

# Association between Eicosanoids in Exhaled Breath Condensate and Type 2 Immunological Mediators in Sputum from Patients with Asthma



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The American Academy of Allergy, Asthma & Immunology  
 COI Disclosure Yuki Hoshino  
 The authors have no financial conflicts of interest to disclose concerning the presentation.

## Rationale

- Inflammatory eicosanoids, including prostaglandin D2 (PGD2) and cysteinyl Leukotriens (CysLTs) are known crucial mediators in asthma, especially in severe asthma.
- Cysteinyl leukotrienes (CysLTs) and leukotrienes B4 (LTB4) are increased in exhaled breath condensate (EBC) of patients with asthma, especially in severe asthma.
- These eicosanoids promote granulocyte and lymphocyte infiltration and activation in airway, which is leading to type 2 airway inflammation and remodeling in asthma.
- The association between eicosanoids in EBC and mediators in sputum remains unclear in patients with asthma.

## Objective

- The objective of this study is to determine whether concentrations of eicosanoids in exhaled breath condensate (EBC) are associated with severity of asthma and particular inflammation type of asthma.

## Methods

- Study design**
- A cross-sectional observational study
- Patients with asthma and healthy control subjects were recruited from the Allergy Center of the Saitama Medical University Hospital.
- Inclusion criteria**
- Adults over 19 years old
- Asthma was diagnosed according to the GINA report
- Patients not having asthma exacerbation in the previous 4 weeks before examination

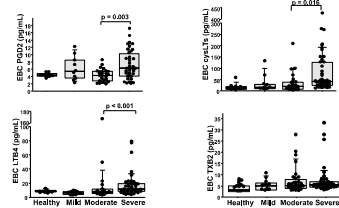
## Methods

- Examination**
  - To classify asthmatic patients into mild, moderate and severe asthma
  - EBC and sputum induction, pulmonary function test
  - Collection of EBC by using recommended methods with EcoScreen™
  - Sputum induction as described previously
- Measurement of EBC and Sputum Eicosanoid Levels**
  - Cysteinyl leukotrienes (CysLTs), leukotriene B4 (LTB4), prostaglandin D2-MOX (PGD2-MOX) and thromboxane B2 (TXB2)
  - Measurement of IL-5, IL-8 and IL-13 concentrations in sputum by ELISA
  - Measurement of eosinophil and neutrophil ratios in sputum
  - Measurement of trypsinase concentrations in sputum by using sandwich enzyme immunoassay kits (Cloud-Clone, Park Row, TX).

## Patient characteristics

	Healthy control subjects	asthmatics			P value
		mild	moderate	severe	
N (%)	10	10	38	44	
Age, y	46.9 (13.6)	44.9 (13.0)	52.8 (17.1)	54.1 (17.2)	N.S.
Female/male, n	4/6	8/2	17/13	32/12	N.S.
Duration of asthma (y)	NA	12.8 (5.0-14.9)	4.5 (1.5-7.2)	17.2 (3.3-34.4)	<0.0001
Atopy, n (%)	0 (0)	18 (100)	29 (76.7)	42 (95.3)	N.S.
ICS dose (µg/d)	NA	200 (100-400)	400 (200-400)	800 (400-900)	<0.0001
LABA, n (%)	NA	0 (0)	22 (57.3)	28 (63.6)	0.001
LTRA / TP, n (%)	NA	4 (40.0)	20 (56.4)	43 (97.7)	<0.0001
Oral corticosteroids, n (%)	NA	0 (0)	0 (0)	19 (43.2)	0.03
Airway hyper-resp., n (%)	NA	0 (0)	0 (0)	33 (75.2)	0.001
Total Log IgE, IU/L	NA	2.7 (1.0)	2.3 (3.5)	2.2 (3.9)	0.03
FEV1, % predicted	NA	99.3 (16.0)	93.5 (16.3)	94.1 (12.9)	0.16
FVC, % predicted	NA	102.5 (15.7)	105.2 (12.5)	95.6 (19.5)	0.0001
FEV1/FVC, %	NA	82.8 (3.8)	77.3 (3.6)	81.3 (7.9)	0.03

Levels of PGD2-MOX, CysLT and LTB4 of EBC in severe asthma were higher than those of moderate asthma

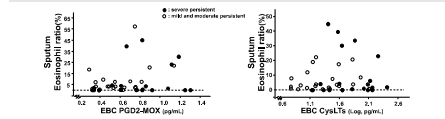


	634 P85) ~ OE		634 4YLBX	
	r	P value	r	P value
76DI, LBS	0%	100%	0%	100%
76DI, % Vred	0%	100%	0%	100%
7D4, LBS	0%	100%	0%	100%
7D4, % Vred	0%	100%	0%	100%
76DI/7D4, %	0%	100%	0%	100%

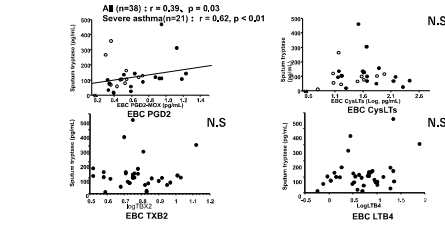
	634 LBS4		634 BE3	
	r	P value	r	P value
76DI, LBS	0%	100%	0%	100%
76DI, % Vred	0%	100%	0%	100%
7D4, LBS	0%	100%	0%	100%
7D4, % Vred	0%	100%	0%	100%
76DI/7D4, %	0%	100%	0%	100%

Any EBC eicosanoid levels were not correlated with sputum eosinophil or neutrophil ratios

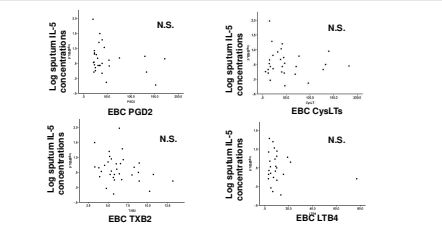


	EBC			
	PGD2-MOX	CysLTs	LTB4	TXB2
Sputum eosinophil ratio	0.09	N.S.	0.04	N.S.
Sputum neutrophil ratio	-0.01	N.S.	0.07	N.S.

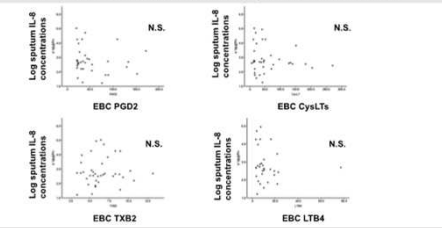
EBC PGD2 concentrations were correlated with sputum trypsinase concentrations in patients with asthma



634 e0UXGTU0 | UTI eTYG0ITX were TUYI UrreRed | won XuYuLS IL-, I UTI eTYG0ITX 0'VG0ITX won GXNS G%



EBC eicosanoid concentrations were not correlated with sputum IL-8 concentrations in patients with asthma.



## Conclusion

- Production of eicosanoids is enhanced in the airway of severe asthma despite of guideline treatment.
- EBC PGD2 might be an alternative marker of activated mast cells in the airway of asthma.