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Cryptosporidium parvum infection and colon cancer. Results of a microarray approach

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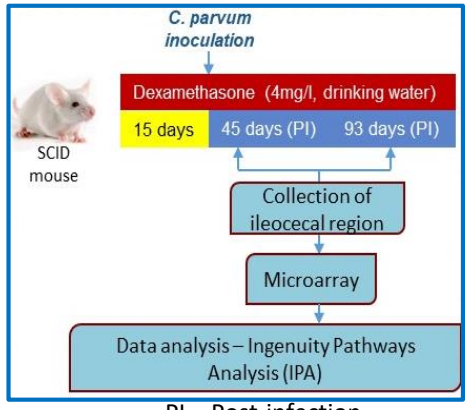
Background

Accumulative experimental and clinical evidences link *Cryptosporidium parvum* infection and digestive adenocarcinoma.

Objective

This study aimed to identify the gene expression profile and significant pathways involved in *C. parvum*-induced neoplasia.

Material and Methods



PI – Post-infection

Results

1. Identification of anti-microbial peptides α-defensins (DEFA) as novel targets of *C. parvum*

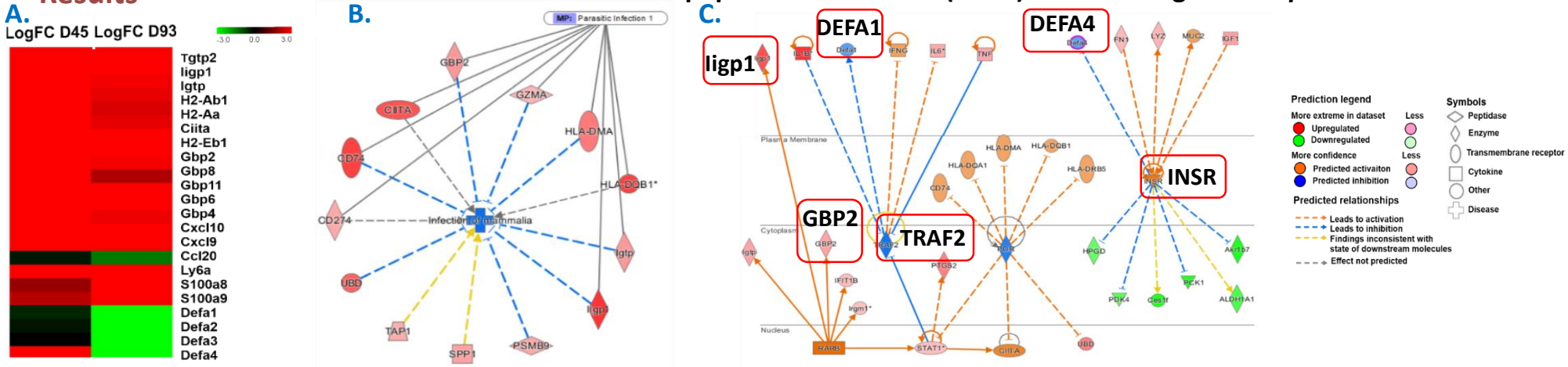
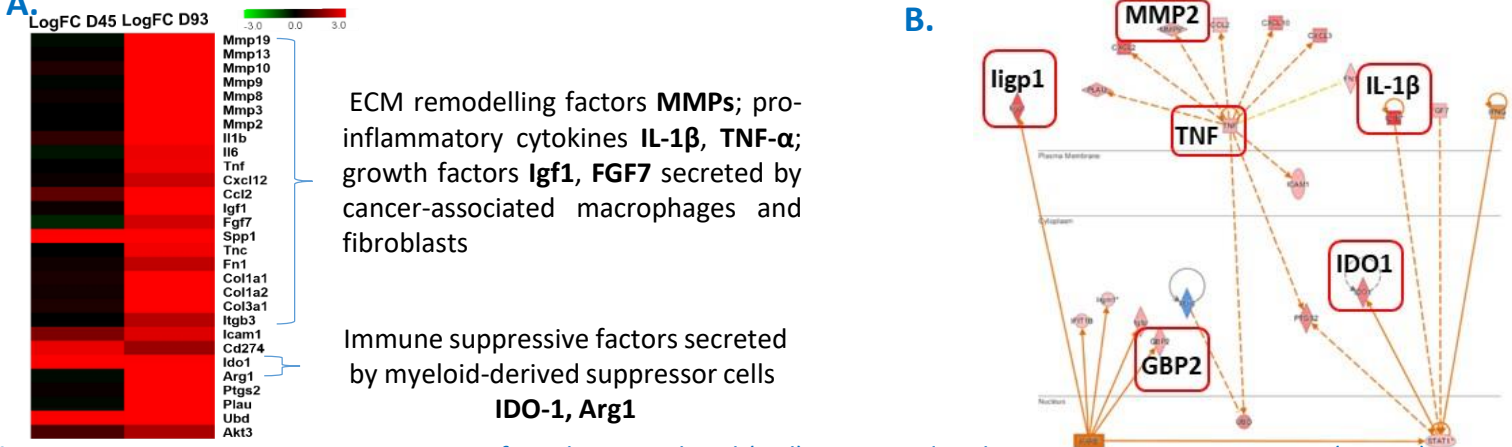


Fig 1. A. Heatmap showing α-defensins to be significantly downregulated (green) at D93 PI. Significant upregulation (red) of host innate immune response genes is observed at D45 and D93. **B**. Molecular network showcasing upregulation of genes involved in immune defence against *C. parvum* infection at D45. **C**. Gene network analysis predicted **INSR** and **TRAF2** to be involved in downregulation of expression of **DEFA1**, and **DEFA4** in response to persistent *C. parvum* infection at D93 by evading the host innate immune response generated by upregulation of **Iigp1**, **GBP2** in intestinal epithelial cells (IECs).

2. Molecular characterization of an immunosuppressive tumour microenvironment



ECM remodelling factors **MMPs**; pro-inflammatory cytokines **IL-1β**, **TNF-α**; growth factors **Igf1**, **FGF7** secreted by cancer-associated macrophages and fibroblasts

Immune suppressive factors secreted by myeloid-derived suppressor cells **IDO-1, Arg1**

Fig 2. A. Heatmap representing genes significantly upregulated (red) associated with tumour microenvironment (D93 PI). **B**. Gene network analysis predicted *C. parvum* to resist host innate immune response (**Iigp1**, **GBP2**) leading to an uncontrolled infection causing inflammatory stimuli (**TNF-α**, **IL-1β**) and leading to epithelial mesenchymal transition (EMT) (**MMP2**), and to protection of cancerous IECs from immune attack by inducing expression of immune suppressive factor (**IDO-1**).

Conclusions

- Identification of anti-microbial peptides **DEFA** as novel targets of *C. parvum.*
- Upregulation of **IFNγ**-stimulated genes and downregulation of **DEFA** contributes to chronic inflammation.
- *C. parvum* induces an immunosuppressive microenvironment.