**SUPPLEMENTAL MATERIAL**

| Metabolite | $[M+H]^+$ | Product Ion | CE (V) | RT (min) |
|---|---|---|---|---|
| **Aspartate** | **134.0** | **88** | **13** | **1.15** |
| **Homocysteine** | **136.1** | **89.99** | **12** | **1.15** |
| **Lysine** | **146.85** | **84.05** | **15** | **0.85** |
| **Glutamic Acid** | **148.1** | **84.01** | **14** | **0.97** |
| **Methionine** | **149.97** | **45.02** | **54** | **1.10** |
| **Histidine** | **155.792** | **83.01** | **28** | **0.92** |
| **Phenylalanine** | **166.08** | **120.04** | **11** | **2.61** |
| **Arginine** | **175.1** | **60.01** | **14** | **0.93** |
| **Citrulline** | **176** | **113** | **16** | **0.93** |
| **Tyrosine** | **182.1** | **91.01** | **28** | **1.34** |
| **Tryptophan** | **205.07** | **146.01** | **21** | **3.81** |
| **Cytidine** | **244.1** | **112** | **31** | **1.00** |
| **Adenosine** | **268.1** | **136** | **18** | **2.03** |

**Table S1**. Endogenous metabolites detected by positive ionization. SRM transitions were developed for the detection of small molecules present in the plasma and urine of individuals receiving either Complera™ or Atripla™ antiretroviral therapy and for those present in the biological samples of non-infected, antiretroviral untreated individuals. The above metabolites were detected by a positive ion mode UHPLC-MS/MS screen using the stated parent mass, $[M+H]^+$, to product ion transitions at the specified collision energies (CE) and resulted in the approximate retention times (RT).

| Metabolite | $[M-H]^-$ | Product Ion | CE (V) | RT (min) |
|---|---|---|---|---|
| **Pyruvate** | **86.7** | **42.5** | **26** | **0.94** |
| **Succinc Acid** | **116.8** | **72.99** | **15** | **1.04** |
| **Malic Acid** | **132.8** | **71.2** | **20** | **0.86** |
| **Citrate** | **190.926** | **110.9** | **13** | **0.98** |
| **Thymidine** | **241.1** | **124.96** | **20** | **1.08** |
| **Uridine** | **242.9** | **109.96** | **20** | **0.99** |

**Table S2.** Endogenous metabolites detected by negative ionization. SRM transitions were developed for the detection of small molecules present in the plasma and urine of individuals receiving either Complera™ or Atripla™ antiretroviral therapy and for those present in the biological samples of non-infected, antiretroviral untreated individuals. The above metabolites were detected by a negative ion mode UHPLC-MS/MS screen using the stated parent mass, $[M-H]^-$, to product ion transitions at the specified collision energies (CE) and resulted in the approximate retention times (RT).

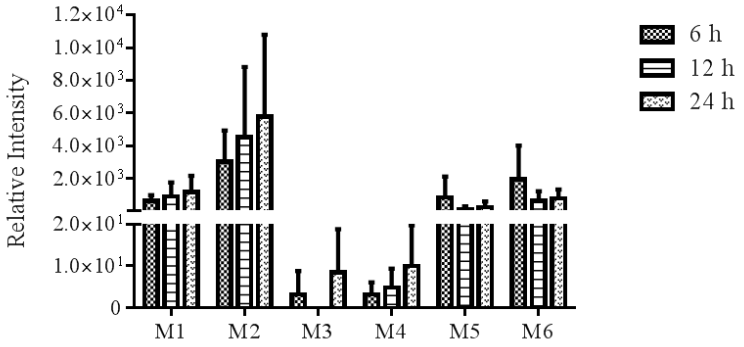


**Figure S1.** Metabolites detected in medium collected from RPV-treated primary human hepatocytes. Hepatocytes from three donors were treated with either DMSO or 10 µM RPV for 6, 12 and 24 h prior to medium collection for UHPLC-MS/MS analysis in SRM mode using the following transitions: 383→222 *m/z* (M1 and M2), 399→183 *m/z* (M3), 399→196 *m/z* (M4), 543→367 *m/z* (M5) and 559→383 *m/z* (M6). Glucuronide M7 formation was not detectable for any of the hepatocyte treatments. Data are representative of the mean relative intensities for three separate hepatocyte preparations n=3 ± SD.