Supplementary Figures

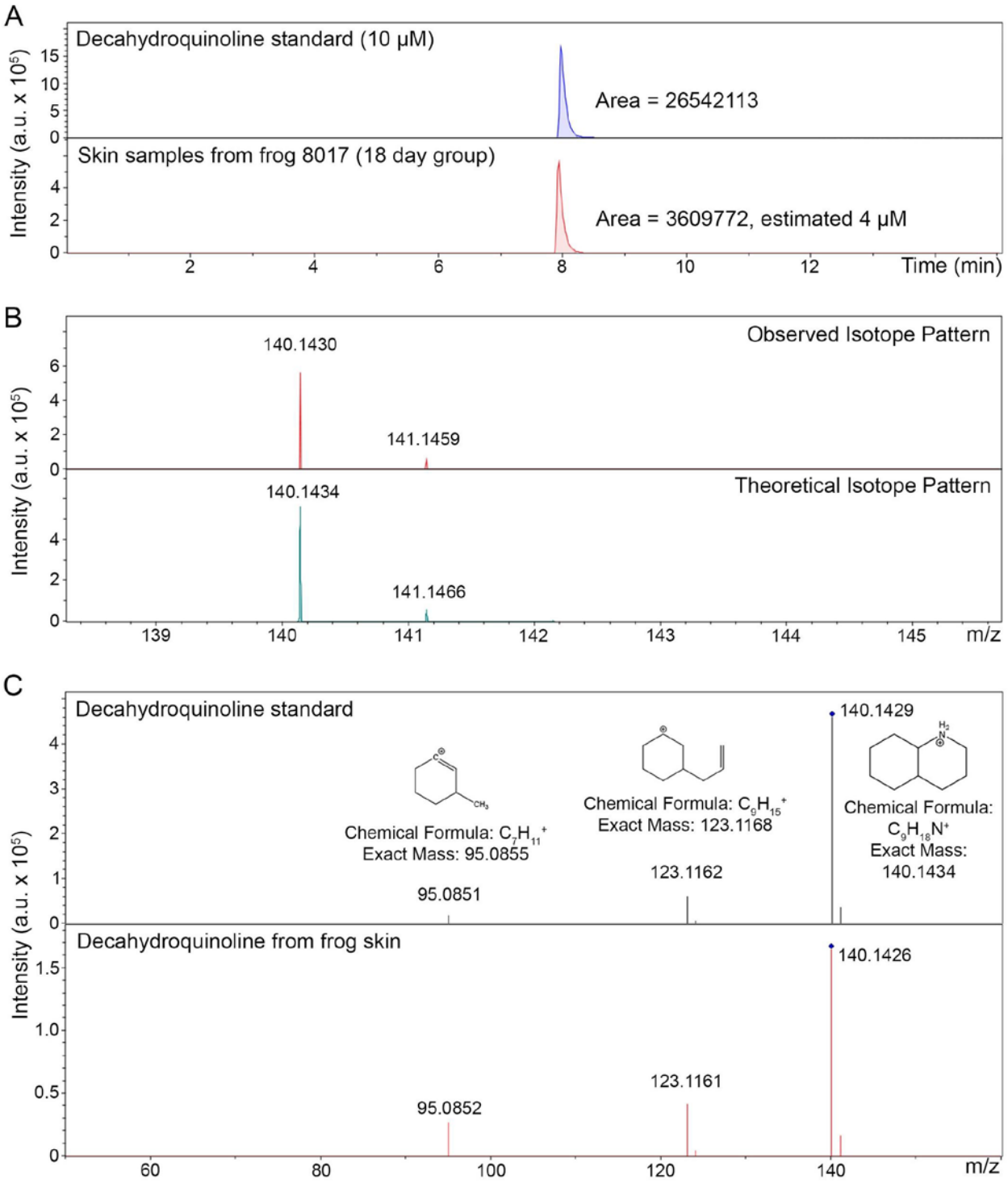

Figure S1. Detection of decahydroquinoline (DHQ) using liquid chromatography / mass spectrometry. (A) DHQ was dissolved at 10μM in methanol and used as a standard (top panel) to quantify tissue samples (bottom panel). **(B)** The observed isotope pattern of the DHQ standard (top panel) matched the theoretical expectation (bottom panel). **(C)** Tandem mass spectrometry was used to confirm the structure of DHQ from frog skin with the standard.

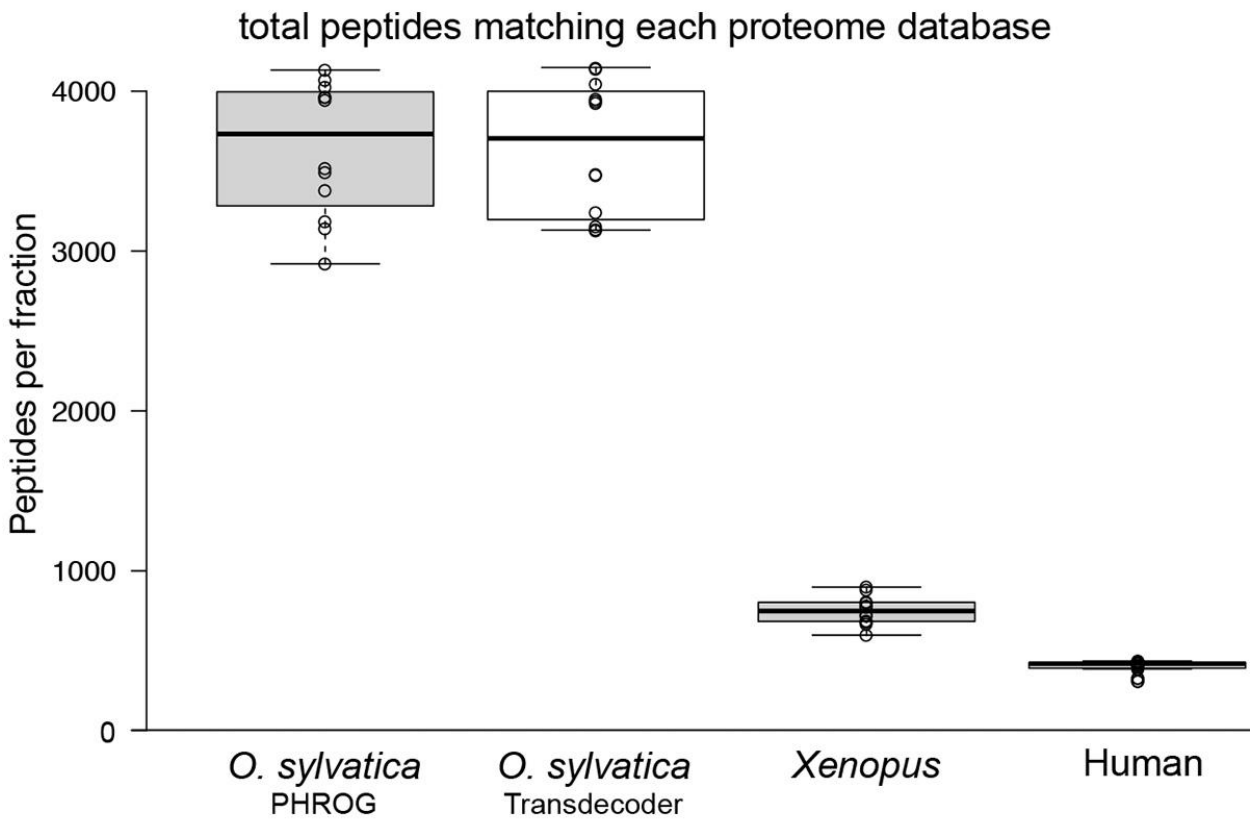

Figure S2. Comparison of proteome databases in peptide matching. The number of matching peptides from all tissues in the DHQ feeding dataset was compared across different proteome references. Two *O. sylvatica* references were equivalent, including one reference generated using the PHROG workflow (proteomic reference with heterogeneous RNA omitting the genome; (Wühr et al., 2014)) and the other generated using Transdecoder (http://**transdecoder**.github.io). We also compared the reference proteomes for *Xenopus* and human, which had fewer matches than the species-specific databases generated from transcriptome data. The *O. sylvatica* PHROG reference proteome was used in the final analysis.

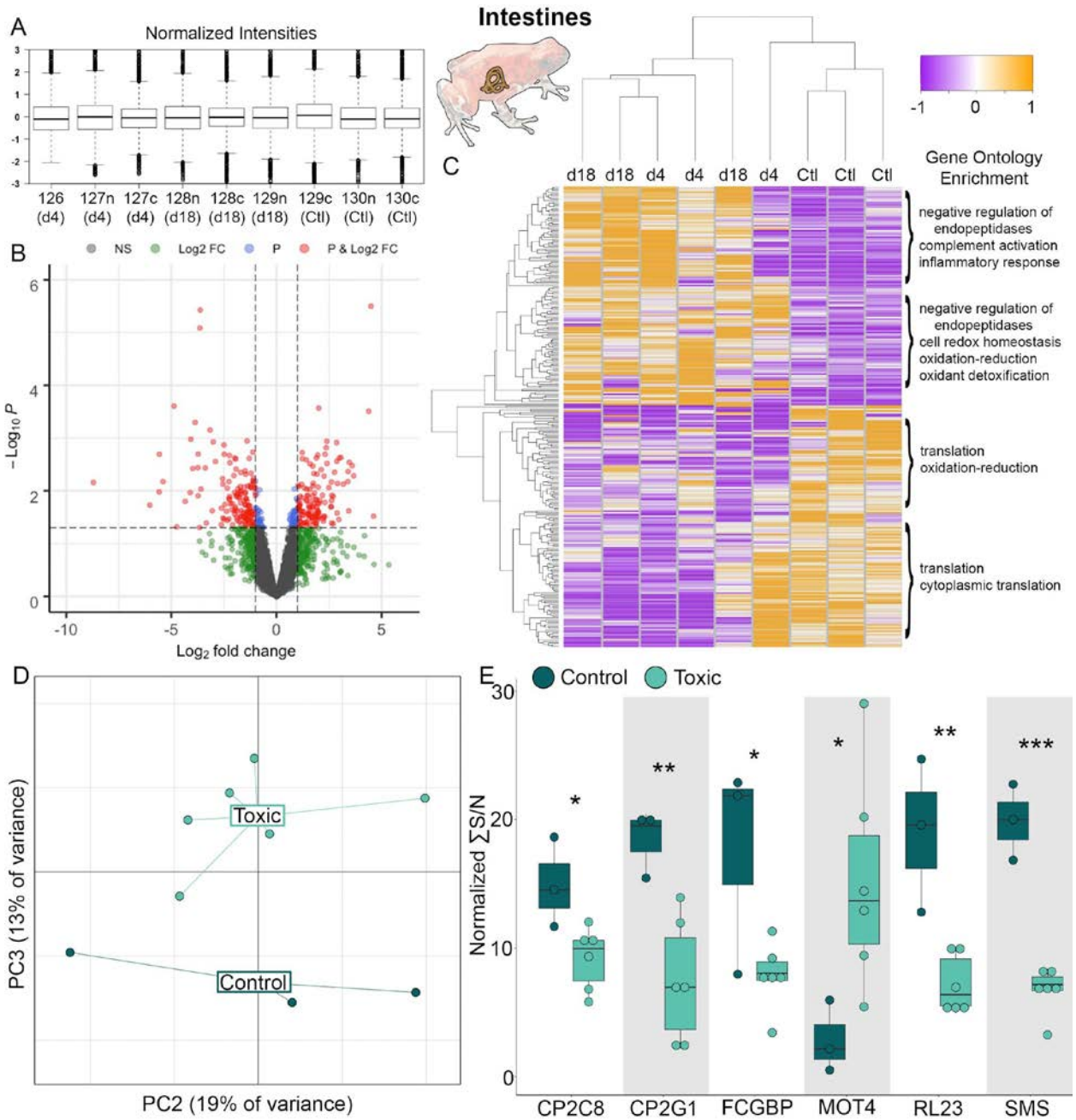

Figure S3. Quantification of protein changes in the intestines with decahydroquinoline bioaccumulation. (A) Protein samples were tandem mass tag (TMT) labeled prior to quantification and channels were z-score normalized prior to analysis. **(B)** Volcano plots show protein contigs that are not significant (NS, black), log fold change greater than one (Log2 FC, green), a p-value < 0.05 (P, blue) or both (red). **(C)** Heatmap of protein contig abundance (rows) between individuals frogs (columns); gene ontology enrichments in different clusters are on the right. **(D)** Visualization of a principal component analysis, where PC3 significantly separated control and toxic frogs (p=0.0008). **(E)** Examples of proteins that are significantly different between non-toxic (N=3) and DHQ-containing (N=6) frogs (* p<0.05, ** p≤0.005, *** p≤0.0005). Data are represented in boxplots that show rectangles as the lower and upper quartiles (with the median as the line) and whiskers that indicate the maximum and minimum values. Abbreviations: CP2C8, Cytochrome P450 Family 2 Subfamily C Member 8; CP2G1, Cytochrome P450 Family 2 Subfamily G Member 1; FCGBP, IgG Fc Binding Protein; MOT4, Monocarboxylate Transporter 4; RL23, Ribosomal Protein L23; SMS, Somatostatin.

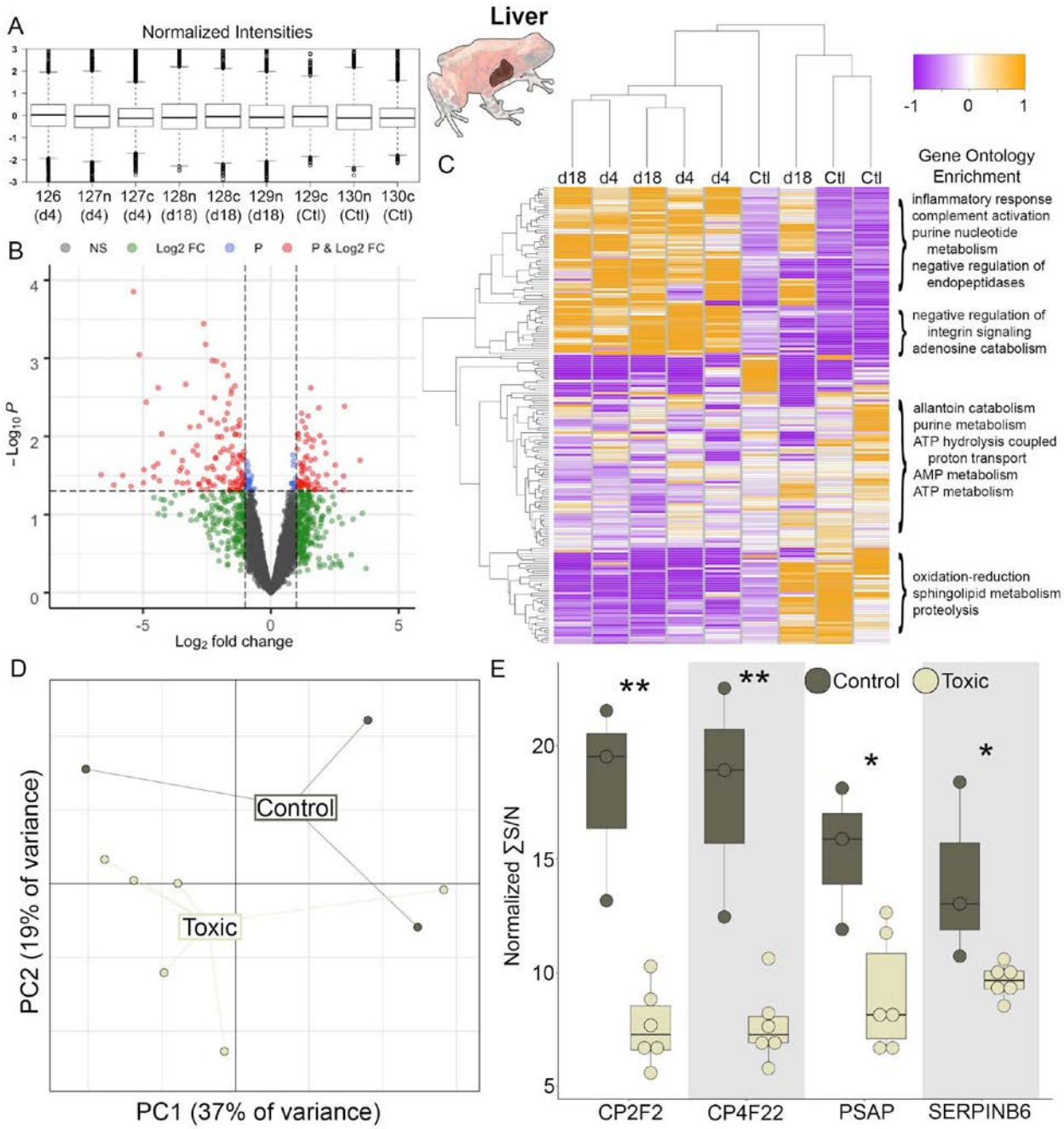

Figure S4. Quantification of protein changes in the liver with decahydroquinoline bioaccumulation. (A) Protein samples were tandem mass tag (TMT) labeled prior to quantification and channels were z-score normalized prior to analysis. **(B)** A volcano plot shows protein contigs that are not significant (NS, black), log fold change greater than one (Log2 FC, green), a p-value < 0.05 (P, blue) or both (red). **(C)** A heatmap of protein contig abundance (rows) between individuals frogs (columns); gene ontology enrichments in different clusters are on the right. **(D)** Visualization of a principal component analysis; groups were not significantly separated in the first three principal components. **(E)** Examples of proteins that are significantly different between non-toxic (N=3) and DHQ-containing (N=6) frogs (* p<0.05, ** p≤0.005, *** p≤0.0005). Data are represented in boxplots that show rectangles as the lower and upper quartiles (with the median as the line) and whiskers that indicate the maximum and minimum values. Abbreviations: CP2F2, Cytochrome P450 Family 2 Subfamily F Member 2; CP4F22, Cytochrome P450 Family 2 Subfamily F Member 22; PSAP, Prosaposin; SERPINB6, Serpin P6.

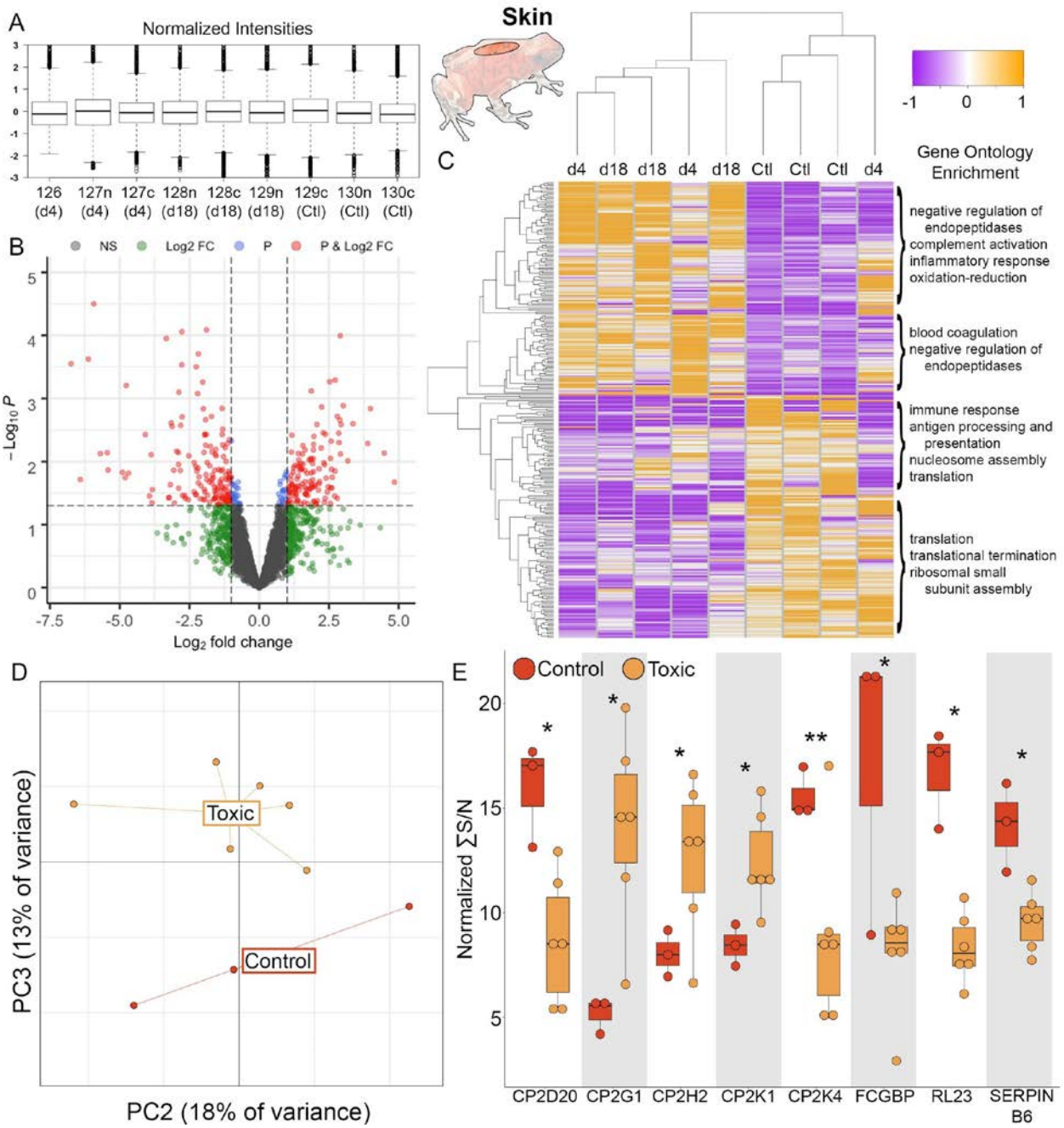

Figure S5. Quantification of protein changes in the skin with decahydroquinoline bioaccumulation. (A) Protein samples were tandem mass tag (TMT) labeled prior to quantification using mass spectrometry. Channels were z-score normalized prior to analysis. **(B)** A volcano plot shows protein contigs that are not significant (NS, black), log fold change greater than one (Log2 FC, green), a p-value < 0.05 (P, blue) or both (red). **(C)** A heatmap of protein contig abundance (rows) between individuals frogs (columns); gene ontology enrichments in different clusters are on the right. **(D)** Visualization of a principal component analysis, where PC3 significantly separated control and toxic frogs (p=0.002). **(E)** Examples of proteins that are significantly different between non-toxic (N=3) and DHQ-containing (N=6) frogs (* p<0.05, ** p≤0.005, *** p≤0.0005). Data are represented in boxplots that show rectangles as the lower and upper quartiles (with the median as the line) and whiskers that indicate the maximum and minimum values. Abbreviations: CP2D20, Cytochrome P450 Family 2 Subfamily D Member 20;

CP2G1, Cytochrome P450 Family 2 Subfamily G Member 1; CP2H2, Cytochrome P450 Family 2 Subfamily H Member 2; CP2K1, Cytochrome P450 Family 2 Subfamily K Member 1; CP2K4, Cytochrome P450 Family 2 Subfamily K Member 4; FCGBP, IgG Fc Binding Protein; RL23, Ribosomal Protein L23.

Table S1

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