**Supplemental Material**

# Comparison of Species and Cell-Type Differences in Fraction Unbound of Liver Tissues, Hepatocytes and Cell-Lines

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Drug Metabolism and Disposition

## Table Legend

Table 1s. Pearson correlation coefficients for $f_{u.}$ Pairwise correlation estimates for all species and cell types using $\log_2$ (geomean $f_u$) per compound per matrix.

## Figure Legend

Figure 1s. Sample variance versus geometric mean of the matrix quadruplicates. A slope of two for a simple linear fit of log(y) vs. log(x) (not shown) suggests a constant coefficient of variation across the range of $f_u$.

Figure 2s. Histogram and normal q-q plot of $\log_2(f_u)$ for 22 compounds in rat liver (representative tissue example). The compound-to-compound variability for $\log_2(f_u)$ is approximately normally distributed.

**Table 1s. Pearson correlation coefficients for $f_{u.}$ Pairwise correlation estimates for all species and cell types using $\log_2$ (geomean $f_u$) per compound per matrix.**

| Correlation Coefficient | Mouse Liver | Rat Liver | Dog Liver | Monkey Liver | Human Liver | Mouse Hepatocyte | Rat Hepatocyte | Dog Hepatocyte | Monkey Hepatocyte | Human Hepatocyte | Huh7 | HEK293 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Mouse Liver** | 1.00 | 0.94 | 0.95 | 0.96 | 0.92 | 0.93 | 0.94 | 0.93 | 0.94 | 0.94 | 0.92 | 0.94 |
| **Rat Liver** | 0.94 | 1.00 | 0.95 | 0.96 | 0.97 | 0.97 | 0.96 | 0.95 | 0.95 | 0.96 | 0.95 | 0.96 |
| **Dog Liver** | 0.95 | 0.95 | 1.00 | 0.96 | 0.95 | 0.93 | 0.95 | 0.93 | 0.94 | 0.91 | 0.95 | 0.94 |
| **Monkey Liver** | 0.96 | 0.96 | 0.96 | 1.00 | 0.95 | 0.95 | 0.97 | 0.94 | 0.93 | 0.95 | 0.94 | 0.95 |
| **Human Liver** | 0.92 | 0.97 | 0.95 | 0.95 | 1.00 | 0.95 | 0.95 | 0.93 | 0.95 | 0.93 | 0.95 | 0.93 |
| **Mouse Hepatocyte** | 0.93 | 0.97 | 0.93 | 0.95 | 0.95 | 1.00 | 0.96 | 0.92 | 0.90 | 0.96 | 0.95 | 0.94 |
| **Rat Hepatocyte** | 0.94 | 0.96 | 0.95 | 0.97 | 0.95 | 0.96 | 1.00 | 0.94 | 0.95 | 0.97 | 0.94 | 0.95 |
| **Dog Hepatocyte** | 0.93 | 0.95 | 0.93 | 0.94 | 0.93 | 0.92 | 0.94 | 1.00 | 0.93 | 0.94 | 0.92 | 0.95 |
| **Monkey Hepatocyte** | 0.94 | 0.95 | 0.94 | 0.93 | 0.95 | 0.90 | 0.95 | 0.93 | 1.00 | 0.93 | 0.90 | 0.94 |
| **Human Hepatocyte** | 0.94 | 0.96 | 0.91 | 0.95 | 0.93 | 0.96 | 0.97 | 0.94 | 0.93 | 1.00 | 0.92 | 0.94 |
| **Huh7** | 0.92 | 0.95 | 0.95 | 0.94 | 0.95 | 0.95 | 0.94 | 0.92 | 0.90 | 0.92 | 1.00 | 0.92 |
| **HEK293** | 0.94 | 0.96 | 0.94 | 0.95 | 0.93 | 0.94 | 0.95 | 0.95 | 0.94 | 0.94 | 0.92 | 1.00 |

**Figure 1s. Sample variance versus geometric mean of the matrix quadruplicates. A slope of two for a simple linear fit of log(y) vs. log(x) (not shown) suggests a constant coefficient of variation across the range of $f_u$.**

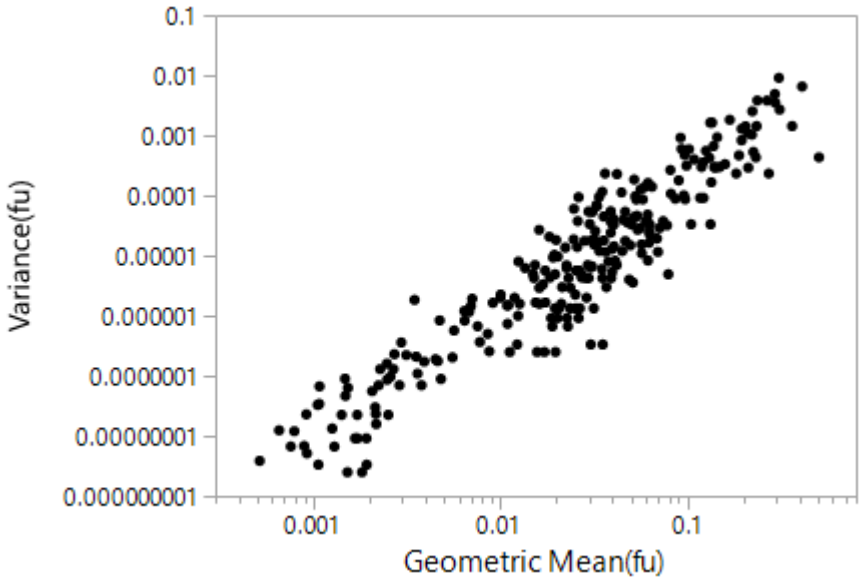

**Figure 2s. Histogram and normal q-q plot of $log_2(f_u)$ for 22 compounds in rat liver (representative tissue example). The compound-to-compound variability for $log_2(f_u)$ is approximately normally distributed.**