TRANSCRIPTIONAL PROFILING OF HOST CELL RESPONSE TO VIRAL RESPIRATORY TRACT INFECTIONS

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INTRODUCTION.

Respiratory syncytial virus (RSV) is one of the most important causes of lower respiratory tract infections in young children and neonates. According to WHO estimates, approximately 64 million human RSV infections cases and 160,000 deaths occur each year. More than 25% of infected infants develop bronchiolitis or pneumonia [1]. There is no RSV vaccine and specific antiviral drugs are limited. Lipid raft microdomains play an important role in RSV maturation process [2] but the dynamics of host-cell interactions and pathway cross-talk associated with RSV-mediated modifications [3] is poorly understood.

MATERIALS AND METHODS.

Relevant host genes that are activated or repressed by RSV in the immediate early phase of infection were delineated using temporal gene expression profiling that covered time points starting 24h after infection. HG-U133 Plus 2 time course results were analyzed using R/Bioconductor package [4] using one-way ANOVA clustering ward method and DAVID [5].

RESULTS AND DISCUSSION.

Clustering resulted in 1,447 genes that were two-fold or greater up/down-regulated in response to RSV infection after 4, 8, 12 and 15 h. Genes involved in sterol, steroid, cholesterol metabolic/biosynthetic processes (Fig. 1) and nuclear envelope-endoplasmic reticulum network were enriched among a cluster of 185 genes with temporally increased expression levels at 4–8 h that decreased again 12h post infection. The results indicate a RSV-modulated convergence of lipid metabolism, changes in lipid raft microdomains, chaperones and the actin network.

CONCLUSIONS.

The development of therapeutic strategies aiming to prevent RSV replication and/or virus particle formation by lipid raft interfering or chaperone targeting drugs require further studies to fully uncover the molecular mechanisms of cell-RSV interactions.

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REFERENCES.

1. Shane S (2010). Respiratory syncytial virus market. *Nat Rev Drug Discov*. 9(1):15-16.
2. Yeo DS, *et al.* (2009). Evidence that selective changes in the lipid composition of raft-membranes occur during respiratory syncytial virus infection. Virology 386(1):168-182.
3. Gentleman RC, *et al.* (2004). Bioconductor: open software development for computational biology and bioinformatics. Genome Biol. 5(10):R80.
4. Huang DW, *et al.* (2009). Bioinformatics enrichment tools: paths toward the comprehensive functional analysis of large gene lists. Nucleic Acids Res. 37(1):1-13.

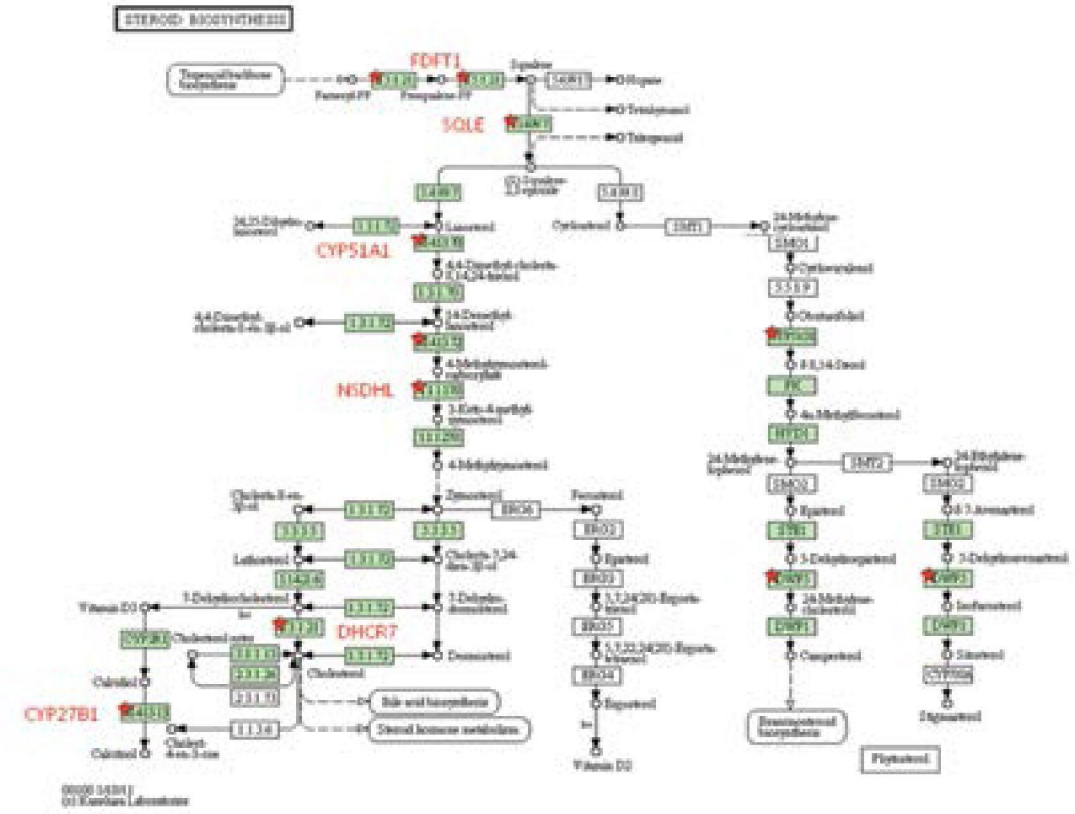

Figure 1. *Increased expression levels of genes involved in steroid biosynthesis (P-value 2.7E-7 Benjamini 1.5E-4) between 4 and 8 h that decrease again 12h after RSV infection. Their gene products are indicated by red asterisks in the KEGG steroid biosynthesis pathway.*