IMPACT ON THE EXPRESSION PROFILE OF TRANSCRIPT ISOFORMS IN MICE HEARTS INFECTED WITH TWO STRAINS OF *TRYPANOSOMA CRUZI*

Nayara Evelin de Toledo[1], Raphael Tavares da Silva[1], Tiago Bruno Rezende de Castro[1], Stellamaris Soares[1], Carlos Renato Machado[1], Andréa Mara Macedo[1], Eric Chiari[2], Glória Regina Franco[1]

[1]*Laboratório de Genética Bioquímica, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Brazil*

[2]*Departamento de Parasitologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Brazil*

INTRODUCTION

Since the description of Chagas disease, caused by the protozoan parasite *Trypanosoma cruzi*, the reasons for its different clinical manifestations have yet to be completely revealed. The aim of the present study is to quantify differential alternative splicing, as well as to identify differentially expressed transcript isoforms from RNA-Seq data of mice hearts infected with two strains of *Trypanosoma cruzi*. We investigated whether different strains of the parasite are remodeling the splicing pattern of the host during the acute phase of infection and if this remodeling is relevant for disease development.

METHODS

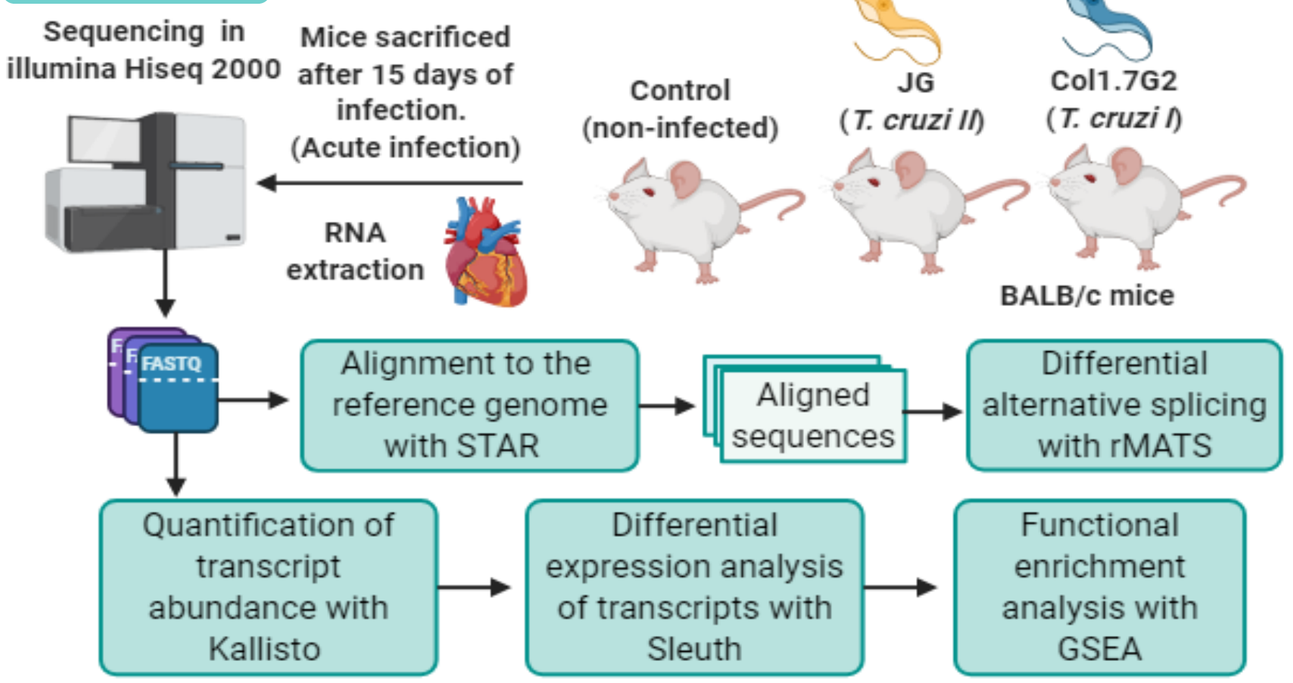

Figure 1: Experimental design. Three Balb/c mice groups containing three independent biological replicates were used in our study. The first group was infected with Col1.7G2, the second with JG and the third group served as a control. After 15 days of infection, each group were sacrificed and heart transcriptomes were sequenced. **Differential isoform expression analysis and alternative splicing analysis.** Alignment to the mouse reference genome with STAR. Detection of alternative splicing events with rMATS. Quantification of transcript abundance with Kallisto. Differential expression analysis of transcripts with Sleuth.

RESULTS

By comparing Col1.7G2 infected mice with the control group, we identified 543 upregulated and 51 downregulated transcripts. By comparing JG with the control group, we identified 256 upregulated and 645 downregulated transcripts. The protein coding transcripts represented the largest group and the non-coding transcripts, the smallest. Despite the greater number of protein coding biotypes, many non-coding transcripts from protein coding genes were found (Table 1). Increase in splicing events were observed, including a rise in the number of skipping exons, retained introns and usage of alternate 5' and 3' splice sites.

Table 1: Biotypes of the differentially expressed transcripts

Col1.7G2-Infect. vs Control

Transcript biotype	Upreg.	Downreg.
Protein coding	472	46
Intron retention	22	2
Nonsense med. decay	9	0
Processed transcript	8	0
Others	32	1

JG-Infect. vs Control

Transcript biotype	Upreg.	Downreg.
Protein coding	214	567
Intron retention	10	13
Nonsense med. decay	5	13
Processed transcript	3	13
Others	27	37

Functional enrichment analysis

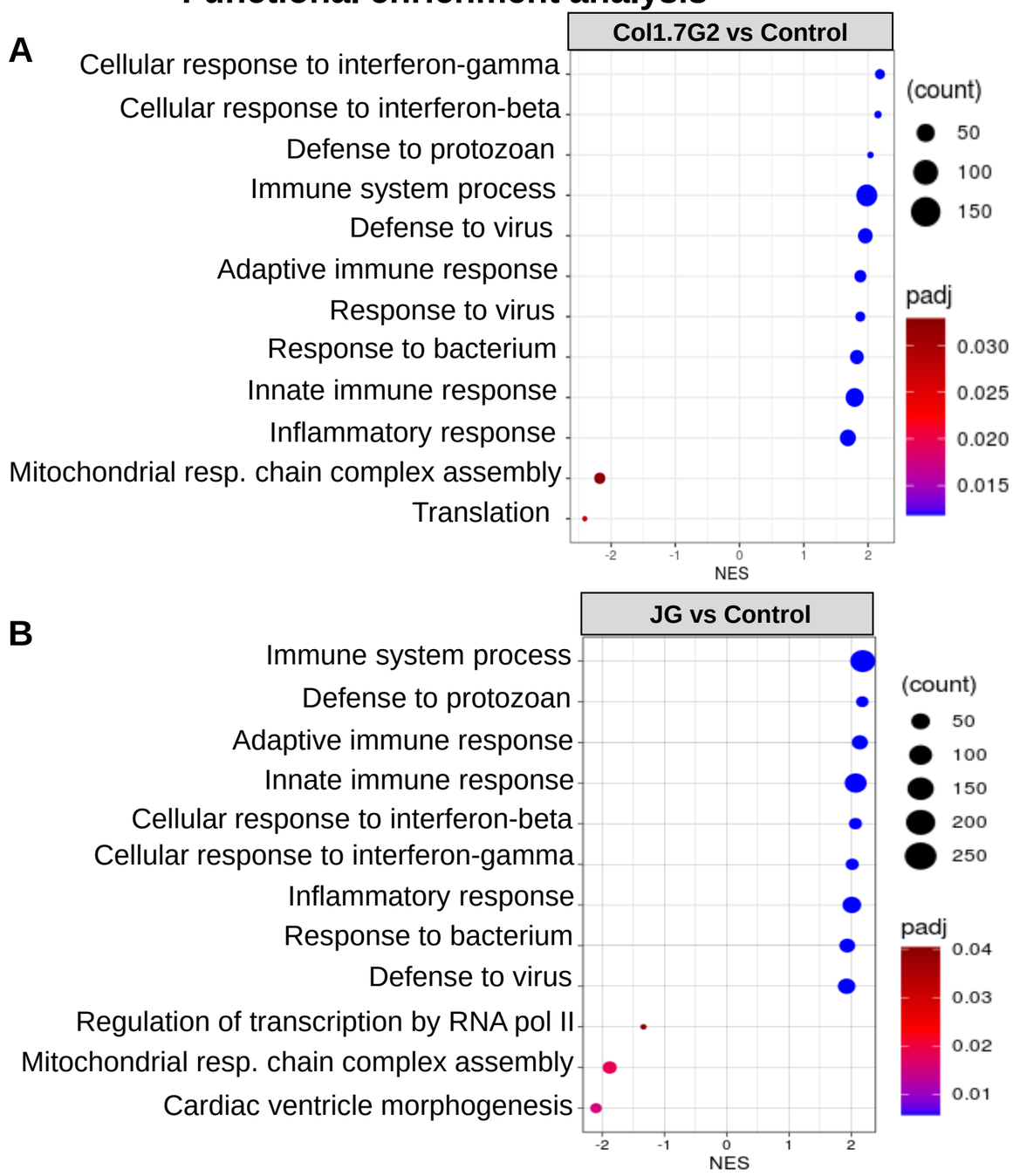

Figure 2: Enriched biological processes. (A) Col1.7G2 and **(B)** JG groups compared with the control group. **NES:** Normalized enrichment scores.

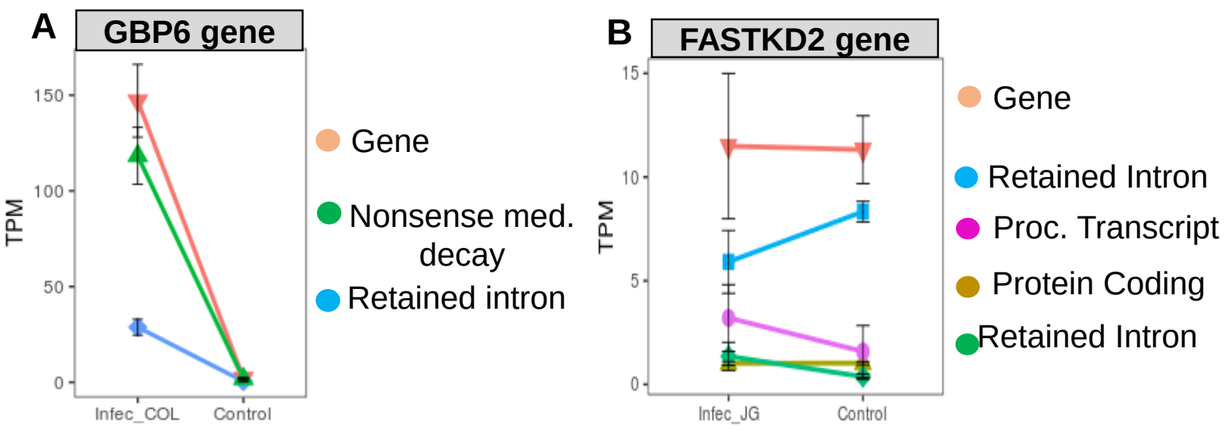

Figure 3: Profile plots. Differential expression of transcript biotypes from protein coding genes**. A.** GBP6 (guanylate binding protein 6- immune response) gene. **B.** FASTKD2 (FAST kinase domains 2-translation) gene.

CONCLUSION

T. cruzi strains can affect the expression levels of different coding and non-coding transcripts of the host and this may be relevant for disease development. Our future steps include the correlation of transcript expression and proteins identified in mass spectrometry data.

ACKNOWLEDGMENT