

Supplementary Table 1: Summary of expression differences in immune related genes in EOO relative to AOO

Gene	Change	Process	Influence	Reference
Hgf	up	Dendritic cell antigen presentation	inhibits	(Okunishi et al. 2005)
Ppapdc2	up	PMN activation	inhibits	(Fukunaga et al. 2006)
Rnd3	up	Leukocyte migration	inhibits	(Sanchez-Madrid and del Pozo 1999)
Dpp4	up	Cytokine cleavage	promotes	(Boonacker and Van Noorden 2003)
H2-Ab1	down	Antigen presentation	promotes	(Stevenson et al. 2000; Wolk et al. 2000)
H2-Eb1	down	Antigen presentation	promotes	(Stevenson et al. 2000; Wolk et al. 2000)
H2-D1	down	Antigen presentation	promotes	(Stevenson et al. 2000; Wolk et al. 2000)
Ccl11	down	Pro-inflammatory signaling	promotes	(Mantovani et al. 2004)
Ccl24	down	Pro-inflammatory signaling	promotes	(Mantovani et al. 2004)
Ccl8	down	Pro-inflammatory signaling	promotes	(Mantovani et al. 2004)
Cxcl10	down	Pro-inflammatory signaling	promotes	(Mantovani et al. 2004)
Cxcl2	down	Pro-inflammatory signaling	promotes	(Mantovani et al. 2004)
Slamf8	down	Lymphocyte activation signaling	promotes	(Graham et al. 2006)
Slamf9	down	Lymphocyte activation signaling	promotes	(Graham et al. 2006)
Tcf7l2	down	T-cell maturation/development	promotes	(Willinger et al. 2006)
Slpi	down	Control of Mast cell/PMN proteases	promotes	(Wright et al. 1999)

Sts1	down	T cell signaling modulation	promotes	(Carpino 2004)
Adam8	down	Soluble IgE release	promotes	(Fourie et al. 2003)
Igfb1	down	Pro-inflammatory cytokine (IL6) production	promotes	(Moller et al. 1994)
Capg	down	Macrophage mobility/phagocytosis	promotes	(Parikh et al. 2003)
Sirpa	down	Modulates macrophage phagocytosis	promotes	(van den Berg et al. 2004)
Itgax	down	Dendritic cell maturation	promotes	(Hebel et al. 2006)
C1qc	down	Antigen recognition/uptake	promotes	(Sontheimer et al. 2005)

Supplementary Discussion of Genes from Supplementary Table 1

The product of Hgf suppresses pulmonary dendritic cell antigen-presenting capacity, thereby inhibiting the immune response to inhaled allergen (Okunishi et al. 2005). Ppapdc2 produces a phosphatase that inhibits PMN activation (Fukunaga et al. 2006). Rnd3 product is a Rho GTPase that negatively regulates the polarization and cytoskeletal rearrangements that are necessary for leukocyte migration (Sanchez-Madrid and del Pozo 1999). Dpp4 protein, CD26, cleaves a number of cytokines involved in leukocyte chemotaxis and targeting, as well as in progenitor cell proliferation and recruitment (Boonacker and Van Noorden 2003). This inactivation of cytokines serves to modulate the immune response.

The type II MHC genes, H2-Ab1 and H2-Eb1, and the type I MHC gene, H2-D1, were down-regulated in EOO mice. Down-regulation of these molecules results in diminished antigen presenting capacity (Stevenson et al. 2000; Wolk et al. 2000). Pro-inflammatory chemokine genes Ccl11 (MIP2), Ccl24 (Eotaxin2), Ccl8 (MCP2), Cxcl10 (IP10), and Cxcl2 (GRO β), produce chemoattractant ligands for the entire range of white blood cells (Mantovani et al. 2004). Their down-regulation would inhibit attraction and accumulation of effector cells for an appropriate immune response.

The signaling lymphocyte activation molecule (SLAM) family of receptor molecules provides signals modulating innate and adaptive responses and polarizing T cells toward Th2 responses (Graham et al. 2006). Hence, down-regulation of Slamf8 and Slamf9 would reduce Th2-mediated allergic responses. T cell factor 7 like 2 (Tcf7l2) is produced by T cells and, with other T cell factors, participates in T cell development through the Wnt pathway (Willinger et al. 2006). Down-regulation of the Wnt pathway could interrupt the differentiation and maturation of T cells. Slpi is a protease inhibitor gene whose product suppresses the inflammatory action of mast cell and PMN proteases (Wright et al. 1999). Suppressor of T cell signaling gene (Sts1) protein negatively regulates the T cell receptor (TCR), thereby dampening the immune response even in the face of antigen-TCR binding (Carpino 2004). ADAM8, a disintegrin metalloprotease, catalyzes cleavage of CD23 (low affinity IgE cell surface receptor). The

resulting soluble CD23 causes up-regulation of IgE and inflammatory cytokine production (Fourie et al. 2003); therefore, down-regulation of Adam8 diminishes inflammatory response. Inducible TGF β (Tgfb1) has a direct positive regulatory effect on production of the pro-inflammatory cytokine, IL6 (Moller et al. 1994). Down-regulation of Tgfb1 decreases IL6 and consequently inflammation. Capg down-regulation alters actin filament capping, disturbs the cytoskeleton, and results in reduced macrophage motility and phagocytosis (Parikh et al. 2003). Sirpa produces an immunoglobulin superfamily protein that inhibits phagocytosis receptors on macrophages and diminishes the innate immune response. Itgax codes for one chain of the heterodimeric mature dendritic cell integrin, CD11c. This molecule is critical to maturation of the dendritic cell into an antigen presenting cell, and down-regulation would decrease the recognition and uptake of antigen by dendritic cells (Hebel et al. 2006). C1QC is a subunit of the recognition member of the complement cascade that promotes antigen recognition, isolation, and up-take (Sontheimer et al. 2005). Down-regulation of the gene responsible for this molecule impacts innate immune response.

All alterations in expression functionally support inhibition or, more correctly, dampening of the immune response. The only apparent inconsistency among genes influencing the immune response was an up-regulation of Ccr11, which encodes a receptor for dendritic and T cell cytokines involved in chemotaxis (Gosling et al. 2000). However, the possibility of Ccr11 involvement in specific negative regulation of dendritic and/or T cells cannot be eliminated.

Supplementary Table 1 References

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