

MiRNA expression profile in genetic FTD

Federica Sorrentino, Chiara Fenoglio, Maria Serpente, Fumagalli Giorgio, Paola Cornelia Maria Muti, Marta Rigoni, Andrea Sacconi, John van Switen, Lize Jiskoot, Harro Seelaar, Barbara Borroni, Raquel Sanchez-Valle, Fermin Moreno, Robert Laforce, Caroline Graff, Matthis Synofzik, Kamen A Tsvetanov, Maura Malpetti, Simon P Jones, Richard Bethlehem, Timothy Rittman, Mario Masellis, Maria Carmela Tartaglia, Elizabeth Finger, Rik Vandenberghe, Alexandre de Mendonça, Fabrizio Tagliavini, Isabel Santana, Simon Ducharme, Chris Butler, Johannes Levin, Markus Otto, Sandro Sorbi, Arabella Bouzigues, Lucy Russell, James B Rowe, Jonathan D Rohrer, Daniela Galimberti

State of The Art

MicroRNAs (miRNA) are regulatory non-coding RNA involved in several cellular processes; recently they gained interest since they appear to be altered in neurodegenerative diseases and therefore have great potential as biomarkers. The aim of this project was to evaluate the expression profile of miRNAs in FTD genetic cases.

Methodology

Patients from Genetic FTD Initiative (GENFI) were retrospectively included in the study. They comprised 10 *C9ORF72* expansion carriers, 10 *MAPT* and 9 *GRN* mutation carriers, and 9 non-carrier subjects.

RNA was extracted from peripheral blood mononuclear cells (PBMC). Real-Time PCR analysis was performed using TaqMan OpenArray technology, which enabled to detect 754 miRNAs simultaneously.

Results

Several miRNAs were altered in patients compared to controls. Two miRNA, hsa-miR-223# and hsa-miR-20b, were overexpressed in *C9ORF72* expansion carriers ($p < 0.05$). A signature of six miRNA was found for *GRN* mutation carriers: hsa-miR-28-3p, hsa-miR-342-3p, hsa-miR-365, hsa-miR-576-5p and hsa-miR-642 were overexpressed, while hsa-miR-590-5p was downregulated ($p < 0.04$). In *MAPT* group, nine miRNA were differentially expressed: hsa-miR-146a, hsa-miR-192, hsa-miR-25, hsa-miR-28, hsa-miR-28-3p, hsa-miR-30c, hsa-miR-339-5p, hsa-miR-576-3p were upregulated, while hsa-miR-532-3p was downregulated ($p < 0.05$).

Conclusions

We showed that several miRNAs are upregulated in genetic FTD. These miRNAs have been previously involved in neuroinflammatory processes, suggesting a role of inflammation in FTD.

Expression profile of miRNA could be helpful in further elucidating neuropathological changes that take place in FTD brain. In this scenario, miRNAs have great potential as biomarkers and therapeutic targets.

Conflicts of interest

N/A