

**Peripheral inflammatory profile in patients with genetic FTD**

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**State of the art:** increasing body of evidence suggests that immunological alterations may play a role in the pathogenesis of genetic Frontotemporal Dementia (FTD). The extent of this alteration has not yet been extensively investigated. The aim of the study was to analyze the protein profile of thirty-seven molecules involved in neuroinflammatory processes.

**Methodology:** a population consisting of 95 symptomatic, 94 presymptomatic FTD-mutation carriers, and 50 family members without mutations was enrolled for the study taking advantage of the international GENFI consortium. The MSD System was used to analyze serum samples.

**Results:** A generalized up regulation of proinflammatory molecules in *GRN* and *MAPT* symptomatic carriers was observed compared with controls, whereas no differences, or a trend to a downregulation, was observed in symptomatic *C9orf72* carriers. IL-5 and IL-8 mean levels $\pm$ SEM were significantly increased in *GRN* symptomatic mutation carriers compared with controls ( $0.51\pm 0.09$  vs  $0.22\pm 0.04$  pg/ml,  $P=0.0037$ ;  $14.12\pm 1.45$  vs  $8.81\pm 1.03$  pg/ml,  $P=0.0002$ , respectively), IL-2 was significantly increased in *MAPT* symptomatic mutation carriers compared with controls ( $0.22\pm 0.03$  vs  $0.14\pm 0.04$  pg/ml,  $P=0.006$ ); IL-7 and VEGF-A were significantly decreased in *C9orf72* symptomatic mutation carriers versus controls ( $5.18$  vs  $11.15\pm 1.37$  pg/ml,  $P=0.05$ ;  $41.37\pm 6.04$  pg/ml vs  $88.26\pm 12.63$  pg/ml  $P=0.05$  respectively).

**Conclusion:** These preliminary results showed a specific inflammatory signature associated with each mutation. The generalized upregulation observed in *GRN*, but not in *C9orf72* carriers, suggest that the inflammatory profile is not driven by TDP-43 deposition. Conversely, the upregulation of inflammatory proteins in *MAPT* and *GRN* suggests that common pathogenic events may occur despite the underlying pathology.

**Conflicts of interest**

N/A