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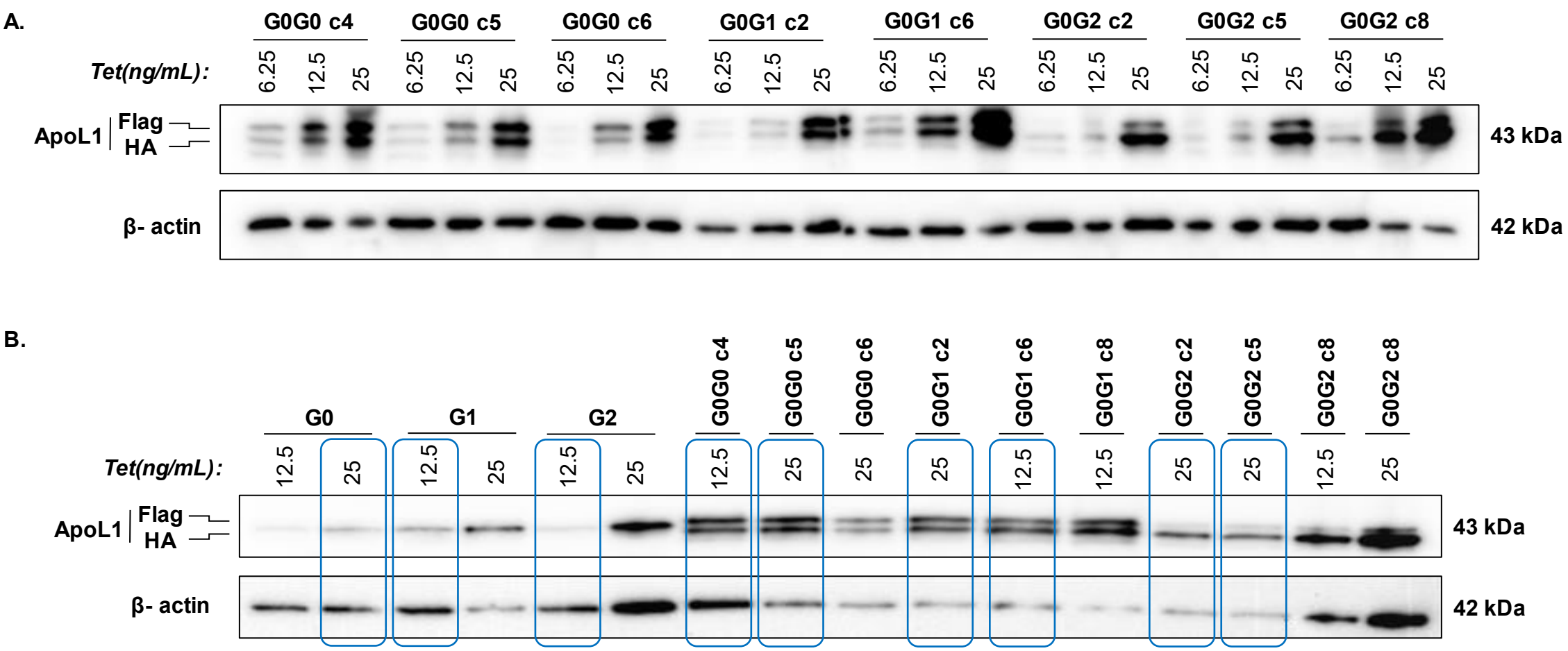
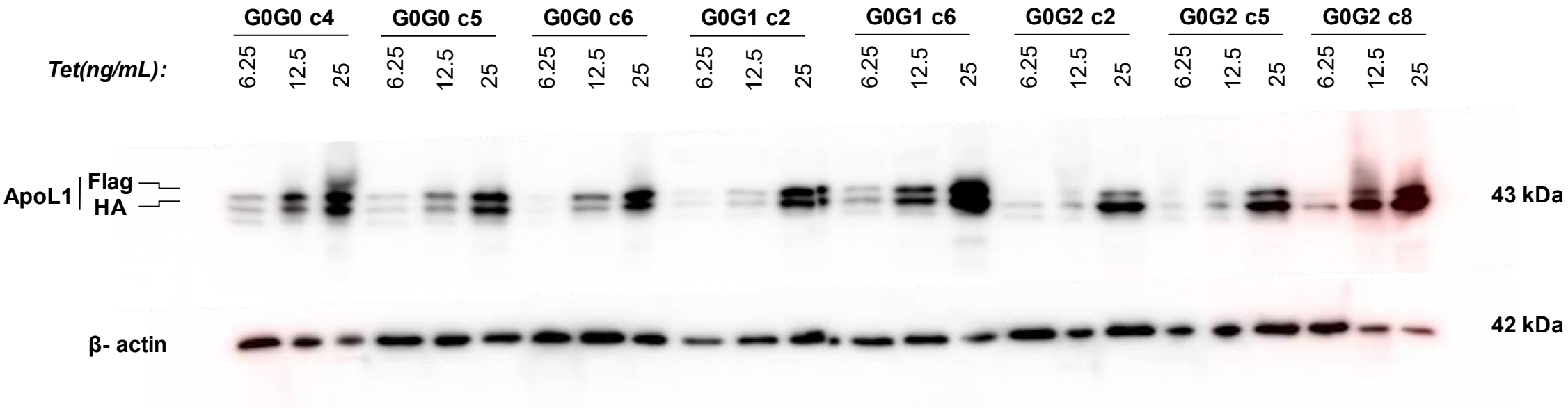
Supple. Figure: 1.



Supple. Figure: 1 A-1



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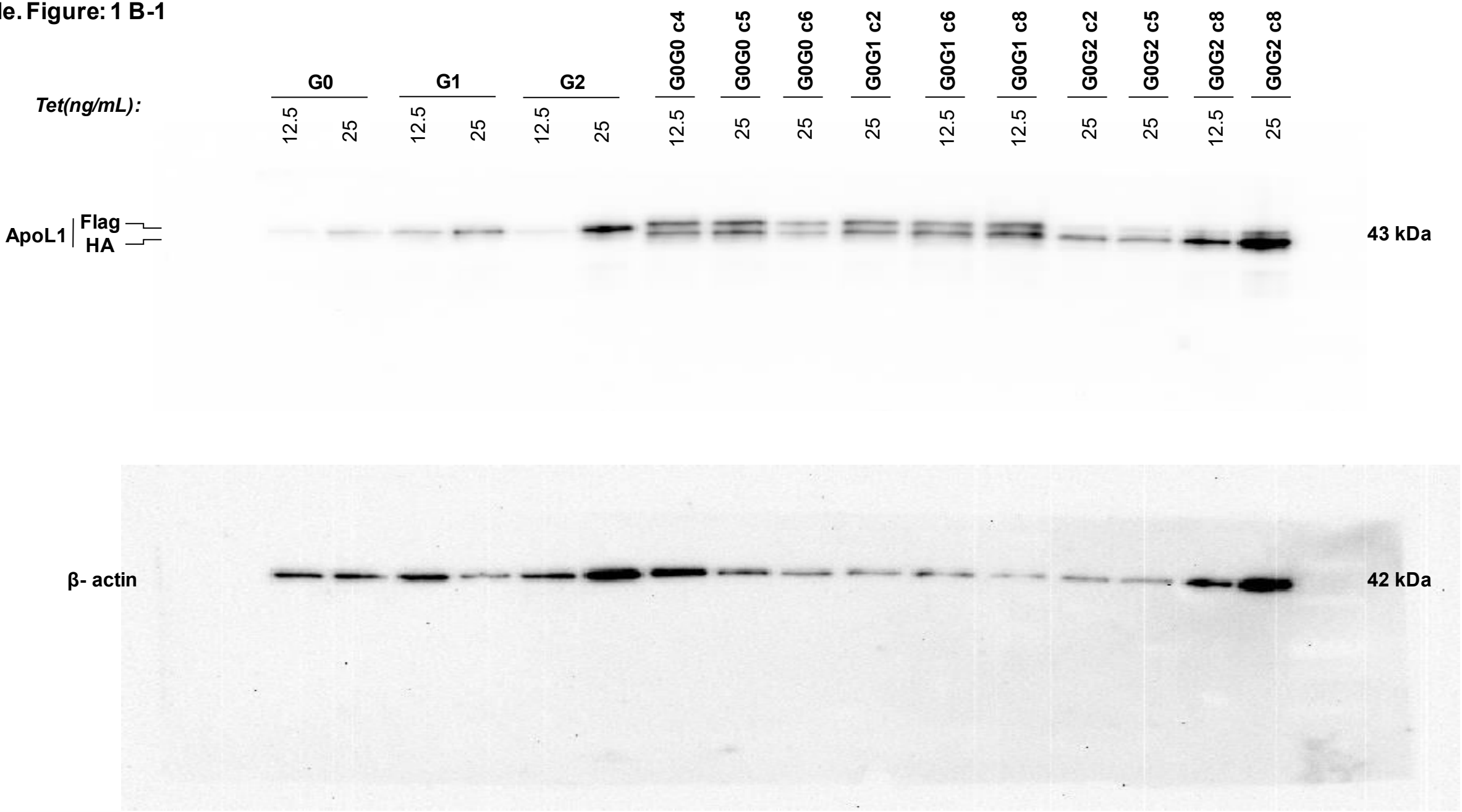

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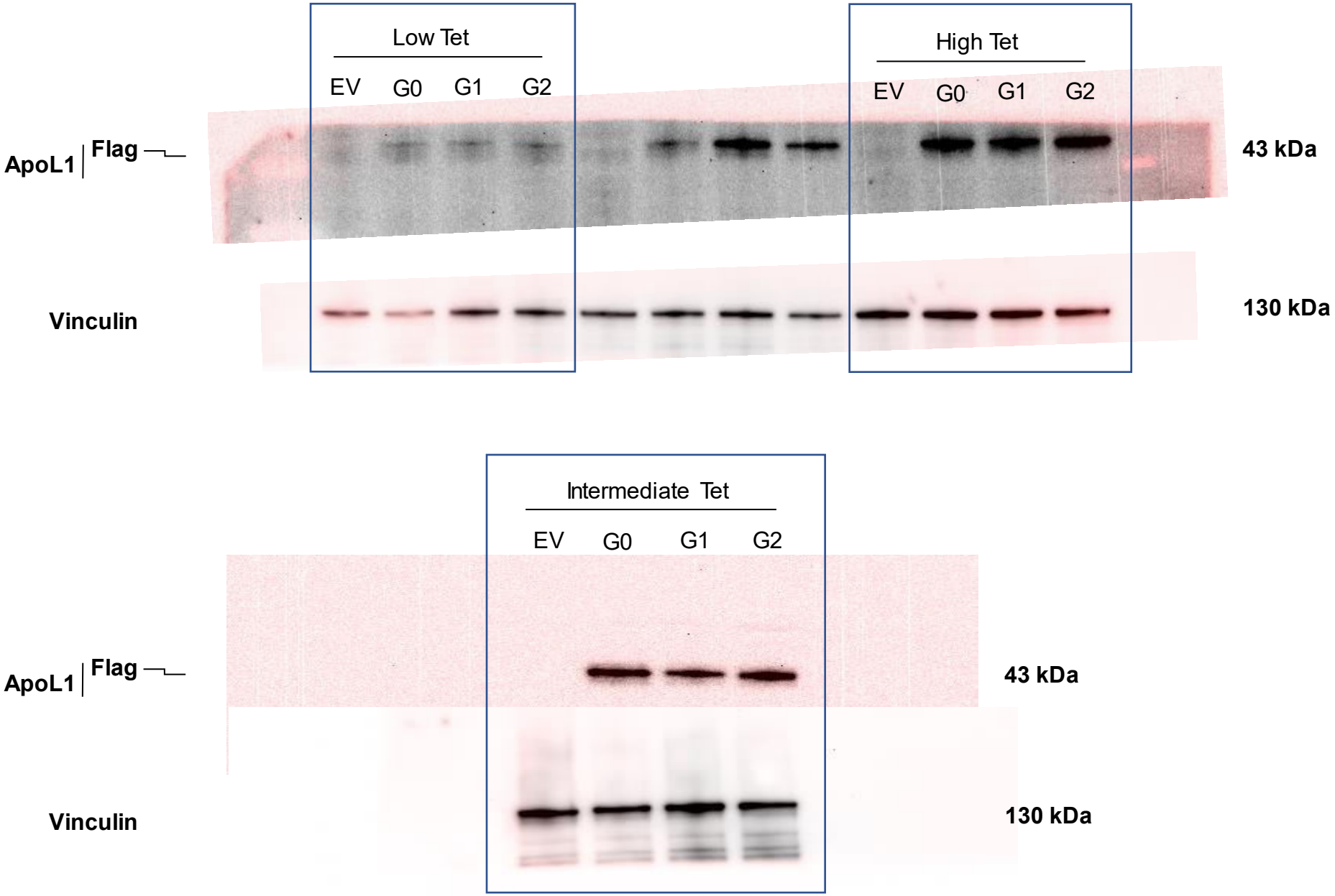

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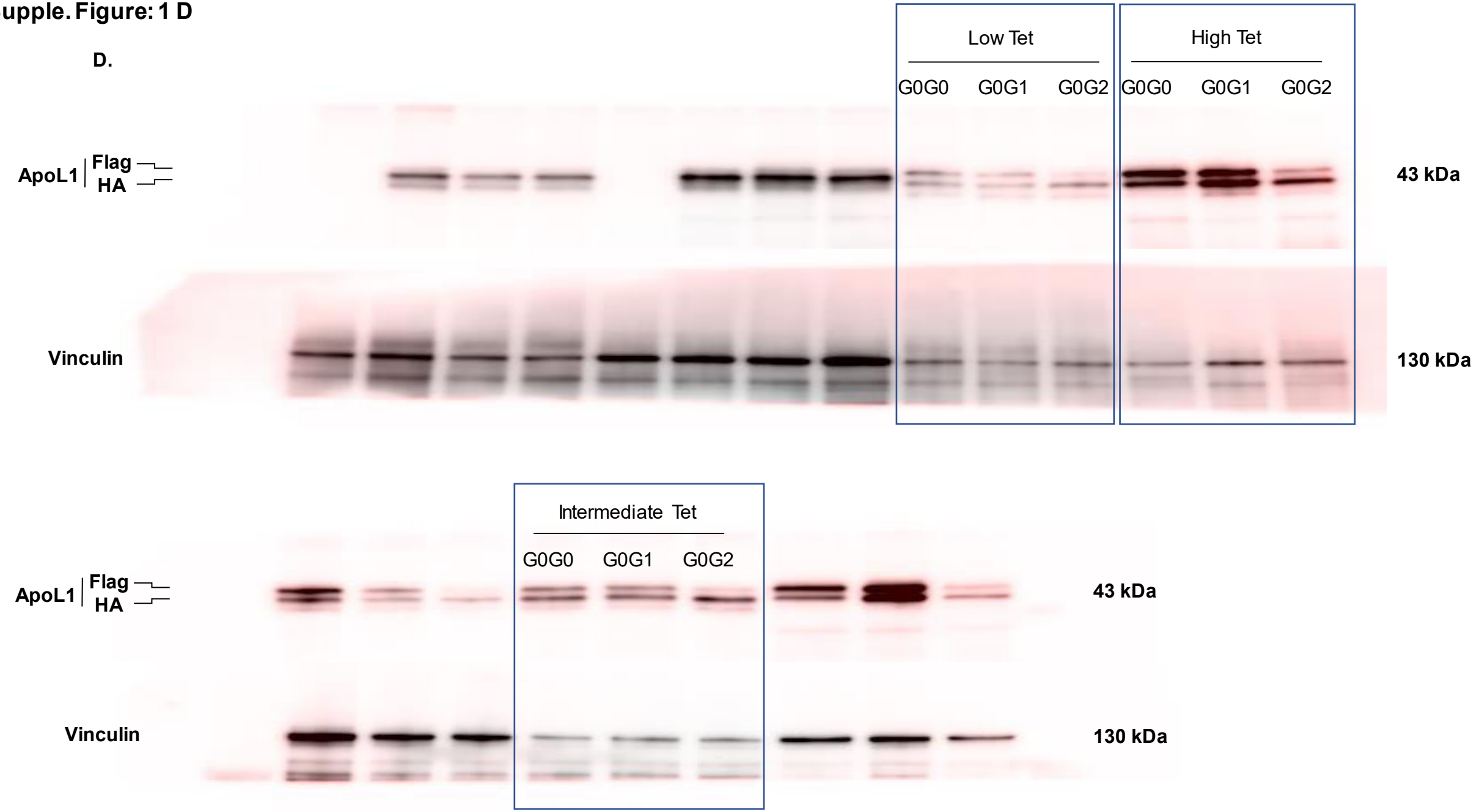

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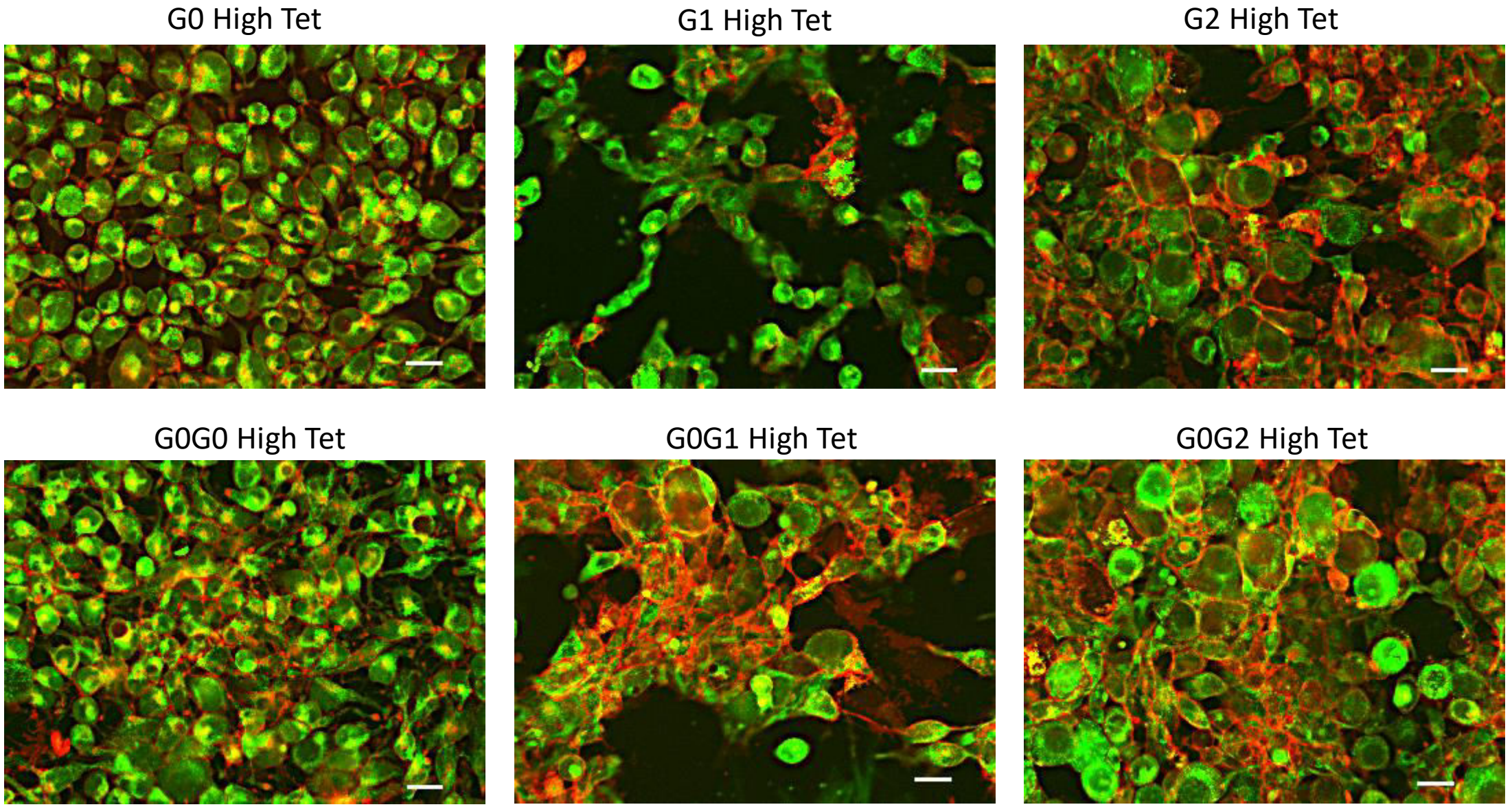

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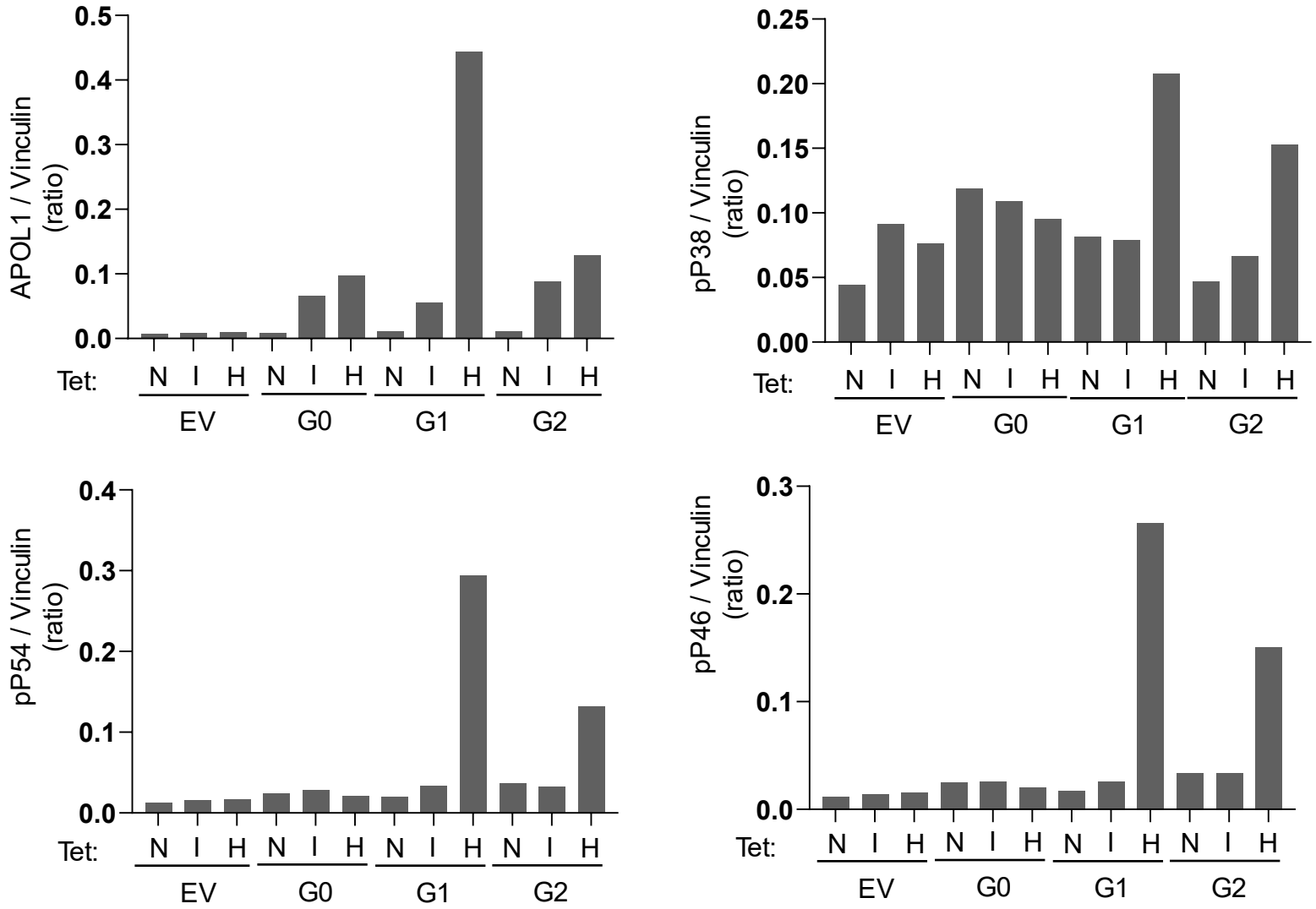

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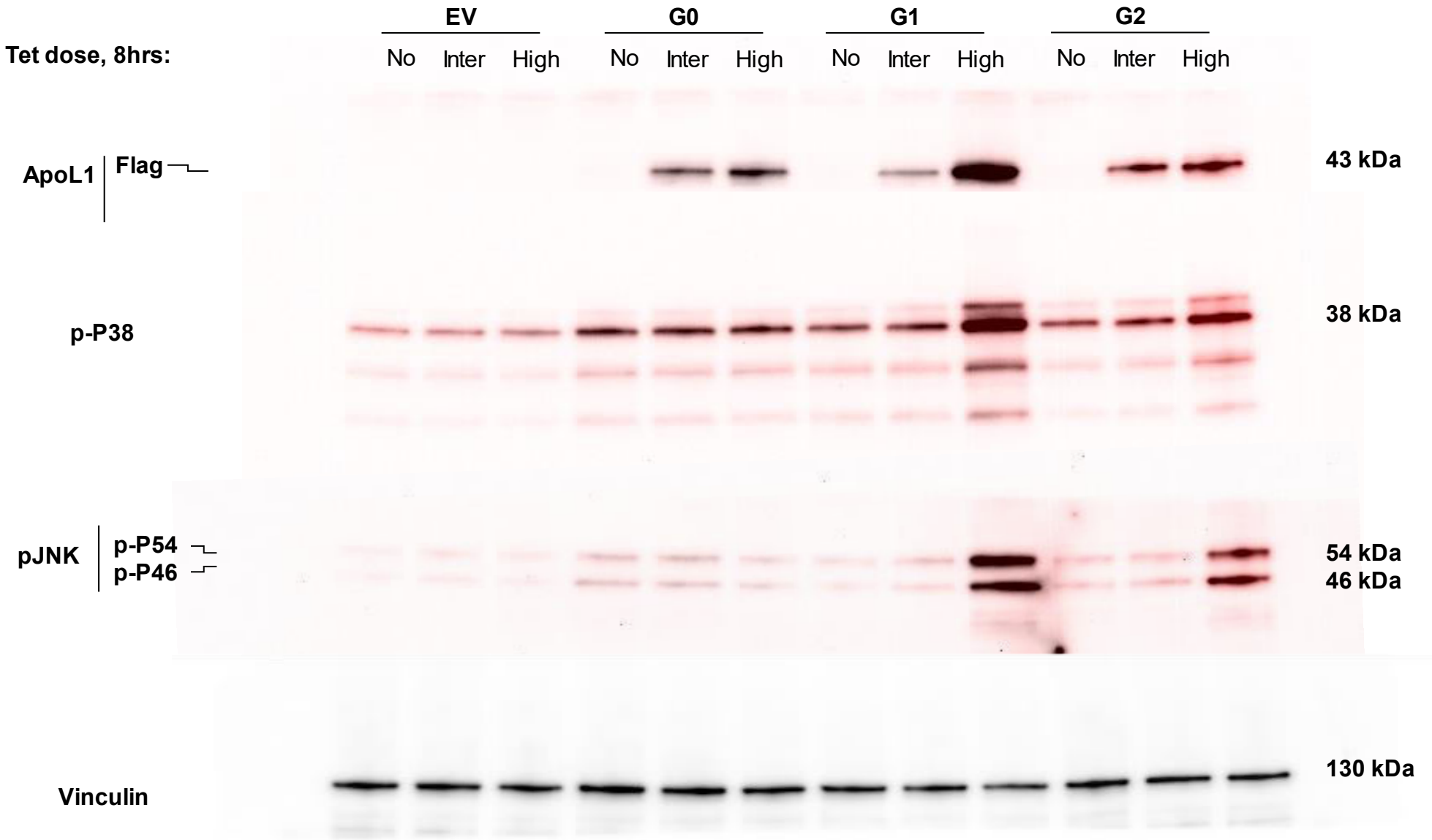

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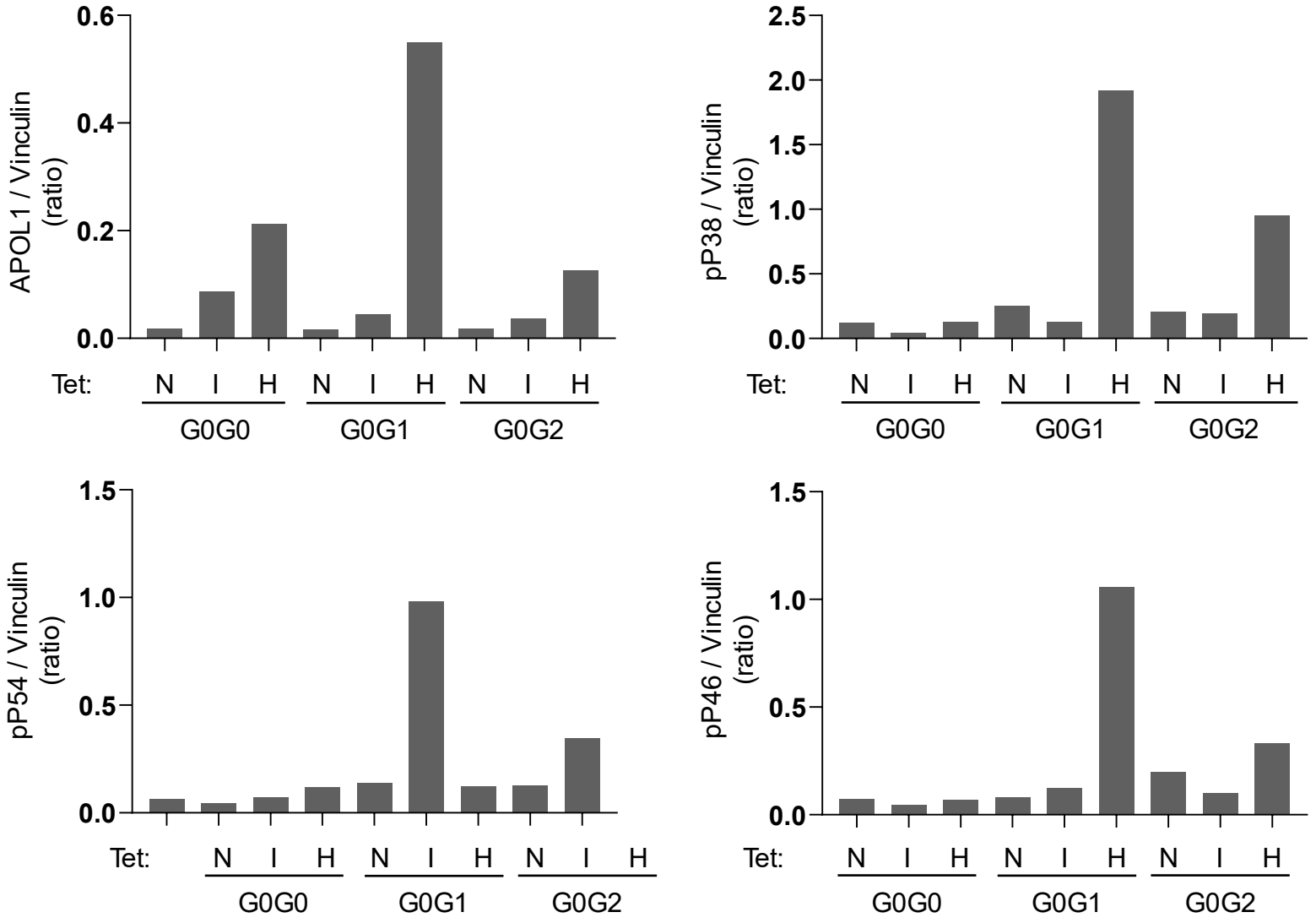

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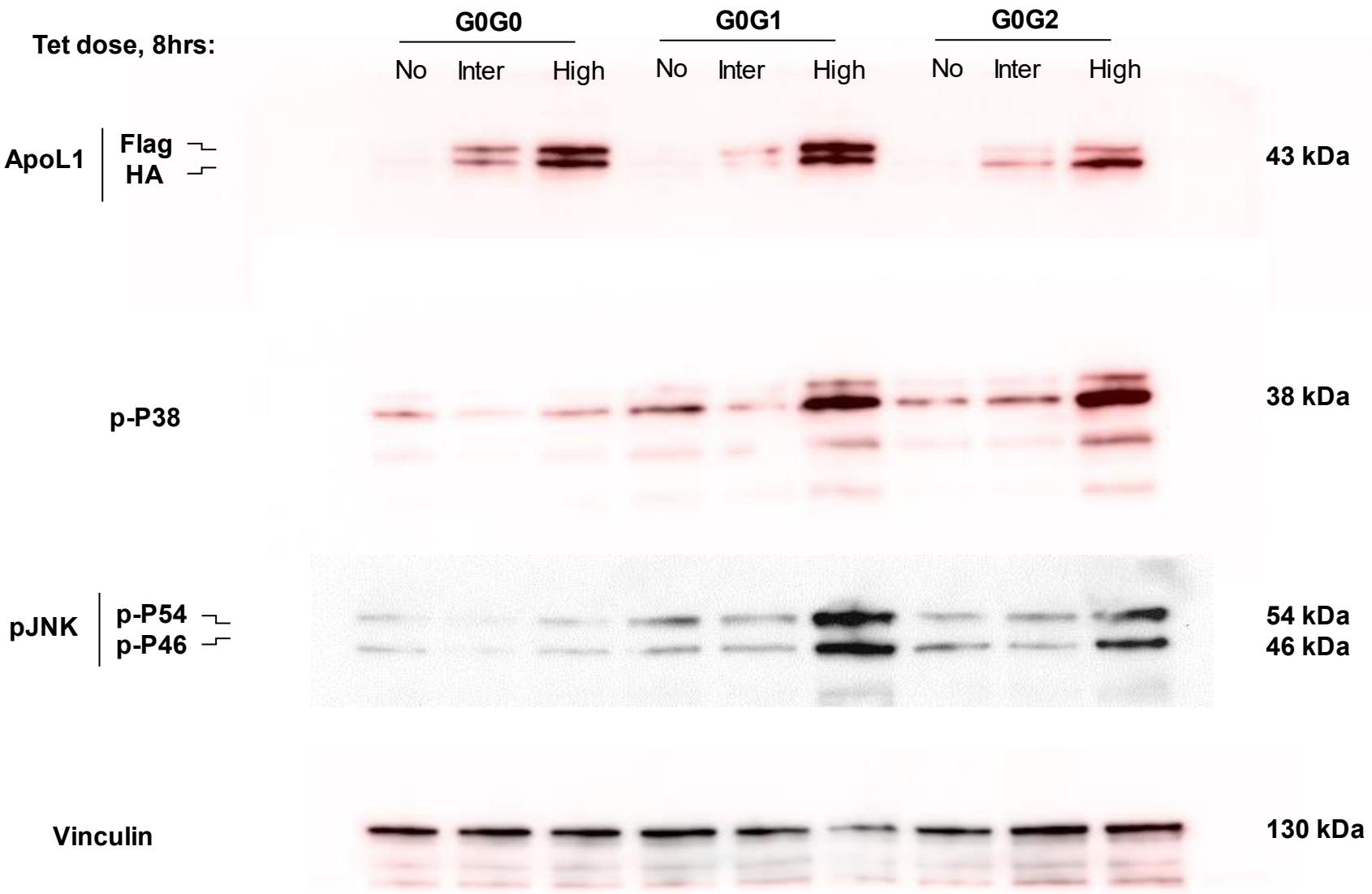

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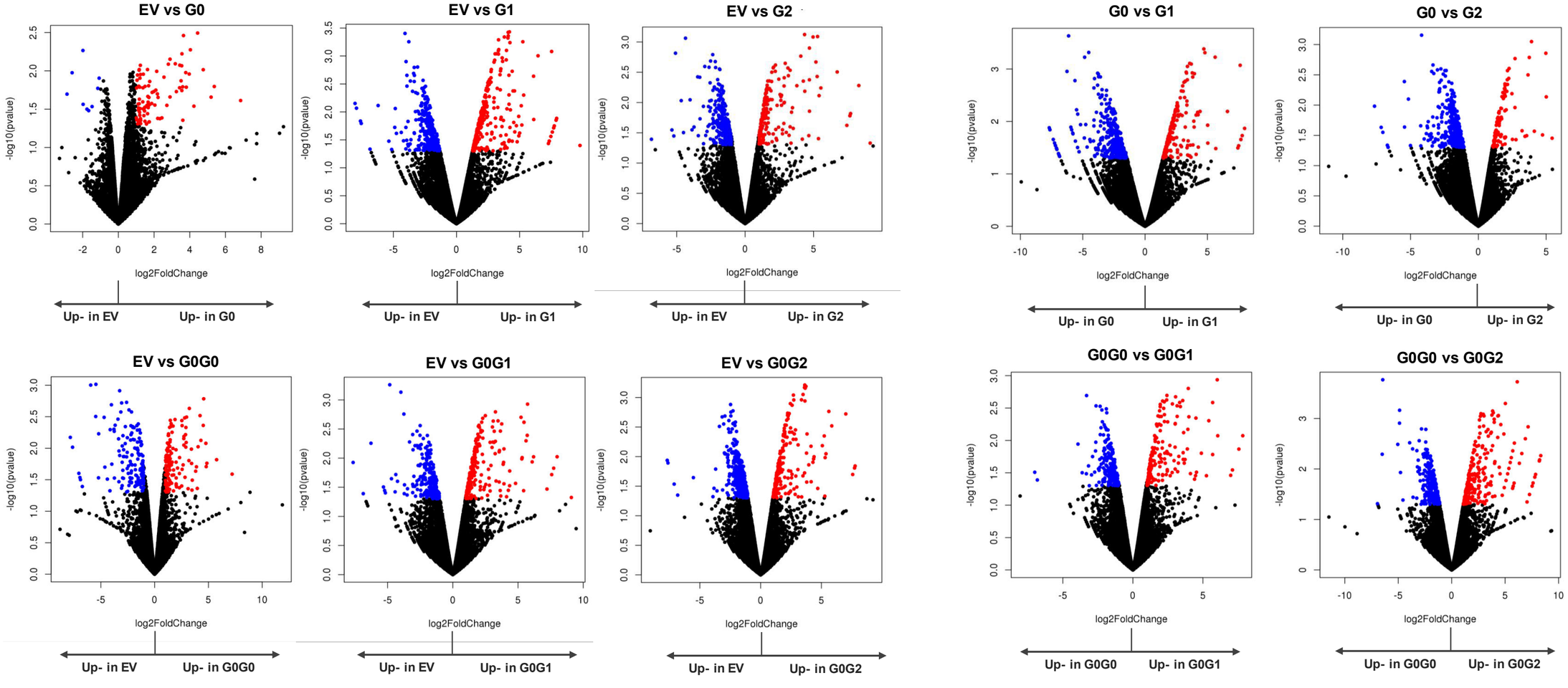

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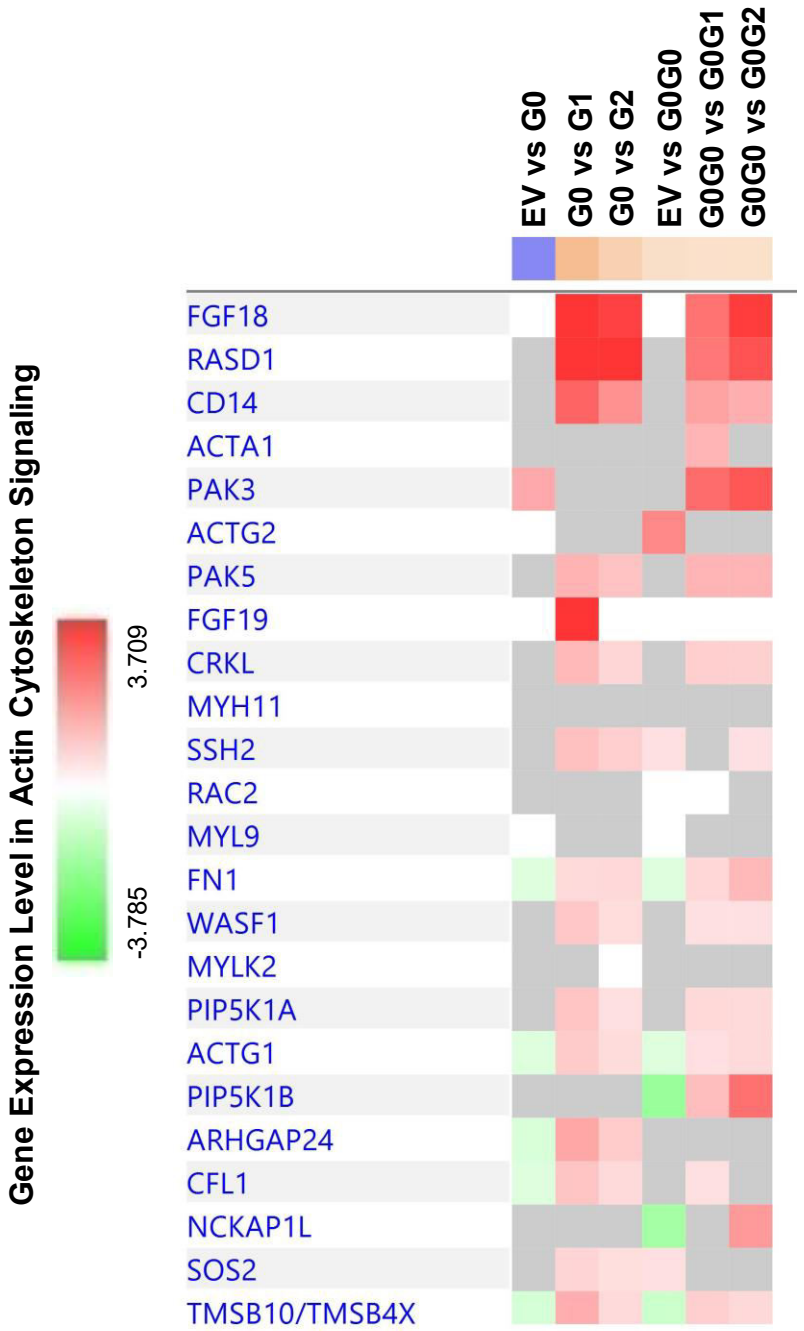

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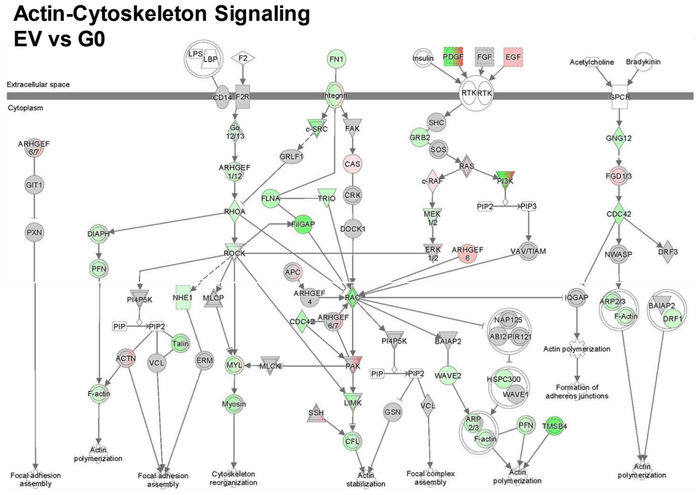

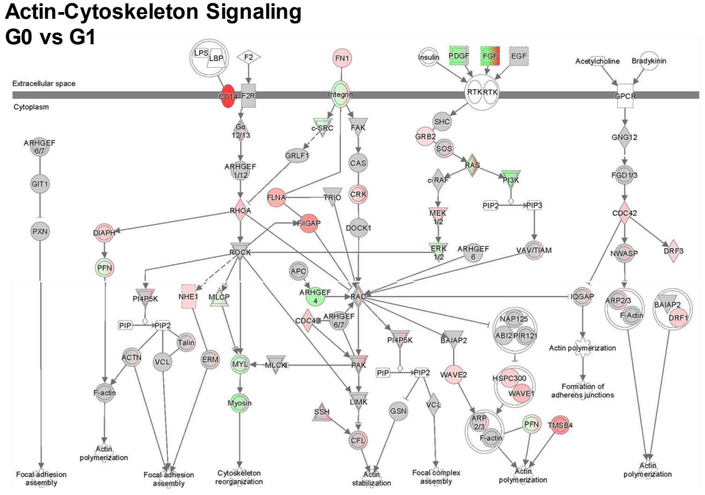

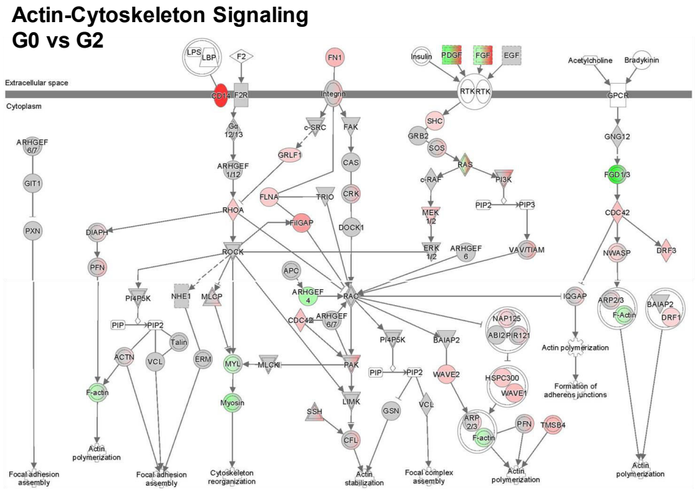

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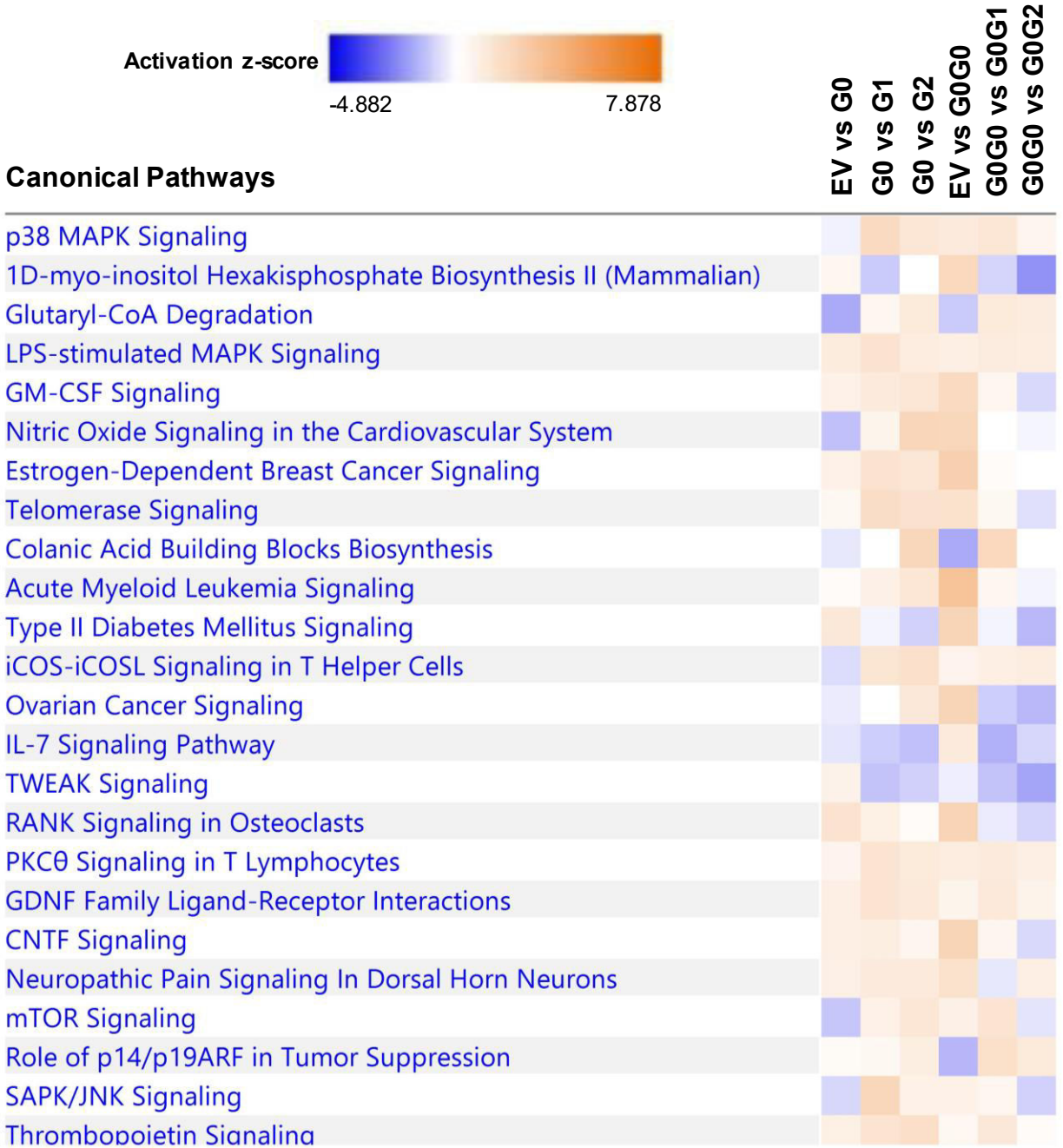

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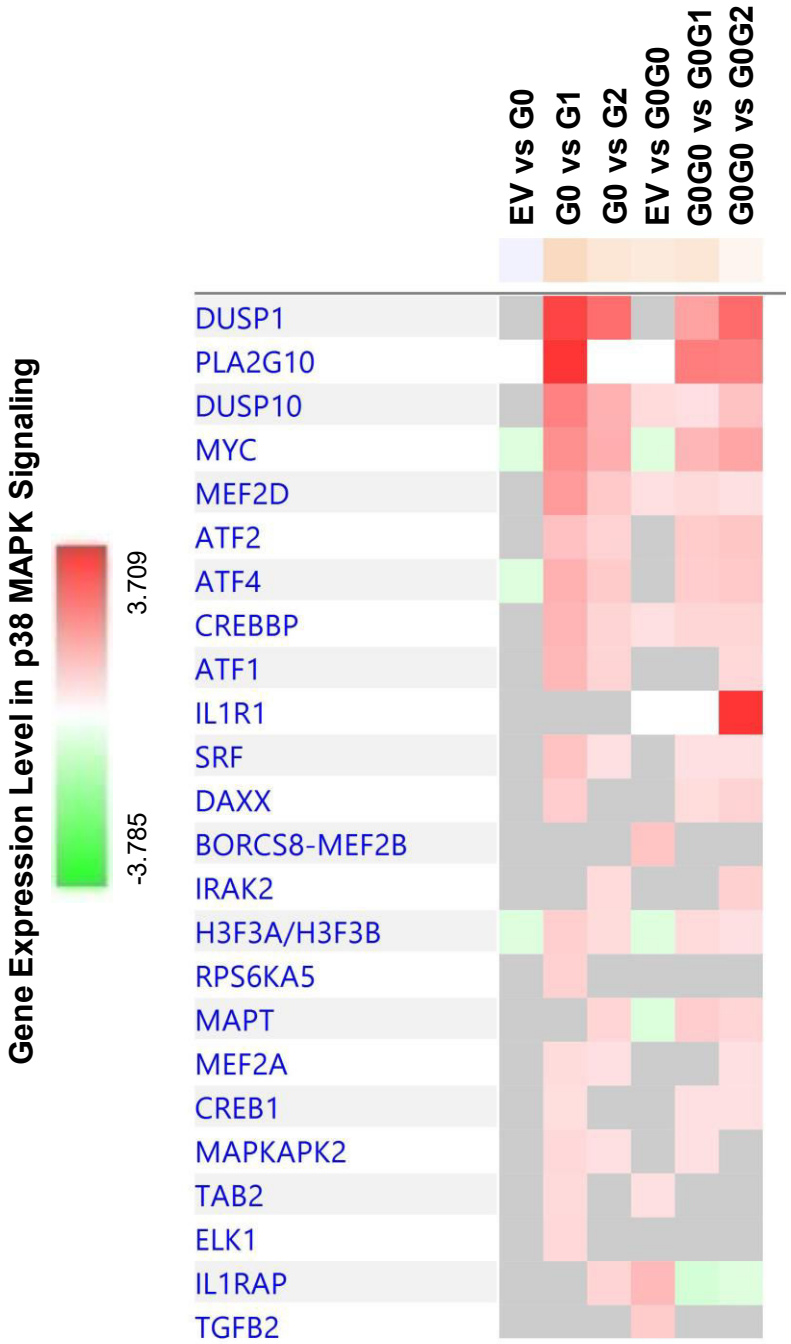

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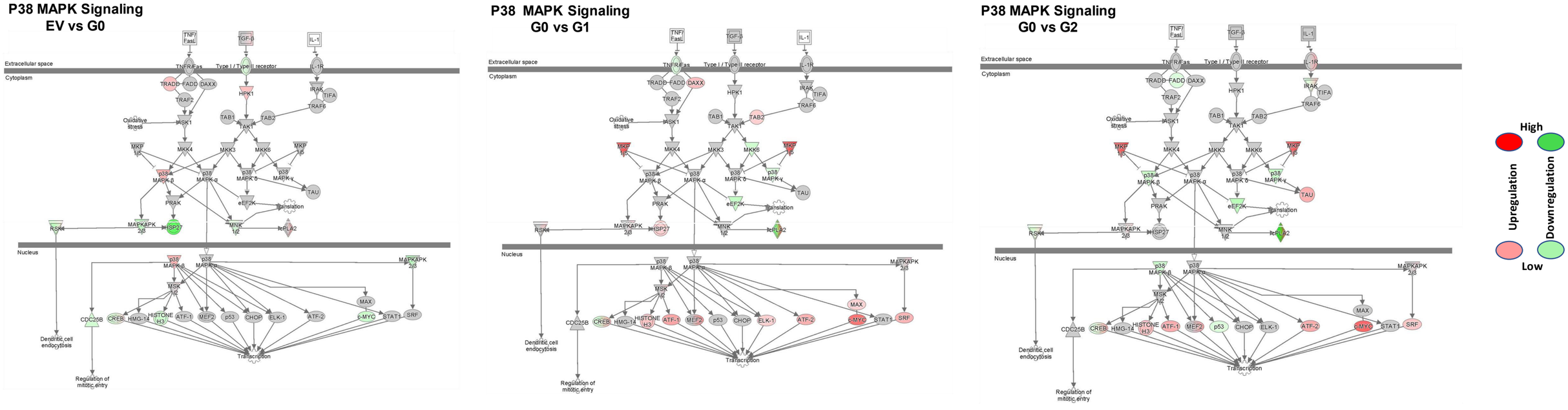

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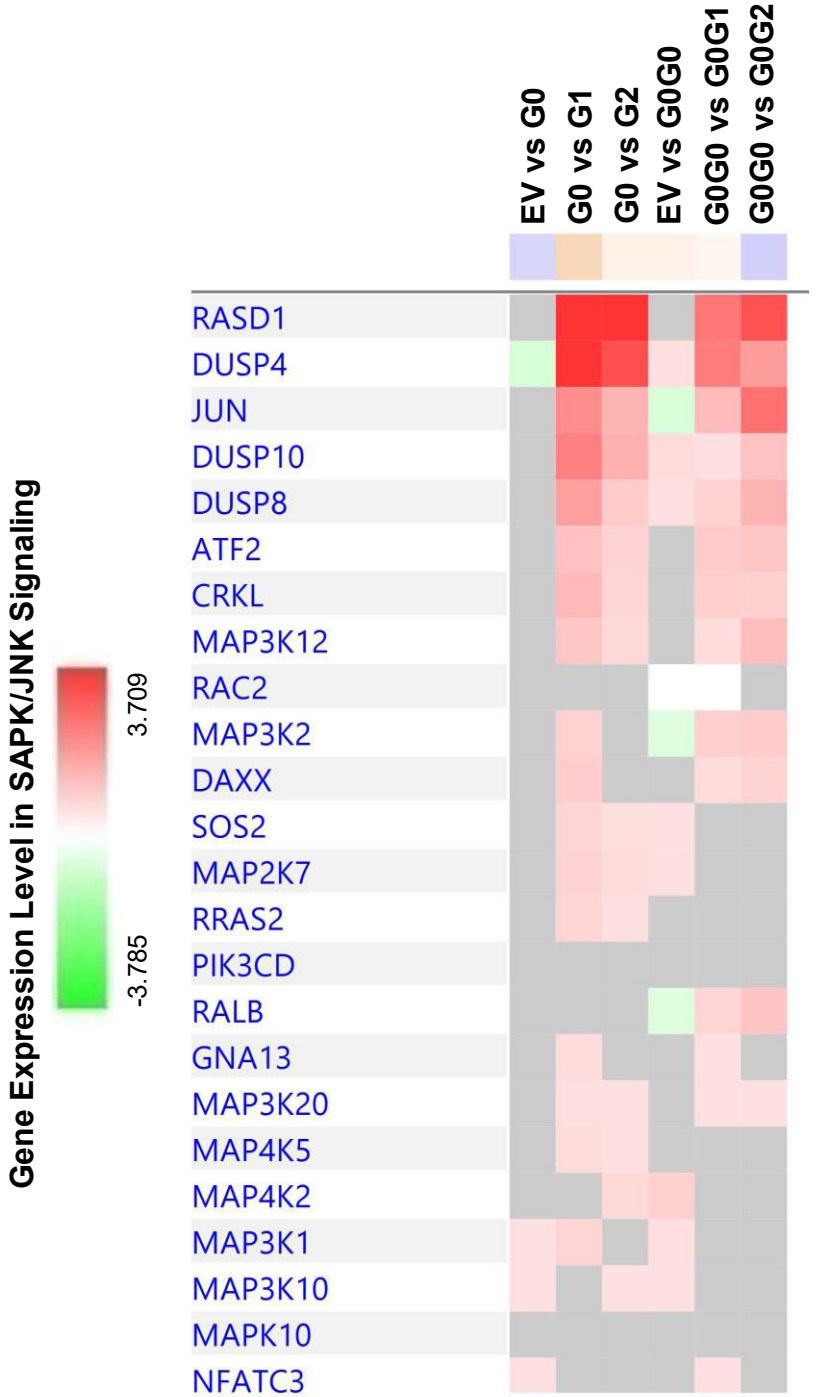

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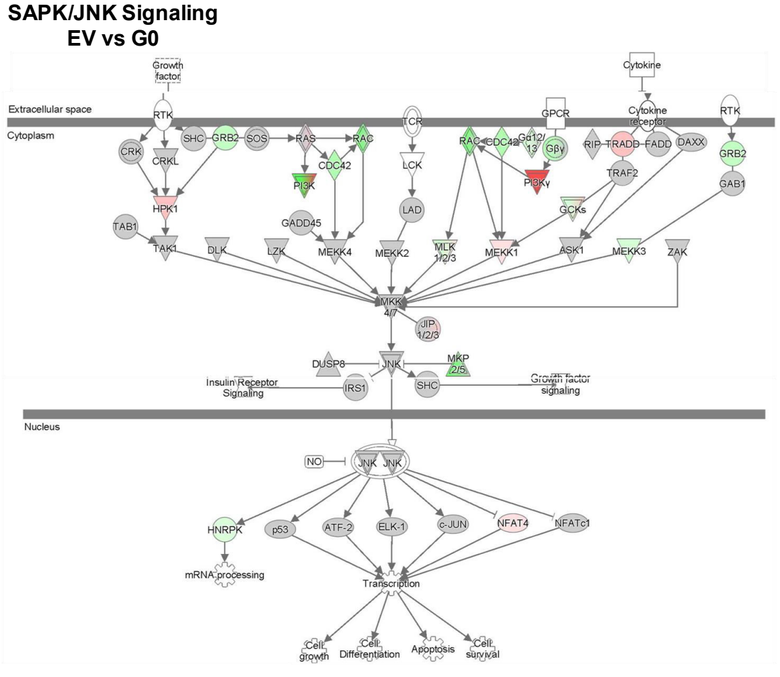

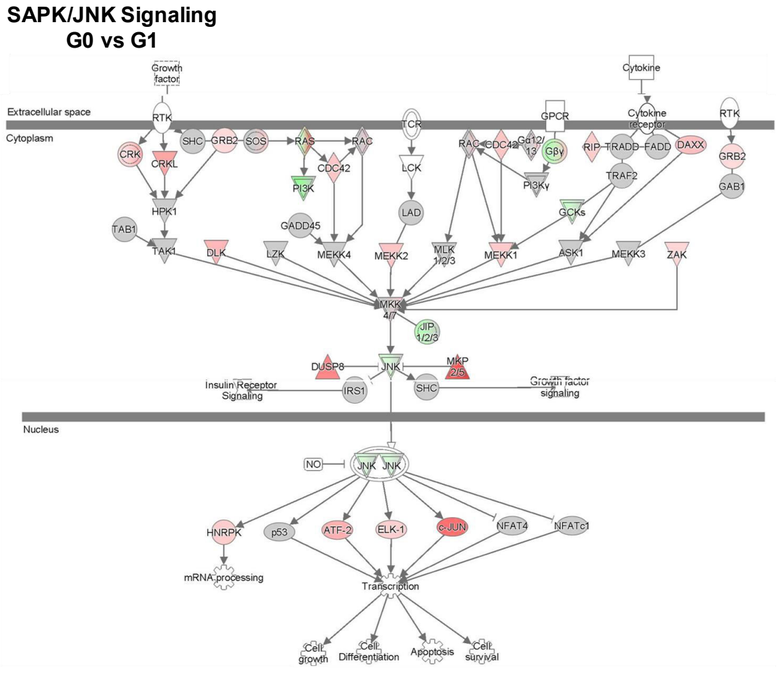

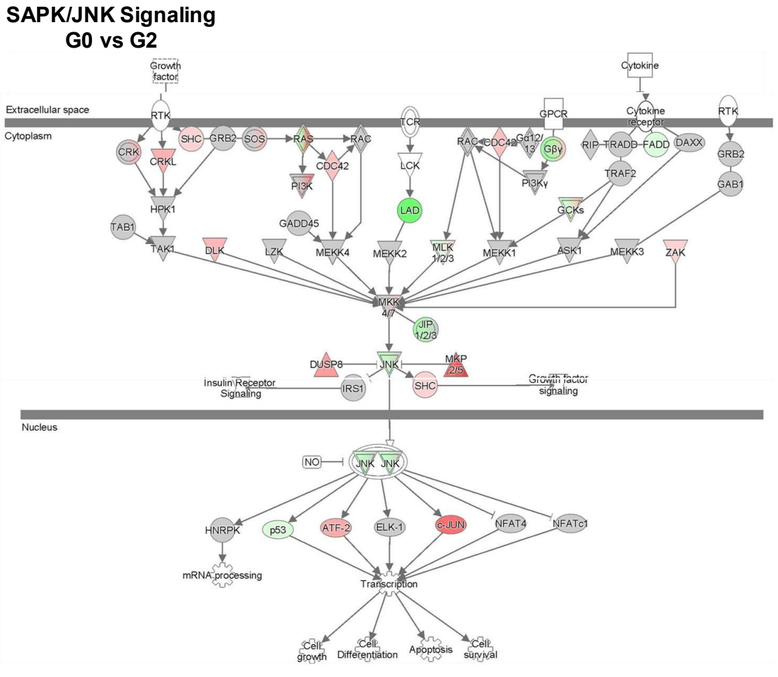

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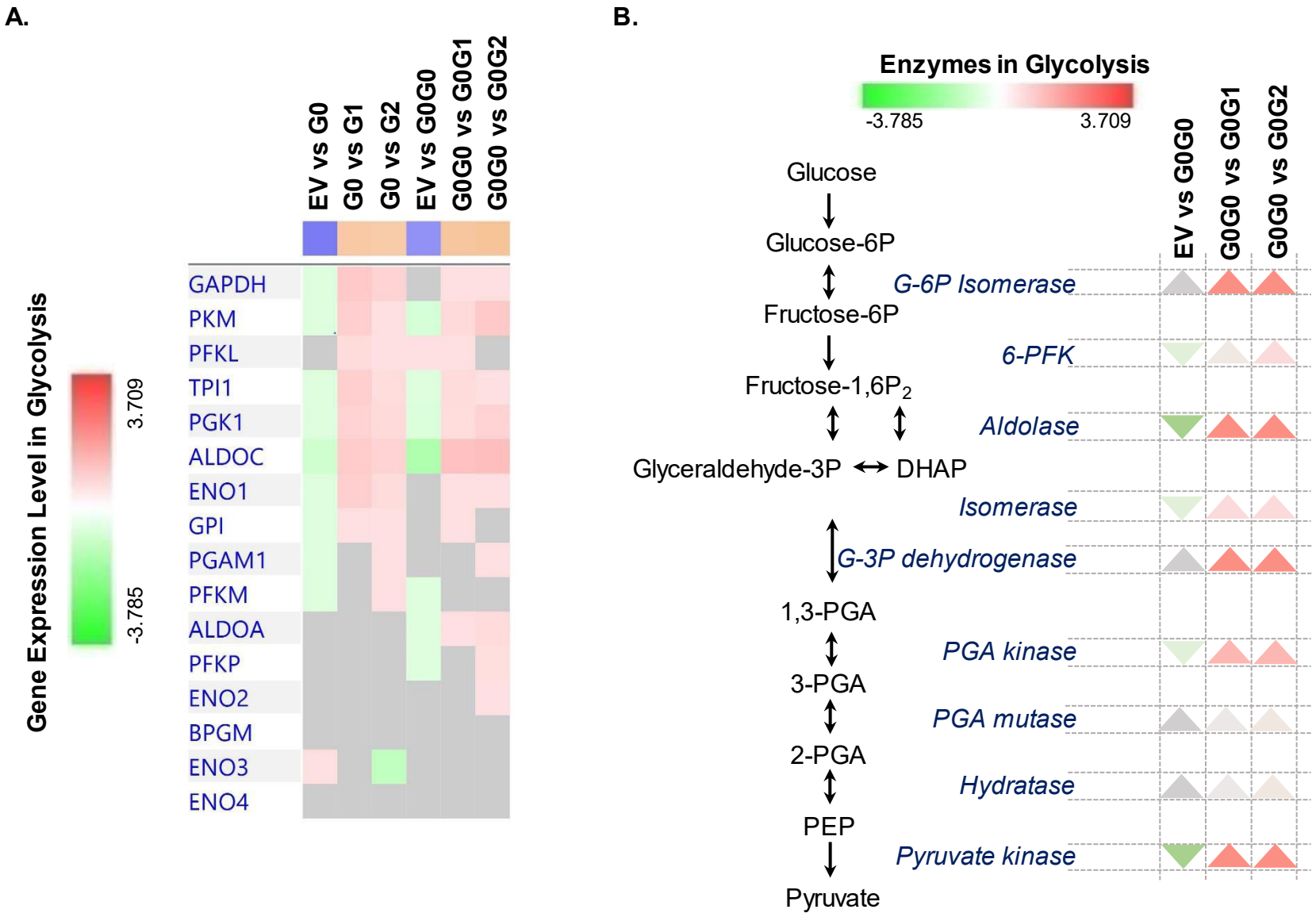

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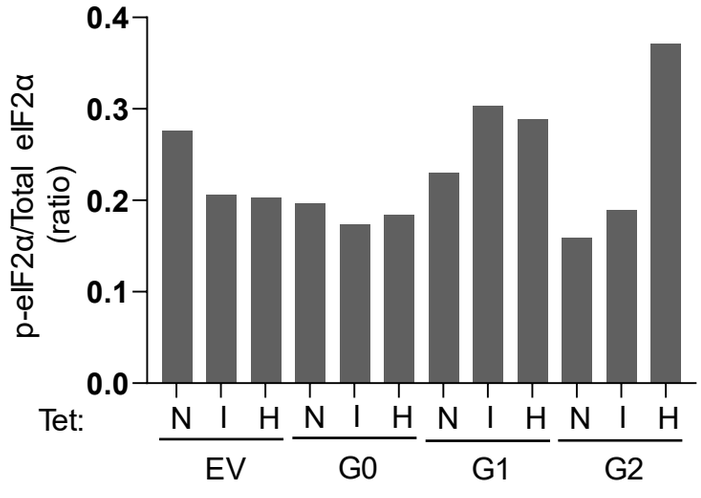

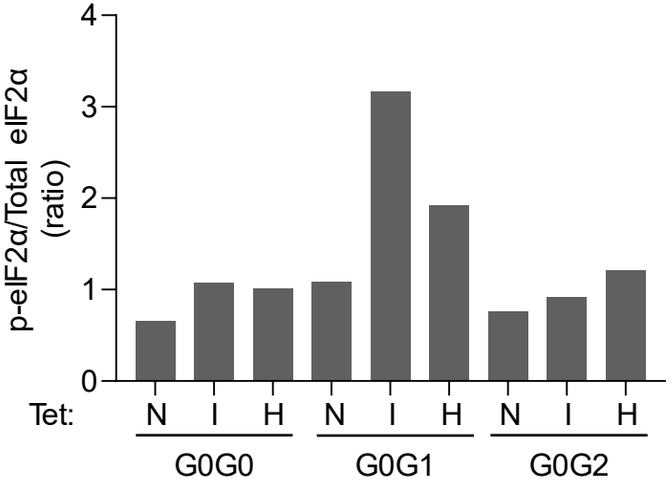

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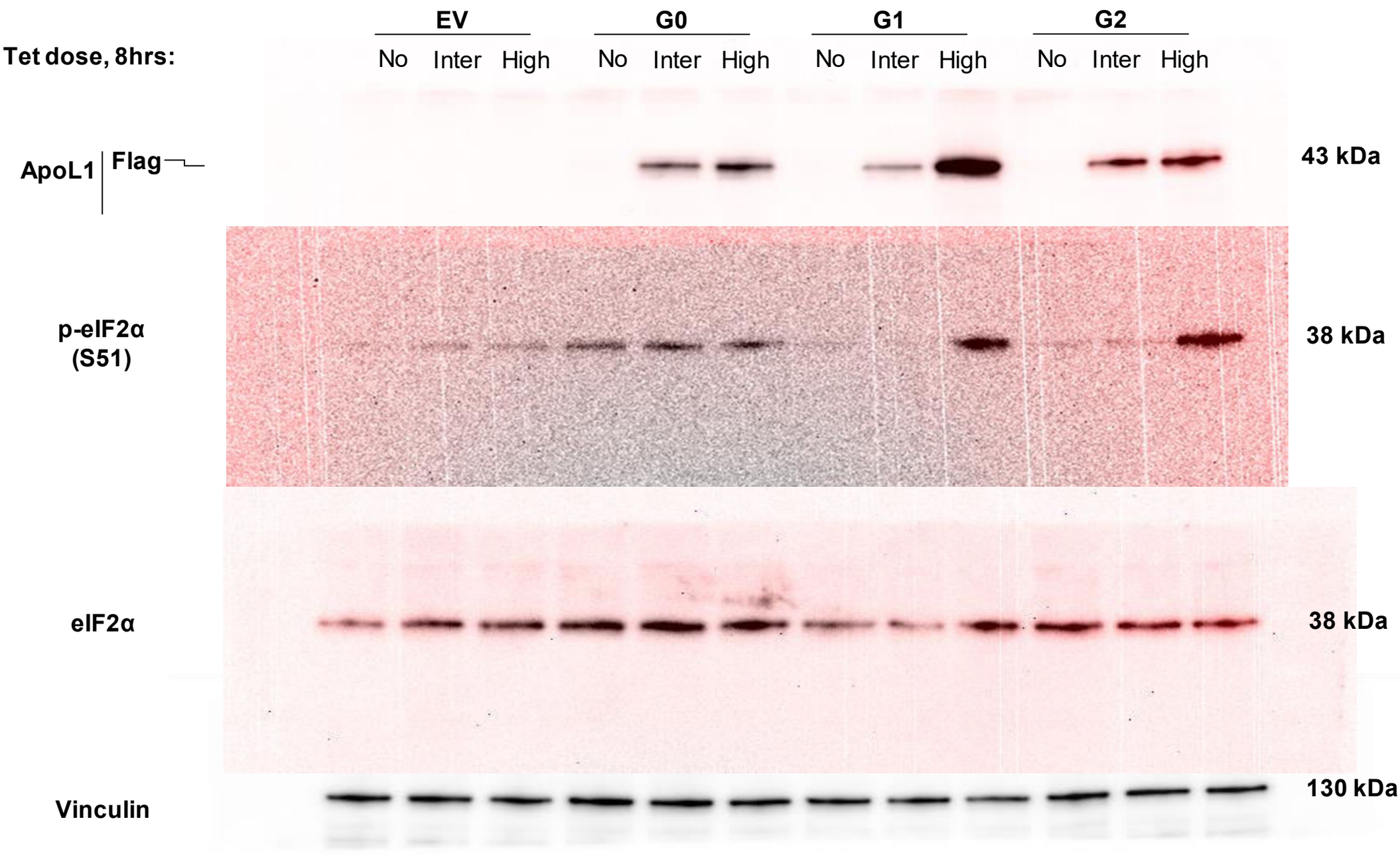

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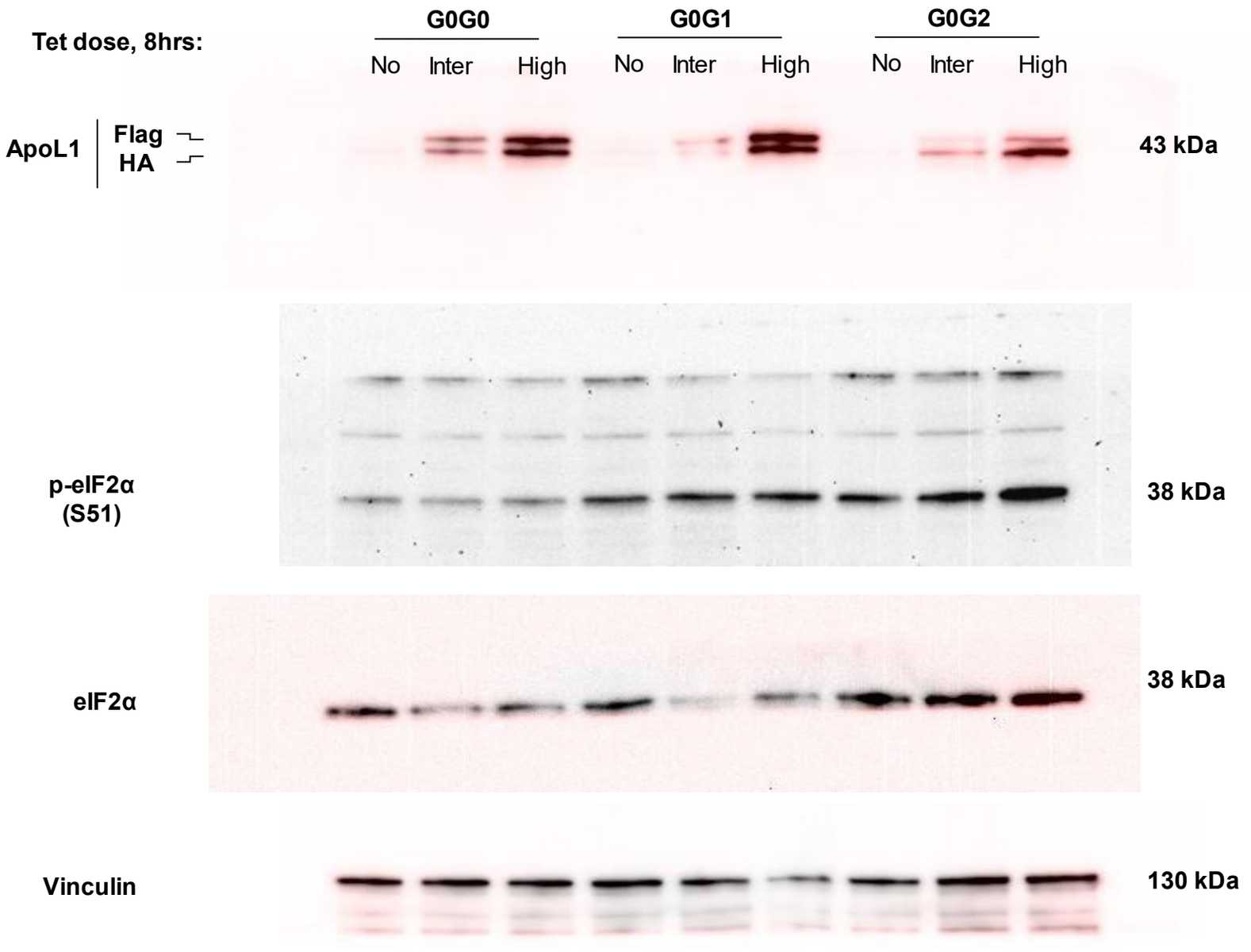

Supple. Table: 1.

		Significant DEGs		
Groups Comparison	**Total number of regulated genes**	**Up**	**Down**	**Total**
EV vs G0	17584	89	9	98
EV vs G1	16923	272	327	599
EV vs G2	16926	177	292	469
EV vs GOG0	17072	133	155	288
EV vs G0G1	16992	210	261	471
EV vs G0G2	17009	191	330	521
G0 vs G1	17292	208	392	600
G0 vs G2	17284	102	344	446
G0G0 vs G0G1	16686	180	212	392
G0G0 vs G0G2	16738	262	258	520

Supple. Figure: 1. Optimization of Tetracycline doses. (A, B) Western blot analysis of APOL1 protein level in cell lysates extracted from T-REx HEK293 mono-allelic and bi-allelic clones after 8hrs of Tet-induction using 6.25, 12.5 and 25ng/mL Tetracycline concentrations. Intermediate Tet dose for individual clones were selected based on similarity in APOL1/β-actin. **(A-1, B-1)** Full length western blots of Supple. Figure 1A and 1B. **(C, D)** Full length western blots of Figure 1B-D and Figure 2B-D. After transferring the proteins onto the PVDF membrane, the membranes were cut horizontally into pieces (using the protein ladder as guide) and incubated with individual antibodies in separate containers.

Supple. Figure: 2. Cellular swelling at High Tet-dose. T-REx HEK293 cells were treated with high Tet-dose (50ng/mL) for 8 hrs and stained with red fluorescence for plasma membrane (Abcam, ab219942) and green fluorescence for cytoplasm (Abcam, ab187967) according to kit protocol. Live cell Imaging was done using Keyence microscope (Scale 20um).

Supple. Figure: 3A. Densitometric analysis of western blot data Figure 4C. (3A-1) Band intensity of each proteins were normalized with band intensity of vinculin (Internal control). **(3A-2)** Full length western blots of Figure 4C. After transferring the proteins onto the PVDF membrane, the membranes were cut horizontally into pieces (using the protein ladder as guide) and incubated with individual antibodies in separate containers.

Supple. Figure: 3B. Densitometric analysis of western blot data Figure 4D. (3B-1) Band intensity of each proteins were normalized with band intensity of vinculin (Internal control). **(3B-2)** Full length western blots of Figure 4D. After transferring the proteins onto the PVDF membrane, the membranes were cut horizontally into pieces (using the protein ladder as guide) and incubated with individual antibodies in separate containers.

Supple. Figure: 4. Volcano plot of RNA-Seq data. The $\log_2$ fold change was plotted on the X-axis and the negative $\log_{10}$ (p-value) was plotted on Y-axis. The red and blue dots were differentially expressed genes (DEGs) which were either up- or down-regulated in one group compare to another with p-value <0.05 and absolute $\log_2$ fold change >1. The black dots represent genes which did not meet both criteria. The genes highlighted blue and red meet the threshold cutoff log2fold change >1 and p value <0.05 [-log10(pvalue) 1.3].

Supple. Figure: 5A. Heatmap showing deregulation of genes associated with actin cytoskeleton signaling in T-REx HEK293 cells for the comparisons provided.

Supple. Figure: 5B. Graphical representation of actin cytoskeleton signaling pathway based on distinct patterns of gene expression profile among mono-allelic T-REx HEK293 cells. Note differential activation of several genes such as CD14, FN1, RHOA, FilGAP, FLNA etc.

Supple. Figure: 6. Heatmap showing deregulation of additional canonical signaling pathways in T-REx HEK293 cells for the comparisons provided. z-score infer the activation state of predicted signaling pathways. Higher z-score (deeper orange) means higher activation and lower z-score (deeper blue) denotes higher inhibition of signaling pathways.

Supple. Figure: 7A. Heatmap showing deregulation of genes associated with p38 MAPK signaling in T-REx HEK293 cells expressing APOL1 variants.

Supple. Figure: 7B. Graphical representation of p38 MAPK signaling pathway showing distinct pattern of gene expression profile in T-REx HEK293 cells. Note differential activation of several genes such as MKP1/5, c-MYC, ATF-1, ATF-2 etc.

Supple. Figure: 8A. Heatmap showing deregulation of genes associated with SAPK/JNK signaling in T-REx HEK293 cells expressing APOL1 variants.

Supple. Figure: 8B. Graphical representation of SAPK/JNK signaling pathway showing distinct pattern of gene expression profile in T-REx HEK293 cells. Note differential activation of several genes such as DUSP8, MKP2/5, ATF-2, c-JUN etc.

Supple. Figure: 9A. Heatmap showing deregulation of genes associated with glycolytic pathway in T-REx HEK293 cells expressing APOL1 variants.

Supple. Figure: 9B. Graphical representation of glycolytic pathway, showing distinct pattern of gene expression of glycolytic enzymes in T-REx HEK293 cells. Note differential activation of several genes such as G-6P Isomerase, Aldolase, G-3P dehydrogenase, Pyruvate kinase etc.

Supple. Figure:10. Estimation of p-eIF2α/total eIF2α ratio. (A) Densitometric analysis and estimation of p-eIF2α/total eIF2α ratio from western blot data Figure 6C-D. N= no Tet, I= Intermediate Tet and H= high Tet. Band intensity of each proteins were normalized with band intensity of vinculin (Internal control). **(B, C)** Full-length western blot data of Figure 6C-D. After transferring the proteins onto the PVDF membrane, the membranes were cut horizontally into pieces (using the protein ladder as guide) and incubated with individual antibodies in separate containers.

Supple. Table: 1. Summary of differential expression analysis. Using DESeq2, a comparison of gene expression between groups of samples was performed. The Wald test was used to generate p-values and log2 fold changes. Genes with a p-value <0.05 and absolute $\log_2$ fold change >1 were called as differentially expressed genes (DEGs) for each comparison. The table shows number of significantly DEGs for all comparisons provided.

Supplementary Videos 1-6: Time-Lapse Imaging at Intermediate-Tet dose. T-REx HEK293 cells were plated on 24-well culture plates (50,000 cells/well) and allowed to attach for 18-24hrs. Time lapse live-cell imaging were done in Keyence chamber (Keyence All-in-One Fluorescence Microscope, BZ-X800E) at 37°C with 5%CO2, starting from 7hrs to 24hrs of post-Tet treatment with intermediate Tet-dose (12.5/25ng/mL). All the Z-stack images from every hour were processed and videos were generated using Keyence BZ-X800 analyzer software (Keyence, Japan).