

Supplementary

Table S1. Demographic Information for Participants with CSF Samples.

| | HIV-/METH- (<i>n</i> =18) | HIV-/METH+ (<i>n</i> =14) | HIV+ /METH- (<i>n</i> =22) | HIV+ /METH+ (<i>n</i> =13) | <i>P</i> value |
|---|--|---|---|---|----------------|
| Age (years) | 44.9 ± 16.2 | 38.4 ± 12.1 | 47.7 ± 16.4 | 38.3 ± 8.3 | 0.029 |
| Sex (%) | M: 61.1; F: 38.9 | M: 64.3; F: 35.7 | M: 95.4; F: 4.5 | M: 92.3; F: 7.8 | 0.016 |
| Ethnicity (%) | Asian: 5.6 Afr Am: 11.1; Hisp: 33.3; Other: 0 Cauc: 50.0 | Asian: 0 Afr Am: 21.4; Hisp: 7.1; Other: 14.3; Cauc: 57.1 | Asian: 0 Afr Am: 18.2; Hisp: 18.2; Other: 9.1; Cauc: 54.5 | Asian: 0; Afr Am: 7.7; Hisp: 69.2; Other: 0; Cauc: 23.1 | NS |
| Education (years) | 14.9 ± 1.6 | 12.9 ± 2.7 | 14.7 ± 2.4 | 13.9 ± 2.5 | 0.018 |
| Age First METH use (years) | - | 25.0 ± 11.4 | - | 24.6 ± 6.7 | NS |
| Days since last METH use (days) | - | 276 ± 563 | - | 93 ± 126 | NS |
| Total quantity METH use (grams) | - | 3654 ± 5507 | - | 2269 ± 2056 | NS |
| Current CD4+ Cell Count (cells/uL) | - | - | 801 ± 307 | 651 ± 250 | NS |
| Estimated Duration HIV Infection (years) | - | - | 15.1 ± 10.6 | 7.4 ± 5.2 | 0.021 |
| Plasma HIV RNA <50 cop- ies/mL (%) | - | - | 95.5 | 84.6 | NS |
| Current ART Use (%) | - | - | 95.5 | 100 | NS |

Data are presented as mean ± standard deviation unless otherwise noted. NS = not significantly different; ART: Anti-retroviral therapy.

Table S2. Summary of Plasma Biomarker Concentrations.

| | HIV-/METH- | HIV-/METH+ | HIV+ /METH- | HIV+ /METH+ | <i>P</i> value | Risk (Cohen's <i>d</i>) |
|----------------|-------------|-------------|----------------|----------------|-------------------|--------------------------|
| 8-iso-prostane | 0.53 ± 0.09 | 0.56 ± 0.10 | 0.58 ± 0.08 | 0.59 ± 0.09 | NS | |
| 8-oxodG | 0.63 ± 0.10 | 0.62 ± 0.06 | 0.65 ± 0.11 | 0.61 ± 0.09 | NS | |
| CRP | 0.20 ± 0.10 | 0.23 ± 0.12 | 0.26 ± 0.15 | 0.18 ± 0.12 | NS | |
| D-dimer | 0.36 ± 0.13 | 0.34 ± 0.15 | 0.37 ± 0.12 | 0.37 ± 0.15 | NS | |
| ICAM1 | 0.45 ± 0.13 | 0.49 ± 0.11 | 0.48 ± 0.12 | 0.49 ± 0.14 | NS | |
| IL-6 | 0.35 ± 0.10 | 0.36 ± 0.11 | 0.41 ± 0.14 | 0.32 ± 0.11 | 0.029 | METH: d=-0.36 |
| IL-8 | 0.38 ± 0.16 | 0.36 ± 0.12 | 0.44 ± 0.13 | 0.47 ± 0.13 | 0.008 | HIV: d=0.47 |
| CXCL10 | 0.30 ± 0.12 | 0.28 ± 0.11 | 0.38 ± 0.15 | 0.40 ± 0.14 | <0.0005 | HIV: d=0.68 |
| Ccl2 | 0.36 ± 0.15 | 0.36 ± 0.15 | 0.44 ± 0.17 | 0.48 ± 0.13 | 0.014 | HIV: d=0.40 |
| MDA | 0.44 ± 0.12 | 0.42 ± 0.14 | 0.44 ± 0.10 | 0.41 ± 0.08 | NS | |
| sCD14 | 0.48 ± 0.15 | 0.46 ± 0.11 | 0.54 ± 0.12 | 0.52 ± 0.13 | 0.006 | HIV: d=0.45 |
| sTNFR2 | 0.41 ± 0.15 | 0.42 ± 0.10 | 0.44 ± 0.15 | 0.46 ± 0.12 | NS | |
| uPAR | 0.43 ± 0.13 | 0.44 ± 0.15 | 0.46 ± 0.16 | 0.40 ± 0.11 | NS | |
| VEGF | 0.37 ± 0.14 | 0.36 ± 0.15 | 0.39 ± 0.14 | 0.43 ± 0.15 | NS | |

Values represent the mean ± S.E.M. of the log transformed Z-scores of the raw biomarker data.

Table S3. Summary of CSF Biomarker Concentrations.

| | HIV-/METH- | HIV-/METH+ | HIV+ /METH- | HIV+ /METH+ | <i>P</i> value | Risk (Cohen's <i>d</i>) |
|----------------|-------------|-------------|----------------|----------------|----------------|---|
| 8-iso-prostane | 0.31 ± 0.17 | 0.40 ± 0.16 | 0.45 ± 0.15 | 0.38 ± 0.11 | 0.017 | H+/M- > H-/M-: d=0.80 |
| 8-oxodG | 0.37 ± 0.17 | 0.33 ± 0.12 | 0.37 ± 0.16 | 0.33 ± 0.16 | NS | |
| CRP | 0.29 ± 0.10 | 0.29 ± 0.21 | 0.35 ± 0.17 | 0.27 ± 0.09 | NS | |
| D-dimer | 0.43 ± 0.13 | 0.45 ± 0.13 | 0.43 ± 0.13 | 0.41 ± 0.10 | NS | |
| ICAM1 | 0.28 ± 0.15 | 0.31 ± 0.16 | 0.38 ± 0.18 | 0.31 ± 0.14 | NS | |

| | | | | | | |
|--------|-------------|-------------|-------------|-------------|--------------|---|
| IL6 | 0.43 ± 0.11 | 0.47 ± 0.14 | 0.43 ± 0.14 | 0.39 ± 0.09 | NS | |
| IL8 | 0.40 ± 0.14 | 0.44 ± 0.14 | 0.52 ± 0.12 | 0.44 ± 0.10 | 0.042 | H+/M- > H-/M-: d=0.40 |
| CXCL10 | 0.27 ± 0.09 | 0.28 ± 0.14 | 0.38 ± 0.15 | 0.34 ± 0.17 | 0.008 | HIV: d=0.60 |
| Ccl2 | 0.42 ± 0.17 | 0.42 ± 0.14 | 0.44 ± 0.15 | 0.41 ± 0.13 | NS | |
| MDA | 0.28 ± 0.15 | 0.32 ± 0.11 | 0.33 ± 0.14 | 0.32 ± 0.11 | NS | |
| NFL | 0.38 ± 0.13 | 0.35 ± 0.15 | 0.44 ± 0.18 | 0.34 ± 0.08 | NS | |
| sCD14 | 0.32 ± 0.12 | 0.34 ± 0.18 | 0.41 ± 0.19 | 0.32 ± 0.11 | NS | |
| sTNFR2 | 0.38 ± 0.14 | 0.39 ± 0.08 | 0.45 ± 0.16 | 0.39 ± 0.12 | NS | |
| uPAR | 0.33 ± 0.16 | 0.32 ± 0.13 | 0.41 ± 0.19 | 0.37 ± 0.08 | NS | |
| VEGF | 0.40 ± 0.14 | 0.52 ± 0.13 | 0.48 ± 0.15 | 0.44 ± 0.14 | NS | |

Values represent the mean ± S.E.M. of the log transformed Z-scores of the raw biomarker data.

Table S4. Factor Loadings of CSF Biomarkers.

| | Factor 1 | Factor 2 | Factor 3 | Factor 4 |
|---------|-----------------|-----------------|-----------------|-----------------|
| ICAM1 | 0.831 | | | |
| uPAR | 0.828 | | | |
| sTNFR2 | 0.796 | | | |
| sCD14 | 0.739 | | | |
| NFL | 0.671 | | | |
| IL8 | 0.663 | | | |
| CXCL10 | 0.536 | | | |
| CRP | 0.491 | | | |
| IL6 | | 0.825 | | |
| Ccl2 | | 0.681 | | |
| D-dimer | | | 0.804 | |
| 8-oxodG | | | 0.696 | |
| MDA | | | | 0.815 |
| 8iso | | | | 0.617 |

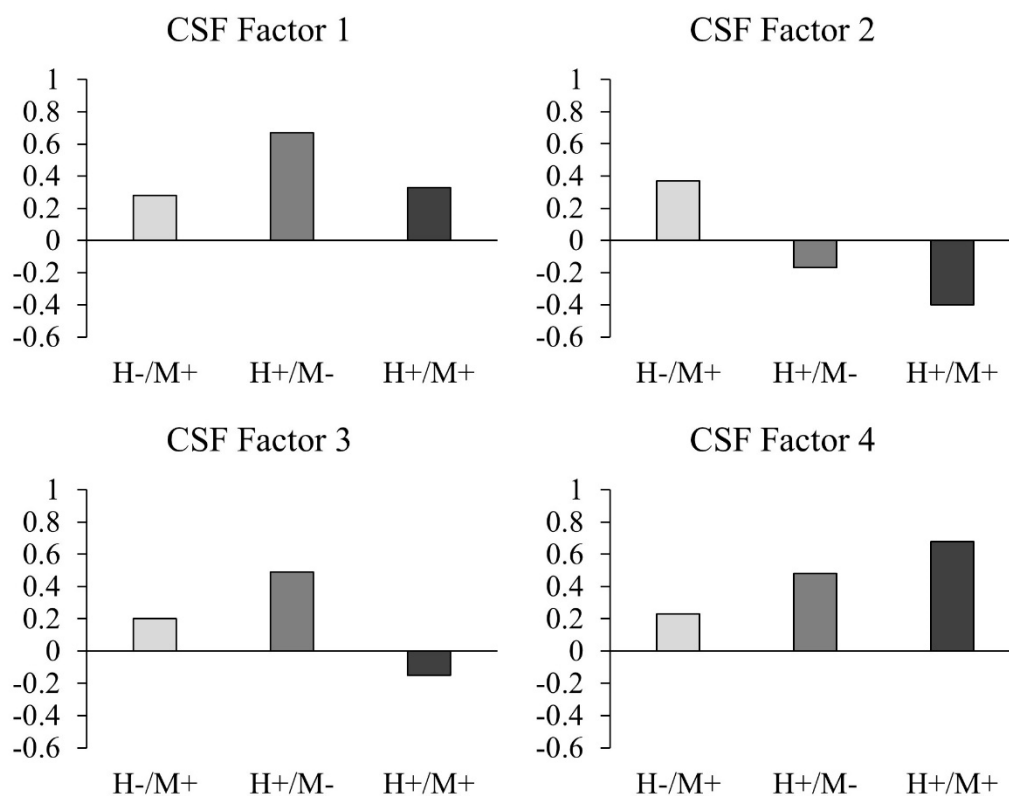


Figure S1. Effect Sizes of Each Group Compared to the HIV-/METH- Group for Each Plasma Factor. Effect sizes (using Cohen's d) were calculated for the HIV-/METH+, HIV+/METH-, and HIV+/METH+ group compared to the control (HIV-/METH-) group for each factor.