



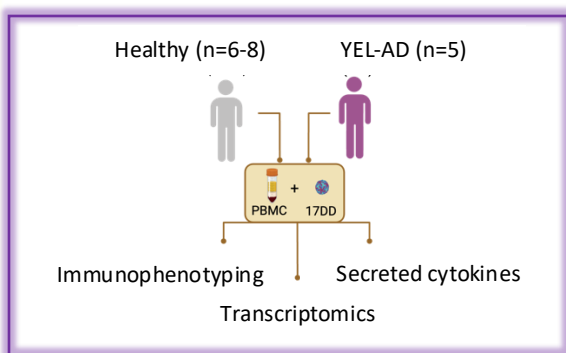
Functional repercussions of type I interferon innate errors in severe adverse events after yellow fever vaccination

Andrea Marques Vieira da Silva^{1*}, Tamiris Azamor^{1*}, Felipe Soares Coelho¹, Lorena Carvalho Rosa¹, Juliana Gil Melgaço¹, Luciana Neves Tubarão¹, Daniela Prado Cunha², Bruna N. S. Agonigi², Camila Dias de Almeida¹, Renata Saraiva Pedro¹, Patrícia Mouta Nunes de Oliveira¹, Maria de Lourdes de Sousa Maia¹, Zilton Vasconcelos², Ana Paula Dinis Ano Bom¹ ¹Instituto de Tecnologia em Imunobiológicos-Bio-Manguinhos. Fiocruz. Brazil. ²Instituto Nacional de Saúde da Mulher, da Criança e do Adolescente Fernandes Figueira. Fiocruz. Brazil. *Authors contributed equally.

Introduction

- Yellow fever vaccine is a gold standard for safety
- Rare vaccine-associated neurotropic or viscerotropic disease
- Participants present Innate immune errors in type I IFN pathway

Methods



Results

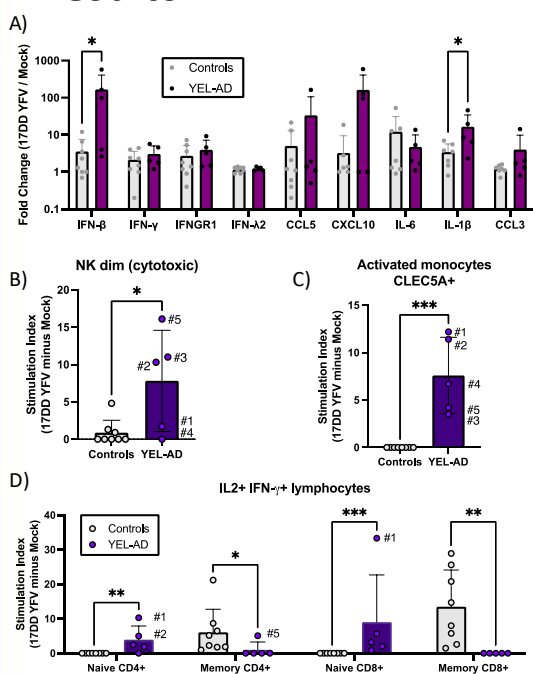


Figure 1. 17DD specific response in PBMC from YEL-ADV cases. The PBMC from healthy controls (n=8) and YEL-ADV cases (n=5) were stimulated *in vitro* with purified 17DD MOI 1 for 48h (A) Fold change (stimulated/mock) of cytokines secreted in the supernatant of Peripheral Blood Mononucleated Cells (PBMCs). (B-D) Immunophenotyping showing 17DD specific response - stimulation index (frequency of cell population in 17DD condition minus mock condition). (B) Activated monocytes CLEC5A+ (CD16+ HLA-DR+ CLEC5A+), (C) NK dim (CD56^{dim} CD16+), and (D) Lymphocytes producing IL2 and IFN-γ: Naive CD4+ (CD3+ CD4+ CD45RA+ CCR7+); Memory CD4+ (CD3+ CD4+ CD45RA-); Naive CD8+ (CD3+ CD8+ CD45RA+ CCR7+) and Memory CD8+ (CD3+ CD8+ CD45RA-). Comparisons using Mann-Whitney test. P-values *** ≤ 0.005 ** ≤ 0.01, and * ≤ 0.05.

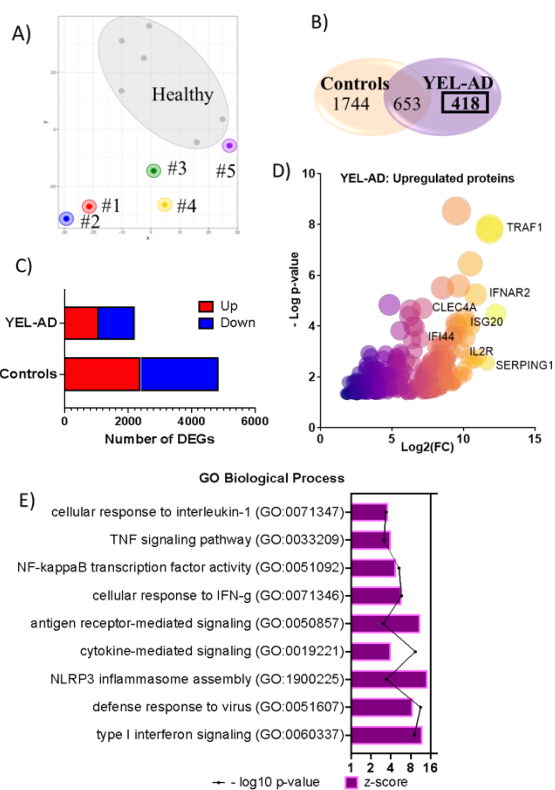
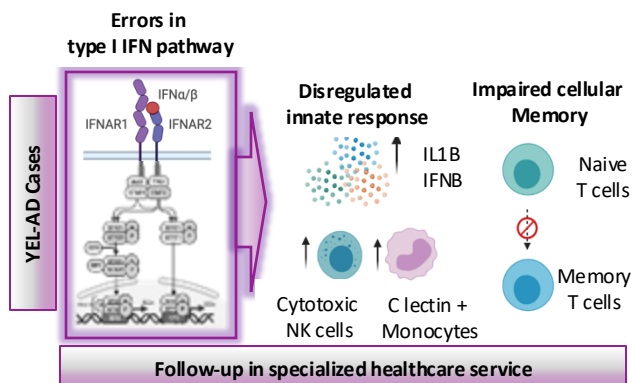


Figure 2. Transcriptomic profile of YEL-AD responses to 17DD. (A) tSNE plot of global transcriptomics for healthy and YEL-AD cases after 17DD stimulation. (B) Number of up and downregulated Differentially Expressed Genes (DEGs). (C) Quantitative comparison of the number of upregulated DEGs in Venn diagrams of YEL-AD group compared to healthy. (D) Bubble plot and (E) Gene Ontology (GO) biological process enrichment analysis considering gene upregulated exclusively in the YEL-AD group. (E)

Conclusions



Perspectives

- Development of therapeutic strategies and alternative vaccines;
- Reduction of vaccine hesitancy by fighting against misinformation