

Fig. S1- Predictive models of tumor metformin concentration. Regression models for tumor metformin concentration as a function of 1) dose, 2) dose + plasma concentration, or 3) dose + plasma concentration + and whole blood concentration (R^2 =coefficient of determination). The average value from replicate measurements for each specimen was used. The predictor as a linear function of the variables is listed below each plot. Regression lines (thick) are plotted \pm standard error of prediction by regression (thin).

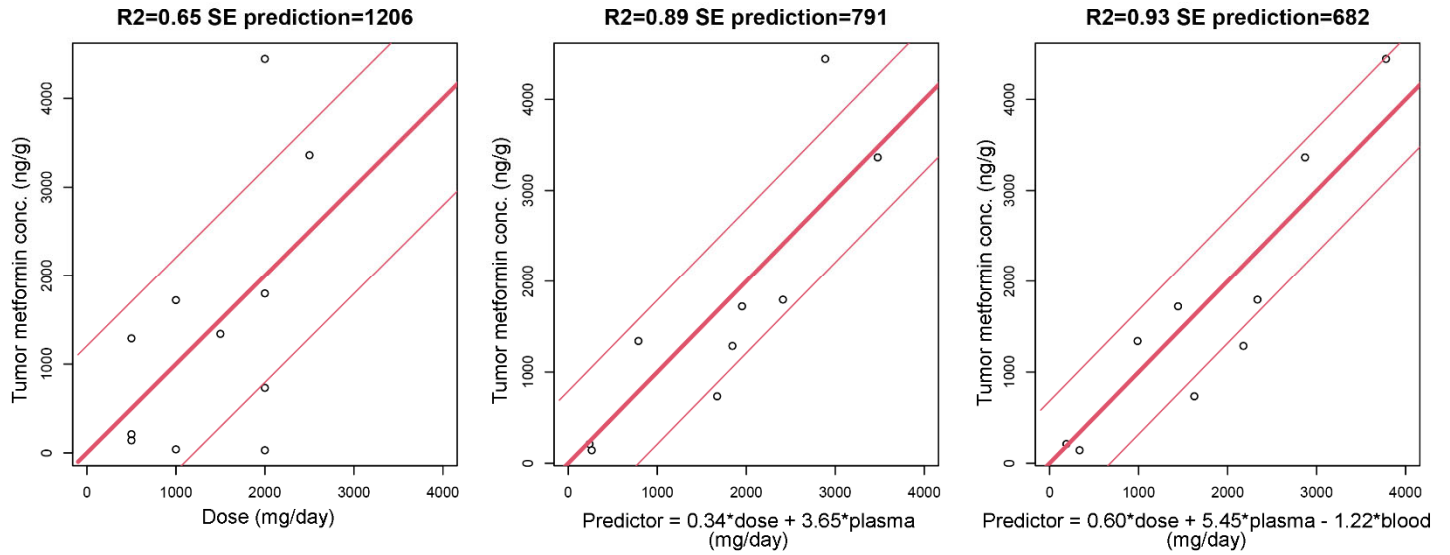


Fig. S2- Pairwise correlation plots of metformin concentrations in tissue. Concentrations of metformin in plasma, blood, adipose tissue, lung tissue, and tumor tissue were compared pairwise by subject. Data are plotted as average of replicates \pm standard deviation for each specimen. Regression lines (thick) were plotted \pm standard error of prediction by regression (thin). p-values were calculated by comparing slopes to null hypothesis.

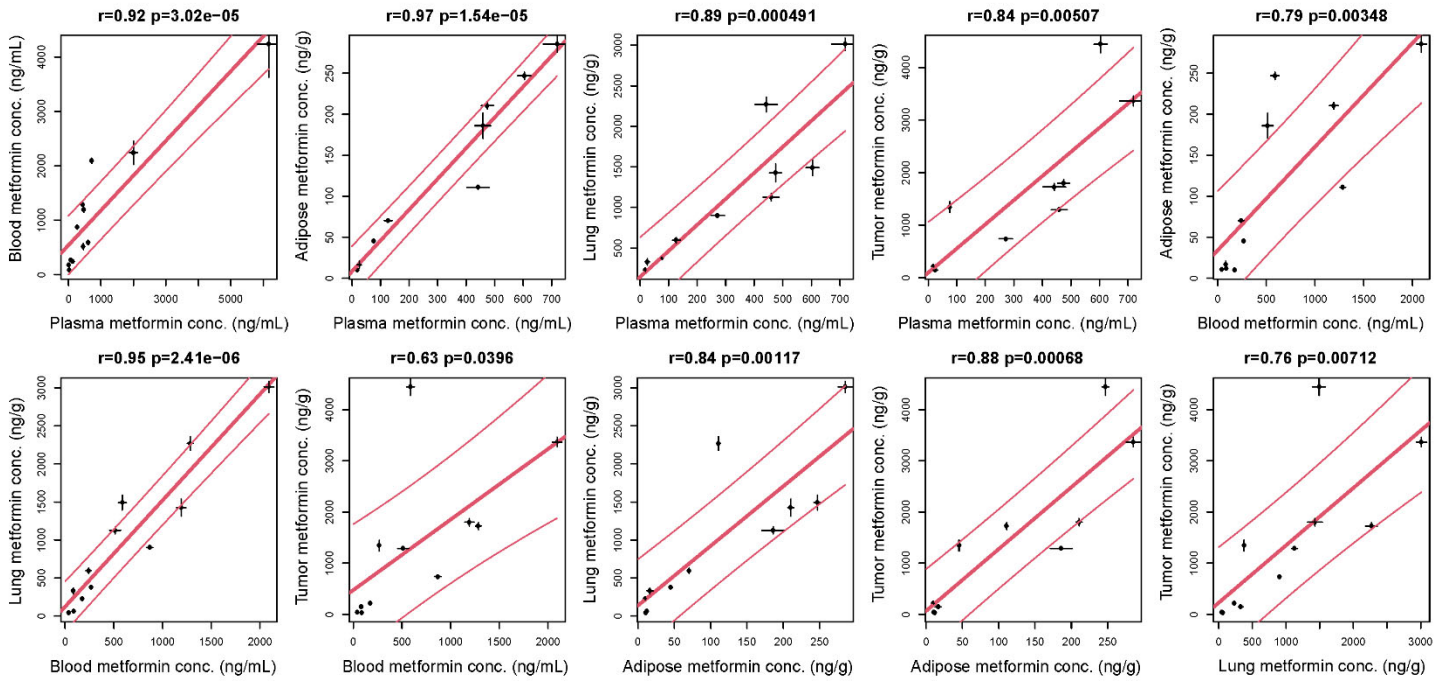


Fig. S3- Adjustment for dose formulation and frequency does not significantly alter model prediction of metformin concentration by dose. A linear mixed-effects model was applied accounting for inter-subject variation to predict tissue metformin concentration compared to daily dose with adjustment for dose formulation (SR or ER) and frequency (QD or BID). Adjusted regression lines (thick) and 95% confidence intervals (thin) are shown for each tissue type. Unadjusted regression lines from Fig. 2 (dotted) and slopes (“Dose slope”) are included for visual comparison. p-values comparing the two regression lines are indicated. Testing included all replicates with metformin concentrations \geq LLOQ.

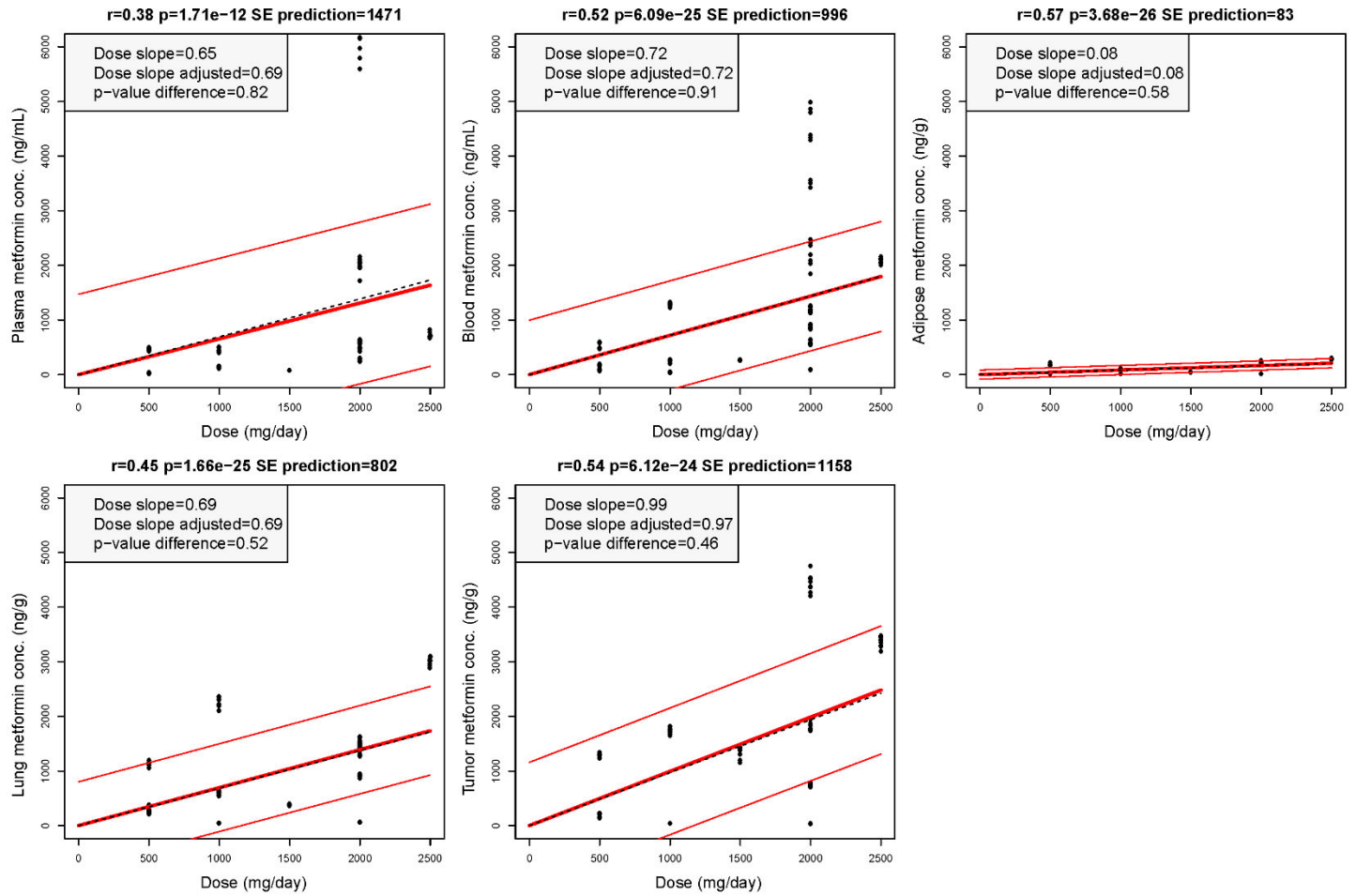


Fig S4- Pairwise comparison of metformin concentrations between tissue compartments. Slopes of lines from Fig. 2 (dose vs. concentration within each tissue compartment) were compared in a pairwise manner. Multiple comparison-adjusted p-values are shown. Cells are colored with white-to-red gradient based on decreasing p-value.

	Plasma	Blood	Adipose	Lung	Tumor
Plasma		0.52452	<0.0001	0.68307	0.00241
Blood	0.52452		<0.0001	0.74936	0.00295
Adipose	<0.0001	<0.0001		<0.0001	<0.0001
Lung	0.68307	0.74936	<0.0001		0.00085
Tumor	0.00241	0.00295	<0.0001	0.00085	