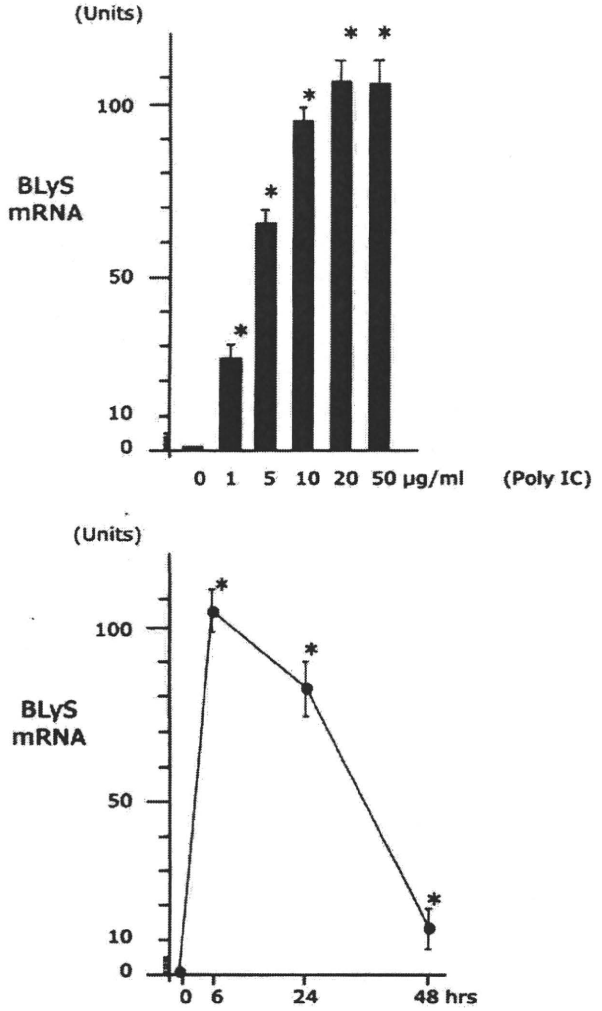

Fig. 3. Dose-dependence and time-course of poly(I:C)-induced BLyS-expression. (A) Human nasal fibroblast cells were cultured either with medium or with various concentrations of poly(I:C) (1, 5, 10, 20, and 50 μg/ml) for 6 h. (B) The cells were stimulated with poly(I:C) (10 μg/ml) and then harvested at 6, 24, 48, or 72 h. RNA was prepared and reverse transcribed to cDNA, followed by real time PCR. Data are expressed as the mean ± SEM ($n = 6$). *$P < 0.05$.

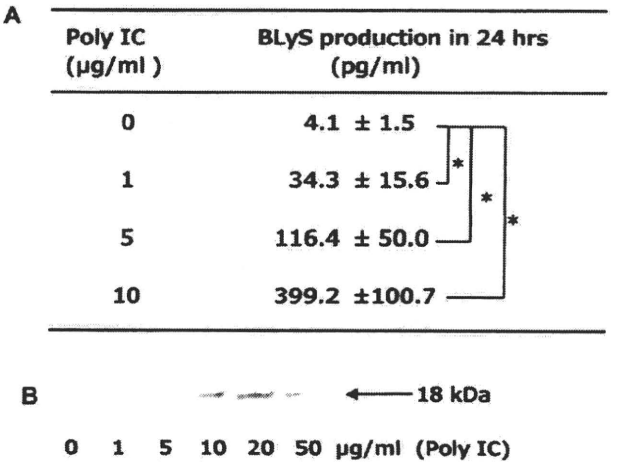

Fig. 4. Poly(I:C) induces BLyS-production from human nasal fibroblasts. (A) The cells were cultured either with medium or with various concentrations of poly(I:C) for 24 h. The supernatants were harvested for analysis of BLyS-production by ELISA. The results are expressed as the mean ± SEM ($n = 6$). *$P < 0.05$. (B) The same amount of supernatant was applied to each lane and blotted with anti-BLyS Ab. The position of BLyS-proteins was indicated to the right with the arrow.

Inhibitor (10 μM)	Poly IC (μg/ml)	BLyS production in 24 hrs (pg/ml)
None	0	4.1 ± 4.4
None	10	391.8 ± 72.7
LY 294002	10	13.3 ± 5.9
Piceatannol	10	245.1 ± 52.8
SB203580	10	279.9 ± 51.2
PD98059	10	322.9 ± 64.9
SP600125	10	296.5 ± 82.3

Fig. 5. The effect of intracellular signal transduction inhibitors on Poly(I:C)-induced BLyS-production from human nasal fibroblasts. After pre-incubation with LY294002, Wortmanin, an inhibitor of PI3-kinase; Piceatannol, an inhibitor of Syk kinase; SB203580, an inhibitor of p38 MAP kinase; PD98059, an inhibitor of MEK; or SP600125, an inhibitor of JNK, the cells were stimulated with poly(I:C) (1, 5, and 10 μg/ml) for 24 h. The supernatants were harvested for analysis of BLyS-production by ELISA. The results are expressed as the mean ± SEM ($n = 6$). *$P < 0.05$.

joints of patients with rheumatoid arthritis [13]. Pre-incubation with the PI3-kinase inhibitor LY294002 or Wortmanin reversed the poly(I:C)-induced production and expression of BLyS. The Syk kinase inhibitor Piceatannol also partially reduced its production and expression. Thus, we were able to show that PI3-kinase signaling is directly involved in poly(I:C)-induced BLyS-expression in nasal airway fibroblasts.

Airway submucosal fibroblasts play important roles, in the innate anti-viral response to human rhinovirus infections and dsRNA [14], while airway fibroblasts support the proliferation of bronchial epithelial cells, which is an important biological process in physiological conditions and various human airway diseases [15]. The inferior turbinate of the human nose is a 'mucosal protector' on the upper airway that acts against viral or bacterial infection and antigen exposure. Nasal fibroblasts of the inferior turbinate produce BLyS strongly when stimulated by dsRNA, leading to the innate anti-viral response including B cell proliferation and Ig secretion. Here, we have demonstrated the high BLyS-expression of nasal fibroblasts originating from nasal mucosa of the inferior turbinate.

Upper airways characteristically consist of a periosteum and bone covered by nasal respiratory mucosa. We also examined BLyS-expression of nasal fibroblasts originating from the periosteum of the inferior turbinate, and poly(I:C) strongly also induced BLyS-expression in these cells (data not shown). Fibroblasts also play key roles in airway remodeling process [16,17] and in nasal polyps, which are products of nasal airway remodeling. BLyS-mRNA was significantly increased in nasal polyps of patients with chronic rhinosinusitis, and its protein was present in mucosal epithelial cells in the nasal polyps along with unidentified cells in the lamina propria[5]. We also found that nasal fibroblasts originating from nasal polyps express BLyS by stimulation with dsRNA and LPS (data not shown).

Due to the high expression of TLR3 and TKR4, nasal fibroblasts can respond to their ligands. Through TLR3 and adaptor molecules, poly(I:C) stimulation induces the activation of IRF-3 transcription factor [10]. When PI3-kinase is not recruited to TLR3 or its activity

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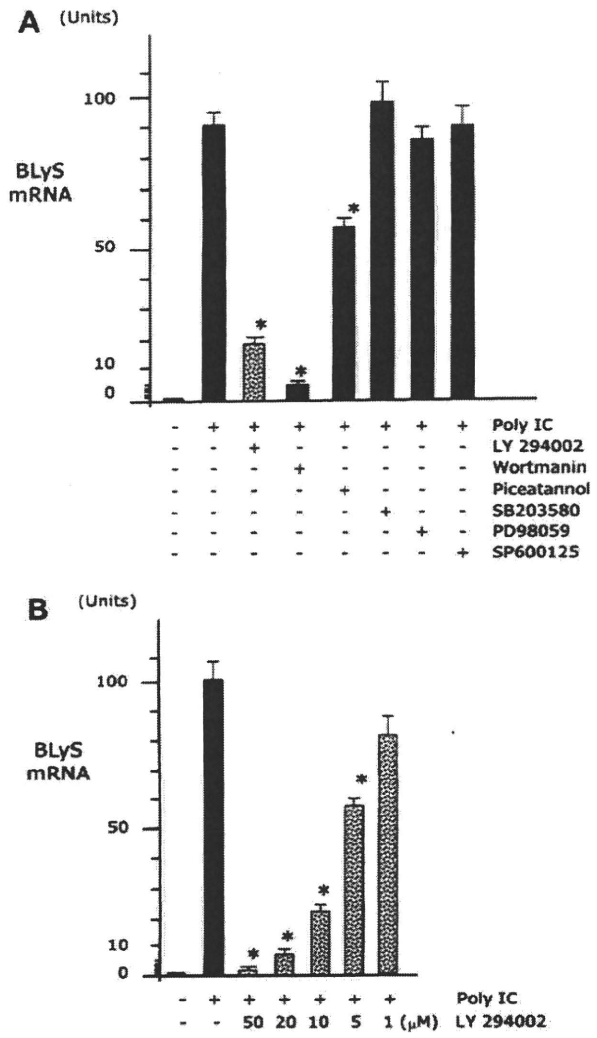

Fig. 6. Suppression of poly(I:C)-induced BLyS-expression by a PI3-kinase inhibitor. (A) Human nasal fibroblasts were pre-incubated with LY294002, Wortmanin, Piceatannol, SB203580, PD98059, or SP600125. The cells were harvested 6 h after stimulation with poly(I:C) (10 μg/ml), and the RNA was prepared for analysis of BLyS-expression by RT-PCR. Data are presented as mean ± SEM compared with the levels without inhibitor using Wilcoxon's signed-ranks test ($n = 6$). *$P < 0.05$. (B) Dose response of PI3-kinase inhibition of poly(I:C)-induced BLyS-expression. The culture conditions were the same as those for the experiment shown in Fig. 5A. except that the concentration of LY294002 was varied as indicated.

is blocked, IRF-3 is only partially phosphorylated and fails to bind to the promoter of its target gene in dsRNA-treated cells [11]. The PI3-kinase pathway plays an essential role in TLR3-mediated gene induction. As a specific PI3-kinase inhibitor reversed the expression of BLyS in dsRNA-stimulated nasal fibroblasts, PI3-kinase is considered to play a pivotal role in dsRNA-induced BLyS-expression in human nasal fibroblasts. PI3-kinase inhibitor also decreased TLR3-experssion in nasal fibroblasts (data not shown). A frequent byproduct of virus infection, dsRNA, is recognized by TLR3 as a method for mediating the innate immune response to virus infection. The most common acute infection in humans, human rhinovirus is a leading cause of exacerbations of airway inflammation. We previously reported that the protein tyrosine kinase Syk is expresses in nasal fibroblasts [18,19] and regulates PI3K activation and human rhinovirus endocytosis [20]. Although the full intracellular signaling pathway for dsRNA-induced BLyS-expression remains to be elucidated, we did find that, a PI3-kinase inhibitor and a Syk kinase inhibitor significantly reduced dsRNA-induced production and expression of BLyS in nasal fibroblasts.

While BLyS is an important survival factor for B lymphocytes, it can enhance immune responses not only by increasing the number of B cells but also by elevating CD4-positive T lymphocyte function and NK cell activity [21]. In BLyS-transgenic mice, the delayed-type hypersensitivity scores were found to correlate directly with BLyS levels in serum [22]. BLyS also provides a co-stimulatory signal to T cells and T cell activation, and bronchial structural cells including fibroblasts might play a critical role in the regulation of inflammation in asthma by increasing the survival of T lymphocytes [23]. Human post-switched IgG-positive B cells respond specifically and exclusively to BLyS by differentiating into IgG-secreting plasma cells [24]. On the contrary, in the presence of IL-4, BLyS induced immunoglobulin class switch recombination to epsilon in a CD40-independent manner [1,2].

BLyS participates in a variety of disorders, and interruption of the BLyS pathway is a candidate for therapeutic targeting of some diseases. In patients treated with belimumab, a fully human monoclonal antibody that inhibits the biological activity of the soluble form of BLyS in patients with systemic lupus erythematosus, significant reductions in the median percentage of CD20 positive B cells were observed versus placebo [25]. In nasal polyps, the expression of BLyS-mRNA in sinonasal tissue was significantly correlated with CD20 and transmembrane activator and CAML interactor (TACI) in sinus tissue [5]. TACI has been identified as a BLyS receptor. In a murine model of airway hyperresponsiveness, using soluble mTACI-Ig, a receptor for BLyS, it was revealed that mTACI-Ig treatment reduced the levels of total and allergen-specific IgE in serum and it was more effective than anti-IgE treatment in reducing airway hyperresponsiveness to inhaled antigens [26]. In human airways, the levels of BLyS-protein were significantly increased in bronchoalveolar lavage fluid after allergen challenge and its level was also correlated with IL-13 [27]. These in vitro and in vivo studies of BLyS and our analysis of BLyS-production reinforce the idea of BLyS being a possible therapeutic modality and its signaling pathway being potential targets for drug interventions against airway diseases.

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References

[1] Litinskiy MB, Nardelli B, Hilbert DM, He B, Schaffer A, Casali P, et al. DCs induce CD40-independent immunoglobulin class switching through BLyS and APRIL. Nat Immunol 2002;3:822–9.
[2] Yamada T, Zhang K, Yamada A, Zhu D, Saxon A. B lymphocyte stimulator activates p38 mitogen-activated protein kinase in human Ig class switch recombination. Am J Respir Cell Mol Biol 2005;32:388–94.
[3] Moore PA, Belvedere O, Orr A, Pieri K, LaFleur DW, Feng P, et al. BLyS: member of the tumor necrosis factor family and B lymphocyte stimulator. Science 1999;285:260–3.
[4] Kato A, Truong-Tran AQ, Scott AL, Matsumoto K, Schleimer RP. Airway epithelial cells produce B cell-activating factor of TNF family by an IFN-beta-dependent mechanism. J Immunol 2006;177:7164–72.
[5] Kato A, Peters A, Suh L, Carter R, Harris KE, Chandra R, et al. Evidence of a role for B cell-activating factor of the TNF family in the pathogenesis of chronic rhinosinusitis with nasal polyps. J Allergy Clin Immunol 2008;121:1385–92.
[6] Jacobs BL, Langland JO. When two strands are better than one: the mediators and modulators of the cellular responses to double-stranded RNA. Virology 1996;219:339–49.

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[7] Alexopoulou L, Holt AC, Medzhitov R, Flavell RA. Recognition of double-stranded RNA and activation of NF-kappaB by toll-like receptor 3. Nature 2001;413:732–8.
[8] Liu Y, Kimura K, Yanai R, Chikama T, Nishida T. Cytokine, chemokine, and adhesion molecule expression mediated by MAPKs in human corneal fibroblasts exposed to poly(I:C). Invest Ophthalmol Vis Sci 2008;49:3336–44.
[9] Steer SA, Moran JM, Christmann BS, Maggi Jr LB, Corbett JA. Role of MAPK in the regulation of double-stranded RNA- and encephalomyocarditis virus-induced cyclooxygenase-2 expression by macrophages. J Immunol 2006;177:3413–20.
[10] Pisegna S, Pirozzi G, Piccoli M, Frati L, Santoni A, Palmieri G. p38 MAPK activation controls the TLR3-mediated up-regulation of cytotoxicity and cytokine production in human NK cells. Blood 2004;104:4157–64.
[11] Sarkar SN, Peters KL, Elco CP, Sakamoto S, Pal S, Sen GC. Novel roles of TLR3 tyrosine phosphorylation and PI3 kinase in double-stranded RNA signaling. Nat Struct Mol Biol 2004;11:1060–7.
[12] Lau C, Wang X, Song L, North M, Wiehler S, et al. Syk associates with clathrin and mediates phosphatidylinositol 3-kinase activation during human rhinovirus internalization. J Immunol 2008;180:870–80.
[13] Ohata J, Zvaifler NJ, Nishio M, Boyle DL, Kalled SL, Carson DA, et al. Fibroblast-like synoviocytes of mesenchymal origin express functional B cell-activating factor of the TNF family in response to proinflammatory cytokines. J Immunol 2005;174:864–70.
[14] Bedke N, Haitchi HM, Xatzipsalti M, Holgate ST, Davies DE. Contribution of bronchial fibroblasts to the antiviral response in asthma. J Immunol 2009;182:3660–7.
[15] Skibinski G, Elborn JS, Ennis M. Bronchial epithelial cell growth regulation in fibroblast cocultures: the role of hepatocyte growth factor. Am J Physiol Lung Cell Mol Physiol 2007;293:69–76.
[16] Boero S, Sabatini F, Silvestri M, Petecchia L, Nachira A, et al. Modulation of human lung fibroblast functions by ciclesonide: evidence for its conversion into the active metabolite desisobutyryl-ciclesonide. Immunol Lett 2007;112:39–46.
[17] Yamauchi E, Shoji S, Nishihara M, Shimoda T, Nishima S. Contribution of lung fibroblast migration in the fibrotic process of airway remodeling in asthma. Allergol Int 2008;57:73–8.
[18] Yamada T, Fujieda S, Yanagi S, Yamamura H, Inatome R, Sunaga H, et al. Protein-tyrosine kinase Syk expressed in human nasal fibroblasts and its effect on RANTES production. J Immunol 2001;166:538–43.
[19] Yamada T, Fujieda S, Yanagi S, Yamamura H, Inatome R, Yamamoto H, et al. IL-1 induced chemokine production through the association of Syk with TNF receptor-associated factor-6 in nasal fibroblast lines. J Immunol 2001;167:283–8.
[20] Yang M, Hase H, Legarda-Addison D, Varughese L, Seed B, Ting AT. B cell maturation antigen, the receptor for a proliferation-inducing ligand and B cell-activating factor of the TNF family, induces antigen presentation in B cells. J Immunol 2005;175:2814–24.
[21] Shan X, Chen L, Cao M, Xu L, Zhang S. Effects of human soluble BAFF synthesized in *Escherichia coli* on CD4+ and CD8+ T lymphocytes as well as NK cells in mice. Physiol Res 2006;55:301–7.
[22] Sutherland AP, Ng LG, Fletcher CA, Shum B, Newton RA, Grey ST, et al. BAFF augments certain Th1-associated inflammatory responses. J Immunol 2005;174:5537–44.
[23] Darveau ME, Jacques E, Rouabhia M, Hamid Q, Chakir J. Increased T-cell survival by structural bronchial cells derived from asthmatic subjects cultured in an engineered human mucosa. J Allergy Clin Immunol 2008;121:692–9.
[24] Ettinger R, Sims GP, Robbins R, Withers D, Fischer RT, Grammer AC, et al. IL-21 and BAFF/BLyS synergize in stimulating plasma cell differentiation from a unique population of human splenic memory B cells. J Immunol 2007;178:2872–82.
[25] Furie R, Stohl W, Ginzler EM, Becker M, Mishra N, Chatham W, et al. Biologic activity and safety of belimumab, a neutralizing anti-B-lymphocyte stimulator (BLyS) monoclonal antibody: a phase I trial in patients with systemic lupus erythematosus. Arthritis Res Ther 2008;10:109.
[26] Bilsborough J, Chadwick E, Mudri S, Ye X, Henderson Jr WR, Waggie K, et al. TACI-Ig prevents the development of airway hyperresponsiveness in a murine model of asthma. Clin Exp Allergy 2008;38:1959–68.
[27] Kato A, Xiao H, Chustz RT, Liu MC, Schleimer RP. Local release of B cell-activating factor of the TNF family after segmental allergen challenge of allergic subjects. J Allergy Clin Immunol 2009;123:369–75.

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研究成果の刊行に関する一覧表（大久保公裕）

雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
◎	Gotoh M, , Hashiguchi K, Okubo K.	Efficacy of Epinastine Hydrochloride for Antigen-provoked Nasal Symptoms in Subjects with Orchard Grass Pollinosis.	Allergol Int.	60 (1)		2011 in press
◎	Gotoh M, Okubo K, Okuda M, Hamada C.	Clinical pharmacology study of the corticosteroid nasal spray dexamethasone cipecilate (NS-126): examination of the durability of efficacy in the nasal induction test.	Expert Opin Investig Drugs.	19 (12)	1475-86	2010
	村山貢司、馬場廣太郎、大久保公裕	スギ花粉症有病率の地域差について	アレルギー	59 (1)	47-54	2010
	太田伸男、鈴木祐輔、後藤崇成、高橋裕一、青柳優、大久保公裕	スギ花粉症患者の QOL と睡眠障害	アレルギー・免疫	17 (2)	250-257	2010
	岡野光博、大久保公裕	2009 年におけるスギ花粉症に対する第 2 世代抗ヒスタミン薬による初期療法の有用性 - JRQLQ No1 を用いた QOL の評価	アレルギー・免疫	17 (1)	102-108	2010
	奥田稔、今野昭義、馬場廣太郎、大久保公裕、竹中洋、浜田知久馬	鼻噴霧用ステロイド薬デキサメタゾンシペシル酸エステル (NS-126P) の通年性アレルギー性鼻炎における用法用量試験	耳鼻臨床	補 125	1-17	2010

	Okubo K, Uchida E, Nogami S .	Levocabastine nasal spray significantly improves perennial allergic rhinitis: A single blind placebo-controlled study.	Auris Nasus Larynx	37	436-442	2010
	指原紀宏、後藤穣、池上秀二、紀光助、竹友直生、伊藤裕之、大久保公裕	乳酸菌Lactobacillus gasseri OLL2809のスギ花粉症改善効果	アレルギーの臨床	30	53-58.	2010
	大久保公裕、後藤穣	専門医のためのアレルギー学講座	アレルギー性鼻炎. アレルギー	59 (2)	75-81	2010
	大久保公裕.	高齢者のアレルギー性鼻炎	アレルギー・免疫	17 (3)	418-423	2010
	大久保公裕.	舌下免疫療法	Medicina	47 (2)	312-315	2010
	Okubo K, Okuda M, Magara H, Kaneko K	Olopatadine hydrochloride in children: efficacy and safety for perennial allergic rhinitis	CMRO	26 (7)	1657-65	2010
	Nishihata S, Murata T, Inoue S, Okubo K, et al	Prevalence of Japanese cedar pollinosis inTokyo: a suvey conducted by Tokyo metropolitan government	Clin Exp Allergy rev	10	8-11	2010
	Okubo K, Gotoh M	Allergen Immunotherapy for allergic rhinitis	J Nippon Med Sch	77 (6)	285-289	2010

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁
	大久保公裕 後藤穣	プライマリケアのための花粉症診療		プライマリケアのための花粉症診療	医薬ジャーナル社	大阪	2010	

研究成果の刊行に関する一覧表（岡本美孝）

雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	Muradil M, Okamoto Y, Yonekura S, Chazono H, Hisamitu M, Horiguchi S, Hanazawa T, Takahashi Y, Yokota K, Okumura S	Reevalution of Pollen Quantitation by an Automatic pollen Counter	Allergy and Asthma Proceedings	31 (5)	422-427	2010
◎	Fujimura T, Yonekura S, Taniguchi Y, Horiguchi S, Saito A, Yasueda H, Nakayanma T, Takemori T, Taniguchi M, Sakaguchi M, Okamoto Y	The Induced Regulatory T Cell Level, Defined as the Proportion of IL-10+Foxp+Cells among CD25+CD4+Leukocytes, Is Potential Therapeutic Biomarker for Sublingual Immunotherapy: A Preliminary Report	Int Arch Allergy Immunology	153	378-387	2010
◎	Fujimura T, Okamoto Y	Antigen-Specific Immunotherapy against Allergic Rhinitins:The State of the Art	Allergology International	59 No. 1	21-31	2010

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雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	Ishida A, Ota N, Koike S, Aoyagi M, and Yamakawa M.	Overexpression of gluco-corticoid receptor-β in severe allergic rhinitis	Auris Nasus Larynx	37	584-588	2010
	Ishida A, Hozumi Y, Goto K, Ito T, Aoyagi M, and Yamakawa M.	Expression of glucocorticoid receptor spliced variants in lymphoma cell lines,	Hematological Oncology.	29	1-4	2010
	鈴木祐輔,太田伸男 櫻井真一,青柳優 深瀬滋	山形市におけるアレルギー性鼻炎患者の花粉抗原陽性率の検討.	アレルギー	58	1619-1628	2009
◎	Yamauchi k, Tamura G, Akasaka T, Chiba T, Honda K, Kishi M, Kobayashi H, Kuronuma T, Morikawa T, Ogawa H, Ohta N, et al	Analysis of the comorbidity of bronchial asthma and allergic rhinitis by questionnaire in 10,009 patients.	Allegol Int.	58	55-61	2009
	太田伸男,鈴木祐輔,後藤崇成,高橋裕一,青柳優,大久保公裕	スギ花粉症患者のQOLと睡眠障害	アレルギー・免疫	17	90-97	2010

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	なし							

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雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	仲田拡人、中込一之、高久洋太郎、西原冬実、山口剛史、杣知行、萩原弘一、金澤寶、加瀬康弘、永田真.	鼻炎症状と喘息症状の連関についてのアンケート調査.	アレルギー	59	688-698	2010;
	Takaku Y,. Nakagome K, Kobayashi T, Yamaguchi T, Nishihara F, Soma T, Hagiwara K, Kanazawa M, and Nagata M.	Changes in airway inflammation and hyperresponsiveness after inhaled corticosteroid cessation in allergic asthma.	Int Arch Allergy Immunol.	152 (Suppl. 1):	41-46	2010
	Nagata M and Nakagome K.	Allergen Immunotherapy in Asthma: Current Status and Future Perspectives.	Allergology International.	59	15-9	2010

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁
	杣知行、永田真	特異的免疫療法―内科―. アレルギ		アレルギー疾患イラストレイテッド	メディカルレビュー社	東京	2010	pp274-281

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雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	Gotoh M., Hashiguchi K, Okubo K.	Efficacy of Epinastine Hydrochloride for Antigen-provoked Nasal Symptoms in Subjects with Orchard Grass Pollinosis.	Allergol Int.	60 (1)		2011 in press
◎	Gotoh M, Okubo K, Okuda M, Hamada C.	Clinical pharmacology study of the corticosteroid nasal spray dexamethasone cipecilate (NS-126): examination of the durability of efficacy in the nasal induction test.	Expert Opin Investig Drugs.	19 (12)	1475-86	2010

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁
	大久保公裕 後藤穣		共著	プライマリケアのための花粉症診療	医薬ジャーナル.	大阪	2010	

研究成果の刊行に関する一覧表（湯田厚司）

雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
	湯田厚司	内科医のための花粉症入門　花粉症の舌下免疫療法	Ｍｅｂｉｏ	27(3)	42-49	2010
	湯田厚司	花粉症の最新治療　小児に対する舌下免疫療法	アレルギーの臨床	30(3)	41-46	2010
◎	荻原仁美，湯田厚司，他	スギ花粉症に対する免疫療法の治療成績	耳鼻臨床	103(3)	215-220	2010
◎	湯田厚司，山中恵一，大久保公裕	スギ花粉症に対する舌下免疫療法臨床効果と誘導性制御性T細胞による免疫調整	日鼻誌	49(1)	15-21	2010
	荻原仁美，湯田厚司，他	スギ花粉症に対する免疫療法のQOL評価　薬物療法と比較して	日鼻誌	49(1)	26-32	2010
◎	湯田厚司，荻原仁美，他	スギ花粉症に対する舌下免疫療法の治療年数による臨床効果の増強と治療終了後の継続効果	アレルギー	59(11)	1552-1561	2010
	垣内舞美，湯田厚司，他	スギ花粉症に対する皮下および舌下免疫療法の花粉飛散数と治療効果	東海花粉症研究会誌	21	30-36	2010
	湯田厚司，他	三重県におけるスギ・ヒノキ科花粉の2009年飛散結果と2010年飛散予想	東海花粉症研究会誌	21	70-74	2010
	Yamanaka K, Yuta A, Okubo K,, et al.	SLIT Improves Cedar Pollinosis by Restoring IL-10 Production from Trl amd Monocytes Productivity Is Critical for Becoming Allergic	Allergol Int.	60(1)	in press	2010

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁

研究成果の刊行に関する一覧表（増山敬祐）

雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	Ouyang Y, Miyata M, Masuyama K, Nakao A, et al.	TGF-β signaling may play a role in the development of goblet cell hyperplasia in a mouse model of allergic rhinitis.	Allergol Int	59	313-319	2010
◎	増山敬祐、松岡伴和、他.	内科医が留意すべき耳鼻咽喉科疾患の診断と治療、予防　患者の症状から見逃さないためのコツとポイント　鼻漏・くしゃみ.	Progress in medicine	30	1063-69	2010

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁
	なし							

研究成果の刊行に関する一覧表（岡野光博）

雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	Okano M, Fujiwara T, Higaki T, Makihara S, Haruna T, Noda Y, Kanai K, Kariya S, Yasueda H, Nishizaki K	Characterization of pollen antigen-induced IL-31 production by peripheral blood mononuclear cells in allergic rhinitis.	Journal of Allergy and Clinical Immunolog	127	277-279	2011
	Hosoya K, Satoh T, Yamamoto Y, Saeki K, Igawa K, Okano M, Moriya T, Imamura O, Nemoto Y, Yokozeki H	Gene silencing of STAT6 with siRNA ameliorates contact hypersensitivity and allergic rhinitis.	Allergy	66	124-131	2011
◎	岡野光博	上気道からみたOne airway, one disease.	喘息	23	643-652	2010
	岡野光博	親がアレルギー性鼻炎ですが、子どもにも遺伝しますか？	JOHNS	26	1402-1405	2010
	岡野光博	DP受容体	鼻アレルギーフロンティア	10	34-38	2010
	岡野光博	ヒノキ花粉のスギ・ヒノキ花粉症に与える影響.	メディカルビューポイント	32	21-26	2011
◎	岡野光博、難波弘行、佐橋紀男	2011年ヒノキ科花粉飛散予測.	アレルギーの臨床	31	21-26	2011

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁
	岡野光博	花粉症に対する初期療法のEBMとは？	池田勝久、武田憲昭、井之口　明、原渕保明、丹生健一	EBM　耳鼻咽喉科・頭頸部外科の治療（第1版）	中外医学社	東京	2010	20-22

	岡野光博	抗アレルギー薬 トロンボキサンA$_2$合成阻害薬・拮抗薬	永倉俊和、森田 寛、足立 満	アレルギー疾患イラストレイテッド（第2版	メディカルビュー社	東京	2010	214-219

研究成果の刊行に関する一覧表（藤枝　重治）

雑誌：

掲載に◎	発表者氏名	論文タイトル名	発表誌名	巻号	頁	出版年
◎	Makino Y, Noguchi E, Takahashi N, Matsumoto Y, Kubo S, Yamada T, Imoto Y, Ito Y, Osawa Y, Shibasaki M, Uchida K, Meno K, Suzuki H, Okubo K, Arinami T, Fujieda S.	Apolipoprotein A-IV is a candidate target molecule for the treatment of seasonal allergic rhinitis.	J Allergy Clin Immunol.	126	1163-9	2010
◎	Yamada T, Lizhong S, Takahashi N, Kubo S, Narita N, Suzuki D, Takabayashi T, Kimura Y, Fujieda S.	Poly(I:C) induces BLyS-expression of airway fibroblasts through phosphatidylinositol 3-kinase.	Cytokine.	50	163-9.	2010
◎	Imoto Y, Enomoto H, Fujieda S, Okamoto M, Sakashita M, Susuki D, Okada M, Hirota T, Tamari M, Ebe K, Arinami T, Noguchi E.	S2554X mutation in the filaggrin gene is associated with allergen sensitization in the Japanese population.	J Allergy Clin Immunol.	125	498-500	2010
◎	Sakashita M, Hirota T, Harada M, Nakamichi R, Tsunoda T, Osawa Y, Kojima A, Okamoto M, Suzuki D, Kubo S, Imoto Y, Nakamura Y, Tamari M, Fujieda S.	Prevalence of allergic rhinitis sensitization to common aeroallergens in a Japanese population.	Int Arch Allergy Immunol.	151	255-61	2010
◎	Yamamoto H, Yamada T, Kubo S, Osawa Y, Kimura Y, Oh M, Susuki D, Takabayashi T, Okamoto M, Fujieda S.	Efficacy of oral olopatadine hydrochloride for the treatment of seasonal allergic rhinitis: A randomized, double-blind, placebo-controlled study.	Allergy Asthma Proc	31	296- 303	2010
◎	Imoto Y, Kojima A, Osawa Y, Sunaga H, Fujieda S.	Cough reflex induced by capsaicin inhalation in patients with dysphagia.	Acta Otolaryngol.	131	96-100	2011
	Yamamoto H, Yamada T, Takabayashi T, Sunaga H, Oh M, Narita N, Kojima A, Fujieda S.	Platelet derived endothelial cell growth factor/Thymidine phosphorylase enhanced human IgE production.	Allegol Int.			
◎	Takabayashi T, Xie MJ, Takeuchi S, Kawasaki M, Yagi H, Okamoto M, Tariqur RM, Malik F, Kuroda K, Kubota C, Fujieda S, Nagano T, Sato M.	LL5beta directs the translocation of filamin A and SHIP2 to sites of phosphatidylinositol 3,4,5-triphosphate (PtdIns(3,4,5)P3) accumulation, and PtdIns(3,4,5)P3	J Biol Chem.	285	16155-65	2010

		localization is mutually modified by co-recruited SHIP2.				
◎	Kimura Y, Sugimoto C, Takabayashi T, Tanaka T, Kojima A, Narita N, Fujieda S.	Bax-gene transfer enhances apoptosis by steroid treatment in human nasal fibroblasts.	Eur Arch Otorhinolaryngol.	267	61-6	2010

書籍：

	著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	頁
	なし							