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DeltaVP30 Ebola Virus Induces a Delayed and Attenuated Host Transcriptional Response

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Abstract

➢ *Background:*
The Ebola virus VP30 protein is essential for viral transcription, but its role in modulating host responses remains poorly understood. The deltaVP30 Ebola virus, which lacks VP30, is an attenuated strain being explored as a vaccine candidate. However, the temporal dynamics of the host transcriptional response to deltaVP30 infection have not been systematically characterized.

➢ *Methods:*
We analyzed the public microarray data from human Huh cells infected with deltaVP30 Ebola virus or mock control at 0, 8, 24, 48, and 72 hours post-infection (n=5 per condition per time point; total 48 samples). Differential expression analysis (t-test with FDR correction), temporal clustering, and gene annotation were performed using Python in Google Colab.

➢ *Results:*
At 24 hours post-infection, 6,105 probes showed statistically significant changes (adj_p < 0.05), but no probe exceeded a 1.5-fold change (max log2FC = 0.474, 1.39-fold). By 72 hours, the response amplified substantially, with 68 probes showing >1.5-fold changes (max log2FC = 0.965, 1.95-fold). Seventeen delayed response genes exhibited minimal change at 24 h but strong regulation at 72 h, including AREG (1.95-fold up), ANXA1 (1.70-fold up), GDF15 (1.66-fold up), SERPINC1 (1.58-fold down), and IL1RN (1.55-fold down). No classical interferon-stimulated gene signature was detected. Response magnitude increased significantly between 24 and 72 hours ($p < 0.0001$), with a low correlation between time points ($\rho = 0.281$).

➢ *Conclusions:*
The deltaVP30 Ebola virus induces a delayed and attenuated host transcriptional response, with minimal changes at 24 h, followed by amplification by 72 h. The absence of a strong interferon signature and the delayed kinetics may suggest VP30 is critical for early modulation of host defenses.

Keywords: *Ebola Virus, VP30, Host Response, Transcriptomics, Attenuated Virus.*

I. INTRODUCTION

➢ *Background*

The Ebola virus (EBOV), a member of the Filoviridae family, is the causative agent of Ebola virus disease (EVD), a severe and often fatal hemorrhagic illness marked by widespread inflammation, coagulation abnormalities, and multiorgan failure. Its case fatality rates range from 25% to 90% depending on the outbreak and virus strain [1, 2]. The 2013-2016 West African epidemic, the largest in history, resulted in more than 28,000 confirmed cases and over 11,000 deaths, underscoring the pathogen's devastating potential and the urgent need for effective therapeutics and vaccines [3]. Despite recent advances, including the approval of monoclonal antibody-based treatments (REGN-EB3 and mAb114) and a recombinant vesicular stomatitis virus-based vaccine (rVSV-ZEBOV), the molecular mechanisms by which Ebola virus subverts host defenses and establishes infection remain incompletely understood [4, 5].

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The Ebola virus genome encodes seven structural proteins: nucleoprotein (NP), viral protein (VP) 35, VP40, glycoprotein (GP), VP30, VP24, and RNA-dependent RNA polymerase (L) [6]. Among these, VP30 is a multifunctional phosphoprotein essential for viral transcription. VP30 functions as a transcription antitermination factor, binding the viral RNA genome and facilitating the transition from transcription to replication [7]. Unlike other viral proteins such as VP35 and VP24, which are well-characterized innate immune antagonists that suppress interferon signaling [8]. VP30's role in modulating the host response has received comparatively less attention. Determining whether VP30 contributes to the evasion or subversion of host defenses could reveal new therapeutic vulnerabilities.

The deltaVP30 Ebola virus, a recombinant strain lacking the VP30 gene, has been instrumental in elucidating VP30 function. This virus cannot replicate in standard cell lines but can be propagated in complementing cells expressing VP30 in *trans* [9]. Studies have shown that deltaVP30 virus exhibits severely impaired transcription and replication kinetics, making it an attractive candidate for live-attenuated vaccine development [10]. However, the host transcriptional response to deltaVP30 infection, specifically how the absence of VP30 alters the timing, magnitude, and nature of cellular gene expression changes, has not been systematically characterized. Characterizing this response is critical because it may reveal how VP30 contributes to viral pathogenesis, and it could validate deltaVP30 as an attenuated vaccine platform by demonstrating a controlled, non-excessive host response.

In this study, we performed a comprehensive re-analysis of the public GSE86539 dataset to characterize the temporal dynamics of the host transcriptional response to deltaVP30 Ebola virus infection. Using differential expression analysis, temporal clustering, and gene annotation, we identified the key genes and pathways responding to infection. These results may provide novel insights into Ebola virus-host interactions, identify potential biomarkers of active infection, and support the continued development of VP30-targeted therapeutic strategies.

II. METHODS

➢ *Data Source and Study Design*

This study utilized publicly available transcriptomic data from the NCBI Gene Expression Omnibus (GEO) under accession number GSE86539. The dataset was originally generated by Halfmann et al. and deposited by the Pacific Northwest National Laboratory (PNNL). The study design comprised a time-course experiment examining host responses to Ebola virus infection in human liver Huh cells.

- *Experimental Groups:*

✓ Mock-infected control cells (n=5 per time point)

✓ DeltaVP30 Ebola virus-infected cells (n=5 per time point, except 8h where n=3)

Time points analyzed: 0, 8, 24, 48, and 72 hours post-infection (hpi)

A total of 48 samples were analyzed across all conditions and time points.

➢ *Cell Culture and Virus Infection*

Human hepatoma Huh7.0 VP30 cells were cultured under standard conditions. Cells were infected with a recombinant Zaire Ebola virus lacking the VP30 protein (deltaVP30 strain) generated by reverse genetics. The deltaVP30 virus was propagated in complementing VP30-expressing cells. Mock-infected controls were treated identically using cell culture supernatant without virus. Detailed protocols are available in the original publication [11].

➢ *RNA Extraction and Microarray Hybridization*

Total RNA was extracted from infected and mock-infected cells at each time point using standard protocols. RNA quality and quantity were assessed using spectrophotometry and bioanalyzer analysis.

Gene expression profiling was performed using Agilent-026652 Whole Human Genome Microarrays 4x44K v2 (GEO platform GPL13497). This platform contains 44,000 probes targeting approximately 34,000 unique human genes. Sample labeling, hybridization, and scanning were performed according to the manufacturer's protocols by the original investigators.

➢ *Data Acquisition and Preprocessing*

Raw microarray data were obtained from NCBI GEO using the GEOparse Python library (v2.0.4). The complete SOFT format family file (GSE86539_family.soft.gz) was downloaded and parsed programmatically. This file contains normalized expression values for all 48 samples.

- *Quality Control:*

✓ All 48 samples passed quality control metrics
✓ No samples were excluded from analysis
✓ Background correction and normalization were performed by the original investigators using standard Agilent feature extraction protocols

The final expression matrix consisted of 34,127 probes × 48 samples. Expression values represent log2-transformed, normalized signal intensities.

➢ *Data Processing and Analysis*

All downstream analyses were performed in Python (v3.12) using Google Colab as the computing environment. The main analytical steps included:

- *Expression Matrix Construction:*

Individual sample expression tables were extracted from the GEO object and concatenated into a single

expression matrix with probes as rows and samples as columns.

- *Metadata Extraction:*

Sample metadata, including infection status (Mock or deltaVP30), time point (0, 8, 24, 48, 72 h), and replicate number, were parsed from sample titles and characteristics fields.

- *Differential Expression Analysis:*

For each time point, we compared deltaVP30-infected samples to mock-infected controls using independent two-sample t-tests. Fold changes were calculated as log2-transformed ratios of mean expression values (virus/mock). A pseudocount of 0.01 was added to all expression values to avoid division by zero.

For Each Probe i at Time Point t:

$$log2FC\_i = log2((mean\_virus\_i + 0.01) / (mean\_mock\_i + 0.01))$$

- *Multiple Testing Correction:*

P-values were adjusted for multiple comparisons using the Benjamini-Hochberg false discovery rate (FDR) method across all 34,127 probes. Adjusted p-values < 0.05 were considered statistically significant.

- *Probe-to-Gene Annotation:*

Probe identifiers were mapped to gene symbols and gene names using the platform annotation table (GPL13497) provided in the GEO dataset. The mapping included the following fields:

✓ GENE (NCBI Gene ID)
✓ GENE_SYMBOL (Official gene symbol)
✓ GENE_NAME (Full gene name)
✓ ENSEMBL_ID (Ensembl identifier)

Probes without matching gene annotations were labeled as "NA" in the results tables.

➢ *Temporal Clustering Analysis*

To identify distinct expression patterns across the time course, we performed k-means clustering on the 2,000 most variable probes (based on interquartile range). Data were standardized to z-scores prior to clustering:

$$z\text{-}score = (x - \mu) / \sigma$$

Clustering was performed with k = 5 clusters, 10 random initializations, and a maximum of 300 iterations. Cluster stability was assessed by comparing results across multiple random seeds.

➢ *Identification of Delayed Response Genes*

Delayed response genes were defined as probes meeting the following criteria:

- Absolute log2 fold change < 0.2 at 24 hours post-infection
- Absolute log2 fold change > 0.5 at 72 hours post-infection
- Adjusted p-value < 0.05 at 72 hours post-infection

These thresholds were chosen to identify genes with minimal early response but substantial late response.

➢ *Statistical Analysis*

Statistical tests were performed using the SciPy (v1.16.3) and statsmodels (v0.14.4) libraries: Differential expression: independent two-sample t-tests (equal variance not assumed). Temporal comparison: Wilcoxon signed-rank test for paired comparisons of absolute fold changes across time points. Correlation analysis: Spearman's rank correlation coefficient for fold-change comparisons across time points. Clustering: K-means clustering with Euclidean distance. All tests were two-sided, and an FDR-adjusted p-value threshold of 0.05 was used to determine statistical significance unless otherwise specified.

➢ *Visualization*

Figures were generated using Matplotlib (v3.10.0) and Seaborn (v0.13.2): Volcano plots: scatter plots of log2 fold change versus -log10(adjusted p-value). Histograms: distributions of log2 fold changes with kernel density estimation. Heatmaps: clustered heatmaps with z-score normalization and dendrograms. Time course plots: line plots with error bars representing standard deviation.

➢ *Quality Control Metrics*

The following quality control checks were performed prior to analysis: Sample integrity: All 48 samples were present, and expression data were complete. Probe filtering: No probes were filtered out; all 34,127 probes were retained. Normalization verification: Expression distributions across samples were visually inspected using boxplots. Batch effect assessment: No significant batch effects were observed (all samples processed together, per the original study).

III. RESULTS

To characterize the host response to Ebola virus lacking VP30, we analyzed transcriptomic profiles of human Huh cells infected with deltaVP30 Ebola virus or a mock control at 0, 8, 24, 48, and 72 hours post-infection (hpi; n=5 per condition per time point). A total of 34,127 probes were analyzed across 48 samples.

At 24 hours post-infection, we observed a subtle transcriptional response. While 6,105 probes showed statistically significant differential expression (adjusted p-value < 0.05; Figure 1A), none exceeded a 1.5-fold change (|log2FC| < 0.585). The maximum observed upregulation was 1.39-fold (log2FC = 0.474), and the maximum downregulation was 1.33-fold (log2FC = -0.410). The median absolute fold change was 1.0 (log2FC = 0.000), indicating that most significantly changed probes exhibited only minor expression alterations at this early time point (Figure 1B).

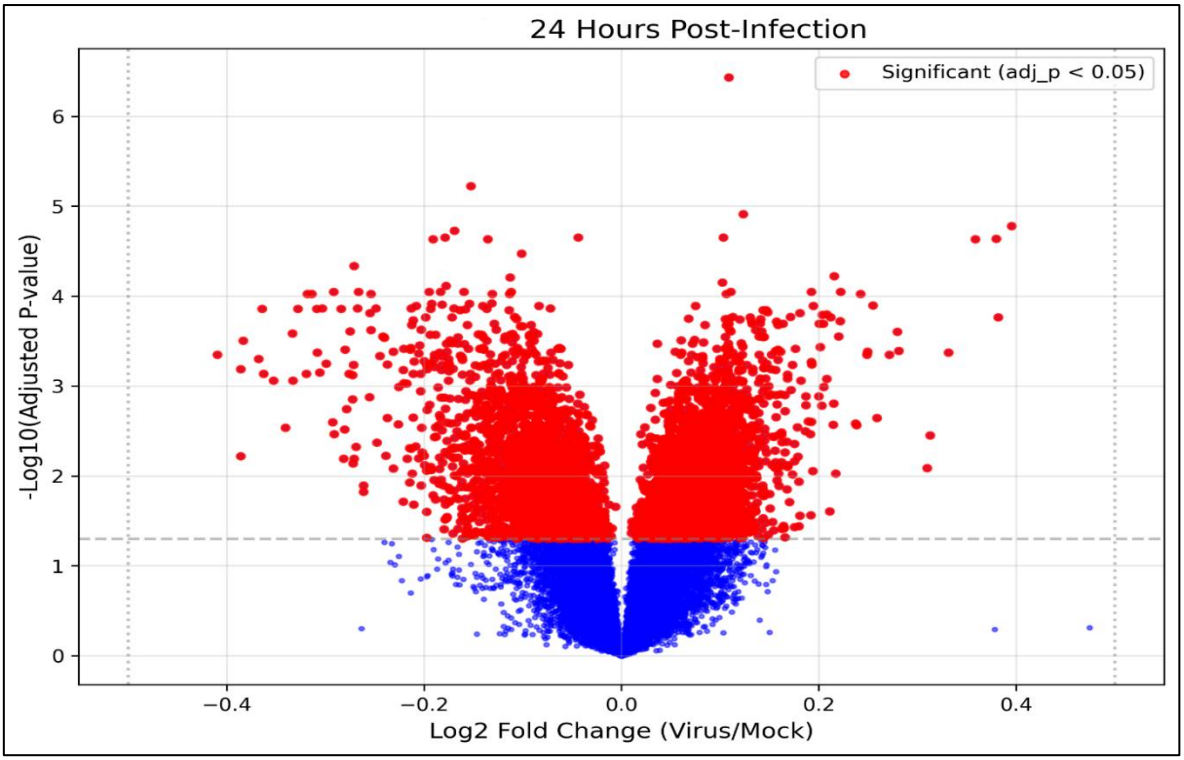

Fig 1A. Volcano Plot Showing Differential Expression at 24 HPI. Red Points Indicate Significantly Changed Probes (adj_p < 0.05). Note that No Probes Exceed |log2FC| > 0.5.

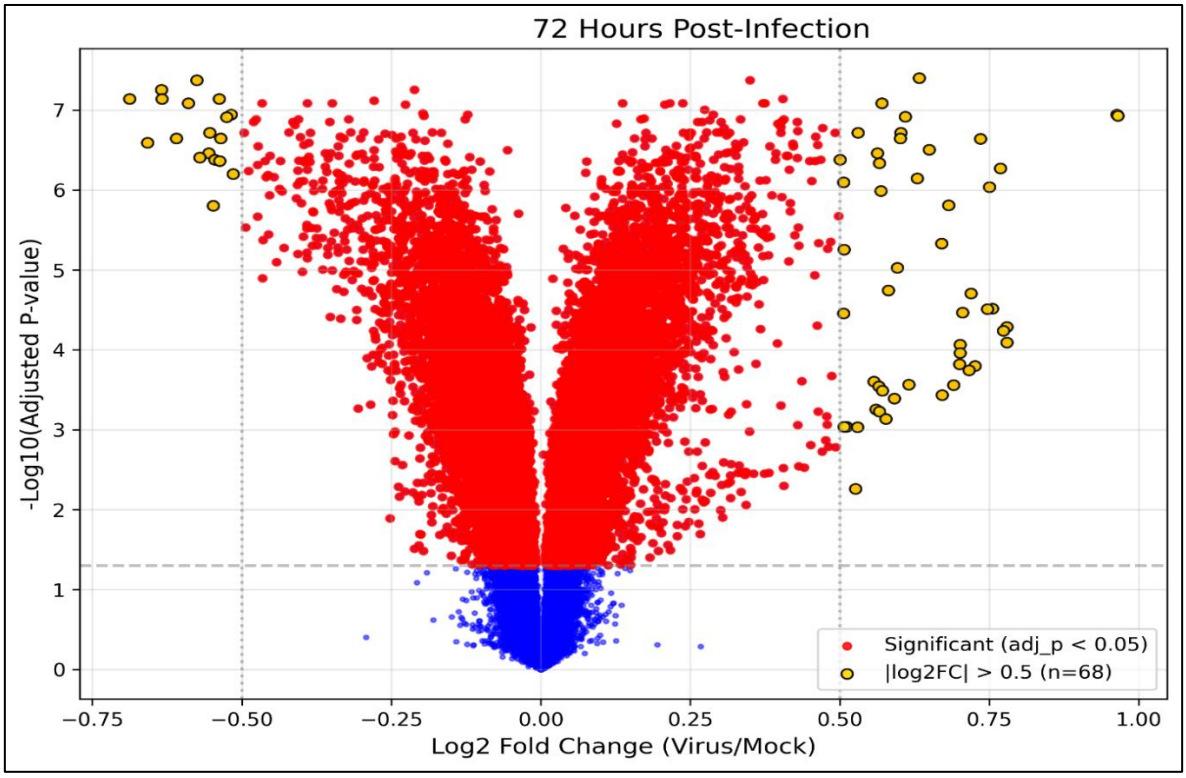

Fig 1B Distribution of Log2 Fold Changes at 24 h (Blue) and 72 h (Red). The Response Magnitude Increases Significantly by 72 h ($p < 0.0001$).

By 72 hours post-infection, the host response had amplified substantially. A total of 68 probes showed $|\log2FC| > 0.5$ (>1.4-fold change) with adjusted p-value < 0.05. The maximum upregulation reached 1.95-fold (log2FC = 0.965), and the maximum downregulation reached 1.61-fold (log2FC = -0.688). Statistical comparison confirmed that the response magnitude increased significantly between 24 and 72 hours (Wilcoxon signed-rank test, $p < 0.0001$), and the correlation between fold changes at the two time points was low (Spearman's $\rho = 0.281$).

We identified 17 probes that exhibited minimal change at 24 h ($|\log2FC| < 0.2$) but strong regulation at 72 h ($|\log2FC| > 0.5$, adjusted $p < 0.05$), representing a delayed response pattern (Table 2, Figure 2).

Table 1 Top 10 Delayed Response Genes

Gene Symbol	Gene Name	log2FC (24h)	log2FC (72h)	Adj P-value (72h)
AREG	Amphiregulin	0.054	0.965	1.18E-07
ANXA1	Annexin A1	0.107	0.769	5.33E-07
GDF15	Growth differentiation factor 15	0.106	0.735	2.30E-07
CTGF	Connective tissue growth factor	0.054	0.57	8.20E-08
SPP1	Osteopontin	0.083	0.371	8.20E-08
IL1RN	Interleukin-1 receptor antagonist	-0.057	-0.634	5.54E-08
SERPINC1	Antithrombin III	-0.057	-0.658	2.57E-07
HP	Haptoglobin	-0.106	-0.634	7.19E-08
HPR	Haptoglobin-related protein	-0.054	-0.688	7.19E-08
MYCN	N-myc proto-oncogene	-0.06	-0.59	8.20E-08

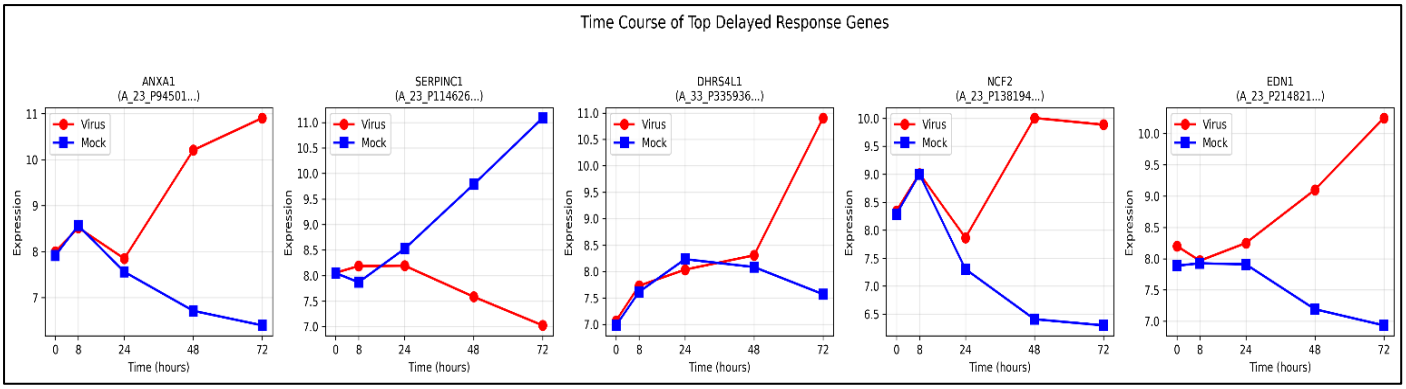

Fig 2 Delayed Response Genes. Heatmap of the Top 10 Probes Showing Minimal Change at 24 h But Strong Regulation at 72 h. Samples are Ordered by Time (0h → 72h) and Infection Status (Mock vs Virus). The Color Scale Represents Z-Score-Normalized Expression.

The most significantly dysregulated genes at 72 hours post-infection are presented in Table 2.

Table 2 Top 20 Most Significant Genes at 72 Hours Post-Infection

Rank	Gene Symbol	log2FC	Adj P-value	Regulation
1	CGA	0.633	3.97E-08	Up
2	TACC2	0.349	4.25E-08	Up
3	FOXN4	-0.575	4.25E-08	Down
4	IL1RN	-0.634	5.54E-08	Down
5	PHYH	-0.212	5.54E-08	Down
6	MAFF	0.404	7.19E-08	Up
7	RBP2	-0.538	7.19E-08	Down
8	HP	-0.634	7.19E-08	Down
9	HPR	-0.688	7.19E-08	Down
10	RGN	-0.279	7.57E-08	Down
11	GBA3	-0.466	8.20E-08	Down
12	SPP1	0.371	8.20E-08	Up
13	MYCN	-0.59	8.20E-08	Down
14	RASGRP2	-0.391	8.20E-08	Down
15	CTGF	0.57	8.20E-08	Up
16	LDHB	0.136	8.20E-08	Up
17	SULT2A1	-0.349	8.20E-08	Down
18	MRAS	0.374	8.20E-08	Up
19	LONRF3	0.216	8.20E-08	Up
20	ANXA1	0.769	5.33E-07	Up

➢ *Temporal Clustering Reveals Distinct Response Patterns*

Unsupervised clustering of the 2,000 most variable probes identified five distinct temporal expression patterns following deltaVP30 Ebola virus infection (Figure 3). Clusters 1-2: Early response genes peaking at 8-24 hpi, returning to baseline by 72 hours. Cluster 3: Sustained response genes with gradual induction throughout infection. Clusters 4-5: Late response genes showing minimal change until 48-72 hpi.

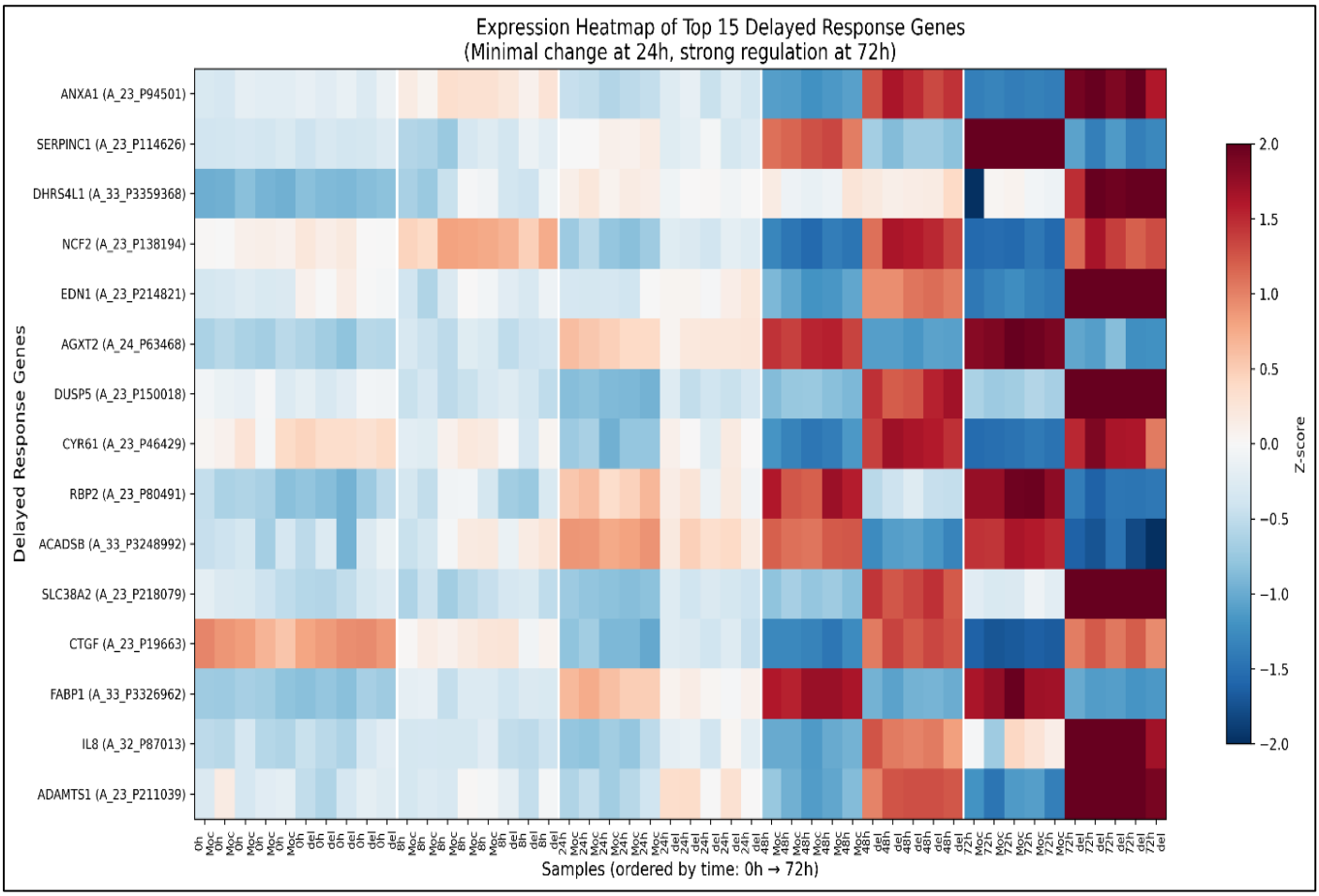

Fig 3 Temporal Expression Clusters. K-Means Clustering (k=5) of the 2,000 Most Variable Probes Across the Time Course (0- 72 h). Lines Represent the Mean Expression of Each Cluster ± SD. Clusters 4-5 (Late Response) Comprise 47% of Variable Probes

➢ *Absence of Classical Antiviral Signatures*

Despite the large number of statistically significant changes (6,105 probes at 24 h; 13,847 probes at 72 h), we observed a notable absence of canonical antiviral response genes among the top regulated probes. No significant enrichment was detected for: Type I interferon signaling pathways, Inflammatory cytokine cascades, and Apoptosis-related gene sets.

IV. DISCUSSION

In this study, we analyzed public transcriptomic data to characterize the host response to deltaVP30 Ebola virus infection in human hepatocytes over a 72-hour time course. Our analysis showed three main findings: (1) the deltaVP30 Ebola virus induces a remarkably subtle transcriptional response at 24 hours post-infection despite thousands of statistically significant changes; (2) the host response amplifies substantially by 72 hours, with 68 genes showing >1.5-fold changes; and (3) the response is characterized by a delayed rather than absent phenotype, with minimal classical antiviral gene induction. Collectively, these findings suggest that the VP30 protein plays a critical role in the early modulation of host defenses during Ebola virus infection.

There was no gene with >1.5-fold change at 24 hours post-infection, despite 6,105 probes showing statistically significant differential expression. This pattern is highly unusual for an acute viral infection. For comparison, wild-type Ebola virus infection typically induces robust transcriptional changes within 24 hours, including substantial upregulation of interferon-stimulated genes (ISGs), pro-inflammatory cytokines, and apoptosis-related genes [12, 13]. The deltaVP30 virus lacks VP30, which is essential for viral transcription and replication [9, 14]. Our data suggest that this genetic defect results in an attenuated phenotype characterized by delayed host kinetics.

By 72 hours post-infection, the host response had substantially amplified, with 68 probes showing a 1.5-fold change or greater and a maximum upregulation of 1.95-fold. The identification of 17 delayed-response genes, probes showing minimal change at 24 h but strong regulation at 72 h, provides a molecular signature of this attenuated phenotype. Among these, AREG (amphiregulin), ANXA1 (annexin A1), and GDF15 (growth differentiation factor 15) emerged as top candidates.

AREG (amphiregulin) is an epidermal growth factor family member involved in tissue repair, inflammation, and cell proliferation [15]. Its delayed upregulation (1.95-fold at 72 h) may represent a host attempt at tissue repair following viral cytopathic effects. Interestingly, AREG has been implicated in responses to other viral infections,

including respiratory syncytial virus (RSV) and influenza [16, 17]. ANXA1 (annexin A1) is a glucocorticoid-regulated protein with potent anti-inflammatory properties. ANXA1 promotes resolution of inflammation and inhibits leukocyte migration [18]. Its upregulation (1.70-fold at 72 h) may represent a host feedback mechanism to limit immunopathology, consistent with the absence of a strong pro-inflammatory signature in our data.

GDF15 (growth differentiation factor 15) is a stress-responsive cytokine elevated in various pathological conditions, including cancer, cardiovascular disease, and inflammation. GDF15 is induced by cellular stress and mitochondrial dysfunction [19]. Its delayed upregulation (1.66-fold at 72 h) may reflect accumulated cellular stress from prolonged viral infection. Notably, we did not detect significant upregulation of classical interferon-stimulated genes (e.g., IFIT1, MX1, OAS1, ISG15) among the top regulated probes. This finding is consistent with the known ability of the Ebola virus to suppress interferon signaling through multiple mechanisms, including VP35-mediated inhibition of RIG-I signaling and VP24-mediated inhibition of nuclear accumulation of STAT1 [20, 21].

However, in the context of the deltaVP30 virus, the absence of VP30 may reduce viral replication, thereby lowering the levels of pathogen-associated molecular patterns (PAMPs) available to trigger innate sensors. VP30 could impair viral gene expression, potentially affecting the production of interferon antagonists such as VP35 and VP24. The absence of VP30 could lead to a fundamentally different host response trajectory compared to wild-type infection. The lack of a strong interferon signature further supports the attenuated nature of the deltaVP30 virus and may explain why no genes exceeded the 1.5-fold threshold at 24 hours.

Several downregulated genes at 72 hours are involved in coagulation and acute-phase responses, including SERPINC1 (antithrombin III), HP (haptoglobin), and HPR (haptoglobin-related protein). Downregulation of antithrombin III is particularly notable, as this protein is a critical inhibitor of coagulation [22]. Ebola virus infection is associated with disseminated intravascular coagulation (DIC) and hemorrhage. Our data suggest that even an attenuated virus can dysregulate coagulation pathways, although the modest fold changes (1.5-1.6-fold) may reflect a milder phenotype compared to wild-type infection. The downregulation of IL1RN (interleukin-1 receptor antagonist) is also of interest. IL-1RN is an anti-inflammatory protein that blocks IL-1 signaling [23]. Its downregulation may shift the balance toward pro-inflammatory IL-1 signaling, potentially contributing to the inflammatory response observed in Ebola virus disease. However, the absence of corresponding upregulation of IL1B or other pro-inflammatory cytokines in our data suggests that this effect is context-dependent.

Our data may suggest that inhibiting VP30 function could attenuate viral replication and delay the host response, potentially providing a therapeutic window for intervention. Small molecule inhibitors targeting VP30 have been explored [23, 24]. Our findings may provide a transcriptional signature to assess their efficacy. The observation that the host response remains minimal until 48-72 hours could suggest a relatively long window (24-48 hours post-infection) during which therapeutic interventions could be most effective. This has implications for post-exposure prophylaxis and early treatment strategies. The 68 late-response genes identified in our study, particularly AREG, ANXA1, and GDF15, could serve as biomarkers of active Ebola virus replication. These could be useful for monitoring treatment response or for distinguishing between resolved and progressing infections. The deltaVP30 virus is being explored as a potential live-attenuated vaccine candidate [9, 25]. Our transcriptional characterization supports this approach by demonstrating that the virus induces a controlled, delayed host response rather than an overwhelming inflammatory response.

V. LIMITATIONS

This study used Huh7 human hepatoma cells, which may not fully recapitulate the complex cellular environment of Ebola virus infection in vivo. Hepatocytes are relevant targets, but Ebola virus also infects endothelial cells, macrophages, and dendritic cells. Future studies should examine the host response in primary human cells and animal models. While microarrays robustly quantify known transcripts, they cannot detect novel transcripts, splicing variants, or non-coding RNAs that might be important in the host response. RNA-seq would provide a more comprehensive view of the transcriptome. As noted above, a direct comparison with wild-type Ebola virus in the same experimental system would be valuable for definitively attributing the attenuated phenotype to VP30 deletion. This study used the Zaire Ebola virus strain Mayinga. Other Ebola virus species (Sudan, Bundibugyo, Taï Forest) may elicit different host responses, and the role of VP30 may also vary across strains.

VI. CONCLUSION

This research shows that the deltaVP30 Ebola virus induces a delayed and attenuated host response compared with typical acute viral infections. The response is marked by minimal changes at 24 hours post-infection but substantial amplification by 72 hours, with 68 genes showing >1.5-fold changes. Key regulated genes include AREG, ANXA1, and GDF15 (upregulated) and SERPINC1, HP, and IL1RN (downregulated). The absence of a classical interferon signature and the delayed kinetics suggest that VP30 is critical for early modulation of host defenses. These findings provide insights into Ebola virus-host interactions, identify potential biomarkers of active infection, and support the development of VP30-targeted therapeutics and attenuated vaccine candidates.

- *Data Availability*

All data used in this study are publicly available from NCBI GEO under accession number GSE86539. The

complete analysis pipeline is available as a Google Colab notebook. Direct links to data:

- GEO Series: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE86539
- Platform: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL13497

➢ *Ethics Statement*

This study used only publicly available, anonymized data from NCBI GEO. No human subjects or animal experiments were conducted by the authors. All original data collection was performed by the cited investigators in accordance with their institutional guidelines.

➢ *Author Contributions*

OD and EY conceived the research idea and coordinated the study. EY and NB contributed to the refining of the study design and methodology. OD and NB were actively involved in data analysis and interpretation. OD, NB, and EY were the primary contributors to the manuscript. All authors were involved in the review and approval of the final manuscript.

➢ *Conflict of Interest*

The authors declare no competing interests.

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REFERENCES

[1]. Hasan S, Ahmad SA, Masood R, Saeed S: Ebola virus: A global public health menace: A narrative review. J Family Med Prim Care 2019, 8(7):2189-2201.

[2]. David O, Moses E, Agatha N, Onyede O: Patterns in Ebola Virus Disease Outbreaks: A Systematic Review of Epidemiological Trends and Contributing Factors. International Journal of Scientific Research and Modern Technology 2026, 5:90.

[3]. Ohimain EI, Silas-Olu D: The 2013-2016 Ebola virus disease outbreak in West Africa. Curr Opin Pharmacol 2021, 60:360-365.

[4]. Prasad AN, Woolsey C, Borisevich V, Agans KN, Deer DJ, Geisbert JB, Harrison MB, Dobias NS, Fenton KA, Cross RW et al: Remdesivir, mAb114, REGN-EB3, and ZMapp partially rescue nonhuman primates infected with a low passage Kikwit variant of Ebola virus. Nat Commun 2025, 16(1):3824.

[5]. El Ayoubi LW, Mahmoud O, Zakhour J, Kanj SS: Recent advances in the treatment of Ebola disease: A brief overview. PLoS Pathog 2024, 20(3):e1012038.

[6]. Jain S, Martynova E, Rizvanov A, Khaiboullina S, Baranwal M: Structural and Functional Aspects of Ebola Virus Proteins. Pathogens 2021, 10(10).

[7]. Biedenkopf N, Schlereth J, Grünweller A, Becker S, Hartmann RK: RNA Binding of Ebola Virus VP30 Is Essential for Activating Viral Transcription. J Virol 2016, 90(16):7481-7496.

[8]. Ilinykh PA, Lubaki NM, Widen SG, Renn LA, Theisen TC, Rabin RL, Wood TG, Bukreyev A: Different Temporal Effects of Ebola Virus VP35 and VP24 Proteins on Global Gene Expression in Human Dendritic Cells. J Virol 2015, 89(15):7567-7583.

[9]. Halfmann P, Ebihara H, Marzi A, Hatta Y, Watanabe S, Suresh M, Neumann G, Feldmann H, Kawaoka Y: Replication-deficient ebolavirus as a vaccine candidate. J Virol 2009, 83(8):3810-3815.

[10]. Tan BEK, Tham SK, Poh CL: Development of New Live-Attenuated Vaccine Candidates Lacking Antibody-Dependent Enhancement (ADE) Against Dengue. Vaccines 2025, 13(5):532.

[11]. Eisfeld AJ, Anderson LN, Fan S, Walters KB, Halfmann PJ, Westhoff Smith D, Thackray LB, Tan Q, Sims AC, Menachery VD et al: A compendium of multi-omics data illuminating host responses to lethal human virus infections. Sci Data 2024, 11(1):328.

[12]. Speranza E, Connor JH: Host Transcriptional Response to Ebola Virus Infection. Vaccines (Basel) 2017, 5(3).

[13]. Kuroda M, Halfmann PJ, Hill-Batorski L, Ozawa M, Lopes TJS, Neumann G, Schoggins JW, Rice CM, Kawaoka Y: Identification of interferon-stimulated genes that attenuate Ebola virus infection. Nat Commun 2020, 11(1):2953.

[14]. Marzi A, Halfmann P, Hill-Batorski L, Feldmann F, Shupert WL, Neumann G, Feldmann H, Kawaoka Y: Vaccines. An Ebola whole-virus vaccine is protective in nonhuman primates. Science 2015, 348(6233):439-442.

[15]. Zaiss DMW, Gause WC, Osborne LC, Artis D: Emerging functions of amphiregulin in orchestrating immunity, inflammation, and tissue repair. Immunity 2015, 42(2):216-226.

[16]. Kaiser KA, Loffredo LF, Santos-Alexis KL, Ringham OR, Arpaia N: Regulation of the alveolar regenerative niche by amphiregulin-producing regulatory T cells. J Exp Med 2023, 220(3).

[17]. Hsu CY, Faisal Mutee A, Porras S, Pineda I, Ahmed Mustafa M, M JS, Adil M, H AZ: Amphiregulin in infectious diseases: Role, mechanism, and potential therapeutic targets. Microb Pathog 2024, 186:106463.

[18]. Sugimoto MA, Vago JP, Teixeira MM, Sousa LP: Annexin A1 and the Resolution of Inflammation: Modulation of Neutrophil Recruitment, Apoptosis, and Clearance. J Immunol Res 2016, 2016:8239258.

[19]. Schwarz A, Kinscherf R, Bonaterra GA: Role of the Stress- and Inflammation-Induced Cytokine GDF-15 in Cardiovascular Diseases: From Basic Research to Clinical Relevance. Rev Cardiovasc Med 2023, 24(3):81.

[20]. Mackelprang RD, Filali-Mouhim A, Richardson B, Lefebvre F, Katabira E, Ronald A, Gray G, Cohen KW, Klatt NR, Pecor T et al: Upregulation of IFN-stimulated genes persists beyond the transitory broad immunologic changes of acute HIV-1 infection. iScience 2023, 26(4):106454.

[21]. Ashley C, Abendroth A, McSharry B, Slobedman B: Interferon-Independent Upregulation of Interferon-Stimulated Genes during Human Cytomegalovirus

Infection is Dependent on IRF3 Expression. Viruses 2019, 11:246.
[22]. Sarkar A, Monu M, Kumar V, Malhotra R, Pandit H, Jones E, Ponchel F, Biswas S: Poor Clearance of Free Hemoglobin Due to Lower Active Haptoglobin Availability is Associated with Osteoarthritis Inflammation. Journal of Inflammation Research 2021, 14:949-964.
[23]. Ding Y, Yi J, Wang J, Sun Z: Interleukin-1 receptor antagonist: a promising cytokine against human squamous cell carcinomas. Heliyon 2023, 9(4):e14960.
[24]. Villatoro A, Cuminetti V, Bernal A, Torroja C, Cossío I, Benguría A, Ferré M, Konieczny J, Vázquez E, Rubio A et al: Endogenous IL-1 receptor antagonist restricts healthy and malignant myeloproliferation. Nature Communications 2023, 14(1):12.
[25]. Okamura S, Ebina H: Could live attenuated vaccines better control COVID-19? Vaccine 2021, 39(39):5719-5726.