

Transcriptomic studies of rainbow trout strains with different susceptibility to viral hemorrhagic septicemia virus provide insight into immunological pathways linked to resistance.

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Introduction

- Viral haemorrhagic septicaemia virus (VHSV) is a highly contagious pathogen affecting salmonid fish populations
- Recent evidence suggests that host genetics play a key role in susceptibility to the virus, with differences in innate antiviral immune responses underlying VHSV resistance in rainbow trout strains
- **The aim of the present study was to investigate gene expression signatures in a VHSV-resistant local German rainbow trout strain (R7) under VHSV infection and to compare them with expression signatures in a highly susceptible commercial strain (R9)**

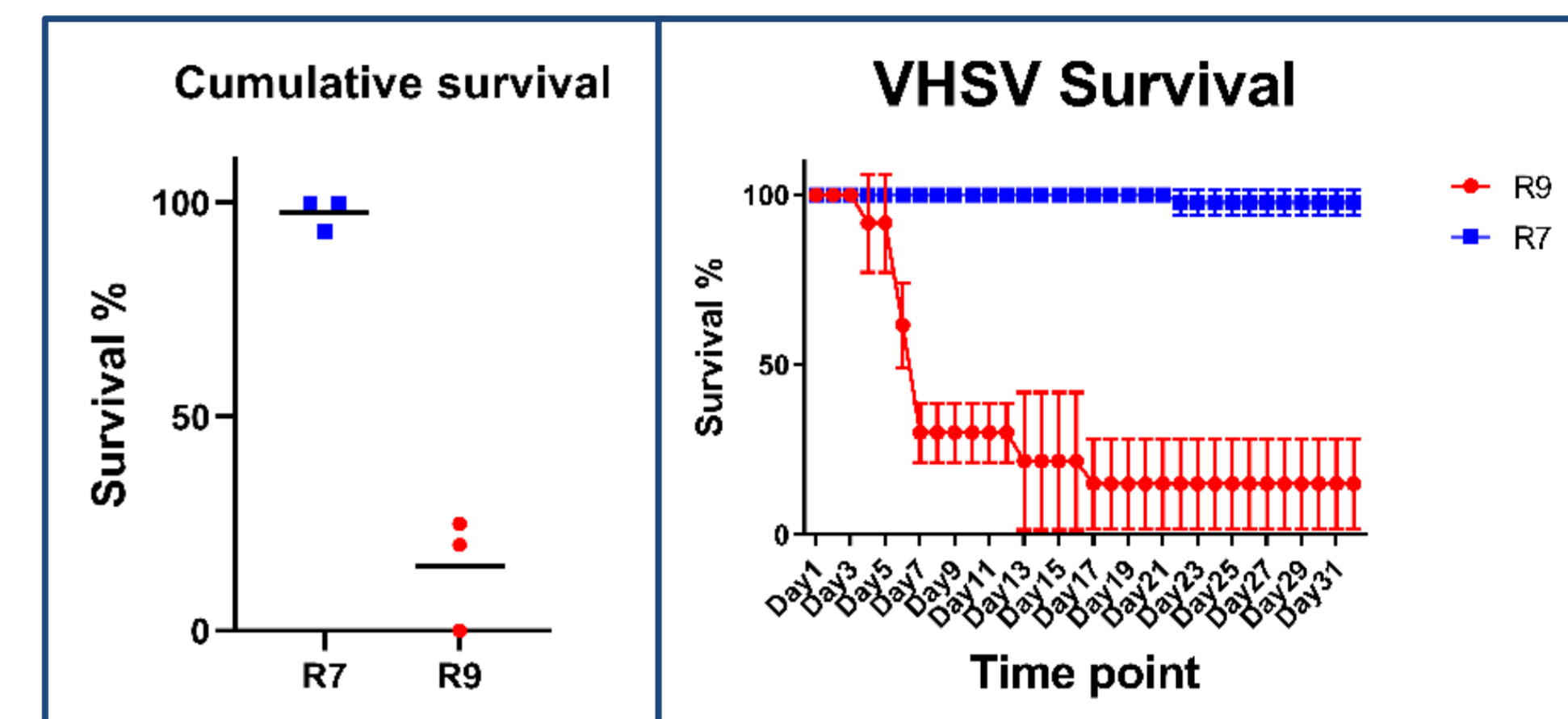


Figure 1: Dot plots showing survival rates from the infection experiment of rainbow trout strains R7 (resistant) and R9 (susceptible) in percent.

Material and Methods

- Fin, gill, gut, kidney and spleen tissues were collected from susceptible and resistant adult rainbow trout at 2 and 4 days post infection with VHSV isolate 07-71
- RNA-seq was performed from kidney samples at 2 dpi
- In addition, gene expression of 27 selected genes was determined by RT-qPCR in all samples collected
- The results were compared with gene expression in primary cell cultures from fins, scales and kidneys of fish of the same strains infected with native and inactivated virus

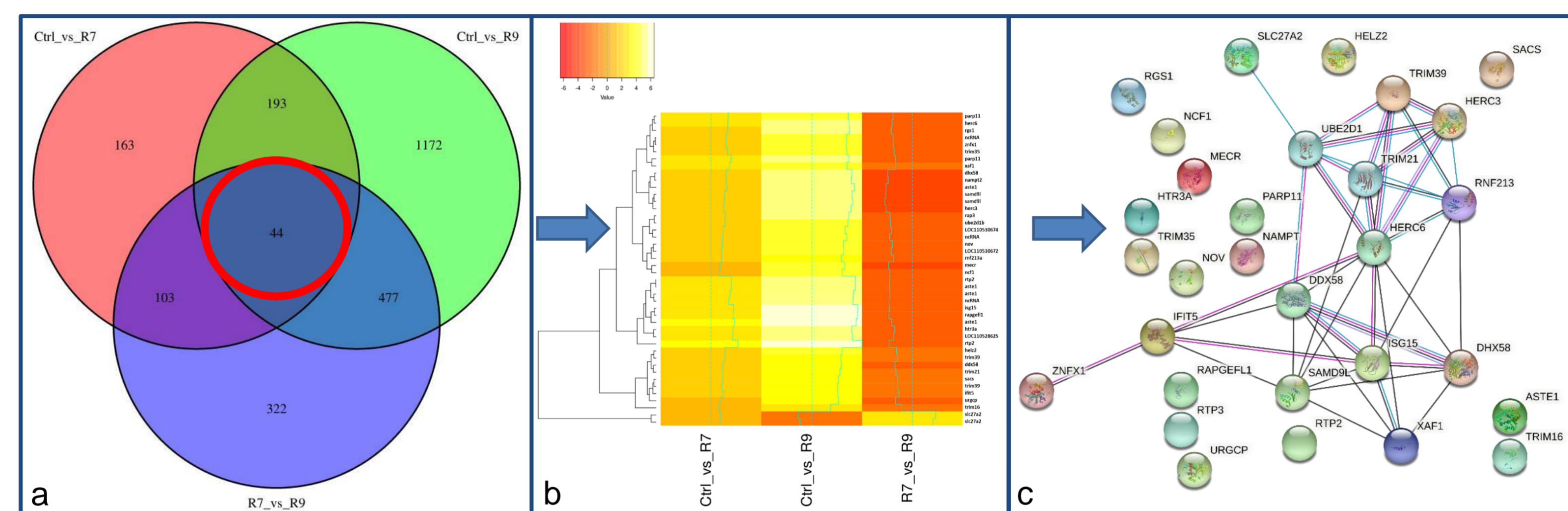


Figure 2: Venn-diagram of the differentially expressed genes in controls and R7 & R9 origin (a); heatmap of the 30 most highly expressed genes in each of the kidneys (b); protein-protein interaction network of the 30 most highly expressed genes (c).

Results

VHSV-N-Protein:

- Detection of VHSV in all five tissues (Figure 3a)
- Highest viral load in spleen 4 dpi in the susceptible strain (R9)
- Lowest viral load in gills 2 dpi in the resistant strain (R7)

Gene expression:

- Genes involved in the interferon response of rainbow trout showed clear differences in gene expression levels between the two origins (Figure 3b-e)
- Especially on day 2 after infection with VHSV, a large number of genes differed significantly ($p < 0.05$), especially in spleen and kidney
- Particularly striking were the gene expressions of pro-inflammatory cytokines and type II interferons
- While gene expression in tissues of resistant origin increased steadily over the observation period, there was a rapid increase (day 2) followed by a decrease in gene expression (day 4) in samples of susceptible origin
- Additionally, the performed *in vitro* experiments confirmed the *in vivo* results that VHSV induces a stronger immune response in cells derived from the R9 strain

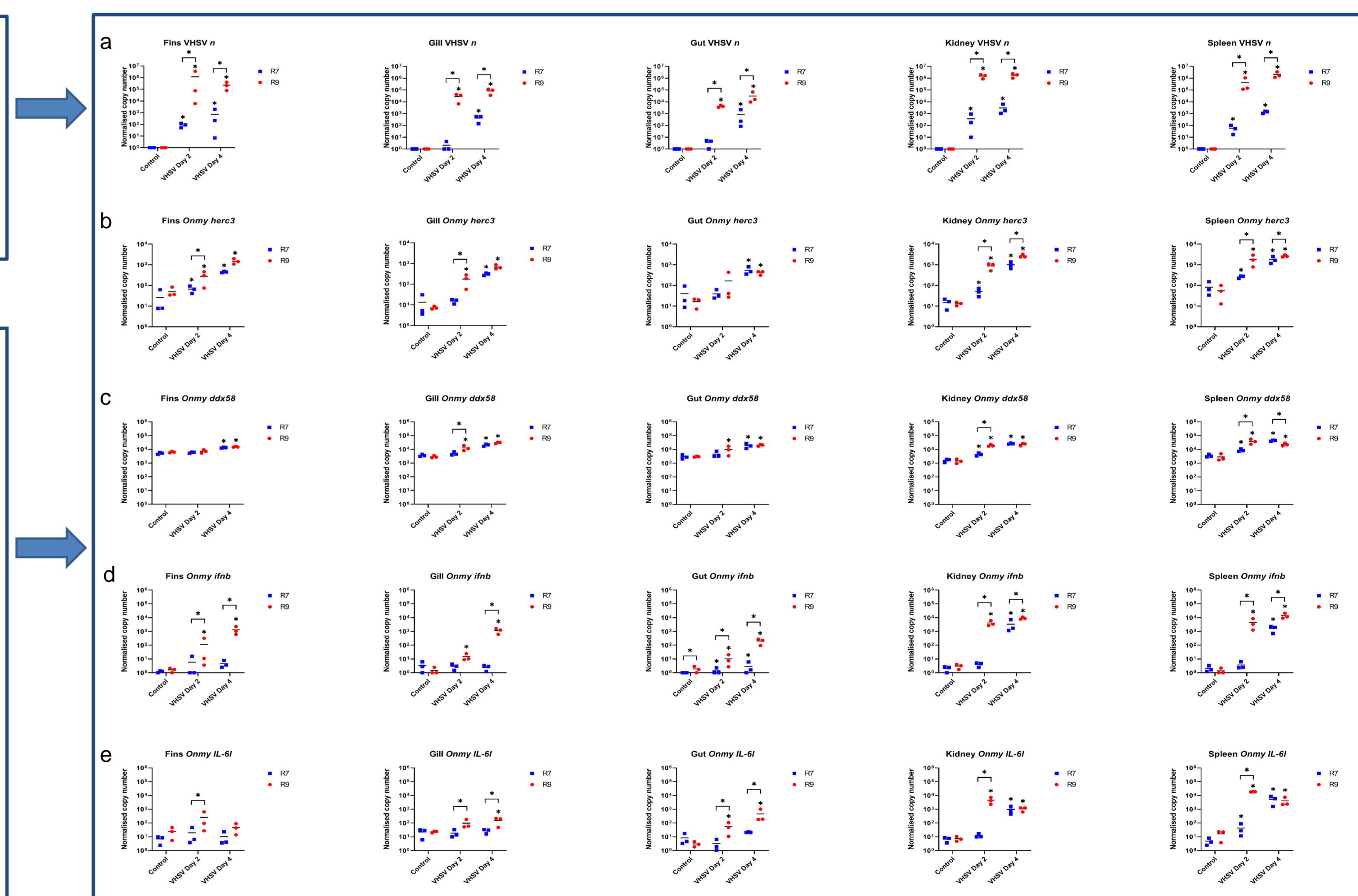


Figure 3: Expression of VHSV-N-Protein as an indicator for the viral load in tissues (a); expression of the mRNA encoding the genes *herc3* (b), *ddx58* (c), *irfb* (d) and *il-6l* (e).

Conclusion

- Explanation of the resistance? - Unfortunately, No!
 - Protein-protein interaction network of the only genes regulated in the R7 strain (Figure 4)
 - Random selection of genes
 - No correlation or signaling pathway identifiable
- Death as a result of a dysregulated inflammatory response and a cytokine storm in trout of the R9 strain (Figure 5)

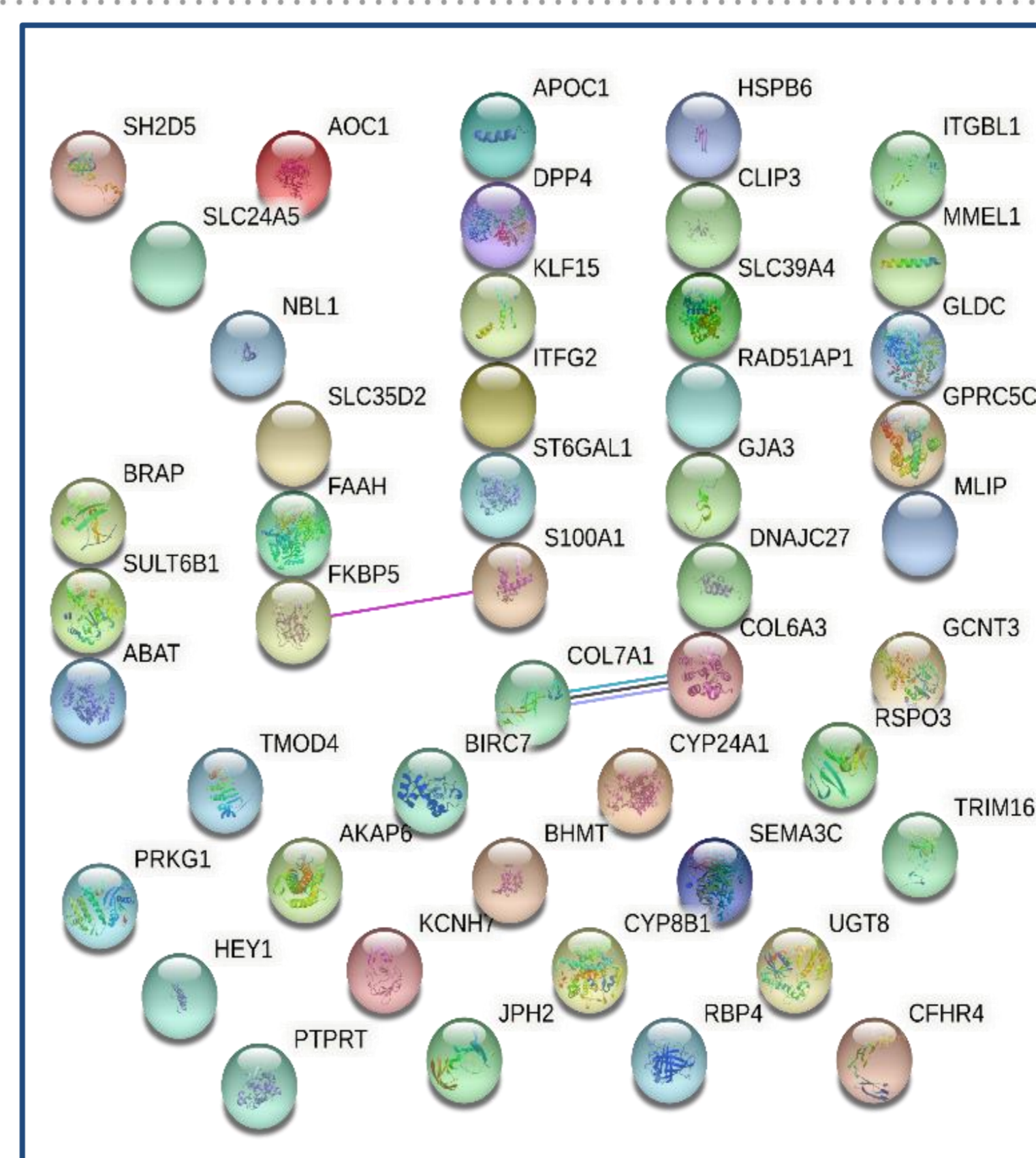


Figure 4: Protein-protein interaction network of the only genes regulated in the resistant strain.

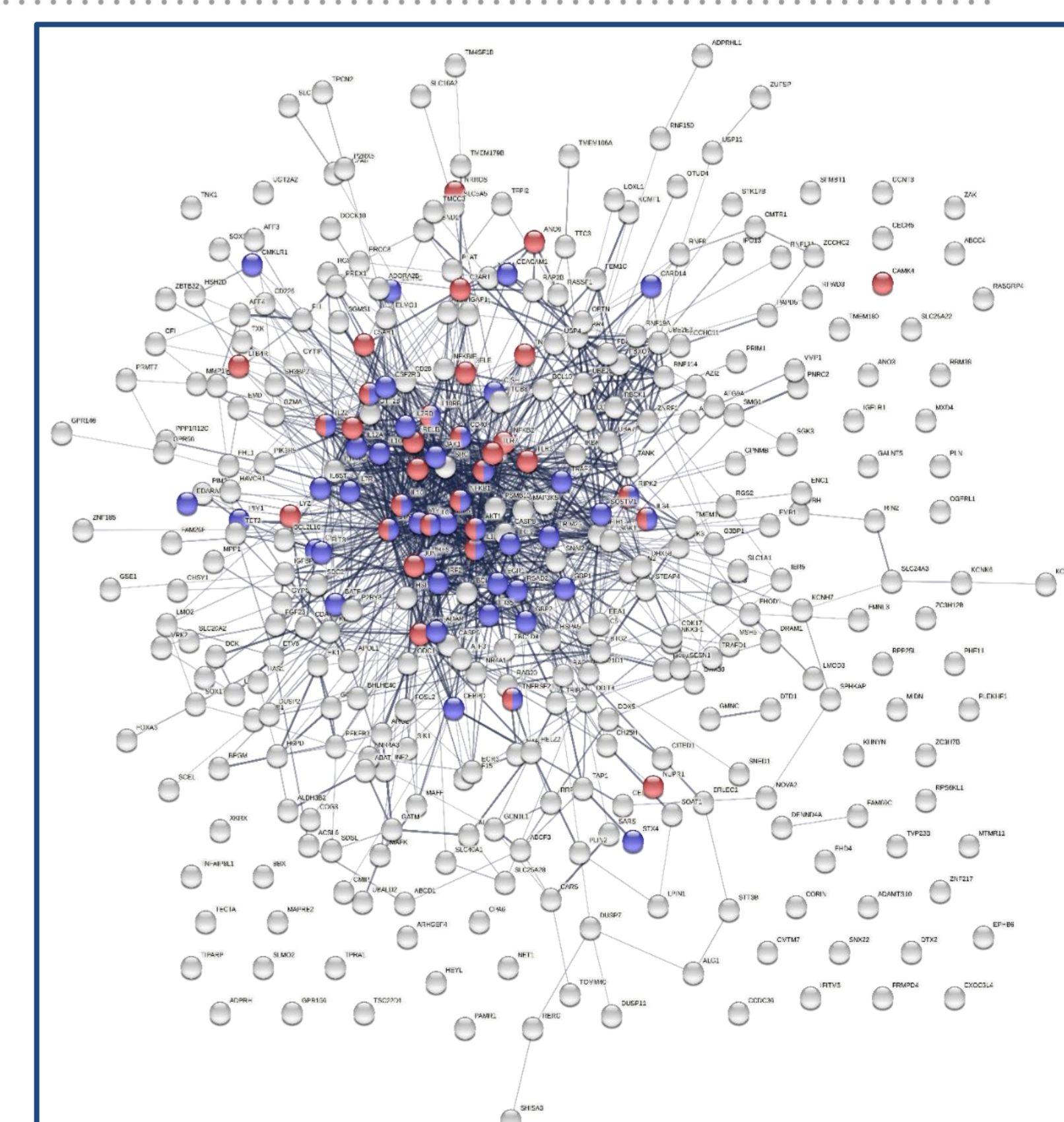


Figure 5: Protein-protein interaction network of only regulated genes that cause inflammation and/or act as cytokines.

Acknowledgement

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