Naïve T cell

Th1
Stat4
T-bet
IFN-γ

Th17
Stat3
RORγt
IL-17a
IL-17f

Th2
Stat6
GATA3
IL-4
IL-13

Th9
Stat6
PU.1+TPA
IL-9
IL-10
IL-13

Dendritic Cell

CD4+ CD62L+

(A)

PGE2
EP2/4
IL-23
IL-1

PGI2
PGF2α
Stat3
RORγt

(B)

IL-17

CD4+ T cell

IL-25
IL-17RA
IL-17RB

PLA2
Arachidonic Acid
COX-2
Prostaglandin H2 Synthases

TXA2
PGD2
PGF2α
PGJ2
PGE2
PGE3
IP3/CA2

Adenyl cyclase
PKA
CREB
IL-17RB

Act1
SAFα
TAK1

Nucleus

IL-5/IL-10
1. COX pathway and prostaglandins on immune tolerance

- People who do not have allergic diseases develop immune tolerance to common allergens such as seasonal pollen and house dust mite antigens.
- The prevalence of allergic diseases has doubled in the past 50 years in developed countries.
- Frequent use of COX-inhibiting drugs was associated with increased risk of developing allergic diseases and asthma.
- COX inhibition suppressed immune tolerance induced by airway allergen exposures.
- Deficiency of prostaglandin I_2 (PGI_2) receptor (IP) suppressed immune tolerance induced by airway allergen exposures.
- COX2-dependent arachidonic acid metabolites were required for oral tolerance induction and the development of functional regulatory T cells.
- COX2 inhibition abrogated immune tolerance induced by oral protein exposures.

2. PGE_2 on pulmonary vascular remodeling in allergic inflammation

- Exogenous administration of PGE_2 suppressed allergen-induced pulmonary inflammation in rat and mouse models of allergic pulmonary disease.
- Deficiency of microsomal PGE_2 synthase (mPGES)-1 increased numbers of vascular smooth muscle cells and the thickness of intrapulmonary vessels in response to sensitization and challenge with dust mite antigen.
- These vascular changes were suppressed by the administration of the stable PGE_2 analog 16, 16-dimethyl PGE_2, or of selective agonists of the EP receptors.

References: