Supplemental Figures (S1-S4)
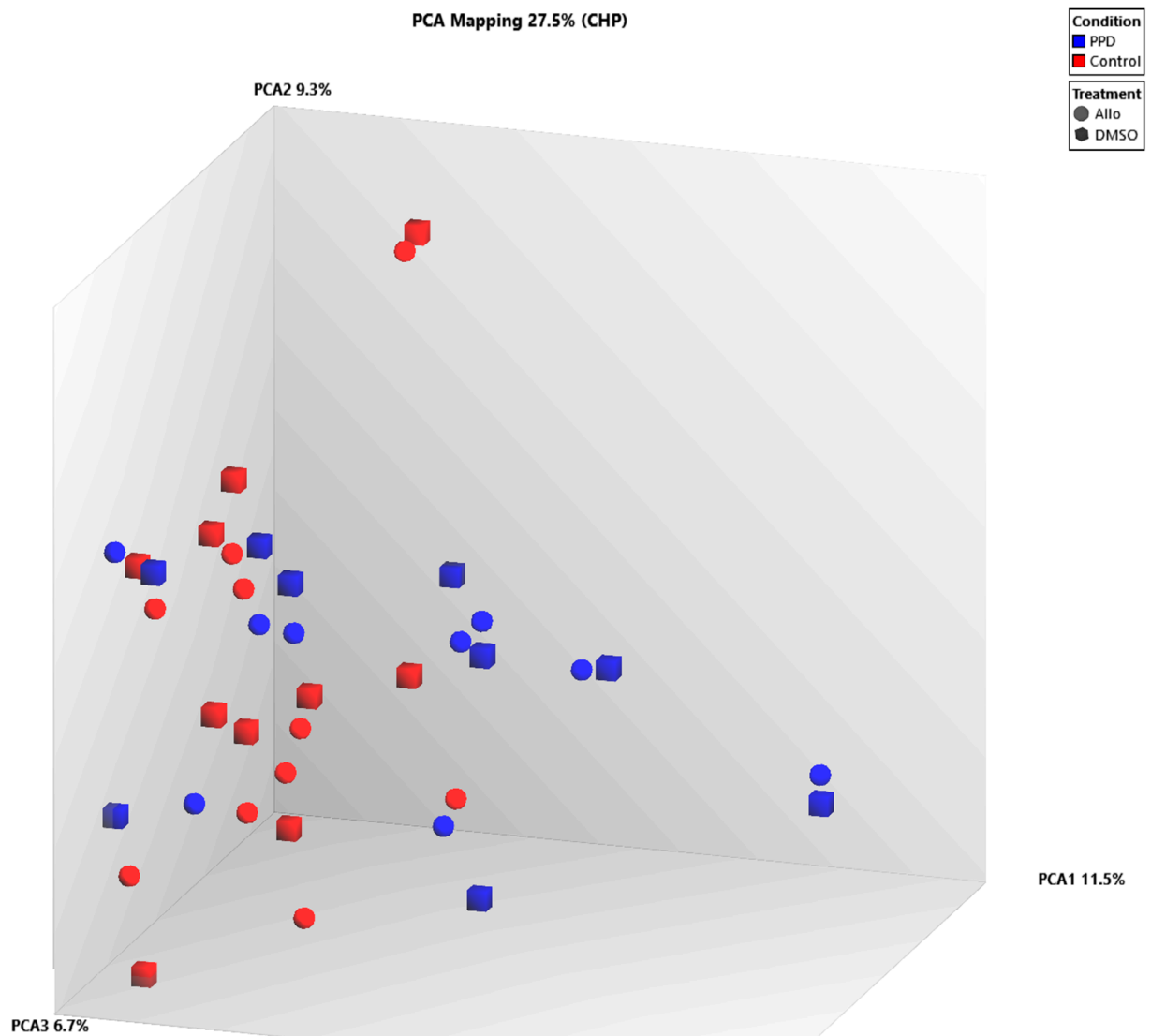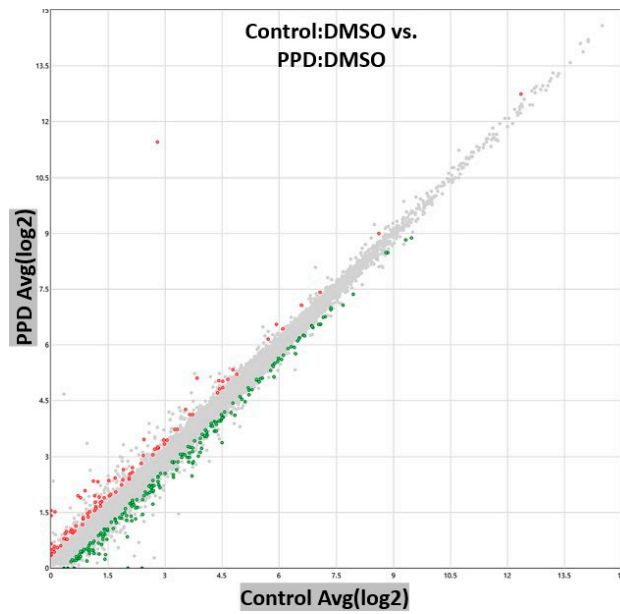
Supplemental Table Captions

Figure S1: Unsupervised Clustering of RNA-sequencing

A) Principal component analysis (PCA) of the transcriptomic output, using default Transcriptome Analysis Console (TAC) 4.0 settings (5000 points, distributed) to plot all samples in the study. Collectively, the first two axes (PCA 1 & 2) explain 20.8% of the variance, and the top three PCs explaining 27.5% of the variance. Clustering shows segregation of LCL samples primarily between diagnostic groups genetic background, e.g., PPD vs. Control.
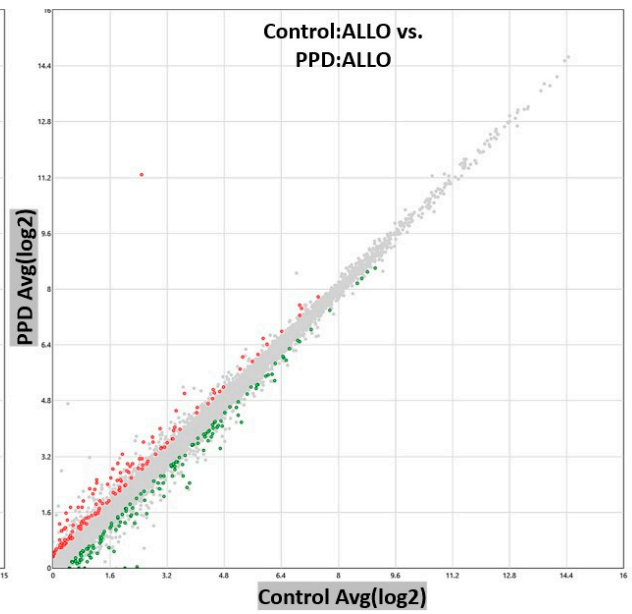
Diagnosis (**Color**): Red = Control, and Blue = PPD

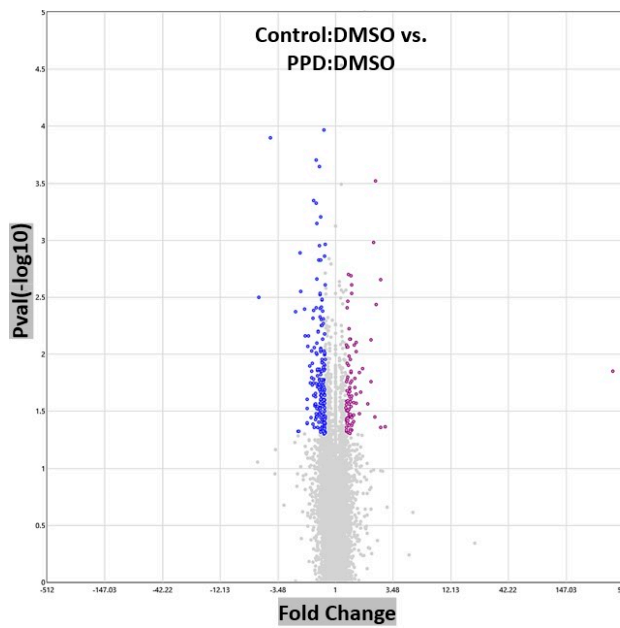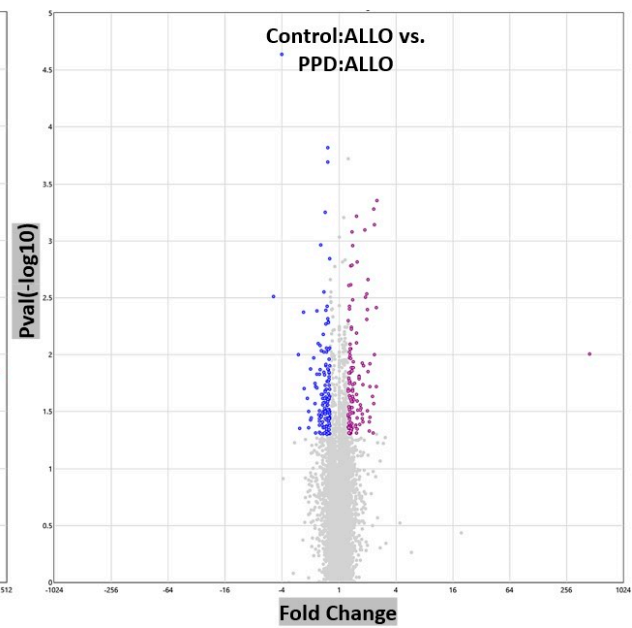Treatment (**Shape**):   = DMSO or **O** = ALLO

Figure S2: Control vs. PPD, Scatter and Volcano plots

A, C) Scatter plots depicting the transcripts changed in PPD vs. Control LCLs at Baseline and after ALLO-treatment, respectively. The log2(Average Counts) Control is plotted on the X-axis, and log2(Average Counts) PPD is plotted on the Y-axis. Each dot represents one gene.

Red: Upregulated Differentially Expressed Gene (DEG, $p_{nominal}<0.05$) in PPD
Green: Downregulated Differentially Expressed Gene (DEG, $p_{nominal}<0.05$) in PPD

B, D) Volcano plots depicting the nominal significance and fold change in transcription for PPD vs. Control LCLs at Baseline and after ALLO-treatment, respectively. Each dot represents one gene. Fold change is plotted on the x-axis, where a positive fold change (purple, right side of volcano) indicates increased expression in PPD LCLs. The y-axis plots gene significance ((p value)-log_{10}).

Blue = Downregulated Differentially Expressed Gene ($p_{nominal}<0.05$)
Purple = Upregulated Differentially Expressed Gene ($p_{nominal}<0.05$)

WikiPathway 2021 Human

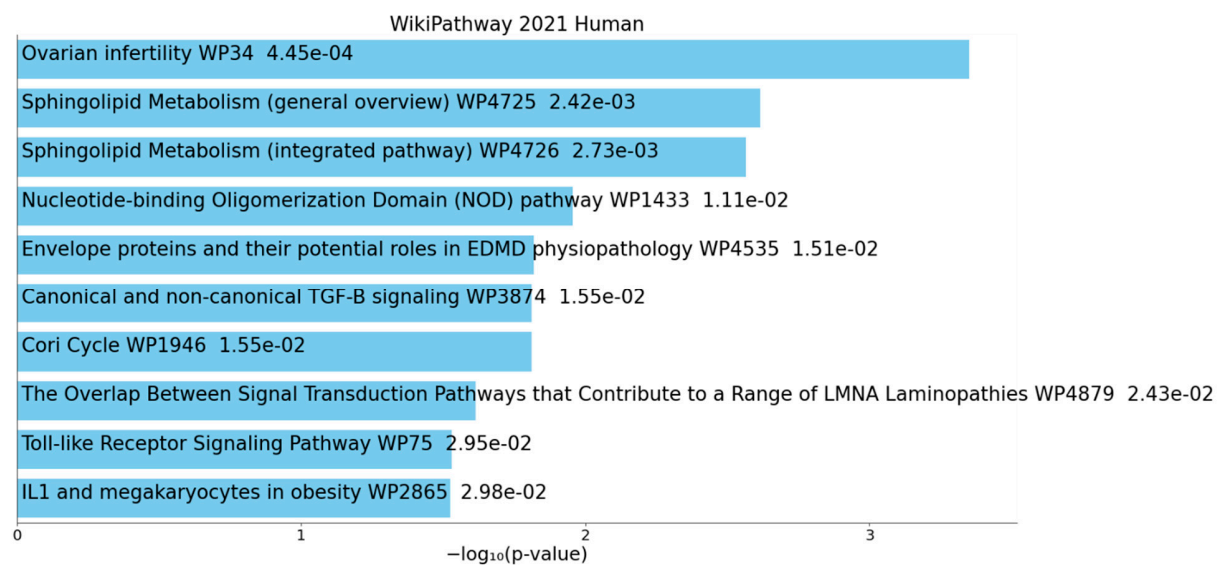| Pathway	−log₁₀(p-value)
Ovarian infertility WP34 4.45e-04	
Sphingolipid Metabolism (general overview) WP4725 2.42e-03	
Sphingolipid Metabolism (integrated pathway) WP4726 2.73e-03	
Nucleotide-binding Oligomerization Domain (NOD) pathway WP1433 1.11e-02	
Envelope proteins and their potential roles in EDMD physiopathology WP4535 1.51e-02	
Canonical and non-canonical TGF-B signaling WP3874 1.55e-02	
Cori Cycle WP1946 1.55e-02	
The Overlap Between Signal Transduction Pathways that Contribute to a Range of LMNA Laminopathies WP4879 2.43e-02	
Toll-like Receptor Signaling Pathway WP75 2.95e-02	
IL1 and megakaryocytes in obesity WP2865 2.98e-02	

Figure S3: WikiPathway results for 226 DEGs significant only at baseline between PPD and Controls.

Data are plotted as the -log(pValue) for each potential functional category of significance. The bar chart shows the top enriched terms in the chosen database's library, where colored bars correspond to terms with significant p-values (<0.05), and an asterisk (*) indicates the term has a significant adjusted p-value.
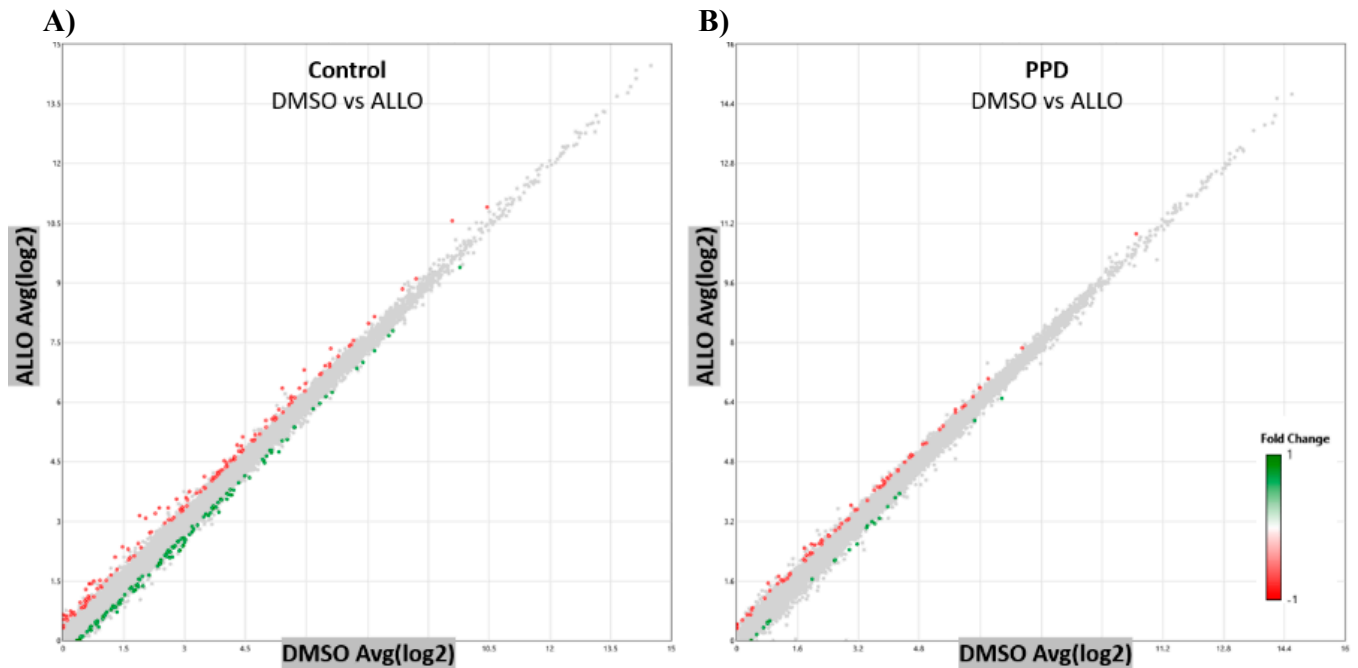
Figure S4: DMSO vs. ALLO (within-diagnosis) Scatterplots

A, B) Scatter plots depicting the transcripts changed after ALLO within Control LCLs and within PPD LCLs, respectively. The log2(Average Counts) DMSO is plotted on the X-axis, and log2(Average Counts) ALLO is plotted on the Y-axis. Each dot represents one gene.

Red: Upregulated Differentially Expressed Gene ($p_{nominal}<0.05$) by ALLO
Green: Downregulated Differentially Expressed Gene ($p_{nominal}<0.05$) by ALLO

Supplemental Tables (Tables are in separate excel sheets):

<u>Table S1,2: RNA-seq results comparing case (PPD) vs. control LCLs within each drug exposure condition</u>

      S1: Control vs. PPD – Baseline/DMSO (60hrs Vehicle)

      S2: Control vs. PPD – ALLO (60hrs ALLO, total 300nM)

<u>Table S3,4: RNA-seq results comparing LCL baseline (DMSO) to ALLO-treatment within each diagnosis</u>

      S3: Control – Baseline/DMSO vs. ALLO

      S4: PPD – Baseline/DMSO vs. ALLO