became M.D., magna cum laude, discussing an experimental thesis on the radiosensitizing properties of aliphatic aldehydes.

He worked in several positions as faculty of Institute of General Pathology at University of Milan from 1969 to present. He was the Associate Professor of General Pathology at University of Milan from 1971 to 1985. He was honored as Assistant to the Chairman of General Pathology, Faculty of Medicine and Surgery at University of Milan from 1973 to 1985. He has more than 100 Publications in high impact journals.

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