Effector Cells & Their Roles in the Early & Late Phase Asthmatic Reactions

Th2 Cells

Th2-specific cytokines play a central role in the cellular response to allergens. These cytokines promote the production of IgE antibodies by B cells, induce the survival and recruitment of mast cells and eosinophils, promote goblet cell hyperplasia and increased mucus secretion, and stimulate structural changes in the airway. Regulatory T cells and Th1 cells produce cytokines, such as IL-10 or IFN-γ, respectively, that can inhibit the allergen-induced Th2 response or Th2 differentiation, suggesting that these cells may be involved in inhibiting the pathogenesis of asthma.

Mast Cells

Mast cells are the primary effector cells of the early asthmatic reaction. Cross-linking of the IgE-FcεRI receptors on these cells causes degranulation and the release of histamine, cysteinyl leukotrienes, and prostaglandins that cause smooth muscle contraction and airway constriction. Allergen binding to IgE-FcεRI complexes also leads to the release of cytokines and chemokines that attract inflammatory cells involved in the late phase asthmatic reaction.

Basophils

Basophils, like mast cells, degranulate following allergen-induced IgE-FcεRI receptor cross-linking. The release of inflammatory mediators by these cells contributes to bronchial constriction in the early phase asthmatic reaction. Cytokines released by the basophils also contribute to the excessive inflammation and structural changes that occur during the late phase reaction.

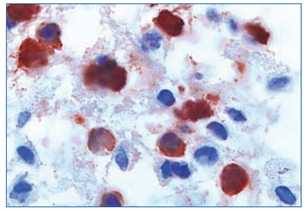
Eosinophils

Eosinophils are the prime regulators of the late phase asthmatic reaction. These cells infiltrate the asthmatic airway, and release cytokines and chemokines that promote their adhesion to the activated endothelium, and generate an inflammatory response at the sites of allergen exposure. Eosinophil degranulation is tightly associated with the structural changes that lead to airway remodeling

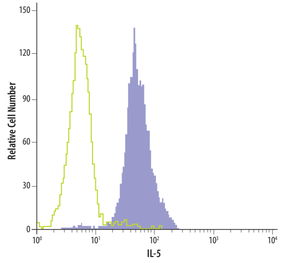
Neutrophils

Neutrophils play an important role in the late phase reaction. They expresss the IgE-FcεRI receptor and release cytokines, lipids, and proteases that contribute to airway constriction and mucus production. While infiltrating neutrophils are a characteristic of severe asthma, neutrophil-mediated responses are not currently well understood.

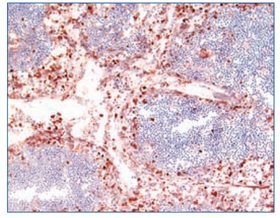
Antibodies



IL-4 in Human Lymph Node. IL-4 was detected in cryostat tissue sections of frozen human lymph node using anti-human IL-4 monoclonal antibody (Catalog # MAB304). Tissues were stained using anti-mouse ABC-HRP with NovaRed™ substrate (red) and counterstained with hematoxylin (blue).



Intracellular Detection of IL-5 in Activated Lymphocytes by Flow Cytometry. Activated human lymphocytes were stained with CFS-conjugated anti-human IL-5 monoclonal antibody (Catalog # IC605F; filled histogram) or CFS-conjugated mouse IgG$_1$ isotype control antibody (Catalog # IC002F; open histogram).

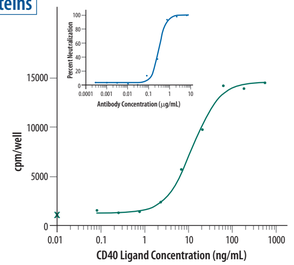


CD14 in Human Lymph Node. CD14 was detected in cryostat tissue sections of frozen human lymph node using biotinylated anti-human CD14 polyclonal antibody (Catalog # BAF383). Tissues were stained using anti-sheep ABC-HRP with AEC substrate (red) and counterstained with hematoxylin (blue).

NovaRed™ is a tradmark of Vector Labs.

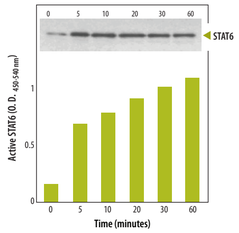
For research use only. Not for use in diagnostic procedures.

Proteins



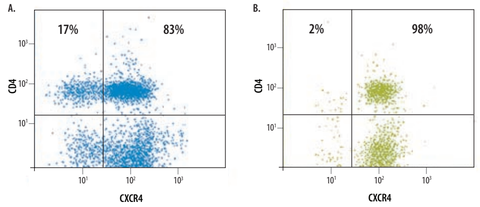
CD40 Ligand Stimulates B Cell Proliferation. Mouse splenic B cells were incubated with increasing concentrations of recombinant mouse CD40 Ligand (Catalog # 1163-CL), in the presence of 20 ng/mL recombinant mouse IL-4 (Catalog # 404-ML). Cell proliferation was determined by measuring ^{3}H-thymidine incorporation. Treatment of the cells with IL-4 alone is indicated (**x**). The ability of recombinant mouse CD40 Ligand to stimulate B cell proliferation was neutralized using increasing concentrations of anti-mouse CD40 Ligand polyclonal antibody (Catalog # AF1163; inset).

ELISAs & Activity Assays



Detection of STAT6 in Mouse DA3 Cells. Mouse myeloid DA3 cells were treated with recombinant mouse IL-4 (Catalog # 404-ML) for the indicated times. Nuclear extracts were prepared and analyzed using the mouse Active STAT6 DuoSet® IC ELISA (Catalog # DYC2169). The same nuclear extracts were also assessed by Western blot analysis using anti-mouse STAT6 monoclonal antibody (Catalog # MAB2169; inset)

Cell Selection



Isolation of CXCR4$^+$ Lymphocytes. The human CXCR4 PlusCellect™ Kit (Catalog # PLS170) was used to enrich for CXCR4$^+$ lymphocytes. The effectiveness of enrichment was assessed by staining cells before (A) or after (B) selection with APC-conjugated anti-human CD4 antibody (Catalog # FAB3791A) and PE-conjugated anti-human CXCR4 antibody (provided in the kit).

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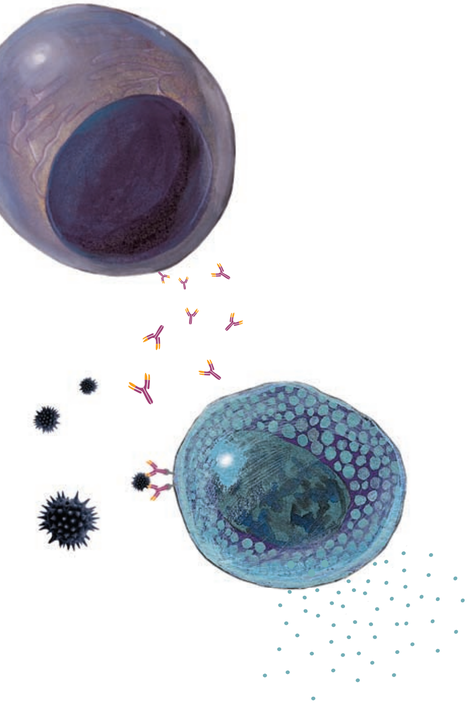
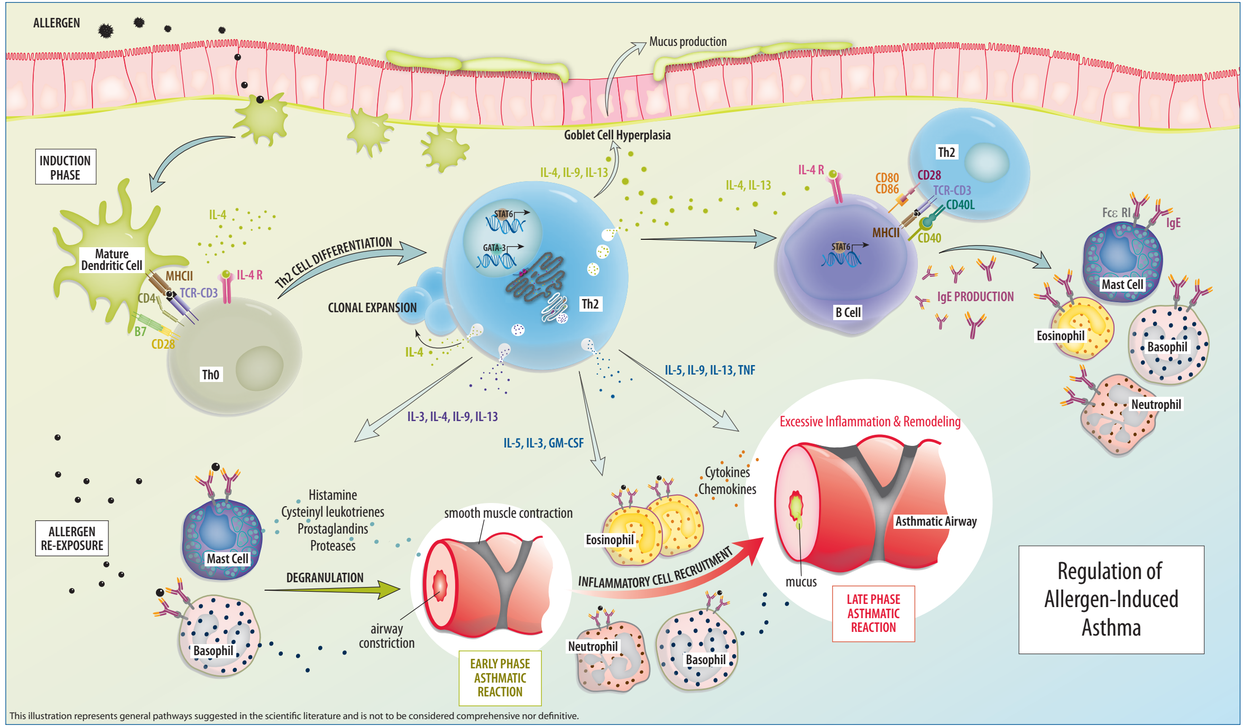
Allergy & Asthma



The Immune Response to Inhaled Allergens: Pathogenesis of Asthmatic Inflammation

Exposure to inhaled allergens, such as pollen, dust mites, mold, or animal dander can initiate an acute immune response in allergen-sensitive individuals that leads to airway inflammation. Persistent inflammation is associated with allergen-induced asthma, a chronic respiratory disorder characterized by the production of IgE antibodies, airway hypersensitivity, increased mucus secretion, and thickening of the airway wall. The asthmatic response to allergens takes place in two phases. The immediate response is the early, acute phase reaction in which mast cells and basophils undergo degranulation to release histamine, and cysteinyl leukotrienes. These mediators cause smooth muscle contraction and bronchial constriction which are manifested by a shortness of breath, wheezing, and coughing. The late phase reaction occurs several hours after the initial reaction and is characterized by excessive inflammation, infiltration of the airway by eosinophils and other cytokine-secreting leukocytes, and structural changes that lead to airway remodeling.

The early and late phase asthmatic responses are initiated by the recognition and processing of allergens by dendritic cells which drive naïve T cells to differentiate into T helper type 2 cells (Th2). Th2 lineage commitment is established by STAT6-dependent expression of GATA-3 which induces the expression of Th2 cytokines, including IL-3, IL-4, IL-5, IL-9, IL-13, and GM-CSF (Induction phase; dark blue arrows). Together these cytokines direct the inflammatory response to allergens (light blue arrows). The hallmark Th2 cytokine, IL-4 promotes clonal expansion and, along with IL-13 and specific co-stimulatory molecules, induces B cells to produce allergen-specific IgE antibodies. IgE antibodies bind to the Fcε RI high affinity receptors found on mast cells, basophils, neutrophils, and eosinophils. Upon allergen re-exposure, allergen binding to the IgE-Fcε RI complexes on mast cells and basophils leads to receptor cross-linking which triggers the release of mediators that cause immediate hypersensitivity (Early phase asthmatic reaction; green arrow). Several hours later the late phase asthmatic reaction occurs. During this phase, Th2- and mast cell-derived cytokines stimulate eosinophil activation and leukocyte recruitment to the sites of allergen exposure (red arrow). The release of pro-inflammatory molecules at these sites by eosinophils, infiltrating basophils, neutrophils, and Th2 cells plays a critical role in promoting chronic inflammation and airway remodeling. R&D Systems offers a wide variety of research reagents useful for the characterization of allergen-induced immune response pathways.



This illustration represents general pathways suggested in the scientific literature and is not to be considered comprehensive nor definitive.

Allergy, Asthma & Inflammation Research Reagents Available from R&D Systems

MOLECULE	ANTIBODIES	PROTEINS	ELISAs & KITS
4-1BB/TNFRSF9	H M	H M	H M
4-1BB Ligand/TNFSF9	H M	H M	
ADAM33	M		
BAFF/BLys/TNFSF13B	H M	H M	H M
BAFF R/TNFRSF13C	H M	H M	M
B7-1/CD80	H M R	H M R	H M
B7-2/CD86	H M R	H M R	R
CCL1/I-309/TCA-3	H M	H M	H M
CCL2/MCP-1/JE	H M Ca CR	H M R Ca	H M Ca
CCL3/MIP-1α	H M CR	H M CR	H M
CCL4/MIP-1β	H M CR	H M CR	H M
CCL5/RANTES	H M CR F	H M CR F	H M
CCL7/MCP-3	H M	H M	H
CCL8/MCP-2	H M	H	H
CCL11/Eotaxin	H M	H M	H M
CCL13/MCP-4	H	H	H
CCL17/TARC	H M	H M	H M
CCL22/MDC	H M	H M	H M
CCL24/Eotaxin-2	H M	H M	H M
CCL26/Eotaxin-3	H	H	H
CCR1	H		
CCR2	H		
CCR3	H M		
CCR4	H		
CCR6	H M		
CCR8	H		
CD3	M		H* M* R*
CD3ε	H M		
CD14	H M P	H M	H / H*
CD23/Fcε RII	H	H	H
CD27/TNFRSF7	H M	H M	M
CD28	H M	H M	
CD30/TNFRSF8	H M	H M	M
CD31/PECAM-1	H M P	H M P	H*
CD40/TNFRSF5	H M	H M	M
CD40 Ligand/TNFSF5	H M	H M	H M

MOLECULE	ANTIBODIES	PROTEINS	ELISAs & KITS
Common γ Chain/IL-2 Rγ	H M	H M	
CTLA-4	H M	H M	M
CXCL1/GROα	H M R	H M R	H M R
CXCL1/2/3/GRO	H	CR	
CXCL6/GCP-2	H	H	H
CXCL8/IL-8	H Ca F P	H Ca F P	H Ca F P
CXCR3	H M		
CXCR4	H M F		H*
DPP10	H		
Galectin-3	H M	H M	M
Galectin-3BP/Mac-2BP	H	H	
GATA-3	H		
GM-CSF	H M R Ca F P	H M R Ca F P	H M R F
GM-CSF Rα	H		
ICAM-1	H M R	H M R	H M R
ICAM-2	H M	H M	
ICOS	H M	H M	
IFN-γ	H M R B Ca CR E F P Pr	H M R B Ca CR E F P Pr	H M R Ca CR F P Pr
IFN-γ R1/CD119	H M	H M	H M
Phospho-IFN-γ R1			H
IFN-γ R2	H M		
IL-1α/IL-1F1	H M R CR P	H M R CR P	H M R
IL-1β/IL-1F2	H M R Ca CR E F P	H M R Ca CR E F P Pr	H M R F P
IL-1ra/IL-1F3	H M E P	H M R E P	H M
IL-1 RI	H M	H M	H
IL-1 RII	H M	H M	H
IL-1 R3/IL-1 R AcP	H	H	
IL-2	H M R B Ca CR E F P	H M R B Ca CR E F P	H M R Ca F
IL-2 Rα	H M	H M	H M / H* M*
Il-2 Rβ	H M	H	
IL-3	H M R	H M R	H M
IL-3 Rα	H M	H M	
IL-3 Rβ	M	M	M
IL-4	H M R B Ca CR E F P	H M R B Ca CR E F P Pr	H M R Ca CR F P
IL-4 R	H M	H M	

MOLECULE	ANTIBODIES	PROTEINS	ELISAs & KITS
IL-5	H M R Ca E F P	H M R B Ca E F P Pr	H M
IL-5 R	H M	H	
IL-6	H M R Ca CR E F P	H M R Ca CR E F P	H M R Ca F P
IL-6 R	H M	H M	H M
IL-9	H M R	H M R	
IL-9 R	H M	H	
IL-10	H M R Ca CR E F P V	H M R Ca CR E F P V	H M R Ca E F P
IL-10 Rα	H M	H M	
IL-10 Rβ	H	H	
IL-11	H M	H M	H M
IL-11 Rα	M	H M	
IL-12	H M R P	H M R Ca F P Pr	H M
IL-12/IL-23p40	H M R Ca F P	H M Ca F	H M F P
IL-12 Rβ1	H M	H M	
IL-12 Rβ2	H	H	
IL-13	H M R	H M R Pr	H M R
IL-13 Rα1	H	H M	H
IL-13 Rα2	H M	H M	H
IL-16	H M	H	H
Integrin α4	H M		
Integrin α6	H M B		
Integrin αL	H		
Integrin αLβ2		H	
Integrin αM	H M		
Integrin αMβ2		H	
Integrin αX	H		
Integrin β1	H M		
Integrin β2	H M		
Integrin β7	H M		
Leukotriene A4 Hydrolase/LTA4H		H	
Leukotriene B_4			Ms
Leukotriene B_4 R1	H		
Mast Cell Protease-6	M	M	
Mast Cell Protease-11	M	M	
Nitric Oxide			Ms

MOLECULE	ANTIBODIES	PROTEINS	ELISAs & KITS
iNOS	H		H
OX40/TNFRSF4	H M	H M	
PD-1	H M	H M	
PGE_2			Ms
E-Selectin	H M R	H M R	H M / H*
P-Selectin	H M	H M	H M
SLAM/SLAMF1/CD150	H M		
STAT6	H M R		M
Phospho-STAT6 (Y641)	H		H M
TACI/TNFRSF13B	H M	H M	H M
TGF-β1	Ms	H P	H M R Ca P
TGF-β2	Ms	H P	H
TGF-β RI/ALK-5	H M	M	
TGF-β RII	H M	H M	
TGF-β RIIb	H	H	
TGF-β RIII	H	H	
TNF-α/TNFSF1A	H M R B Ca CR E P Pr	H M R B Ca CR E F P Pr	H M R Ca E F P Pr
TNF-β/TNFSF1B	H M	H M	H
TNF RI/TNFRSF1A	H M	H M Ca	H M
TNF RII/TNFRSF1B	H M	H M	H M
Tryptase α	H		
Tryptase β1	M	M	
Tryptase γ-1/TPSG1	H	H	
TSLP	H M	H M	H M
TSLP R	H M	H M	
VCAM-1	H M	H M	H M / H*
VEGF	H M R Ca Z	H M R Ca Z	H M R Ca
VEGF R1/Flt-1	H M	H M	H M
VEGF R2/KDR/Flk-1	H M	H M	H M / H*
VEGF R3/Flt-4	H M	H M	H M

* Denotes Cell Selection Kits

KEY: H: Human M: Mouse R: Rat B: Bovine Ca: Canine CR: Cotton Rat E: Equine F: Feline Ms: Multi-species P: Porcine Pr: Primate V: Viral Z: Zebrafish

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