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Gene expression in active systemic JIA after anti-IL1 and anti-IL6R treatment

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Introduction

We have previously found specific genes upregulated in PBMCs of active sJIA [1]. Biologics to block IL-1 and IL-6 signalling have both been shown to be effective in early clinical trials. In this study we examine the expression before and after anti-IL1 and anti IL-6R treatment in PBMCs and their constitutive cell types; using gene expression analysis to further understand the disease pathways.

Methods

PBMCs were collected before and after treatment from patients that responded to treatment: two patients were treated with tocilizumab, one with anakinra and another with an experimental anti-IL1 antibody (Novartis). A proportion of PBMCs were reserved and positive selection of B cells, T cells and monocytes performed on the rest. RNA was extracted and hybridised to Affymetrix U133 Plus 2.0 arrays. Paired significance analysis was performed using LIMMA.

Results

In the B cell population we found 1902 genes differentially expressed after anti-IL1 treatment and 165 after anti-IL6R treatment. While genes involved in transcriptional regulation and the immune response were differentially expressed after both treatments there were only 24 genes that were common to both lists including *TCL1A* and *CD69*. Differential expression unique to the anti-IL1 blockade included downregulation of complement-mediated immunity genes e.g. *CD55*. Other genes downregulated after anti-IL1 include *IL12RB2*, and *CREB1*. Genes upregulated after anti-IL6R treatment include *CEBPδ* and *BTLA*. We are currently characterising gene expression in the remaining cell types.

Conclusion

We have found that the majority of changes in gene expression in B cells differ according to the specific cytokine modulation.

References

1. Ogilvie EM, Khan A, Hubank M, Kellam P, Woo P: **Specific gene expression profiles in systemic juvenile idiopathic arthritis.** *Arthritis Rheum* 2007, **56:**1954-65.