Clinical, Immune, and Neuro-Motor Profiles Linked to STING1 Gene Variants in People Living With HIV

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BACKGROUND

- Older PLWH in ART → persistent immune activation and type I interferon signaling → accelerated aging and comorbidities;
- cGAS-STING mediates IFN I and inflammaging;
- Hypomorphic STING1/TMEM173 variants may attenuate the pathway;
- Clinical impact in aging PLWH remains unclear.

This study was conducted to test the hypothesis that common STING1 variants may be associated with more favorable aging in PLWH.

METHODS

- Cross-sectional, single center, pilot study;
- PLWH ≥ 50 years, long-term efficient ART;
- Demographic, immunologic and comorbidities data were collected from medical records;
- STING1/TMEM173 genotyping by PCR amplification and Sanger sequencing;
- Cognitive (MMSE, CDT) and physical (SPPB) performance were assessed during a single study visit;
- Analyses compared groups stratified by genetic variants (HAQ haplotype and R232H variant) adjusting for age and HIV duration when appropriate.

All combinations tested:

WT/WT vs any polymorphism
WT/WT vs all HAQ/AQ/A carriers
WT/WT vs only HAQ/AQ/A carriers
WT/WT vs all HAQ carriers
All HAQ/AQ/A vs all other patients
All HAQ vs all other patients
WT/WT vs all H232 carriers
WT/WT vs only H232 carriers
All H232 carriers vs all other patients
Only H232 carriers vs all other patients
Only HAQ/AQ vs only H232 carriers

Hypomorphic STING1 variants may support immuno-metabolic resilience in aging PLWH

RESULTS

- Sixty older PLWH were included (median age: 69.5 years, median CD4+ count ~546 cells/mm³, 58% had ≥2 comorbidities);
- No differences in demographic or immunological parameters;
- No differences in cognitive or physical performance;
- Higher n. comorbidities in WT/WT group vs HAQ (2.44 vs 1.56; p= 0.037);
- R232H carriers vs WT/WT → higher CD4 T-cell counts (median 553.2 vs 796.9, p = .022) [Fig. 1];
- HAQ carriers vs WT/WT → lower dyslipidemia prevalence (26% vs 56% p = 0.031) [Fig. 2].

Genotypes prevalence

Genotype	N (%)
WT/WT	28 (46.7)
WT/H232	10 (16.7)
H232/H232	1 (1.7)
WT/HAQ	16 (26.7)
HAQ/HAQ	1 (1.7)
WT/AQ	1 (1.7)
A/H232	1 (1.7)
HAQ/H232	2 (3.3)
TOT	60 (100)

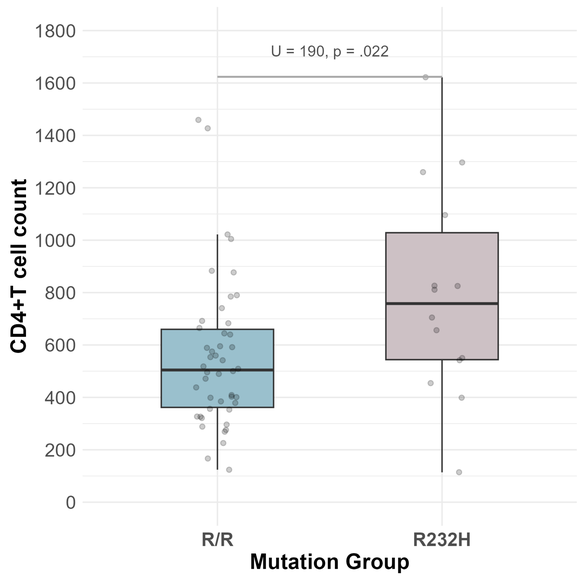


Fig. 1

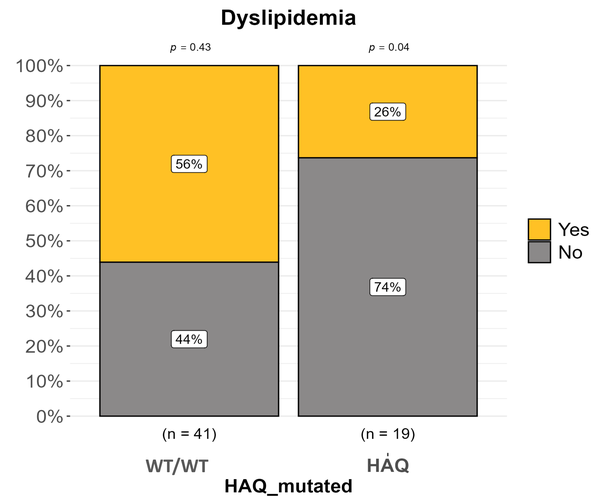


Fig. 2

CONCLUSIONS

What this suggests

STING variants may reduce inflammaging and the burden of medical comorbidities in older PLWH.
Hypomorphic STING1 (HAQ and R232H) variants may modulate immune recovery dynamics.

What this does NOT show

No evidence for neurocognitive impact.
No mechanistic IFN data.

Why this matters

Host genetics may shape aging trajectories in PLWH on ART.
STING pathway could represent a modifier of immune-metabolic risk.

ADDITIONAL KEY INFORMATION

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PLAIN LANGUAGE SUMMARY

PLWH with common hypomorphic genetic variations in the STING1 gene maintain stronger immune systems and fewer metabolic health problems. These findings suggest that natural differences in immune genes could influence how well people age with HIV.