WORLDLAB · EUROMEDLAB

ROMA 2023

IFCC-EFLM WorldLab • EuroMedLab Roma 2023
Rome, Italy

25th International Congress of Clinical Chemistry and Laboratory Medicine
25th European Congress of Clinical Chemistry and Laboratory Medicine
55th Congress of the Italian Society of Clinical Biochemistry and Clinical Molecular Biology

May 21-25, 2023, Rome, Italy

La Nuvola, Viale Asia 40 /44 - 00144 Roma RM

Dementia and neurological diseases

P0732

EVALUATION OF PLASMA PROGRANULIN LEVELS IN FRONTOTEMPORAL DEMENTIA (FTD) PATIENTS: NEED FOR STANDARDIZATION

A. Poulopoulou [3], A. Simoudis [3], V. Papastefanopoulou [3], N. Petri [3], C. Koros [2], R. Antonellou [2], E. Stanitsa [2], J. Papatriantafyllou [2], L. Stafanis [1], S. Papageorgiou [2], C. Kroupis [3]

[1]*1st Neurology Department, Aiginiteion Hospital, Medical School, National and Kapodistrian University of Athens, Greece*

[2]*2nd Neurology Department, Attikon University General Hospital, Medical School, National and Kapodistrian University of Athens, Greece*

[3]*Department of Clinical Biochemistry, Attikon University General Hospital, Medical School, National and Kapodistrian University of Athens, Greece*

BACKGROUND-AIM

Granulin gene (GRN) encodes for a 593-amino acid secreted protein named progranulin that is important in proper lysosomal function of neurons. It can be easily measured in plasma where significantly lower levels can assist in identifying candidates for loss of function (null) GRN mutations. When heterozygous, these mutations lead to Frontotemporal Dementia (FTD). FTD is as common as Alzheimer's disease in patients <65y and can be attributed to mutations in one of many genes (C9orf72, MAPT, GRN, TARDBP etc).

METHODS

In 37 well-ascertained FTD patients, we collected EDTA peripheral blood after obtaining their informed consent. We performed both plasma progranulin measurements with an ELISA method (Adipogen) and genetic analysis in GRN gene with DNA Sequencing and MLPA.

RESULTS

Four patients were detected with null mutations (one with the c.264+1G>A mutation that has been deposited only once in ClinVar database as likely pathogenic), one patient with a rare missense variant of unknown clinical significance (p.T310P) and 32 were negative for any alteration in the GRN gene. Plasma progranulin measurement of the 32 negative patients showed a normal distribution (average 233 ng/ml, SD±49) while the 4 positive patients showed a range between 39-92 ng/ml. The p.T310P patient had an intermediate value and bioinformatics tools evaluated this alteration as benign.

CONCLUSIONS

Based on the used method and statistical analysis, FTD patients with plasma progranulin levels >135 ng/ml do not bear GRN mutations (95% confidence), while patients with <92 ng/ml most probably bear null mutations. This low-cost screening test can allow them to be included in clinical trials such as intracisternal PGRN gene therapy or intrathecal anti-sortilin antibodies. The low progranulin level assisted in the final adjudication of the c.264+1G>A mutation as pathogenic. However, there is need for an international effort in order to harmonize all assays with a certified reference material and establish universal cutoffs not only for null mutations but also for those with intermediate plasma progranulin protein levels due to either hypomorphic mutations or epigenetic or other genetic factors; they could also benefit by therapeutic enhancement of their progranulin level.