### Supplementary Table. Summary table of the articles reviewed

<table>
<thead>
<tr>
<th>Article</th>
<th>Sample size</th>
<th>Race/ethnicity</th>
<th>Cohort/geographic location</th>
<th>Study design</th>
<th>Tissue/genotyping method</th>
<th>Haplogrouping method</th>
<th>Adjusted for ART</th>
<th>Phenotype</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hulgan, et al. 2008[18]</td>
<td>54</td>
<td>White</td>
<td>ACTG (Protocol 384/IUS) Cohort</td>
<td>Peripheral blood/TaqMan</td>
<td>10 SNP genotyped following Torroni[77]</td>
<td>Yes</td>
<td>Lipodystrophy</td>
<td>No statistically significant associations; haplogroup J tended to have lower risk (p = 0.07)</td>
<td></td>
</tr>
<tr>
<td>Hendrickson, et al. 2008[19]</td>
<td>1,833</td>
<td>White</td>
<td>MACS, SFDC, HGCS, MHCE, ALIVEUS Cross-sectional</td>
<td>Lymphophatiod B-cell line/TaqMan</td>
<td>32 SNP genotyped</td>
<td>No*</td>
<td>AIDS progression</td>
<td>Haplogroups U5a and J associated with AIDS progression; IXK, UK, and H5 associated with delayed or decreased AIDS</td>
<td></td>
</tr>
<tr>
<td>Navi, et al. 2008[20]</td>
<td>346</td>
<td>White</td>
<td>Clinical cohort/ northern italy Cross-sectional</td>
<td>Peripheral blood/restriction enzyme</td>
<td>Restriction-enzyme recognition sites</td>
<td>Yes</td>
<td>Multiple metabolic (including lipodystrophy) and virus-immunologic parameters</td>
<td>No statistically significant associations</td>
<td></td>
</tr>
<tr>
<td>Hendrickson, et al. 2010[22]</td>
<td>503</td>
<td>White</td>
<td>LSOSA Cross-sectional</td>
<td>White blood cells/TaqMan</td>
<td>Haplogroup SNP list from Hendrickson[72]</td>
<td>No</td>
<td>Neuroretinal disorder</td>
<td>Haplogroup J associated with decrease in progression; haplogroup U5a and H5 protective</td>
<td></td>
</tr>
<tr>
<td>Canter, et al. 2010[23]</td>
<td>156</td>
<td>Black</td>
<td>ACTG (Protocol 384/IUS) Cohort</td>
<td>Peripheral blood/ Affymetrix</td>
<td>Haplogroup SNP list defined by Hernnstadt[86]</td>
<td>Yes</td>
<td>Peripheral neuropathy</td>
<td>Haplogroup L.t associated with increased risk</td>
<td></td>
</tr>
<tr>
<td>Hulgan, et al. 2011[24]</td>
<td>231</td>
<td>White</td>
<td>ACTG (Protocol 384/IUS) Cohort</td>
<td>Peripheral blood/TaqMan</td>
<td>10 SNP genotyped following Torroni[77]</td>
<td>Yes</td>
<td>Serum lipids, lipodystrophy</td>
<td>Haplogroup J associated with higher baseline non-HDL cholesterol; greater decrease in non-HDL cholesterol, increased baseline extremity fat, greater decrease in extremity fat and lipodystrophy</td>
<td></td>
</tr>
<tr>
<td>Michaloud, et al. 2011[27]</td>
<td>248</td>
<td>White</td>
<td>HIV/HCV coinfected cohort/Spain Cross-sectional</td>
<td>Peripheral blood/Sequenom MassARRAY platform using the iPLEX Gold Assay design system</td>
<td>Haplogroup SNP list from Hendrickson[72]</td>
<td>Yes</td>
<td>Insulin resistance, atherogenic risk, serum HGF, c-HSP, and adiponectin levels</td>
<td>Haplogroup HV and H had decreased insulin resistance and high atherogenic risk; haplogroup U increased insulin resistance; haplogroup JT and T increased atherogenic risk</td>
<td></td>
</tr>
<tr>
<td>Grady, et al. 2011[28]</td>
<td>423</td>
<td>49% White 31% Black 18% Hispanic 3% other</td>
<td>ACTG (Protocol 384/IUS) Cohort</td>
<td>Peripheral blood/ Affymetrix</td>
<td>Haplogroup SNP list defined by Hemnostad[86]</td>
<td>No</td>
<td>CD4 T-cell recovery on ART</td>
<td>Haplogroup L.t associated with decreased likelihood of ≥ 100 cells/mm³ CD4 count increase</td>
<td></td>
</tr>
<tr>
<td>Garcia-Avarez, et al. 2011[29]</td>
<td>231</td>
<td>White</td>
<td>HIV/HCV coinfected cohort/Spain Cross-sectional</td>
<td>Peripheral blood/Sequenom MassARRAY</td>
<td>Haplogroup SNP list defined by Hemnostad[86]</td>
<td>Yes</td>
<td>Advanced fibrosis, cirrhosis, fibrosis progression rate</td>
<td>Haplogroup HV and H associated with less fibrosis, cirrhosis, slower fibrosis progression; haplogroup U associated with increased cirrhosis, faster fibrosis progression</td>
<td></td>
</tr>
<tr>
<td>Arenas-Pinto, et al. 2011[30]</td>
<td>90</td>
<td>87% Black 13% White</td>
<td>Clinical cohort/South Africa, Denmark, UK, Switzerland Cohort</td>
<td>Peripheral blood and buccal smears/Sanger</td>
<td>SNP from hypervariable region 1</td>
<td>Yes</td>
<td>Severe hyperlactatemia</td>
<td>No associations between severe hyperlactatemia and haplogroups</td>
<td></td>
</tr>
<tr>
<td>De Lucia, et al. 2012[31]</td>
<td>187</td>
<td>White</td>
<td>Clinical cohort/ central Italy Cross-sectional</td>
<td>Peripheral blood/restriction enzyme</td>
<td>Restriction-enzyme recognition sites</td>
<td>Yes</td>
<td>Lipodystrophy</td>
<td>Haplogroup K associated with increased risk</td>
<td></td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Article</th>
<th>Sample size</th>
<th>Race/ethnicity</th>
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<tr>
<td>Holzinger, et al. 2012</td>
<td>549</td>
<td>44% White, 43% Black, 10% Hispanic, 2% other</td>
<td>CHARITER/US Cohort</td>
<td>Peripheral blood/ Affymetrix</td>
<td>Haplogroup SNP list defined by Hernstadt 86</td>
<td>Yes</td>
<td>HIV-associated sensory neuropathy</td>
<td>Haplogroup L1c associated with lower risk</td>
<td></td>
</tr>
<tr>
<td>Sinwadi, et al. 2013</td>
<td>171</td>
<td>Black African</td>
<td>Metabolic and neuropathy cohort/ South Africa</td>
<td>Cross-sectional</td>
<td>Peripheral blood/ Affymetrix</td>
<td>PhyloTree 18</td>
<td>Yes</td>
<td>Dyslipidemia, lipodystrophy, peripheral neuropathy Sub-haplogroup L3e1 associated with triglyceride levels and hypo-triglyceridaemia; no associations with lipodystrophy or neuropathy</td>
<td></td>
</tr>
<tr>
<td>Guzmán-Fulgencio, et al. 2013</td>
<td>469</td>
<td>White</td>
<td>CoRIS and cohort of LTNP/Spain</td>
<td>Cross-sectional</td>
<td>Peripheral blood/ Sequenom MassARRAY</td>
<td>Haplogroup SNP list from Hendrickson 72</td>
<td>No</td>
<td>Patterns of AIDS progression Haplogroup H and H associated with lower risk of AIDS progression</td>
<td></td>
</tr>
<tr>
<td>Guzmán-Fulgencio, et al. 2013</td>
<td>275</td>
<td>White</td>
<td>Clinical cohort/Spain</td>
<td>Cohort</td>
<td>Peripheral blood/ Sequenom MassARRAY</td>
<td>Haplogroup SNP list from Hendrickson 72</td>
<td>Yes</td>
<td>CD4 T-cell recovery on ART Haplogroup H and H associated with better CD4 recovery</td>
<td></td>
</tr>
<tr>
<td>Hulgan, et al. 2013</td>
<td>76</td>
<td>White</td>
<td>ACTG (Protocol A1552s)/US Cohort</td>
<td>Peripheral blood/TaqMan 10 SNP genotyped following Torroni 77</td>
<td>Yes</td>
<td>Brachial artery FMD; cardiovascular biomarkers</td>
<td>Haplogroup U associated with greater increase in HOMA-IR; no associations with FMD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ACTG: AIDS Clinical Trials Group; ALIVE: AIDS Linked to Intravenous Experiences cohort; ART: antiretroviral therapy; CHARTER: DNS Andrological Therapy Effects Research; CoRIS: Cohort of the Spanish HIV Research Network; FMD: flow mediated dilation; GCDS: Hemophilia Growth and Development Study; HOMA-IR: Homeostatic model assessment-insulin resistance; LSDDCA: Longitudinal Study of the Ocular Complications cohort; LTNP: long-term non-progressor; MACS: Multicenter AIDS Cohort Study; MHCS: Multicenter Hemophilia Cohort Study; OXPHOS: oxidative phosphorylation; SFCC: San Francisco City Clinic Study; SHCS: Swiss HIV Cohort Study.

*Clinical data was collected before the widespread use of potent combination ART.*
The Other Genome: A Systematic Review of Studies of Mitochondrial DNA Haplogroups and Outcomes of HIV Infection and Antiretroviral Therapy

Anna B. Hart¹, David C. Samuelson² and Todd Hulgan¹
¹Department of Medicine, Division of Infectious Diseases, Vanderbilt University School of Medicine, Nashville, TN, USA; ²Department of Molecular Physiology and Biophysics, Center for Human Genetics Research, Vanderbilt University School of Medicine, Nashville, TN, USA

**ABSTRACT**

Structured summary

1. Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.

**INTRODUCTION**

Rationale

3. Describe the rationale for the review in the context of what is already known.

Objectives

4. Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICO(S)).

**METHODS**

Protocol and registration

5. Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.

Eligibility criteria

6. Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.

Information sources

7. Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.

Search

8. Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.

Study selection

9. State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).

Data collection process

10. Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.

Data items

11. List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.

Risk of bias in individual studies

12. Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.

Summary measures

13. State the principal summary measures (e.g., risk ratio, difference in means).

Synthesis of results

14. Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²) for each meta-analysis.

Risk of bias across studies

15. Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).

Additional analyses

16. Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.

**RESULTS**

Study selection

17. Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.

Study characteristics

18. For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.

Risk of bias within studies

19. Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).

Results of individual studies

20. For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.

Synthesis of results

21. Present results of each meta-analysis done, including confidence intervals and measures of consistency.

Risk of bias across studies

22. Present results of any assessment of risk of bias across studies (see item 15).

Additional analysis

23. Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see item 16]).

**DISCUSSION**

Summary of evidence

24. Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).

Limitations

25. Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).

Conclusions

26. Provide a general interpretation of the results in the context of other evidence, and implications for future research.

**FUNDING**

Funding

27. Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

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PRISMA 2009 Flow Diagram

Records identified through database searching (n = 45)

Additional records identified through other sources (n = 1)

Records after duplicates removed (n = 44)

Records screened (n = 44)

Records excluded (n = 20)

Full-text articles assessed for eligibility (n = 24)

Full-text articles excluded (Reason: articles did not perform haplogroup analysis) (n = 3)

Studies included in qualitative synthesis (n = 21)

Studies included in quantitative synthesis (meta-analysis) (n = )