Diabetes Res Clin Pract. 73(2):215-217,2006

Nagai S, Shimizu C, Kimura Y, Umetsu M, Taniguchi S, Takeuchi J, Atsumi T, Yoshioka N, Kubo M, Koike T.
A case of reversed pituitary dysfunction with intrasellar mass.
J Endocrinol Invest. 29(4):367-372,2006

Amengual O, Atsumi T, Koike T.
Pathophysiology of the antiphospholipid syndrome: roles of anticardiolipin antibodies in thrombosis and fibrinolysis.
APLAR J Rheumatol. 9:377-386,2006

Mizukami K, Nakabayashi T, Naitoh S, Takeda M, Tarumi T, Mizoguchi I, Ieko M, Koike T.
One novel and one recurrent mutation in the PROS1 gene cause type I protein S deficiency in patients with pulmonary embolism associated with deep vein thrombosis.
Am J Hematol. 81:787-797,2006

Ieko M, Tarumi T, Nakabayashi T, Yoshida M, Naito S, Koike,T.
Factor Xa inhibitors: new anti-thrombotic agents and their characteristics.
Frontiers in Bioscience. 11:232-248,2006

Furusaki A, Judo S,Yamashita Y, Amasaki Y, Atsumi T, Koike T.
TRAIL-mediated cytotoxicity: Impacts of sTRAIL and vTRAIL microvesicles.
J Biol Sci. 6(1):150-159,2006

Niwa H, Koumoto C, Shiga T, Takeuchi J, Mishima S, Segawa T, Atsumi T, Shimizu C, Koike T, Yoshioka N.
Clinical analysis of cognitive function in diabetic patients by MMSE and SPECT.
Diabetes Res Clin Pract. 72:142-147,2006

Hashimoto T, Nishio M, Sakai T, Fujimoto K, Sato N, Endo T, Koike T.
Acute schizophrenic symptoms as the initial manifestation of HIV infection that respond to highly active antiretroviral therapy.
Clinical Infectious Diseases. 42:1653-1655,2006

Furukawa S, Yasuda S, Amengual O, Horita T, Atsumi T, Koike T.
Protective effect of pravastatin on vascular endothelium in patients with System Sclerosis: a pilot study.
Ann Rheum Dis. 65(8):1118-1120,2006

Nishio M, Fujimoto K, Yamamoto S, Endo T, Sakai T, Obara M , Kumano K, Minauchi K, Yamaguchi K, Takeda Y, Sato N, Koizumi K, Mukai M, Koike T.
Hypogammaglobulinemmia with a selective delayed recovery inmemory B cells and an impaired Isotype expression after rituximab administration as an adjuvant to autologous stem cell transplantation for non-Hodgkin lymphoma.
Eur J Haemato. 77:226-232,2006

H.知的財産権の出願・登録状況（予定を含む）

なし

表1．健常人とSLE患者間におけるRasGRP1スプライスバリアントの頻度の

	(%)	オッズ比	95% C.I.	p-value
エクソン 11の欠損				
健常人	11.0			
SLE	26.6	2.94	1.43 – 6.07	0.0129
何らかのスプライス異常				
健常人	13.0			
SLE	36.0	3.76	1.92– 7.37	0.0001

表2，患者の臨床像とRasGRP1スプライスバリアントの出現頻度

	スプライス異常なし	スプライス異常あり	p値
年齢	26.0 ± 6.0	36.0 ± 11.0	0.024
性別（男性/女性）	3/7	2/18	
疾患活動性 (BILAG)	9.8 ± 5.3	11.4 ± 7.0	0.494
罹病期間 (月)	53.8 ± 72.9	152 ± 116	0.020
PSL (mg/day)	11.1 ± 15.1	12.1 ± 14.2	0.790
治療なし/治療開始前	34	11	
治療中	65	40	0.153
(クローン数)			

図1; 末梢血単核球分画におけるRasGRP1発現

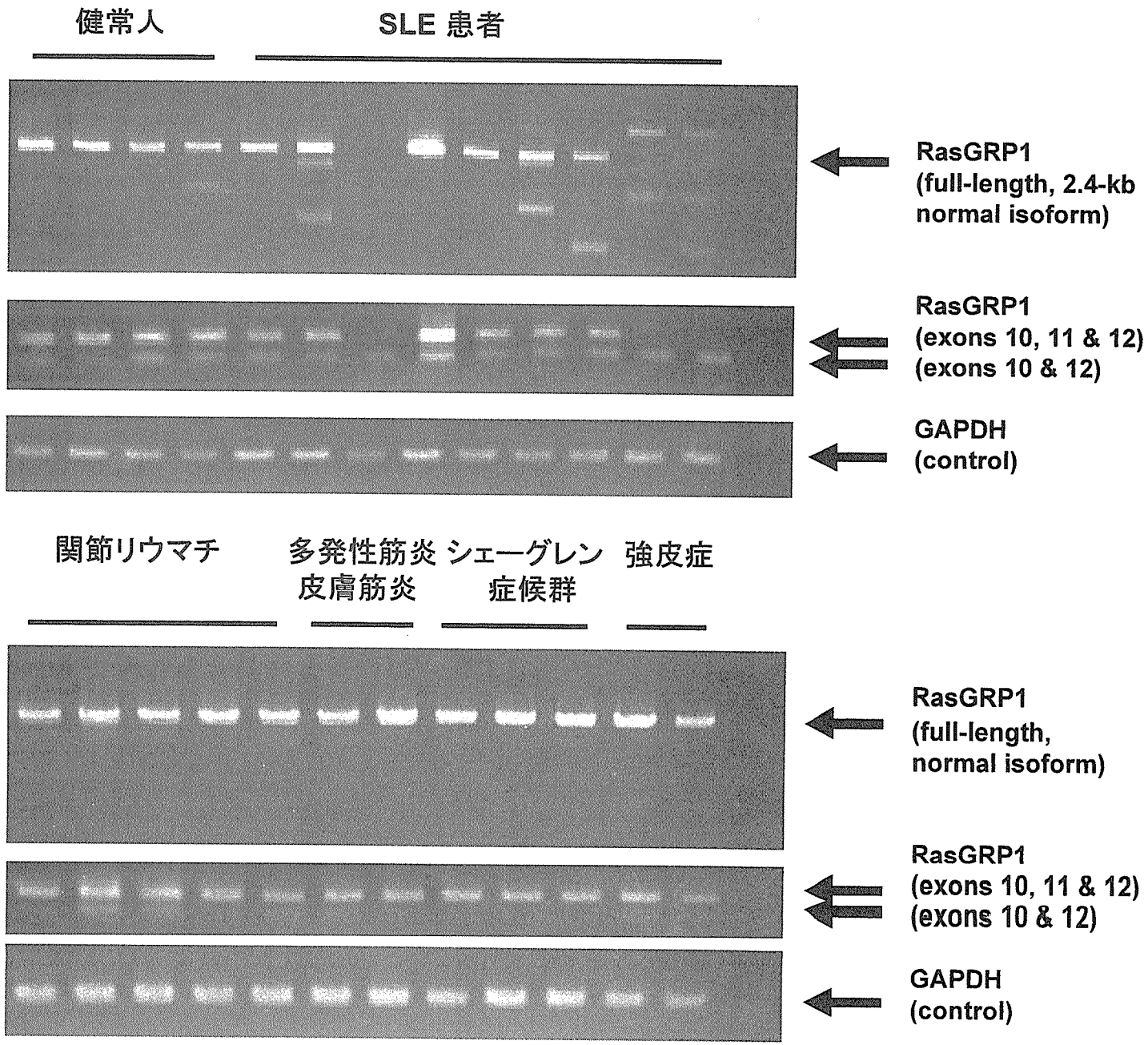
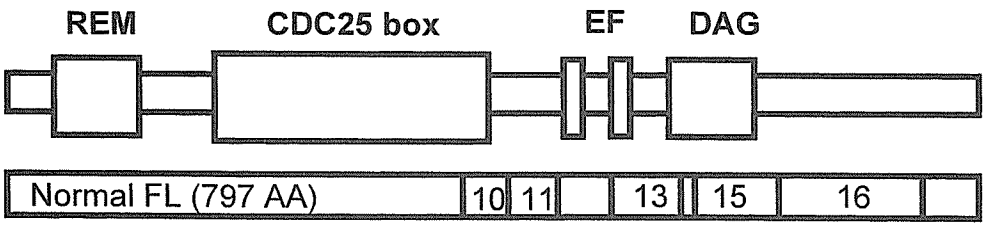


図2；RasGRP1 新規スプライス異常



	健常人 (100 clones)	SLE (150 clones)	治療（なし vs. あり） (45 vs. 105 clones)
Splice variant A (762 AA)	6 (6.0)	16 (10.7)	5 vs. 11
Splice variant B (597 AA)	1 (1.0)	9 (6.0)	3 vs. 6
Splice variant C (481 AA)	0	5 (3.3)	1 vs. 4
Splice variant D (546 AA)	4 (4.0)	8 (5.3)	0 vs. 8
Splice variant E (737 AA)	0	3 (2.0)	1 vs. 2
Splice variant F (632 AA)	2 (2.0)	2 (1.3)	0 vs. 2
Splice variant G (581 AA)	0	3 (2.0)	0 vs. 3
Splice variant H (523 AA)	0	2 (1.3)	0 vs. 2
Splice variant I (711 AA)	0	1 (0.7)	1 vs. 0
Splice variant J (735 AA)	0	1 (0.7)	0 vs. 1
Splice variant K (516 AA)	0	1 (0.7)	0 vs. 1
Splice variant L (746 AA)	0	1 (0.7)	0 vs. 1
Splice variant M (173 AA)	0	1 (0.7)	0 vs. 1
		clones (%)	clones

図3; 末梢血T細胞におけるRasGRP1蛋白発現の検討

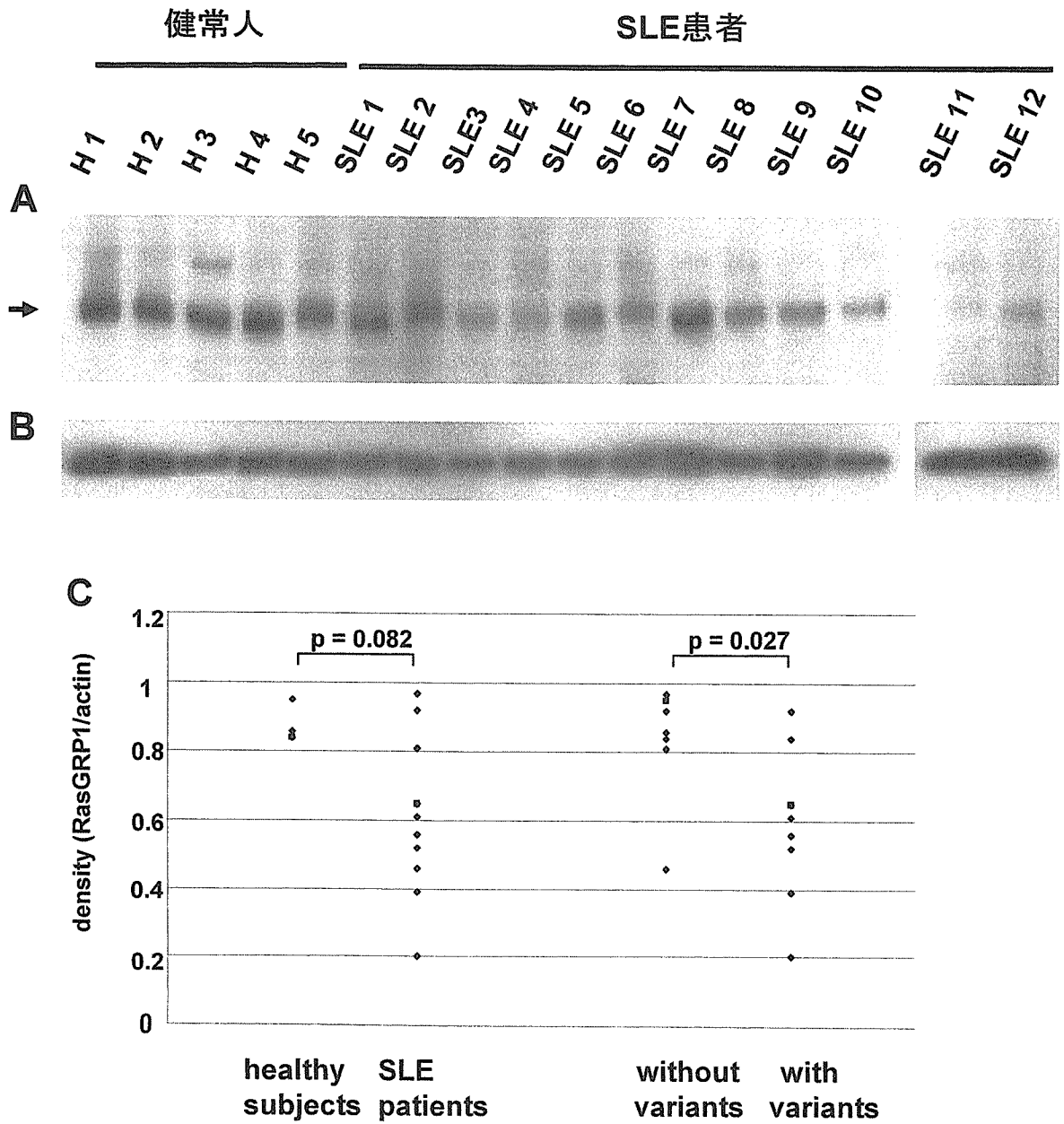
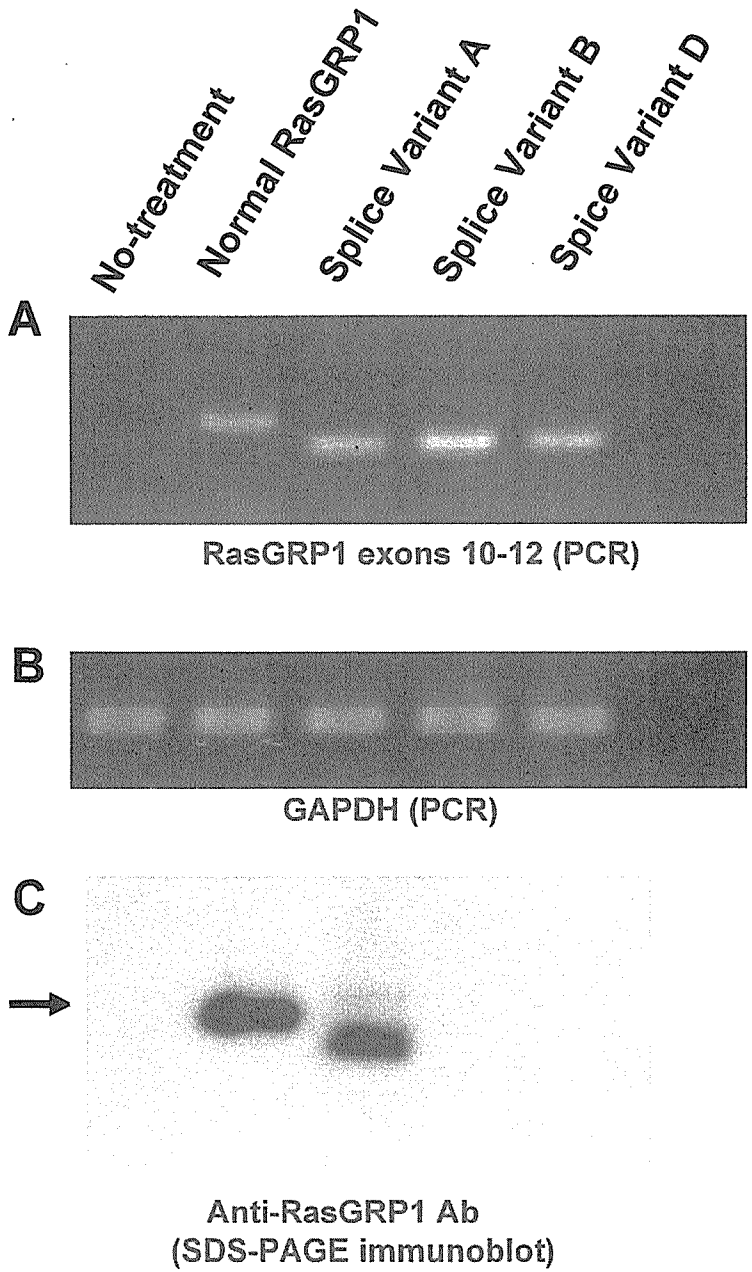


図. 4;HEK-293細胞を用いたRasGRP1 およびスプライスバリアントの発現検討



IV　研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表(平成18年度)

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Wakamatsu, E., Nakamura, Y., Matsumoto, I., Goto, D., Ito, S., Tsutsumi, A., and Sumida, T.	DNA microarray analysis of labial salivary glands from patients with Sjogren's syndrome.	Ann. Rheum. Dis.		in press	
Yoshioka, H., Ito, S., Handa, S., Tomiha, S., Kose, K., Haishi, T., Tsutsumi, A., and Sumida, T.	Low-field compact magnetic resonance imaging system for the hand and wrist in rheumatoid arthritis.	J.Magn, Res. Ima.	23	370-376	2006
Wakamatsu, E., Matsumoto, I., Naito, Y., Goto, D., Mamura , M., Ito, S., Tsutsumi , A., and Sumida, T.	Overexpression of phosphorylated STAT-1 α in the labial salivary glands of patients with Sjogren's syndrome.	Arthritis. Rheum.	54	3476-3484	2006
Kori, Y., Matsumoto, I., Zhang, H., Yasukochi, T., Hayashi, T., Iwanami, K., Goto, D., Ito, S., Tsutsumi, A. and Sumida, T.	Characterization of Th1/Th2 type, glusoce-6-phoshate isomerase reactive T cells in the generation of rheumatoid arthritis.	Ann. Rheum. Dis.	65	968-969	2006
Naito, Y., Matsumoto, I., Wakamatsu, E., Goto, D., Ito, S., Tsutsumi, A., and Sumida, T.	Altered peptide ligands regulate muscarinic acetylcholine receptor reactive T cells of patients with Sjogren's syndrome.	Ann. Rheum. Dis.	65	269-271	2006
Suzuki, E., Tsutsumi, A., Sugihara, M., Mamura, M., Goto, D., Matsumoto, I., Ito, S., Ikeda, K., Ochiai, N., Sato, Y., and Sumida, T.	Expression of TNF- α, tristetraprolin, T-cell intracellular antige-1 and Hu antigen R genes in snovium of patients with rheumatoid arthritis.	Int. J. Mol. Med.	18	273-278	2006
Suzuki, E., Tsutsumi, A., Goto, D., Matsumoto, I., Ito, S., Otsu, M., Onodera, M., Takahashi, S., Sato, Y., and Sumida, T.	Gene transduction of tristetraprolin or its active domain reduces TNF- α production by Jurkat T cells.	Int. J. Mol. Med.	17	801-809	2006
Chino, Y., Murata, H., Goto, D., Matsumoto, I., Tsutsumi, A., Sakamoto, T., Ohtsuka, M., Sekisawa, K., Ito S., and Sumida, T.	T cell receptor BV gene repertoire of lymphocytes in bronchoalveolar lavage fjuid of polymyositis/dermatomyositis patients with interstitial pneumonitis.	Int. J. Mol. Med.	17	101-109	2006
Hirata, S., Matsuyoshi, H., Fukuma, D., Kurisaki, A., Uemura, Y., Nishimura, Y.* and Senju, S.* (*equal contribution)	Involvement of regulatory T cells in the experimental autoimmune encephalomyelitis- preventive effect of dendritic cells expressing myelin oligodendrocyte glycoprotein plus TRAIL[1]	J. Immunol.	178	918-925	2007
千住 覚, 西村泰治	第１３章　T細胞応答の抑制性制御	免疫応答と免疫病態の統合的分子理解に向けて(仮称)(南山堂, 東京)		印刷中	
千住 覚, 西村泰治	MHCとは何か	アニテックス2007年3月号「動物MHC」(研成社, 東京)		印刷中	

Yamamoto K, Okamoto A, Fujio K.	Antigen-specific immunotherapy for autoimmune diseases.	Expert Opin. Biol. Ther.		in press	
Fujio K, Okamura T, Okamoto A, Yamamoto K.	T cell receptor gene therapy for autoimmune disease.	Ann N Y Acad Sci.		in press	
Shoda H, Fujio K, Yamaguchi Y, Okamoto A, Sawada T, Kochi Y, Yamamoto K.	Interactions between IL-32 and tumor necrosis factor alpha contribute to the exacerbation of immune-inflammatory diseases.	Arthritis Res Ther.	8(6)	R166	2006
Fujio K, Okamoto A, Araki Y, Shoda H, Tahara H, Tsuno NH, Takahashi K, Kitamura T, Yamamoto K.	Gene therapy of arthritis with TCR isolated from the inflamed paw[1].	J Immunol.	177 (11)	8140-8147	2006
Ohata J, Miura T, Hori S, Ziegler SF, Kohsaka H	Enhanced efficacy of regulatory T cell transfer by elevated Foxp3 expression against increasing resistance induced in arthritic hosts	Arthritis Rheum		in press	
大畑順子、上阪 等	Foxp3遺伝子導入によるレギュラトリーT細胞の作成	臨床免疫・アレルギー科	46(3)	258-261	2006
Tokunaga M, Saito K, Kawabata D, Imura Y, Fujii T, Nakayamada S, Tsujimura S, Nawata M, Iwata S, Azuma T, Mimori T, Tanaka Y	Efficacy of rituximab (Anti-CD20) for refractory systemic lupus erythematosus involving the central nervous system.	Ann Rheum Dis		in press	
Yoshifuji H, Fujii T, Kobayashi S, Imura Y, Fujita Y, Kawabata D, Usui T, Tanaka M, Nagai S, Umehara H, Mimori T	Anti-aminoacyl- tRNA synthetase antibodies in clinical course prediction of interstitial lung disease complicated with idiopathic inflammatory myopathies.	Autoimmunity	39(3)	233-241	2006
Miyachi K, Hosaka H, Nakamura N, Miyakawa H, Mimori T, Shibata M, Matsushima S, Chinoh H, Horigome T, Hankins RW, Zhang M, Fritzler MJ	Anti-p97/VCP antibodies: an autoantibody marker for a subset of primary biliary cirrhosis patients with milder disease?	Scand J Immunol	63(5)	376-382	2006
三森経世	抗リウマチ薬（DMARDs）の種類と選び方	治療	89(2)	272-276	2007
三森経世，橋本求	抗シトルリン化蛋白抗体	内科	97(4)	721-723	2006
三森経世	治療薬の使い方とピットフォール 免疫抑制薬.	内科	97(4)	641-645	2006
三森経世	関節リウマチの早期診断とその有用性.	日本医師会雑誌	135 (5)	1038-1042	2006
三森経世	関節リウマチと抗シトルリン化蛋白抗体.	BIO Clinica	21 (10)	901-907	2006
三森経世	関節リウマチの最新治療ガイドライン	Mebio	23 (12)	16-21	2006
野島崇樹，三森経世	自己抗体	Medical Practice	23(4)	605-609	2006
大村浩一郎，三森経世	抗シトルリン化蛋白抗体（抗CCP抗体）	リウマチ科	35(1)	8-15	2006

川端大介，三森経世	抗リウマチ薬の現状	治療学	40(7)	765-768	2006
吉藤元，三森経世	関節リウマチの血清学的検査の進歩	Current Therapy	24(5)	406-410	2006
三森経世	関節リウマチ	薬局(病気と薬の説明ガイド)	57(増刊号)	1035-1043	2006
Pyz E, Naidenko O, Miyake S, Yamamura T, Berberich I, Cardell S, Kronenberg M, Herrmann T.	The complementarity determining region 2 of BV8S2 (V beta 8.2) contributes to antigen recognition by rat invariant NKT cell TCR.	J. Immunol.	176 (12)	7447-7455	2006
Miyamoto K, Miyake S, Mizuno M, Oka N, Kusunoki S and Yamamura T.	Selective COX-2 inhibitor celecoxib prevents experimental autoimmune encephalomyelitis through COX-2 independent pathway.	Brain	129	1984-1992	2006
Croxford JL, Miyake S, Huang Y-Y, Shimamura M and Yamamura T.	Invariant Vα19i T cells regulate autoimmune inflammation.	Nat. Immunol.	7(9)	987-994	2006
Aranami T, Miyake S and Yamamura T.	Differential expression of CD11c by peripheral blood NK cells reflects temporal activity of multiple sclerosis.	J. Immunol.	177 (8)	5659-5667	2006
Satoh J-i, Nakanishi M, Koike F, Onoue H, Aranami T, Yamamoto T, Kawai M, Kikuchi S, Nomura K, Yokoyama K, Ota K, Saito T, Ohta M, Miyake S, Kanda T, Fukazawa T, Yamamura T.	T cell gene expression profiling identifies distinct subgroups of Japanese multiple sclerosis patients.	J. Neuroimmunol.	174 (1)	108-118	2006
Ogawa, Y., Razzaque, M.S., Kameyama, K., Hasegawa, G., Shimmura, S., Kawai, M., Okamoto, S., Ikeda, Y., Tsubota, K., Kawakami, Y., and Kuwana, M.	Role of heat shock protein 47, a collagen-binding chaperon, in lacrimal gland pathology in patients with cGVHD.	Invest. Ophthalmol. Vis. Sci.		in press	
Sato, S., Kuwana, M., and Hirakata, M.	Clinical characteristics of Japanese patients with anti-OJ (anti-isoleucyl-tRNA synthetase) autoantibodies.	Rheumatology		in press	
Kajihara, M., Okazaki, Y., Kato, S., Ishii, H., Kawakami, Y., Ikeda, Y., and Kuwana, M.	Evaluation of platelet kinetics in patients with liver cirrhosis: Similarity to idiopathic thrombocytopenic purpura.	J. Gastroenterol. Hepatol.	22	112-118	2007
Takahashi, H., Amagai, M., Tanikawa, A., Suzuki, S., Ikeda, Y., Nishikawa, T., Kawakami, Y., and Kuwana, M.	T helper type 2-biased natural killer cell phenotype in patients with pemphigus vulgaris.	J. Invest. Dermatol.	127	324-330	2007
Nagata, E., Hamada, J., Shimizu, T., Shibata, M., Suzuki, S., Osada, T., Takaoka, R., Kuwana, M., and Suzuki, N.	Altered levels of serotonin in lymphoblasts derived from migraine patients.	Neurosci. Res.	57	179-183	2007
Namboodiri, A.M., Rocca, K.M. Kuwana, M., and Pandey, J.P.	Antibodies to human cytomegalovirus protein UL83 in systemic sclerosis.	Clin. Exp. Rheumatol.	24	176-178	2006

Kuwana, M., Kaburaki, J., Okazaki, Y., Yasuoka, H., Kawakami, Y., and Ikeda, Y.	Increase in circulating endothelial precursors by atorvastatin in patients with systemic sclerosis.	Arthritis Rheum.	54	1946-1951	2006
Kuwana, M., Kaburaki, J., Okazaki, Y., Miyazaki, H., and Ikeda, Y.	Two types of autoantibody-mediated thrombocytopenia in patients with systemic lupus erythematosus.	Rheumatology	45	851-854	2006
Kuwana, M., Kurata, Y., Fujimura, K., Fujisawa, K., Wada, H., Nagasawa, T., Nomura, S., Kojima, T., Yagi, H., and Ikeda, Y.	Preliminary laboratory-based diagnostic criteria for immune thrombocytopenic purpura: Evaluation by multi-center prospective study.	Thromb. Haemost.	4	1936-1943	2006
Ohnishi, Y., Tsutsumi, A., Matsumoto, I., Goto, D., Ito, S., Kuwana, M., Uemura, Y., Nishimura, Y., and Sumida, T.	Altered peptide ligands control type II collagen-reactive T cells from rheumatoid arthritis patients.	Mod. Rheumatol.	16	226-228	2006
Yamazaki, R., Kuwana, M., Mori, T., Okazaki, Y., Kawakami, Y., Ikeda, Y., and Okamoto, S.	Prolonged thrombocytopenia after allogeneic haematopoietic stem cell transplantation: Associations with impaired platelet production and increased platelet turnover.	Bone. Marrow. Transplant.	38	377-384	2006
Kuwana, M.	Potential benefit of statins for vascular disease in systemic sclerosis.	Curr. Opinion. Rheumatol.	18	594-600	2006
Asahi, A., Kuwana, M., Suzuki, H., Hibi, T., Kawakami, Y., and Ikeda, Y.	Effects of *Helicobacter pylori* eradication regimen on anti-platelet autoantibody response in infected and uninfected patients with idiopathic thrombocytopenic purpura.	Haematologica	91	594-600	2006
Kuwana, M., Ikeda, Y.	*Helicobacter pylori* and immune thrombocytopenic purpura: unsolved questions and controversies.	Int. J. Hematol.	84	309-315	2006
Kuwana, M., Okazaki, Y., Kodama, H., Satoh, T., Kawakami, Y., and Ikeda, Y.	Endothelial differentiation potential of human monocyte-derived multipotential cells.	Stem Cells	24	2733-2743	2006
桑名正隆	膠原病のプライマリケア-早期診断と治療指針；ベーチェット病	綜合臨床		印刷中	
桑名正隆	治療/膠原病治療のポイントと実際；強皮症（全身性強皮症）	Medical Practice	23	669-673	2006
桑名正隆	けんさ質問箱；*Helicobacter pylori*の除菌で特発性血小板減少症が軽減する？	検査と技術	34	485-487	2006
香月有美子、鈴木重明、高橋勇人、佐藤隆司、野川茂、田中耕太郎、鈴木則宏、桑名正隆	症例報告；重症筋無力症を伴うGood症候群の一例：免疫評価機能に関する検討	日本臨床免疫学会会誌	29	102-106	2006
桑名正隆	自己免疫疾患のアレルギーのトピックス；特発性血小板減少性紫斑病	Medicina	43	944-946	2006
桑名正隆	免疫能から血液疾患病態を探る；自己免疫疾患の病態と自己反応性T細胞	Sysmex Journal	29	19-26	2006

桑名正隆	話題の疾患と治療；*H. pylori*感染症と特発性血小板減少性紫斑病	感染・炎症・免疫	36	70-71	2006
桑名正隆	解説；抗血小板膜糖蛋白抗体	リウマチ科	36	95-102	2006
桑名正隆	自己免疫疾患；特発性血小板減少性紫斑病とピロリ感染	BIO Clinica	21	39-43	2006
Wakamatsu E, Nakamura Y, Matsumoto I, Goto D, Ito S, Tsutsumi A, Sumida T.	DNA microarray analysis of labial salivary gland of patients with Sjogren's syndrome.	Ann. Rheum. Dis.		in press	
Sumida T, Wakamatsu E, Nakamura Y, Matsumoto I.	Autoantibodies against muscarinic acetylcholine receptor in patients with Sjogren's syndrome.(review)	In Textbook of autoantibodies Second edition		681-686	2007
Chino Y, Murata H, Goto D, Matsumoto I, Tsutsumi A, Sakamoto T, Ohtsuka M, Sekisawa K, Ito S, Sumida T.	T cell receptor BV gene repertoire of lymphocytes in bronchoalveolar lavage fluid of polymyositis/dermatomyositis patients with interstitial pneumonitis.	Int. J. Mol. Med	17	101-109	2006
Naito Y, Matsumoto I, Wakamatsu E, Goto D, Ito S, Tsutsumi A, Sumida T.	Altered peptide ligants regulate muscarinic acetylcholine receptor reactive T cells of patients with Sjogren's Syndrome.	Ann. Rheum. Dis.	65	269-271	2006
Suzuki E, Tsutsumi A, Goto D, Matsumoto I, Ito S, Otsu M, Onodera M, Takahashi S, Sato Y, Sumida T.	Gene transduction of tristetraprolin or its active domain reduces TNF-α production in Jurkat T cells.	Int.I.Mol.Med.	17	801-809	2006
Ito S, Sugihara M, Suzuki T, Mamura M, Goto D, Matsumoto I, Tsutsumi A, Sumida T.	Diagnosis of Chlamydia-induced reactive arthritis.	Intern Med	45	37	2006
Kai H, Shibuya K, Wang Y, Kameta H, Kameyama T, Tahara-Hanaoka S, Miyamoto A, Honda S, Matsumoto I, Koyama A, Sumida T, Shibuya A.	Critical role of M. tuberculosis for dendritic cell maturation to induce collagen-induced arthritis in H-2b background of C57Bl/6 mice.	Immunology	118	233-239	2006
Kori Y, Matsumoto I, Zhang H, Yasukochi T, Hayashi T, Iwanami K, Goto D, Ito S, Tsutsumi A, Sumida T.	Characterization of Th1/Th2 type, glucose-6-phosphate isomerase reactive T cells in the generation of rheumatoid arthritis.	Ann Rheum Dis.	65	968-969	2006
Tsutsumi A, Hayashi T, Chino Y, Goto D, Matsumoto I, Ito S, Sumida T.	Significnace of antiprothrombin antibodies in patients with systemic lupus erythematosus: clinical evaluation of the antiprothrombin assay and the antiphosphatidylserine/prothrombin assay, and comparison with other antiphospholipid antibody assays.	Mod.Rheumatol.	16	158-164	2006

Ohnishi Y, Tsutsumi A, Matsumoto I, Goto D, Ito S, Kuwana M, Uemura Y, Nishimura Y, Sumida T.	Altered peptide ligands control typeII collagen-reactive T cells from RA patients.	Mod.Rheumatol.	16	226-228	2006
Wakamatsu E, Matsumoto I, Yasukochi T, Naito Y, Goto D, Mamura M, Ito S, Tsutsumi A, Sumida T.	Overexpression of phosphorylated stat1-α in labial salivary glands of patients with Sjogren's Syndrome.	Arthritis Rheum.	54	3476-3484	2006
Suzuki E, Tsutsumi A, Sugihara M, Mamura M, Goto D, Matsumoto I, Ito S, Ikeda K, Ochiai N, Sato Y, Sumida T.	Expression of TNF-α, tristetraprolin, T-cell intracellular antigen-1 and Hu antigen R genes in synovium of patients with rheumatoid arthritis.	Int.J.Mol.Med.	18	273-278	2006
松本功	自己抗体誘導性関節炎モデル	内科	97	355-358	2006
松本功	関節リウマチにおける抗glucose-6-phosphate isomerase (GPI) 抗体	分子リウマチ	3	21-27	2006
松本功	関節炎における自己抗体と炎症性サイトカインの関係	臨床免疫	45	292-296	2006
松本功	抗glucose-6-phosphate isomerase 抗体の病原性	臨床免疫	45	640-644	2006
松本功、住田孝之	抗ＧＰＩ(glucose-6-phosphate isomerase)抗体	リウマチ科	36	81-87	2006
Koike T, Atsumi T.	"Resurrection of Thrombin "in the pathophysiology of the antiphospholipid syndrome.	Arthritis Rheum.		in press	
Minauchi K, Nishio M, Itoh T, Yamamoto S, Fujimoto K, Sato N, Koike T.	Hepatosplenic alpha/beta T cell lymphoma presenting with cold agglutinin disease.	Ann Hematol.	86(2)	155-157	2007
Nakamura A, Shimizu C, Nagai S, Taniguchi S, Umetsu M, Atsumi T, Wada N, Yoshioka N, Ono Y, Tanizawa Y, Koike T	A novel mutation of *WFS1* gene in a Japanese man of Wolfram syndrome with positive diabetes-related antibodies.	Diabetes Res Clin Pract.	73(2)	215-217	2006
Nagai S, Shimizu C, Kimura Y, Umetsu M, Taniguchi S, Takeuchi J, Atsumi T, Yoshioka N, Kubo M, Koike T.	A case of reversed pituitary dysfunction with intrasellar mass	J Endocrinol Invest.	29(4)	367-372	2006
Amengual O, Atsumi T, Koike T.	Pathophysiology of the antiphospholipid syndrome: roles of anticardiolipin antibodies in thrombosis and fibrinolysis.	APLAR J Rheumatol.	9	377-386	2006
Mizukami K, Nakabayashi T, Naitoh S, Takeda M, Tarumi T, Mizoguchi I, Ieko M, Koike T	One novel and one recurrent mutation in the PROS1 gene cause type I protein S deficiency in patients with pulmonary embolism associated with deep vein thrombosis.	Am J Hematol	81	787-797	2006

Ieko M, Tarumi T, Nakabayashi T, Yoshida M, Naito S, Koike,T.	Factor Xa inhibitors: new anti-thrombotic agents and their characteristics.	Frontiers in Bioscience.	11	232-248	2006
Furusaki A, Judo S,Yamashita Y, Amasaki Y, Atsumi T, Koike T.	TRAIL-mediated cytotoxicity: Impacts of sTRAIL and vTRAIL microvesicles.	J Biol Sci.	6(1)	150-159	2006
Niwa H, Koumoto C, Shiga T, Takeuchi J, Mishima S, Segawa T, Atsumi T, Shimizu C, Koike T,Yoshioka N.	Clinical analysis of cognitive function in diabetic patients by MMSE and SPECT.	Diabetes Res Clin Pract.	72	142-147	2006
Hashimoto T, Nishio M, Sakai T, Fujimoto K, Sato N, Endo T, Koike T.	Acute schizophrenic symptoms as the initial manifestation of HIV infection that respond to highly active antiretroviral therapy	Clinical Infectious Diseases.	42	1653-1655	2006
Furukawa S, Yasuda S, Amengual O, Horita T, Atsumi T, Koike T.	Protective effect of pravastatin on vascular endothelium in patients with System Sclerosis: a pilot study.	Ann Rheum Dis.	65(8)	1118-1120	2006
Nishio M, Fujimoto K, Yamamoto S, Endo T, Sakai T, Obara M , Kumano K, Minauchi K, Yamaguchi K, Takeda Y, Sato N, Koizumi K, Mukai M, Koike T.	Hypogammaglobulinemmia with a selective delayed recovery inmemory B cells and an impaired Isotype expression after rituximab administration as an adjuvant to autologous stem cell transplantation for non-Hodgkin lymphoma.	Eur J Haemato.	77	226-232	2006

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 ページ
Mimori T	Autoantibodies in rheumatoid arthritis	Pollard M	Wiley-VCH	2006
		Autoantibodies and Autoimmunity	Weiheim, Germeny	277-290
三森経世	膠原病，および類縁疾患の治療の動向	山口徹，北原光夫，福井次矢	医学書院	2006
		今日の治療指針2007年	東京	586
三森経世	混合性結合組織病	住田孝之	診断と治療社	2006
		EXPERT膠原病・リウマチ改訂第2版	東京	298-306
桑名正隆	ベーチェット病(Behçet's Disease)	山口徹、北原光夫、福井次矢	医学書院	印刷中
		今日の治療指針 2008年版-私はこう治療している	東京	
桑名正隆	抗リン脂質抗体症候群(Antiphospholipid Syndrome:APS)	山口徹、北原光夫、福井次矢	医学書院	2007
		今日の治療指針 2007年版-私はこう治療している	東京	596-597
桑名正隆	関節穿刺と関節液検査	池田康夫、鈴木則宏	南江堂	2006
		内科研修マニュアル(改訂第2版)	東京	526-527
桑名正隆	強皮症	池田康夫、鈴木則宏	南江堂	2006
		内科研修マニュアル(改訂第2版)	東京	540-543
桑名正隆	Behçet病	池田康夫、鈴木則宏	南江堂	2006
		内科研修マニュアル(改訂第2版)	東京	561
桑名正隆	抗リン脂質抗体症候群	池田康夫、鈴木則宏	南江堂	2006
		内科研修マニュアル(改訂第2版)	東京	564
桑名正隆	血清蛋白とその分画	橋本信也	医学書院	2006
		最新 臨床検査のABC	東京	142-145
桑名正隆	免疫ブロブリンG, A, M, D(IgG, IgA, IgM, IgD)	橋本信也	医学書院	2006
		最新 臨床検査のABC	東京	146-148
桑名正隆	免疫ブロブリンE(IgE)	橋本信也	医学書院	2006
		最新 臨床検査のABC	東京	149

Ⅴ　平成18年度班会議プログラム

平成18年度班会議プログラム

13：00～13：05　開会の辞
13：05～13：15　厚生労働省　挨拶
13：15～　研究発表

1．　13：15～13：35
アナログペプチドによる抗原特異的免疫分子制御法の開発に関する研究
筑波大学大学院人間総合科学研究科先端応用医学専攻臨床免疫学
住田　孝之

2．　13：35～13：55
遺伝子導入樹状細胞を用いた抗原特異的免疫制御法の開発
熊本大学大学院医学薬学研究部免疫識別学分野
千住　覚

3．　13：55～14：15
関節炎局所に集積しているＴ細胞レセプターを用いた治療モデルの開発
東京大学医学部アレルギーリウマチ内科
山本　一彦

4．　14：15～14：35
免疫制御性分子発現多機能ウイルスベクターを用いた疾患特異的免疫制御法の開発
京都大学大学院医学研究科臨床免疫学
三森　経世

5．　14：35～14：55
IL-2を介したヒトCD4陽性NKT細胞クローンにおけるTh2サイトカイン産生に関する研究
国立精神・神経センター神経研究所免疫研究部
山村　隆

… … …　　コーヒーブレイク　14：55～15：10　　… … …

6．　15：10～15：30

制御性CD8T細胞の解析と抗原特異的治療への応用に関する研究

東京医科歯科大学大学院医歯学総合研究科膠原病・リウマチ内科学

上阪　等

7．　15：30～15：50

天疱瘡モデルマウスを用いた自己反応性T細胞株のin vivo病原性のスクリーニング法に関する研究

慶應義塾大学内科

桑名　正隆

8．　15：50～16：10

自己抗原および関節炎誘導分子修飾による自己抗体産生制御

筑波大学大学院人間総合科学研究科先端応用医学専攻臨床免疫学

松本　功

9．　16：10～16：30

全身性エリテマトーデスにおけるRas-guanyl releasing protein 1発現異常に関する研究

北海道大学大学院医学研究科病態内科学講座・第二内科

小池　隆夫

16：30～16：40　　閉会の辞

VI　研究成果刊行物・別刷

ARTHRITIS & RHEUMATISM
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Overexpression of Phosphorylated STAT-1α in the Labial Salivary Glands of Patients With Sjögren's Syndrome

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Objective. **To clarify the molecular mechanisms of Sjögren's syndrome (SS), we analyzed the functional role of the STAT-1 gene, one of the interferon-γ (IFNγ)–inducible genes, in labial salivary glands (LSGs) from SS patients.**

Methods. **The expression of STAT-1 messenger RNA (mRNA) was examined by real-time polymerase chain reaction (PCR) analysis, and the phosphorylation of STAT-1 protein (Tyr^{701} and Ser^{727} pSTAT-1) was investigated by Western blot and immunohistochemical analyses. The expression of IFNγ-inducible 10-kd protein (IP-10), IFN regulatory factor 1 (IRF-1), and Fas was also examined by real-time PCR and immunohistochemical analyses.**

Results. **STAT-1α and STAT-1β mRNA were highly expressed in LSGs from SS patients. The level of STAT-1α protein in SS LSGs was higher than that in 3 control LSGs, whereas STAT-1β protein was not clearly detected by Western blot analysis. Moreover, Tyr^{701} and Ser^{727} pSTAT-1α proteins were specifically detected in SS LSGs. Immunohistochemical analysis showed localization of Tyr^{701} pSTAT-1 in infiltrating lymphocytes and the adjacent ductal epithelium from SS patients. Ser^{727} pSTAT-1 was localized only in the ductal epithelium of SS LSGs. The STAT-1–inducible genes IP-10 and IRF-1 and the Fas genes were highly expressed in SS LSGs and were colocalized with Ser^{727} pSTAT-1–positive, but not Tyr^{701} pSTAT-1–positive, cells.**

Conclusion. **We found evidence of the up-regulation of STAT-1α mRNA and protein in LSGs from SS patients, as well as the presence of pSTAT-1α in ductal epithelium from SS patients. Our findings suggest that STAT-1α, especially Ser^{727} pSTAT-1, may function as a key molecule in the pathogenesis of SS.**

Sjögren's syndrome (SS) is a chronic autoimmune disease characterized by focal infiltration of lymphocytes into lacrimal and salivary glands, which leads to dry eyes and dry mouth. In SS, several autoantibodies are produced, and they are classified as non–organ-specific antibodies, such as anti-SSA and anti-SSB (1), and organ-specific antibodies, such as anti–type 3 muscarinic acetylcholine receptor antibody (2). SS in the absence of other autoimmune diseases is classified as primary, and SS in the presence of rheumatoid arthritis, systemic lupus erythematosus, or other connective tissue diseases is classified as secondary.

The infiltrating lymphocytes are mainly CD4+ α/β T cells (3), especially Th1-type T cells, because they produce both interferon-γ (IFNγ) and interleukin-2 (4–6). B cells, macrophages, and natural killer cells are found less frequently than T cells (7). These cells lead to salivary gland destruction via the production of inflammatory cytokines and the interaction between Fas and FasL (8–10). However, the mechanisms of the onset and progression of SS are poorly understood.

To clarify the pathogenesis of SS, several molecules in labial salivary glands (LSGs) have been investigated in animal models of SS as well as in humans with SS. In the MRL/*lpr* mouse, the expression of sialadenitis-associated genes was analyzed by microarray, and 13 genes were found to be up-regulated (11). Highly expressed genes in the conjunctival epithelium in patients with SS were examined using the introduced amplified fragment length polymorphism method (12). Moreover, the expression of Fas, FasL, CTLA-4, and programmed

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