

Sex-specific modulation of the host transcriptome in the spleen of *Schistosoma mansoni* infected mice

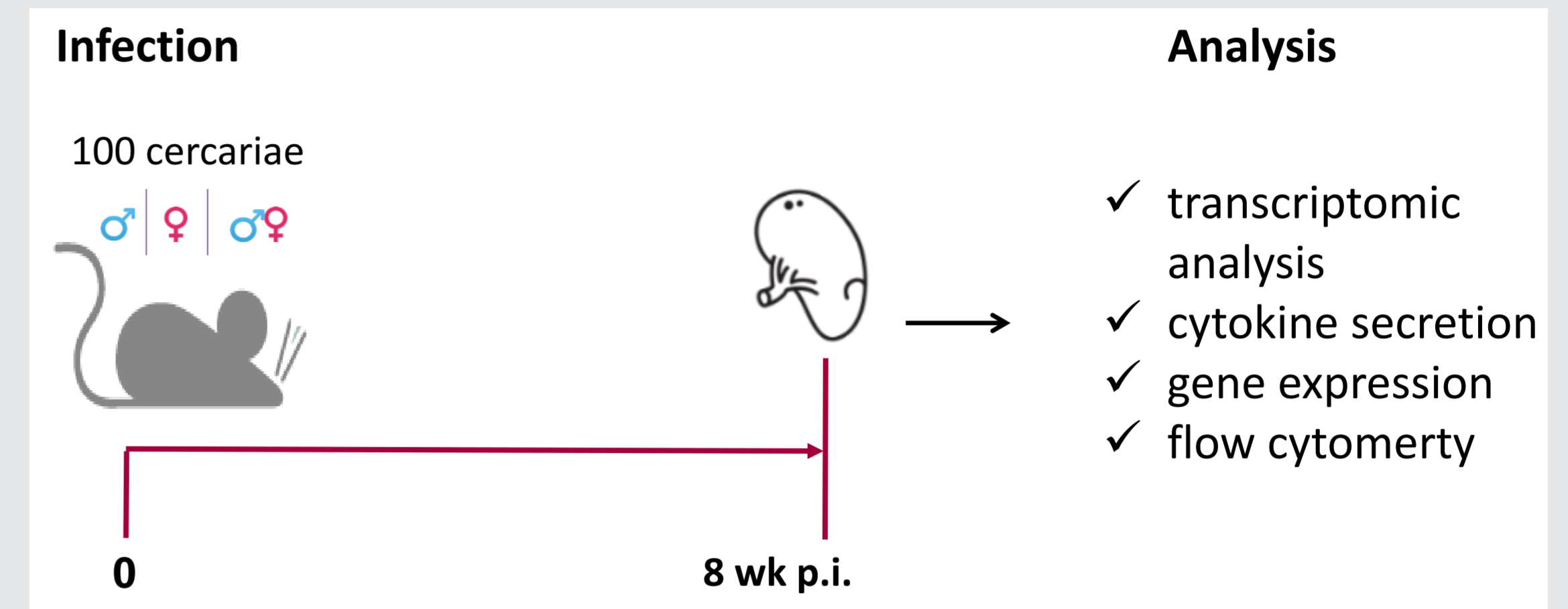
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Introduction

Intestinal schistosomiasis, caused by the helminth parasite *Schistosoma mansoni*, results in hepatosplenic disease triggered by parasite eggs trapped in the liver. Beside the egg antigens, antigens of gonochoric adult worms circulate in the blood of the host. We have recently reported on effects of unisexual infection differentially affecting the host immune system (). However, there are limited data on the sex-specific immunogenic potential. To shed more light on the underlied mechanisms of differential immunogenicity of female and male worms, we performed comparative transcriptomic and flow cytometric analyses of spleen tissue from unisexually and bisexually infected mice and examined the immunostimulatory capacity of worm antigens *in vitro*.

Mouse Model



Statistics: Values are expressed as mean ± SEM. Differences between groups were analysed by Kruskal-Wallis test followed by a Dunn's correction, p values < 0.05 were considered statistically significant. * p < 0.05, ** p < 0.01, *** p < 0.001. Differentially expressed genes (DEG) were identified using filter parameters, fold-change > 2 or < -2, LIMMA p values < 0.05, and FDR q values < 0.05

Results

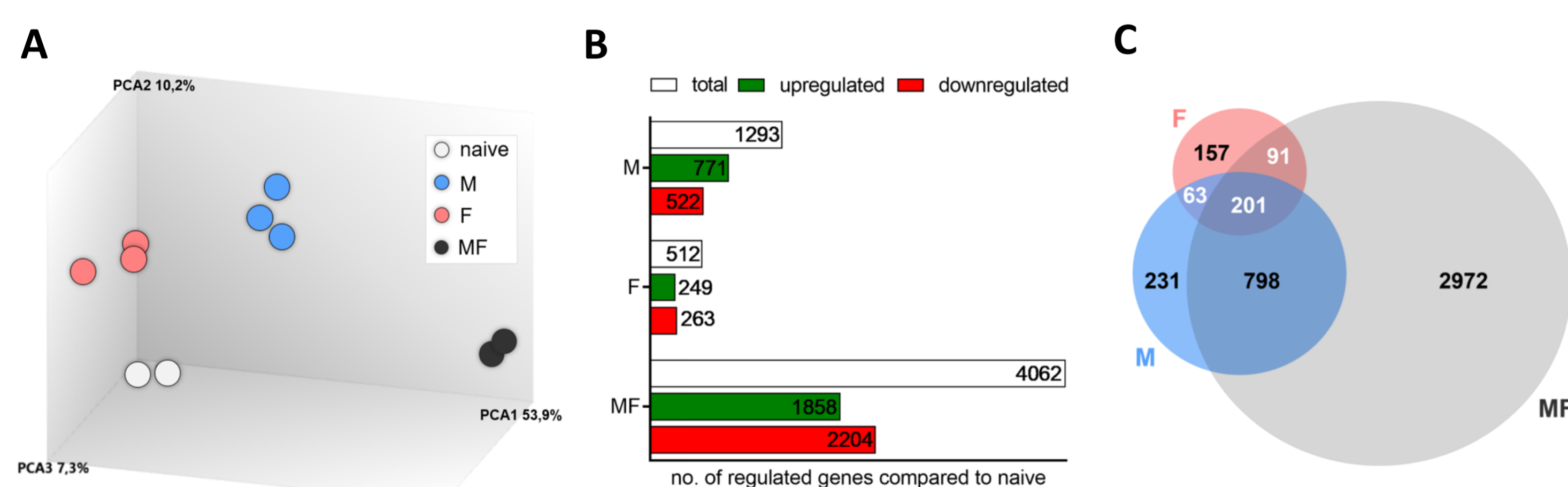


Figure 1: Male schistosomes and pairs regulate a higher number of genes than female schistosomes. Transcriptomic analysis of spleens reveal different gene expression profiles after infection with *Schistosoma mansoni*. (A) Principal Component Analysis, (B) bar chart and (C) Venn diagram represent an overview of transcriptomic analyses of spleens (n=2-3).

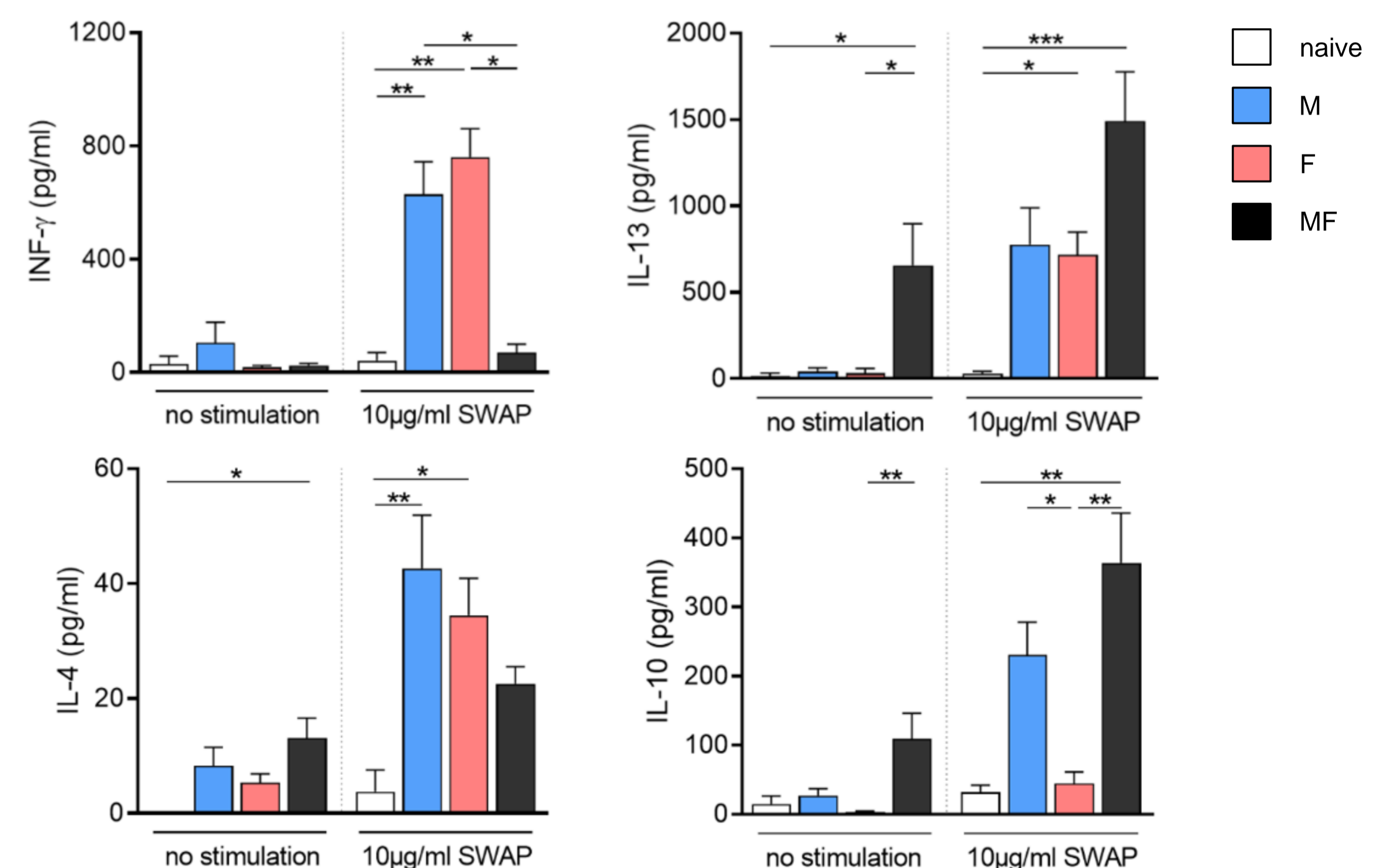


Figure 3: Male and female schistosomes enhance secretion of Th-1 cytokines by splenocytes. Splenocytes were isolated and stimulated with 10 µg/ml soluble worm antigen preparation (SWAP). Supernatants were collected after 72 h and amounts of INF-γ, IL-13, IL-4 and IL-10 were quantified using ELISA (n=5-8).

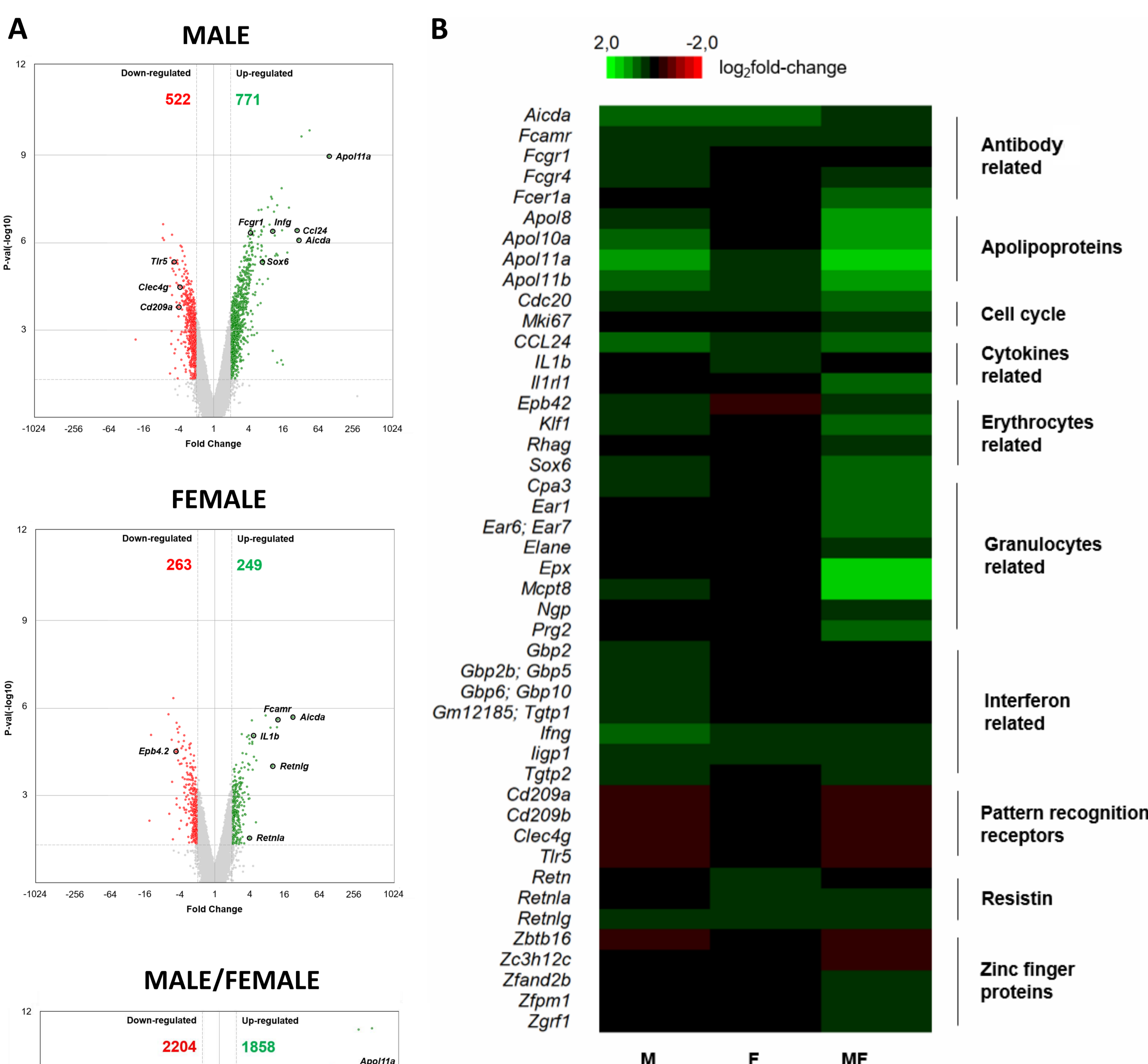


Figure 2: Females schistosomes express less genes involved in biological processes.

(A) The volcano plots showing gene expression (fold change) plotted against the significance level (negative log₁₀ p-value) and show significantly (p < 0.05) increased (green) and decreased (red) genes in the spleen. (B) Heatmap of genes in splenic tissue of infected (M, F, MF) compared to control (naive) mice (n=2-3). The color scale on the top illustrates the log₂ fold-change values shown in the heatmap.

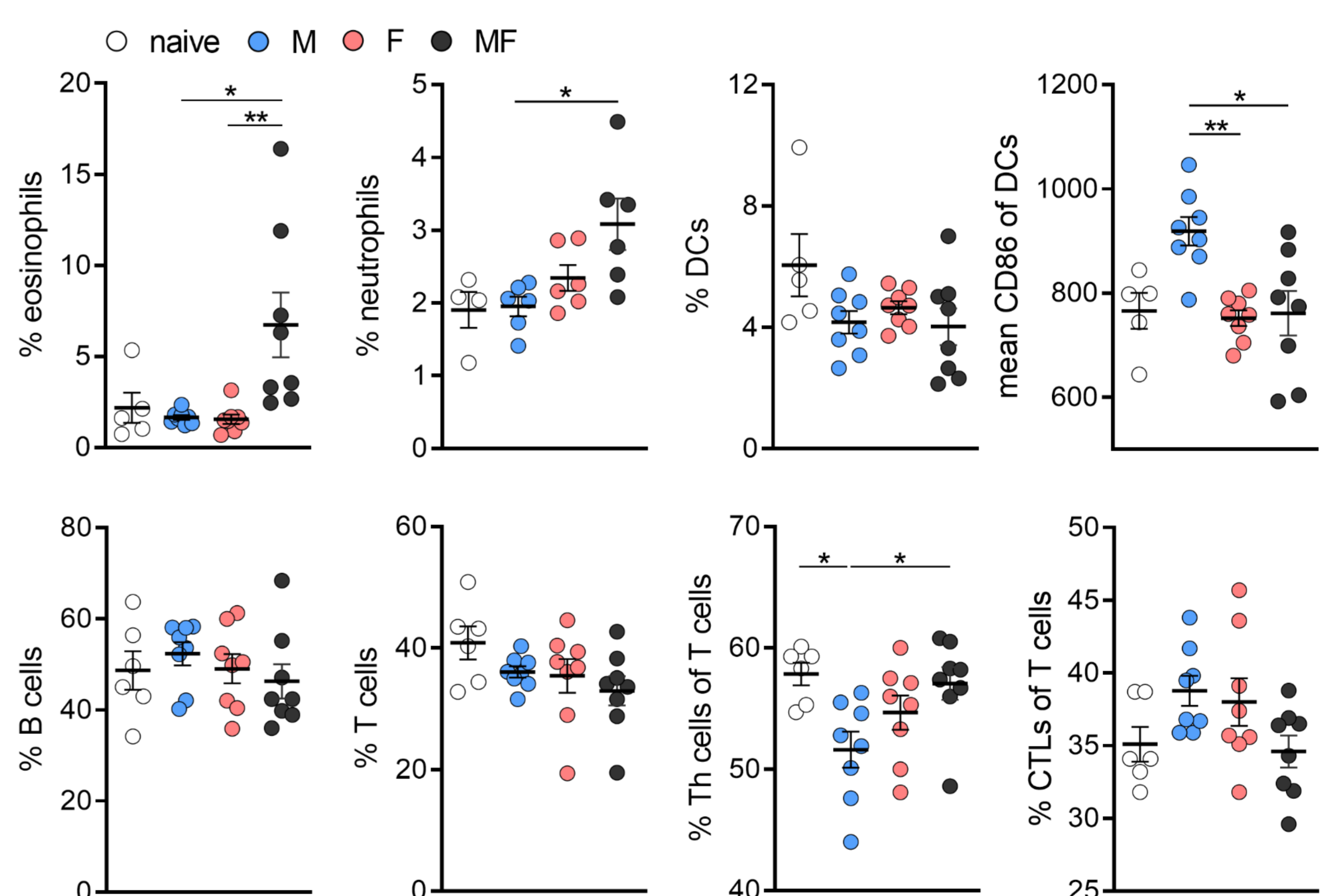


Figure 4: Male schistosomes induces significant enhance proportion of CD86 on dendritic cells. Percentages of eosinophils, neutrophils, dendritic cells (DCs), B cells, T cells, Th cells and cytotoxic T cells as well as the proportion of CD86 on dendritic cells were analysed in the spleens of infected (M, F and MF) and control (naive) mice (n=4-8).

Conclusion

Transcriptomic analysis display clear clustering of experimental groups. Single-sex *Schistosoma mansoni* induce an unpolarised Th1/Th2 immune response. Paired worms have the greatest effect on gene regulation, most likely triggered by eggs. Females from unisexual infection have less impact on regulation of biological processes compared to males and pairs at gene expression level.