

Divergent Nasal Immune Responses of HRV VS RSV Infection in Childhood Asthma

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Abstract. HRV and RSV are the two most common viruses that trigger asthma attacks in children, yet how they affect the nasal immune system in different ways is still not fully clear. This study used RNA-seq data (GSE115770) to compare nasal gene expression between asthmatic children infected with HRV (n=129) and those with RSV (n=7). HRV infection changed 2,822 genes, mainly activating antiviral responses (such as IFIT1, IRF7, CXCL10) and attracting neutrophils. In contrast, RSV altered over 21,000 genes, strongly activating Th2/IL-33 related genes (IL1B, CSF3R) and the NF- κ B pathway. By comparing virus-specific genes, the study found clear differences: HRV-specific genes linked to immune regulation, MAPK signaling and miRNA-related gene control; RSV-specific genes were tied to typical immune reactions like adaptive immunity, virus defense and MAPK pathways. establishes a random forest model to accurately distinguish between HRV or RSV infected children and non infected children (AUC of HRV=0.952, AUC of RSV=1.000). These results indicate that HRV and RSV elicit different immune responses in children's noses and provide genetic markers that may help identify which virus is causing asthma attacks.

Keywords: RNA-seq, asthma, human rhinovirus, respiratory syncytial viral, host immune response

1. Introduction

Respiratory virus infection is the main cause of worsening asthma in children, with human rhinovirus (HRV) and respiratory syncytial virus (RSV) being particularly severe. 92.2% of children suffer from severe side effects, which can be detected through virus testing. HRV is the deadliest virus, followed by RSV [1]. Severe infections of respiratory viruses often occur before breathing again, and can even lead to childhood cancer in subsequent stages, placing a huge burden on healthcare systems and these families. Therefore, learning the most accurate methods for preventing the occurrence of rheumatoid arthritis virus through various prevention pathways is crucial for early and accurate intervention. However, their different effects on nose prevention are still unclear.

Previous studies have confirmed that the immune response increases asthma and plays an important role in controlling the viral burden and stress during human asthma virus and asthma virus infection [2]. Most tests focus on blood samples or lower breath, and cannot accurately detect objects in the nose. The nasal cavity is the first place where the virus enters and recovers, indicating

the cause of the virus infection and initiating a preventive response. Therefore, analyzing the changes in gene expression of individual units can more accurately reflect the main immune responses caused by HRV and RSV.

Despite rapid progress in production and a large number of product sequences, few people are able to accurately compare trends in epidemic changes. To treat this difference, researchers analyzed nasal and nasal RNA sequence data (GSE115770) from children infected with human asthmal virus or human asthmal virus. Compared to children who are not affected by the virus, metastatic changes are eliminated to isolate specific responses to the virus. This study includes enhanced pathway analysis and automatic learning to detect specific prevention patterns of all viruses. This paper aims to explain HIV in children's oral cavity and the different immune responses caused by HIV, identify possible oral genetic symptoms and control methods, and provide a basis for virus classification, early diagnosis and personalized treatment strategies.

2. Materials and methods

2.1. Data source and sample description

Gene expression data were obtained from the GEO database under accession number GSE115770 [3]. The dataset comprised nasal epithelial RNA-seq samples from pediatric subjects: 129 children with HRV infection, 7 with RSV infection and 181 without detectable viral infection. All samples were collected via nasal swabs.

2.2. Principal component analysis (PCA)

PCA was performed using the iDEP web platform (<http://bioinformatics.sdstate.edu/idep/>). Raw RNA-seq count data were uploaded, and variance stabilization transformation (VST) was applied automatically. PCA was conducted using the top 500 most variable genes, with the first two principal components (PC1, PC2) employed to visualize sample grouping. This analysis evaluated whether HRV, RSV and non-infected groups exhibited distinct gene expression profiles.

2.3. Differential gene expression analysis

Differential gene expression analysis was conducted using the DESeq2 R package. Genes with $|\log_2(\text{fold change})| > 1$ and adjusted p-value < 0.05 were defined as significantly differentially expressed. Results were visualized using volcano plots.

2.4. Pathway and functional enrichment analysis

Gene Ontology (GO) biological process and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed using the clusterProfiler and org.Hs.eg.db packages in R. Only terms with adjusted p-value < 0.05 were retained. Metascape (<https://metascape.org>) was utilized for complementary GO enrichment analysis, integrating multiple databases to group related pathways and generate network visualizations. Results were filtered based on p-value and gene set size, with top-ranked pathways selected for interpretation. Enrichment results were visualized using dot plots and bar plots.

2.5. Random forest modeling

A random forest classifier was constructed using the randomForest R package to identify key immune genes that distinguish between HRV infected and non infected children. This article selects input genes from the genes with the highest differential expression and evaluates model performance using 10 fold cross validation. The classification accuracy is quantified by the area under the working characteristic curve (AUC) of the subjects. Important genes were ranked based on mean decrease in Gini index.

2.6. Statistical analysis

All statistical analyses were conducted using R software (version 4.5.1). Using DESeq2 to identify differentially expressed genes, an adjusted p-value<0.05 is considered statistically significant. Filter the enrichment results using the same threshold. Ggplot2 generates data visualization and summary statistics.

3. Results

3.1. HRV infection alters the nasal transcriptome expression of asthma children

PCA is executed on the iDEP platform. The samples infected with human nasal virus were significantly separated from the uninfected samples (see Figure 1), indicating that the human nasal virus caused extensive changes in gene expression of human cells in the nasal cavity of children.

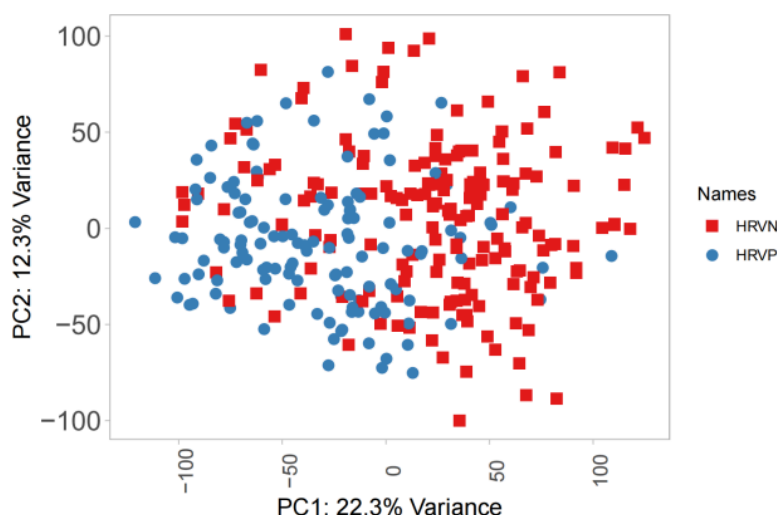


Figure 1. Infection with human asthma virus can stimulate different nasal features in children with asthma

This PCA chart is the highest change rate of gene expression in PC1, from the red dot representing the global HIV infection pattern to the blue dot representing the non infection pattern, in children with HRV and children without asthma. This reflects the continuous response of the narrow space of each human nose transcription group dominated by HRV infection to HIV infected children. This significant difference confirms that the human asthma virus can cause deep and uniform text remodeling in nasal tissue.

3.2. Gene expression differences between HRV infection and non viral infection in children with asthma

Compared with uninfected children, HRV infection induced 2822 significantly differentially expressed genes (638 up-regulated and 2184 down regulated; adjusted $p < 0.05$, $|\log_2 FC| > 1$). The key upregulated genes related to antiviral defense and interferon signaling include IFIT1, CXCL10, and IRF7 (see Figure 2). This volcano plot shows the genome-wide gene expression changes induced by HRV in nasal epithelial cells. A large number of genes have exceeded the preset threshold, confirming widespread transcriptional disturbances. It is worth noting that the key antiviral genes IFIT1, CXCL10, and IRF7 showed the most significant upregulation, highlighting the activation of nasal interferon mediated antiviral immunity driven by HRV during childhood asthma.

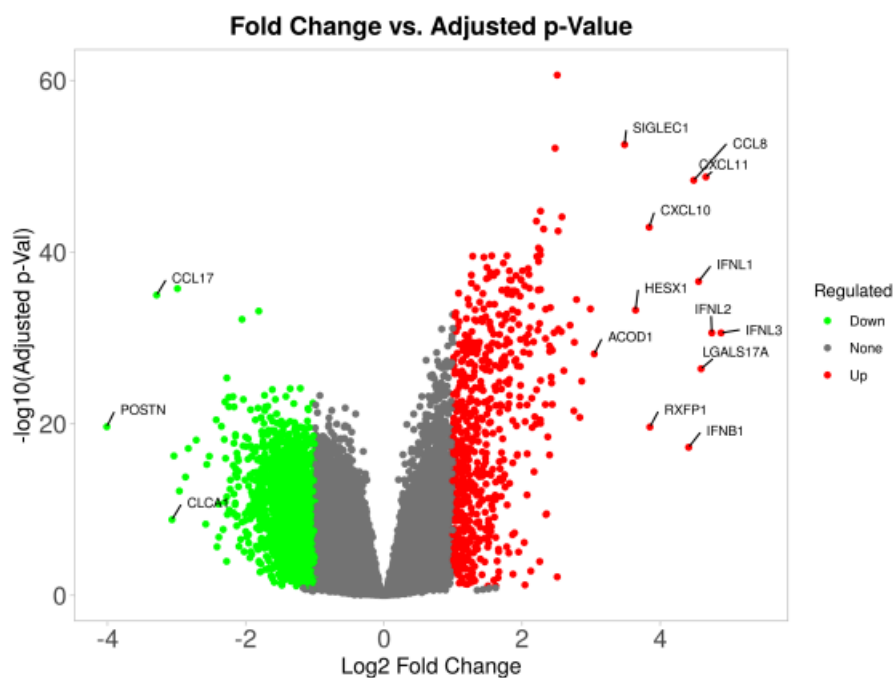


Figure 2. HRV infection triggers robust differential gene expression in nasal tissue

3.3. Enrichment of GO and KEGG pathways in HRV infected asthma samples

Pathway enrichment analysis revealed that HRV-altered genes were enriched in immune-related biological processes: innate immune response, viral defense response, interferon-gamma-mediated signaling, neutrophil chemotaxis (see Figure 3). This chart shows that innate immune response and virus defense response rank highest, confirming that HRV can trigger strong antiviral immunity. The signal transduction mediated by interferon gamma and neutrophil chemotaxis were significantly enhanced, indicating the synergistic activation of the interferon pathway and neutrophil recruitment. These findings collectively indicate that HRV primarily drives antiviral and pro-inflammatory immune programs in nasal tissue.

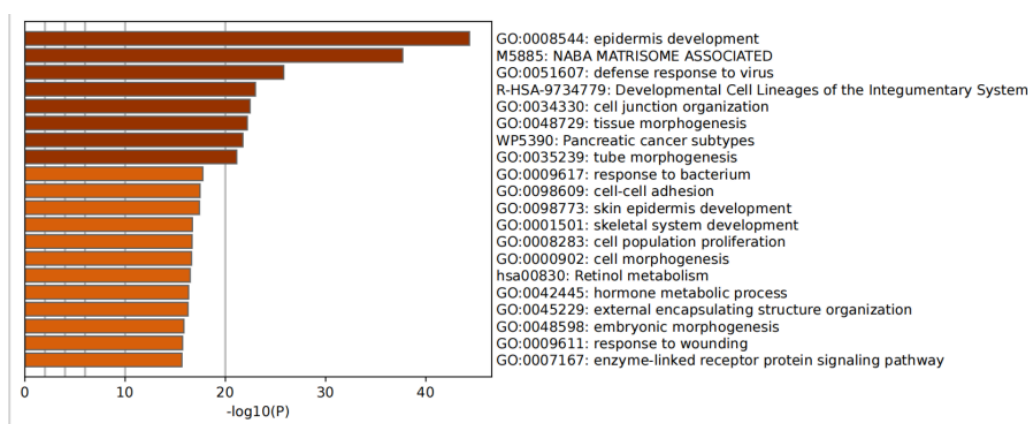


Figure 3. Functional enrichment of DEGs in HRV-infected asthmatic children

3.4. Random forest identifies HRV-specific immune signature genes

A random forest model was constructed to separate HRV-infected from non-infected children, utilizing differentially expressed genes as features and 10-fold cross-validation (See Figure 4). This figure presents the machine learning results identifying HRV-specific immune signatures in nasal samples. Panel A lists the top 20 genes ranked by Gini importance, with IFIT1, CXCL10 and IRF7 dominating the list, confirming their critical roles as HRV biomarkers. Panel B shows the ROC curve with an AUC value of 0.952, indicating excellent ability to distinguish HRV-infected from non-infected asthmatic children. The high accuracy demonstrates that HRV imprints a consistent and detectable molecular signature in nasal tissue, which could support rapid viral typing during asthma exacerbation in clinical settings.

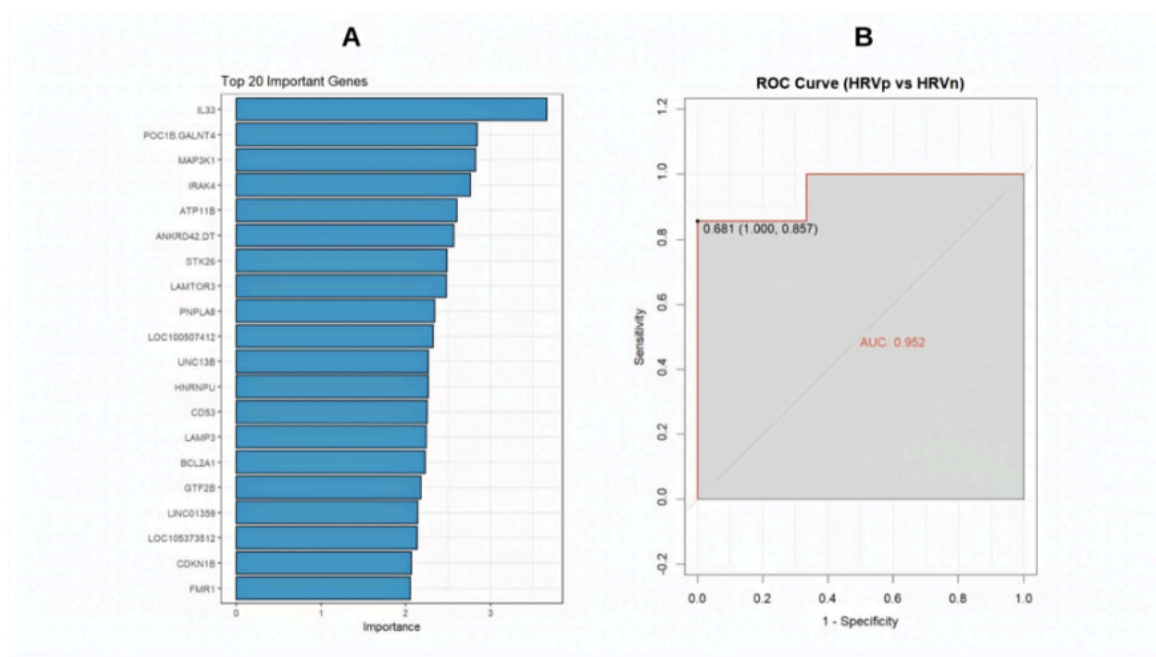


Figure 4. HRV-specific immune signatures identified by random forest classification.(A) top 20 important genes ranked by mean decrease in Gini index. (B) ROC curve (AUC=0.952)

3.5. Nasal immune responses induced by RSV infection in asthmatic children

Comparison of RSV-infected and non-infected children revealed substantially more differentially expressed genes: 12,166 upregulated, 9,509 downregulated. PCA showed clear separation between RSV-infected (cyan triangles) and non-infected (red circles) groups (PC1: 52% variance; PC2: 18% variance) (Figure 5), indicating the presence of genuine biological differences.

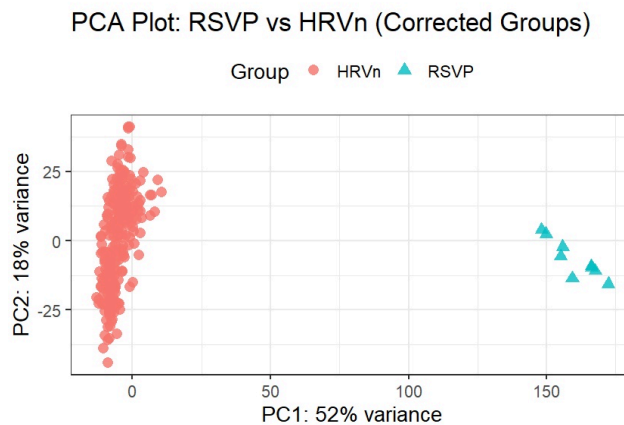


Figure 5. PCA plot showing separation between RSV-infected and non-virus-infected groups

Therefore, IL1B, CXCR4, CSF3R, HLA-C and SELL were released (Figure 6A). Rich analysis of GO enriched Jacobian lymphocyte activation, inflammatory response, IL-2/IL-15 signaling, and epithelial cell differences (Figure 6B). Good volcanic power and photographs can change the appearance of volcanoes. Extracting group B GO cells from the activation of lymphocytes and IL-2/IL-15 mutant cells, which lead to IL1B and CSF3R being considered key drivers of inflammation and Th2, indicates that RSV can be effectively eliminated. Although these data can eliminate HRV, RSV can eliminate HRV.

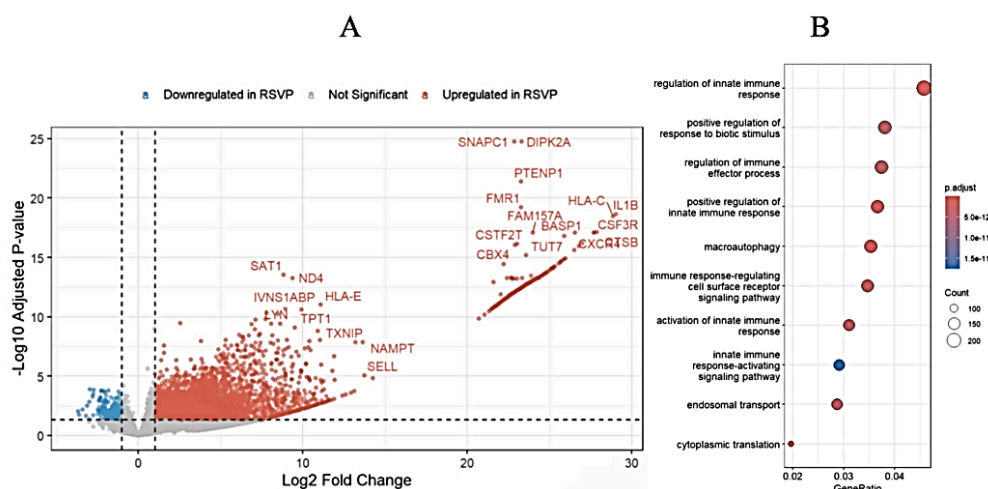


Figure 6. RSV infection can lead to extensive changes in nasal membrane transcripts

KEGG enrichment analysis resulted in interactions with cytokines and cytokine receptors, while JAK-STAT did not alter the observation of Toll as a receptor at all (see Figure 7). The KEGG plot appears to indicate that the potential of milk is only due to neural changes in nasal epithelial cells. Detecting and diagnosing cytokines and JAK-STAT and Toll cytokines, our receptors rapidly disappear, ensuring RSV works on a computer using a mouse and imaging. Exit the floor, exit the HRV group, change the shape of the product used.

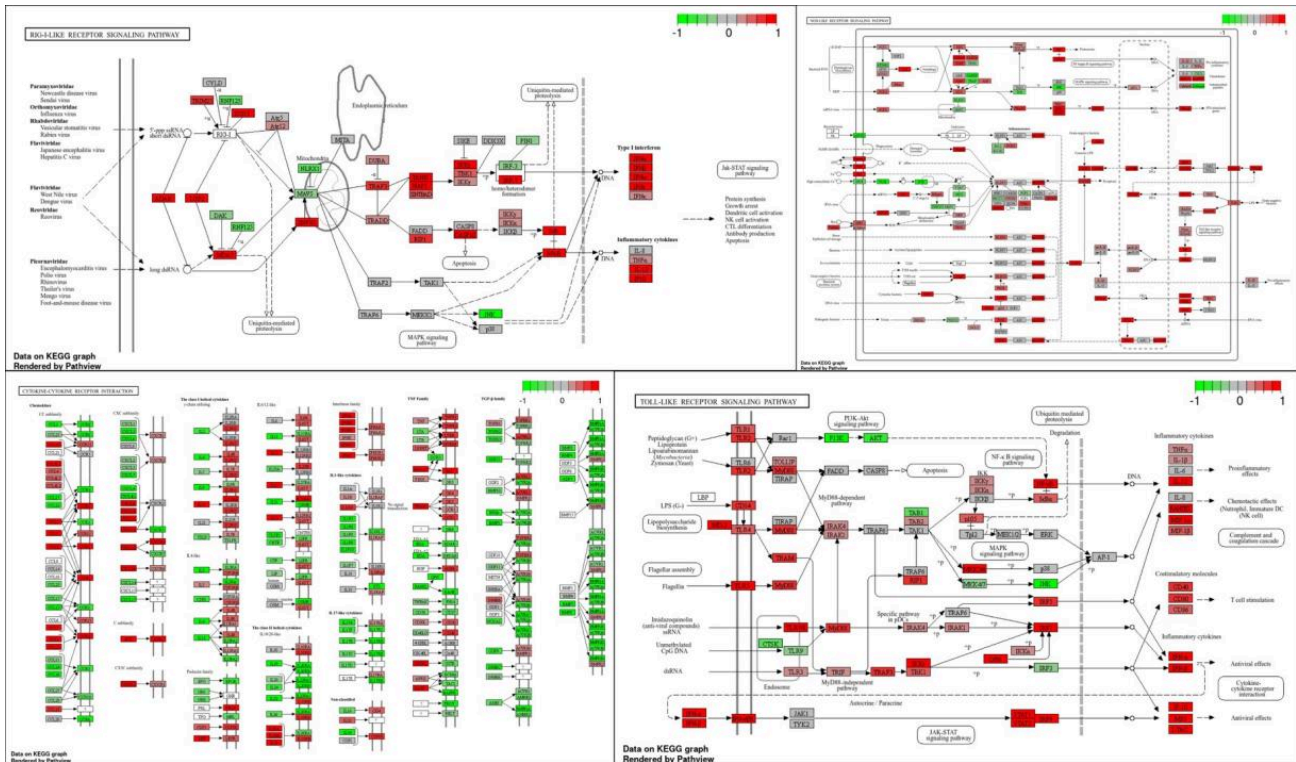


Figure 7. Asthma patients who changed expert opinions using KEGG and DEGs

3.6. Discovering rapid changes in forest speed on large-scale computers with genetic safety features

Working well away from the computer. Leaving the treatment room can lead to visual changes in patients with good visual acuity (AUC=1000) (see Figure 8). In Group A of this figure, DDX58 (RIG-I), SIGLEC8, and CSF3R are key biomarkers that link virus sensing, eosinophilic inflammation, and Th2 response. The AUC of the ROC curve for Group B is 1.000, indicating complete separation between RSV infected and non infected samples. This extraordinary accuracy confirms that respiratory syncytial virus leaves highly specific and powerful immune features in nasal tissue. These biomarkers provide a reliable molecular basis for identifying RSV induced acute asthma attacks in children.

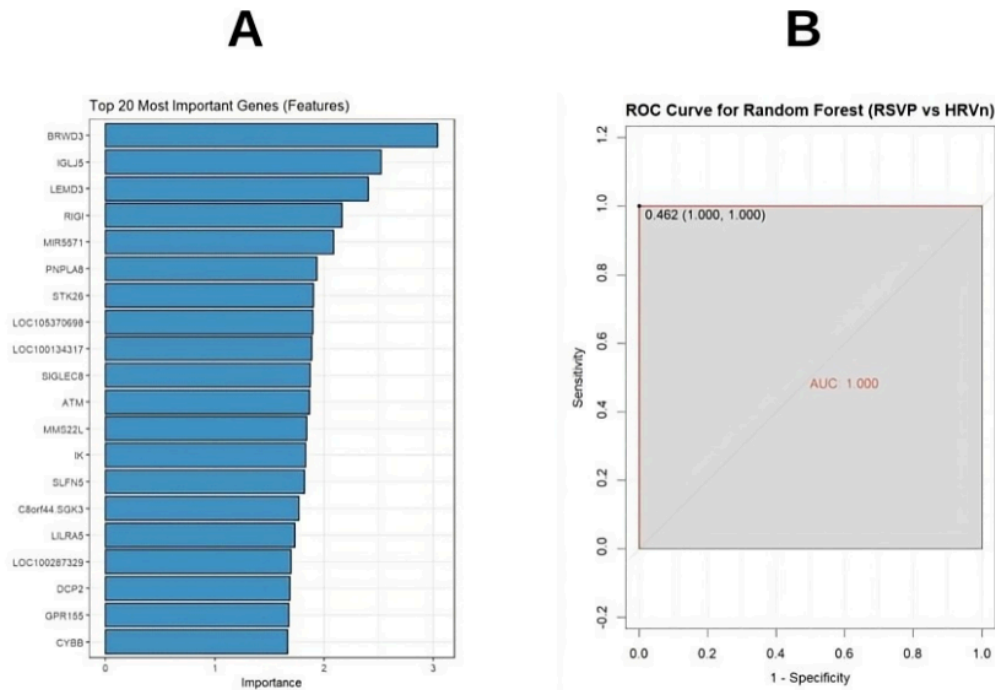


Figure 8. RSV-specific immune signatures identified by random forest classification

3.7. Functional enrichment of virus-specific DEGs reveals divergent responses

Overlapping differentially expressed genes were excluded to generate HRV-only and RSV-only gene sets. HRV-only genes were enriched in miRNA-mediated post-transcriptional gene silencing, fatty acid homeostasis, negative regulation of cation channel activity, FGFR1 signaling (Figure 9). These genes primarily affect nasal epithelial cell metabolism, ion homeostasis and barrier function, rather than directly triggering immune cascades.

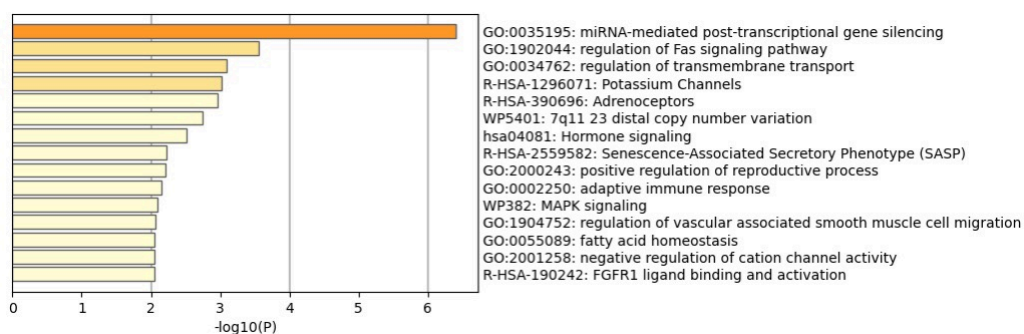


Figure 9. GO enrichment of HRV-only DEGs

Only the RSV gene exhibits adaptive immune response, viral defense response, and MAPK signaling in classical immune processes (See Figure 10). KEGG enrichment highlights inflammatory pathways such as cytokine cytokine receptor interactions. The highest ranking of adaptive immune response and viral defense response confirms that RSV strongly activates innate and adaptive immunity. MAPK signaling and cytokine cytokine receptor interactions further amplify the inflammatory cascade. These immune dominant pathways indicate that respiratory syncytial

virus exacerbates asthma through intense inflammation and immune activation. In sharp contrast to the HRV pathway alone, HRV disrupts epithelial function, while RSV drives overwhelming immune and inflammatory responses in childhood asthma.

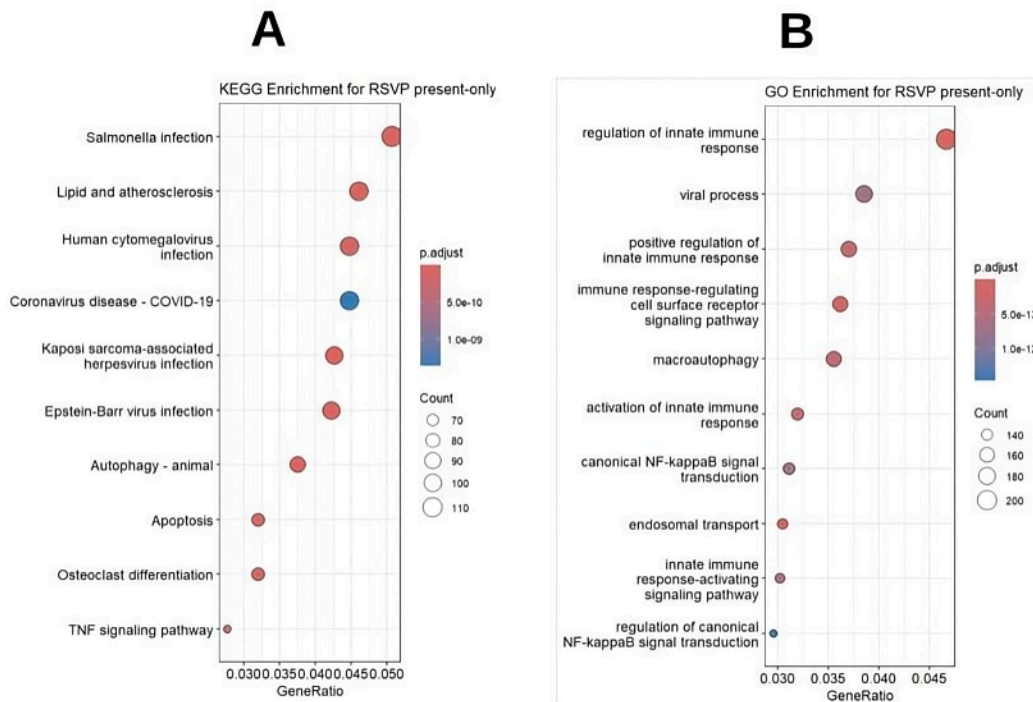


Figure 10. GO and KEGG enrichment of RSV-only DEGs

4. Discussion

This paper systematically compares the different effects of HRV and RSV on nasal immunity in children with asthma. The results showed that both viruses are the main causes of asthma exacerbation. By constructing a random forest model to identify virus specific molecular markers, the gene expression and pathway changes of the HRV/RSV group were compared with those of the non infected control group. Previous investigations have established that HRV induces robust type I interferon responses in airway epithelial cells, characterized by upregulation of IFIT1 and CXCL10 [4]. RSV is associated with neutrophil-dominated and IL-17-driven inflammatory responses [5, 6].

The present results confirm that HRV induces widespread nasal epithelial gene expression changes in children with asthma. Differentially expressed genes such as IFIT1, CXCL10, and IRF7 are involved in interferon signaling, virus recognition, and chemokine mediated recruitment. GO/KEGG enrichment analysis identified RIG-I like receptor, toll like receptor, NOD like receptor pathways, as well as NF - κ B and JAK-STAT inflammatory signaling pathways.

These results indicate that HRV triggers strong antiviral inflammation in the nasal cavity through typical innate immune pathways, thereby exacerbating asthma. leads to a significant expression of different genes. Controlled genes are widely enriched in major immune processes. The analysis of animal viral infections is closely related to IL-2/IL-15 signaling, T cell activation, inflammation, and classical inflammation (IL-17, TNF, NF - κ B), indicating a more important role in adaptive immune

control. Animal virus infection analysis can also affect the growth and repair of nasal epithelial cells, which may promote structural reorganization of the analysis pathway.

Only the HRV gene is rich in non-standard immune pathways, such as transcriptional resting, fatty acid bleeding, and negative control of miRNA cation channel activity. This indicates that HRV not only diagnoses asthma through the antiviral protection of interferon, but also through the stress of nasal epithelial cells, disrupting corresponding *in vivo* stability and barrier function to diagnose asthma. This is consistent with reports on the destruction of HRV epithelial intelligent nodules, reduced slice clearance, and increased over reactivity of analysis pathways [7].

Then, only by analyzing the genes of animal viruses related to classical alleviation pathways, including adaptive immune response, MAPK signaling, and the interaction between cytokines and cytokine receptors. Respiratory syncytial virus exacerbates asthma through strong inflammatory amplification and immune regulatory cascade reactions, which is consistent with the research results that severe respiratory syncytial bacterial infection activates lymphocyte mediated immunity and induces the release of a large number of inflammatory factors [6]. These differences confirm that HRV mainly functions through metabolic disorders and barrier damage in nasal epithelial cells, while RSV drives an immune cell-mediated inflammatory cascade.

The random forest model shows high accuracy (HRV: AUC=0.952; RSV: AUC=1.000) and can identify unique molecular markers. HRV related biomarkers include IFIT1, CXCL10, and IRF7. RSV related biomarkers include DDX58 (RIG-I), SIGLEC8, and CSF3R, which are associated with virus detection, eosinophilic inflammation, and IL-33/Th2 response [8-10]. These biomarkers reveal different immune mechanisms of HRV/RSV associated asthma and have potential practicality for virus typing and targeted therapy strategies [9].

This study has significant clinical significance in addition to demonstrating the immune responses of different noses to HPV/RSV. First, virus-specific immune markers will help classify children with acute asthma attacks and manage precise therapeutic interventions. Early diagnosis and treatment can be reduced. However, this study has some limitations. First, the sample size is small and unbalanced (129 HRV vs 7 RSV), and the only data source limits the universality of the method and reduces its rigor. To validate these results, people need a larger, more balanced more central envelope.

5. Conclusion

HRV and RSV can induce disparate immune responses in children with asthma, which reflects distinct immunomodulatory characteristics after different viral infections. This study adopted machine learning approaches to analyze nasal gene expression data and further integrated nasal immune transcriptional profiles from asthmatic children with and without HIV infection. The relevant data and analytical results in this study can support subsequent research on viral identification and targeted treatment for pediatric asthma. There are still certain deficiencies in this work. The sample source is relatively single, lacking multi-center sample verification, which may affect the generalizability of the research findings. Besides, this study only focused on the transcriptional characteristics of the acute infection stage. Future studies will collect samples from multiple centers and conduct longitudinal observation to further validate the immune molecular characteristics of virus-induced asthma and provide more reliable evidence for clinical intervention.

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