PROGRANULIN PLASMA LEVELS IN THE DIAGNOSIS OF LATE ONSET NEURODEGENERATIVE DISEASES

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Introduction: Recently, attention was drawn to a role for progranulin (PGRN) in the central nervous system with the identification of mutations in the gene encoding PGRN as an important cause of frontotemporal lobar degeneration (FTLD). Of note, PGRN mutations are associated with widely variable clinical phenotypes. We recently proposed the dosage of plasma PGRN as a useful tool for a quick and inexpensive large-scale screening of carriers of progranulin mutations (Ghidoni R et al. Neurology. 2008;71:1235-9).

Aims: To establish the best cutoff threshold for normal versus abnormal levels of plasma progranulin.

Methods: Participants: 250 cognitively intact PGRN (\textsuperscript{-}) adults (25-87 years of age) and 54 affected and unaffected PGRN mutations carriers (21-86 years of age). Participants were enrolled at the Memory Clinic, IRCCS S. Giovanni di Dio-Fatebenefratelli, Brescia, Italy and at the Alzheimer Unit, Ospedale Maggiore Policlinico, Milano, Italy. Plasma PGRN levels were measured using an ELISA kit (AdipoGen Inc., Korea).

Results: In the control group, plasma PGRN (mean values\pm SD: 138.9\pm 60.7 ng/mL) did not correlate with age \((r = 0.100, p=0.116)\). We established a new plasma progranulin protein cutoff level of 61.5 ng/mL that identifies, with specificity of 100\% and sensitivity of 92.6\%, mutation carriers. Plasma screening allowed the identification of PGRN mutations in patients presenting with vascular dementia, Alzheimer disease, Lewy Body dementia, Mild Cognitive Impairment, along with the previously described FTLD and CBD cases.

Conclusions: Circulating PGRN is a suitable biomarker to detect PGRN-related neurodegeneration.