

Role of Fecal MicroRNA Profile in Alzheimer's Disease

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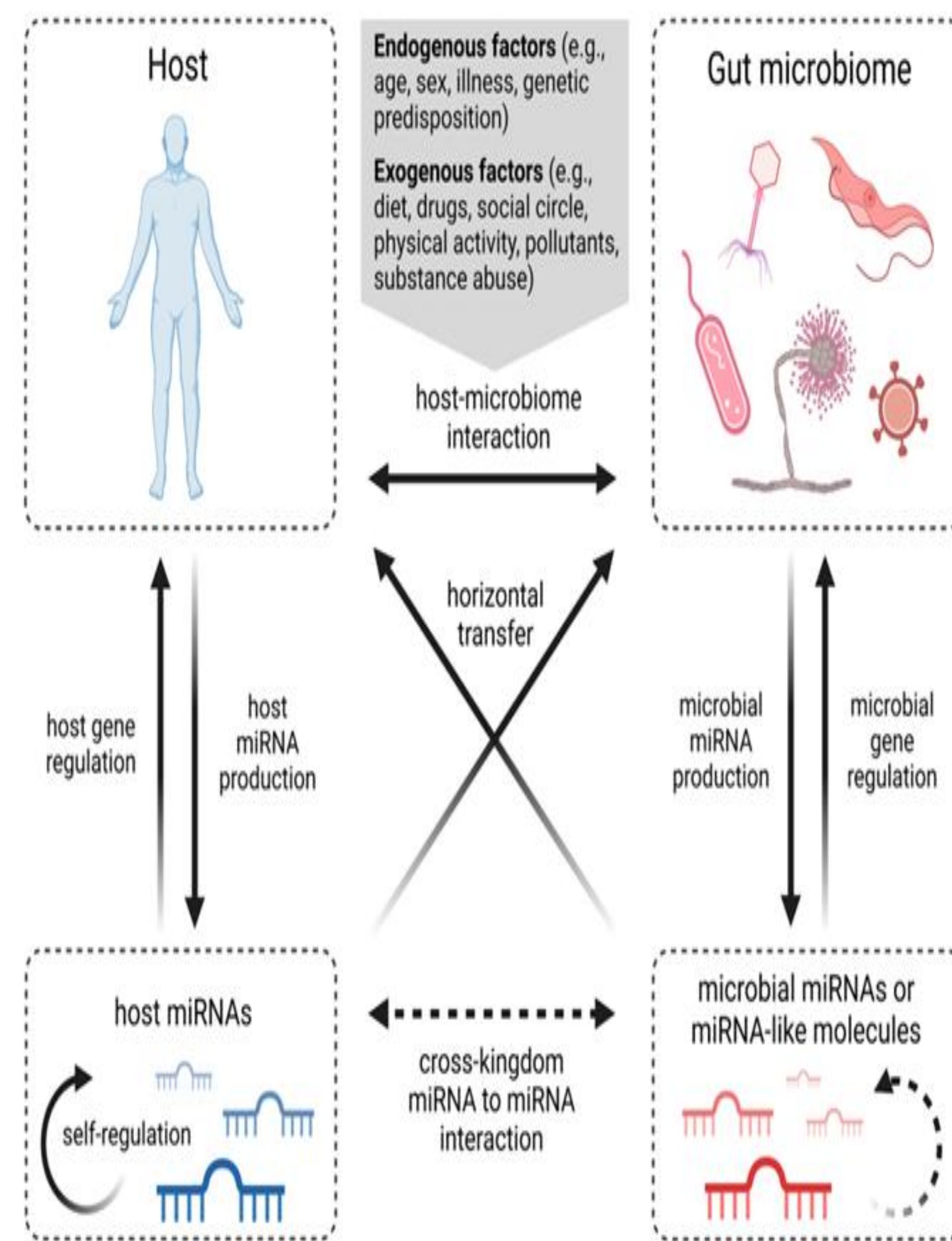


BACKGROUND

- Alzheimer's Disease (AD) is a complex neurodegenerative disorder characterized by cognitive decline and memory loss. Emerging research suggests that gut microbiota play a significant role in AD progression through mechanisms like neuroinflammation and neurotransmitter dysregulation.
- Fecal microRNAs (miRNAs) have gained attention as non-invasive biomarkers reflecting gut-brain communication, offering potential insights into disease pathogenesis and therapeutic targets.
- This research examines the significance of fecal miRNA profiles in AD, focusing on their role in early diagnosis, disease monitoring, and potential therapeutic intervention.

OBJECTIVE

- This research aims to investigate the relationship between fecal microRNA expression and Alzheimer's disease pathology at the preclinical stage by comparing CU+ and CU- participants based on brain amyloid-beta deposition.
- To examine the association between selected fecal microRNA expression and microbial metabolites, particularly short-chain fatty acids, in relation to Alzheimer's disease progression.
- To determine the combined association between Alzheimer's disease pathology, microbial metabolites, and fecal microRNA expression, with the aim of developing a predictive model for Alzheimer's disease progression.

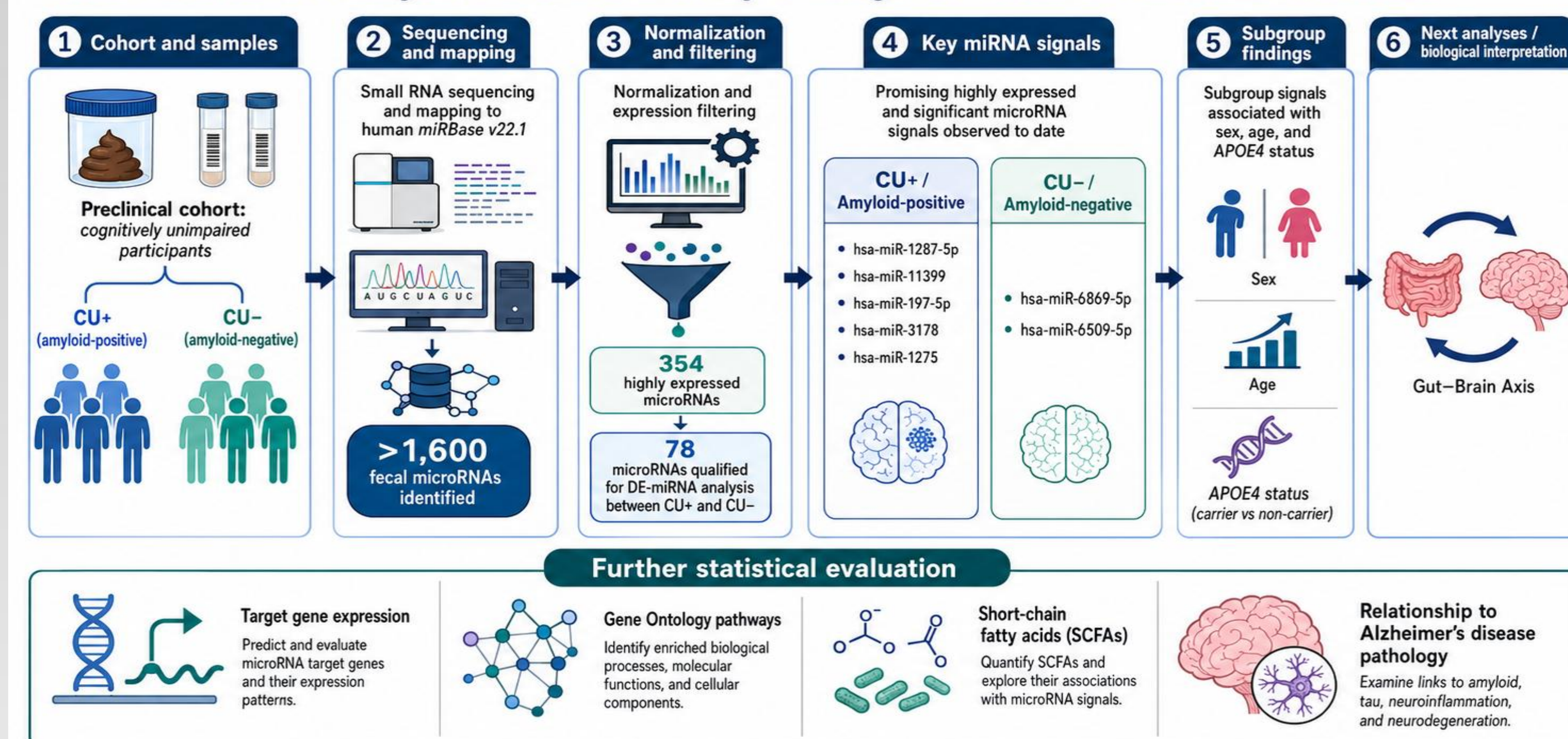


METHODS

- 60 fecal samples were obtained from highly characterised cognitively unimpaired participants from the AIBL and WAMS cohorts, representing the preclinical stage of Alzheimer's disease.
- Participants were grouped as CU+ and CU- based on brain amyloid-beta deposition status. Fecal RNA was extracted, and small RNA sequencing was performed to profile fecal microRNA expression.
- Differential microRNA expression between CU+ and CU- individuals was assessed using edgeR and DESeq2 differential expression analysis.
- Significant miRNAs were further evaluated across subgroups, including age, sex, and APOE ε4 status, to explore their relationship with Alzheimer's disease pathology.
- GO pathway enrichment and target gene expression analyses will also be conducted for significant miRNAs to investigate their potential biological functions and regulatory targets related to AD pathology.

RESULTS

Fecal microRNA Analysis Workflow and Key Findings in Preclinical Alzheimer's Disease



- After mapping to human miRBase v22.1, analysis identified more than 1,600 fecal microRNAs across the preclinical Alzheimer's disease cohort.
- Following normalisation and expression filtering, 354 microRNAs were classified as highly expressed, and 78 microRNAs qualified for differential microRNA expression analysis between the CU+ and CU- preclinical groups. Several promising microRNA signals have been observed to date.
- Highly expressed and significant microRNAs identified in CU+ individuals included hsa-miR-1287-5p, hsa-miR-11399, hsa-miR-197-5p, hsa-miR-3178 and hsa-miR-1275, while hsa-miR-6869-5p and hsa-miR-6509-5p were identified in CU- individuals.
- Subgroup analyses within the CU+ and CU- groups, including sex, age and APOE4 status, also showed significant correlations with these microRNAs.
- Further statistical evaluation will investigate their relationship with target gene expression, Gene Ontology pathways, short-chain fatty acids and their overall association with Alzheimer's disease pathology.

CONCLUSION

- Fecal microRNA profiling identified promising miRNA signals associated with CU+ and CU- individuals in the preclinical stage of Alzheimer's disease.
- Significant miRNAs showed potential relationships with key subgroup factors, including age, sex, and APOE ε4 status, suggesting biological heterogeneity within preclinical AD pathology.
- Further target gene expression and GO pathway analyses may help clarify the functional relevance of these miRNAs and their potential role as non-invasive biomarkers for early AD detection.

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MY CONTACT

