Targeting ICAM-1 regulation in human retinal endothelial cells to treat uveitis

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The disease: Uveitis

- Uveitis is the term used to define diseases characterised by **intraocular inflammation**
- It has an incidence rate of 22 per 100,000 person-years in Australia
- Symptoms are non-specific, including **eye redness, visual floaters and blurred vision**
- Current therapies include **corticosteroids** (prednisolone) and **immunomodulatory drugs** (methotrexate); multiple side effects
- ICAM-1, an adhesion molecule expressed on endothelial cells is involved in leucocyte migration to site of infection/ disease

Research aims

1. To identify transcription factors (TFs) that bind to *ICAM1* promoter in human retinal endothelial cells
2. To determine effect of silencing TFs on human retinal endothelial ICAM-1 protein expression & leucocyte interaction

Research methods

Transcription factors regulating *ICAM1* gene expression determined via *in silico* analysis and literature reviews

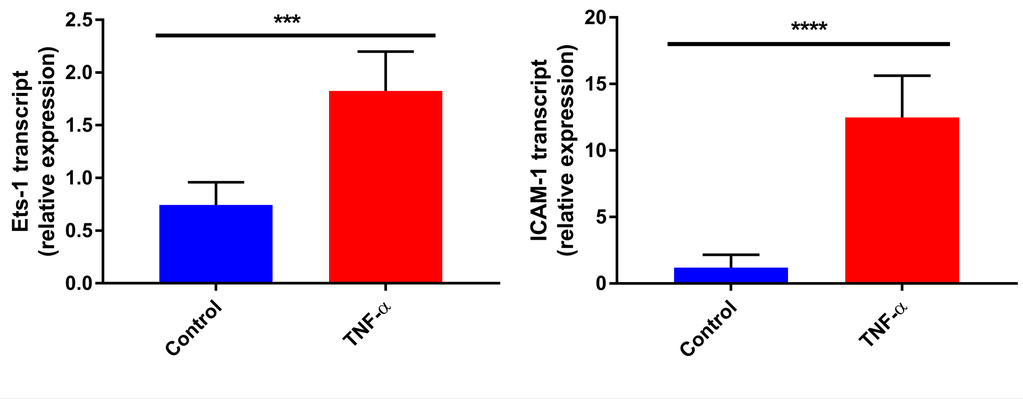
ICAM-1 transcript expression in human retinal endothelial cells quantified by RT-qPCR

Cellular ELISA to detect ICAM-1 protein expression; leucocyte binding assay to assess binding of monocytes to retinal endothelial cells

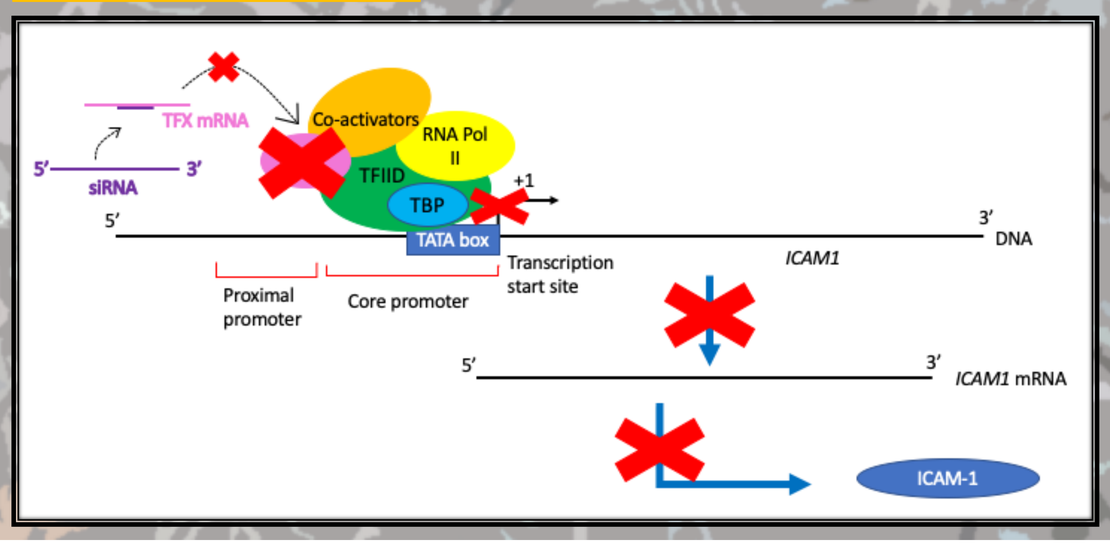
The findings

- ICAM-1 transcript & protein levels were significantly increased following TNF-α & IL-1β stimulation in human retinal endothelial cells
- A significant difference in ICAM-1 protein expression was noted between donor samples for each cytokine treatment, TNF-α & IL-1β
- An increased in leucocyte-endothelial cell interaction was observed following TNF-α & IL-1β stimulation
- Transcription factor, Ets-1 predicted to bind to ICAM-1 promoter following *in silico* analysis
- Ets-1 transcript levels were significantly elevated following both TNF-α & IL-1β stimulation

Ets-1 and ICAM-1 expression are upregulated by TNF-α stimulation



Target TFs using siRNA



Future experiments

- Measure Ets-1 expression in cytokine-stimulated human retinal endothelial cells following transfection with Ets-1 siRNA
- Assess ICAM-1 mRNA and protein expression with Ets-1 transfected siRNA in human retinal endothelial cells with cytokines stimulation

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INSPIRING ACHIEVEMENT

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