miR-155 is essential for proliferation and survival of plasmablast B-cells

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mir-155 is essential for the proliferation of plasmablast B-cells

After establishing that mir-155 was critical for the plasmablast B-cell response, we next sought to determine the underlying cellular mechanisms. We started by monitoring the proliferation of antigen specific B-cells.

**Methods**

In order to elucidate the effects of mir-155 on plasmablast B-cell differentiation, SWM B-cells (CD43.2) sufficient or deficient in mir-155 were injected into B6.PL (CD43.1) mice and then measured with HEL antigen coupled to sheep red blood cells (SRBCs, Figure 2).

**Results**

**mir-155 is required for the plasmablast response**

We analyzed B-cell differentiation of antigen activated mir-155 sufficient and deficient B-cells using flow cytometry by staining for the transgenic HEL BCR and B220.

**mir-155 regulates genes**

We next set out to determine the molecular pathways disrupted in Mir-155 deficient plasmablast B-cells by comparing the transcriptome of mir-155 deficient B-cells with their wild type counterparts. CD44.2+/− HEL BCR+/− B220+ plasmablasts were generated in mir-155 sufficient or −/− deficient mice to recover 98% purity and their transcriptome was analyzed by micro array at 4.5 days post immunisation. We defined differentially expressed genes as those genes with a fold change of at least 3 between mir-155 deficient and mir-155 sufficient plasmablasts and a corrected p-value of less than 0.05. We observed 804 upregulated and 653 downregulated genes in mir-155 −/− plasmablasts relative to their wild type counterparts. We then use the gene ontology enrichment analysis tool GOMA (7) to look for pathway enrichment in the differentially expressed genes. Down- and upregulated genes were sorted into functional processes and ranked according to their p-value (Figure 6).

**Conclusions**

- **mir-155 is required to sustain the plasmablast response and is essential for plasmablast survival and proliferation.**
- **mir-155 deficient, HEL-specific plasmablast B-cells showed an increase in apoptosis and defects in cell cycle progression and DNA replication compared to wild type controls.**
- Through transcriptional analysis of mir-155 sufficient and deficient SWM B-cells we determined that mir-155 indirectly regulates genes involved in cellular processes such as the DNA metabolic process, DNA nucleosome assembly, DNA replication initiation and the mitotic cell cycle process which provides new insight into antibody production during the early response to infection and vaccination.

**References**


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