

9. **Shirakata Y**, Tokumaru S, Yamasaki K, Sayama K, Hashimoto K: So-called biological dressing effects of cultured epidermal sheets are mediated by the production of EGF family, TGF- β and VEGF. *J Dermatol Sci* 2003, 32:209-15

日本語論文

山崎研志、**白方裕司**、佐山浩二、橋本公二：
角化細胞の幹細胞 再生医学 40:218-225,
2003

学会発表

1. Yamasaki K, Dai X, Nanba D, Shiraishi K, Yahata Y, Tokumaru S, Tohyama M, **Shirakata Y**, Sayama K, Higashiyama S, Hashimoto K: PLZF regulates and suppresses melanoma proliferation and tumor growth. International Investigative Dermatology 2003. Miami Beach May 2003, USA
2. Ishii K, Harada R, Matsuo I, **Shirakata Y**, Hashimoto K, Amagai M: In vitro keratinocyte dissociation assay to evaluate blister-inducing activity of pemphigus IgG autoantibodies. International Investigative Dermatology 2003. Miami Beach May 2003, USA
3. Yahata Y, **Shirakata Y**, Tokumaru S, Yamasaki K, Hashimoto K: Novel role of

angiotensin II in fibroblasts: induction of fibroblast migration by angiotensin II via HB-EGF-mediated EGF receptor transactivation. International Investigative Dermatology 2003. Miami Beach May 2003, USA

4. **Shirakata Y**, Tokumaru S, Yamasaki K, Yahata Y, Tohyama M, Sayama K, Higashiyama S, Hashimoto K: Keratinocyte-specific HB-EGF-deficient mice show marked retardation of skin wound healing. International Investigative Dermatology 2003. Miami Beach May 2003, USA
5. Nanba D, **Shirakata Y**, Nakanishi Y, Hieda Y, Ishiguro H, Higashiyama S, Hashimoto K: Epidermal hyperplasia and impaired morphogenesis of hair follicles in mice overexpressing a soluble form of heparin-binding EGF-like growth factor. International Investigative Dermatology 2003. Miami Beach May 2003, USA
6. Dai X, Yamasaki K, Yahata Y, Tokumaru S, Tohyama M, **Shirakata Y**, Sayama K, Hashimoto K: All trans-retinoic acid induces production of IL-8 in human keratinocytes via increased phosphorylation of I κ B α in the NF κ B pathway. International Investigative Dermatology 2003. Miami Beach May

2003, USA

7. Tohyama M, Shirakata Y, Yamasaki K, Sayama K, Tsuda T, Tan E, Hashimoto K: production of MIP-1a/CCL3 is mediated via toll-like receptor 3 in human keratinocytes. International Investigative Dermatology 2003. Miami Beach May 2003, USA

8. Sayama K, Komatsuzawa H, Yamasaki K, Shirakata Y, Dai X, Sugai M, Ichijo H, Hashimoto K: Epidermal differentiation regulates the production of innate antimicrobial peptides in the skin. International Investigative Dermatology 2003. Miami Beach May 2003, USA

9. Tokumaru S, Shirakata Y, Yamasaki K, Yahata Y, Tohyama M, Sayama K, Hashimoto K: EGF receptor transactivation by UV-irradiation is mediated via HB-EGF shedding in human keratinocytes. International Investigative Dermatology 2003. Miami Beach May 2003, USA

H. 知的所有権の出願・登録状況（予定を含む）

1. 特許取得
なし
2. 実用新案登録
なし
3. その他
なし

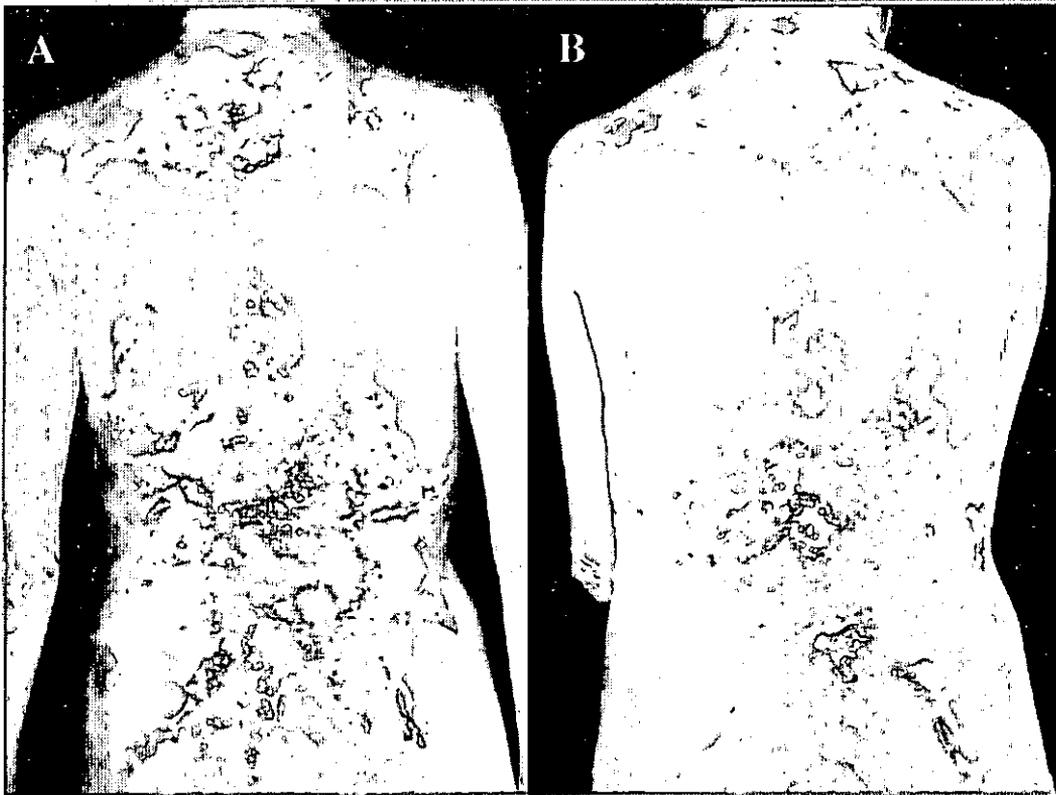


図1 栄養障害型表皮水疱症に対する自己培養表皮シート移植例（症例1）

A；自己培養表皮シート移植前

B；自己培養表皮シート移植後1ヶ月

潰瘍面積の著名な縮小を認める。



図2 栄養障害型表皮水疱症に対する自己培養表皮シート移植例（症例2）

A；自己培養表皮シート移植前

B；自己培養表皮シート移植後3ヶ月

潰瘍面積の著名な縮小を認める。

[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

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Hashimoto K , Yasukawa M, Tohyama M	Human herpesvirus 6 and drug allergy.	Curr Opin Allergy Clin	3	255-260	2003
Nanba D, Mammoto A, Hashimoto K , Higashiyama S	Proteolytic release of the carboxy-terminal fragment of proHB-EGF causes nuclear export of PLZF.	J Cell Biol	163	489-502	2003
Iwamoto R, Yamazaki S, Asakura M, Takashima S, Hasuwa H, Miyado K, Adachi S, Kitakaze M, Hashimoto K , Raab G, Klagsbrun M, Nanba D, Higashiyama S, Hori M, Mekada E	HB-EGF and ErbB signaling is essential for heart function	Proc Natl Acad Sci USA	100	3221-3226	2003
Yahata Y, Shirakata Y, Tokumaru S, Yamasaki K, Sayama K, Hanakawa Y, Detmar M, Hashimoto K	Nuclear translocation of phosphorylated STAT3 is essential for VEGF-induced human dermal microvascular endothelial cell migration and tube formation.	J Biol Chem	278	40026-31	2003
Shirakata Y, Tamai K, Nakaoka H, Tokumaru S, Sayama K, Murakami S, Hashimoto K	Severe Palmo-plantar Hyperkeratosis in Koebner Epidermolysis Bullosa Simplex	J Dermatol	30	135-140	2003
Wada T, Shirakata Y, Takahashi H, Murakami S, Iizuka H, Suzuki H, Hashimoto K	A Japanese Case of Segmental Darier's Disease Caused by Mosaicism for the ATP2A2 Mutation	Br J Dermatol	149	185-8	2003
Tsuda T, Thoyama M, Yamasaki K, Shirakata Y, Yahata Y, Tokumaru S, Sayama K, Hashimoto K	Lack of evidence for TARC/CCL17 production by normal human keratinocytes in vitro	J Dermatol Sci	31	37-42	2003

Nakamura Y, Fukami K, Yu H, Takenaka K, Kataoka Y, Shirakata Y, Nishikawa SI, Hashimoto K , Yoshida N, Takenawa T	Phospholipase Cdelta(1) is required for skin stem cell lineage commitment.	EMBO J	22	2981-2991	2003
Masaki T, Fukunaga A, Tohyama M, Koda Y, Okuda S, Maeda N, Kanda F, Yasukawa M, Hashimoto K , Horikawa T, Ueda M	Human herpes virus 6 encephalitis in allopurinol-induced hypersensitivity syndrome	Acta Derm Venereol	83	128-31	2003
Midorikawa K, Ouhara K, Komatsuzawa H, Kawai T, Yamada S, Fujiwara T, Yamazaki K, Sayama K, Taubman MA, Kurihara H, Hashimoto K , Sugai M	Staphylococcus aureus susceptibility to innate antimicrobial peptides, beta-defensins and CAP18, expressed by human keratinocytes.	Infect Immun	71	3730-9	2002
Shibata R, Kai H, Seki Y, Kato S, Wada Y, Hanakawa Y, Hashimoto K , Yoshimura A, Imaizumi T	Inhibition of STAT3 prevents neointima formation by inhibiting proliferation and promoting apoptosis of neointimal smooth muscle cells	Hum Gene Ther	14	601-10	2003
Yamasaki K, Hanakawa Y, Tokumaru S, Shirakata Y, Sayama K, Hanada T, Yoshimura A, Hashimoto K	SOCS1/JAB and SOCS3/CIS3 negatively regulate the STATs signaling pathway in normal human epidermal keratinocytes	J Invest Dermatol	120	571-80	2003
Yamasaki K, Toriu N, Hanakawa Y, Shirakata Y, Sayama K, Takayanagi A, Ohtsubo M, Gamou S, Shimizu N, Fujii M, Miyazono K, Hashimoto K	Keratinocyte growth inhibition by high-dose epidermal growth factor is mediated by transforming growth factor β autoinduction: A negative feedback mechanism for keratinocyte growth	J Invest Dermatol	120	1030-1037	2003

Hamada K, Kohno S, Iwamoto M, Yokota H, Okada M, Tagawa M, Hirose S, Yamasaki K, Shirakata Y, Hashimoto K , Ito M	Identification of the Human IAI.3B Promoter Element and Its Use in the Construction of a Replication-selective Adenovirus for Ovarian Cancer Therapy	Cancer Res	63	2506-12	2003
Yanai F, Ishii E, Kojima K, Hasegawa A, Azuma T, Hirose S, Suga N, Mitsudome A, Zaitzu M, Ishida Y, Shirakata Y, Sayama K, Hashimoto K , Yasukawa M	Essential roles of perforin in antigen-specific cytotoxicity mediated by human CD4+ T lymphocytes: analysis using the combination of hereditary perforin-deficient effector cells and Fas-deficient target cells	J Immunol	170	2205-13	2003
Shirakata Y, Tokumaru S, Yamasaki K, Sayama K, Hashimoto K	So-called biological dressing effects of cultured epidermal sheets are mediated by the production of EGF family, TGF- β and VEGF.	J Dermatol Sci	32	209-15	2003
Kawase Y, Yanagi Y, Fujimoto M, Okochi H	Characterization of multipotent stem cell in the skin-positive effect of TGF-beta on sphere colony formation.	Exp Cell Res			in press
Itoh M, Hiraoka Y, Kataoka K, Huh NH, Tabata Y, Okochi H	Novel collagen sponge reinforced with polyglycolic acid fiber produces robust, normal hair in murine hair reconstitution model.	Tissue Engineering			in press
Yano S, Komine M, Fujimoto M, Okochi H , Tamaki K	Mechanical stretching in vitro regulates signal transduction pathways and cellular proliferation in human epidermal keratinocytes.	J Invest Dermatol			in press
Yazawa N, Fujimoto M, Sato S, Miyake K, Asano N, Nagai Y, Takeuchi O, Takeda K, Okochi H , Akira S, Tedder TF, Tamaki K	CD19 regulates innate immunity by the toll-like receptor RP105 signaling in B lymphocytes.	Blood	102	1374-80	2003

Yano S, Komine M, Fujimoto M, <u>Okochi H</u> , Tamaki K	Interleukin 15 induces the signals of epidermal proliferation through ERK and PI 3-kinase in a human epidermal keratinocyte cell line, HaCaT.	Biochem Biophys Res Commun	301	841-7	2003
Tsunemi Y, Ihn H, Idezuki T, <u>Okochi H</u> , Tamaki K	Psoriasis guttata in association with hepatocellular carcinoma.	Acta Derm Venereol	83	70-1	2003
Mitsui H, Komine M, Shirai A, Kanda N, Asahina A, <u>Okochi H</u> , Hitomi S, Kimura S, Tamaki K	Chronic active EB virus infection complicated with IgG3 subclass deficiency: an adult case treated with intravenous immunoglobulin and IFN-alpha.	Acta Derm Venereol	83	31-5	2003
Nagaoka Y, <u>Okochi H</u> , Tamaki K	Leukocytopenia after administration of itraconazole.	Mycoses	46	240-1	2003
Oshima K, Shimamura M, Mizuno S, <u>Tamai K</u> , Doi K, Morishita R, Nakamura T, Kubo T, Kaneda Y	Intrathecal injection of HVJ-E containing HGF gene to cerebrospinal fluid can prevent and ameliorate hearing impairment in rats.	FASEB J	120	308-12	2003
Umegaki N, Moritsugu R, Katoh S, Harada K, Nakano H, <u>Tamai K</u> , Hanada K, Tanaka K	Photodynamic therapy may be useful to debulk cutaneous lymphoma prior to radiotherapy.	British J Dermatol			in pres
Kaneda Y, <u>Tamai K</u>	Current status and future prospects of gene therapy technologies toward the treatment of intractable skin diseases.	Arch Dermatol Res	295	S63-6	2003
<u>Tamai K</u> , Hashimoto I, Hanada K, Ikeda S, Imamura S, Ogawa H	Japanese guidelines for diagnosis and treatment of junctional and dystrophic epidermolysis bullosa.	Arch Dermatol Res	295	S24-8	2003
Matsuzaki Y, <u>Tamai K</u> , Kon A, Sawamura D, Uitto J, Hashimoto M	Keratinocyte responsive element 3 (KRE3): Analysis of a keratinocyte-specific regulatory sequence in the 230-kD bullous pemphigoid antigen (BPAG1) gene promoter.	J Invest Dermatol	120	308-12	2003

Potten CS, Booth C, Tudor GL, Booth D, Brady G, Hurley P, Ashton G, Clarke G, Sakakibara S, Okano H	Identification of a putative intestinal stem cell marker and early lineage marker; Musashi 1	Differentiation	71	28-41	2003
Kayahara T, Sawada M, Takaishi S, Fukui H, Seno H, Fukuzawa H, Suzuki K, Hiai H, Kageyama R, Okano H , Chiba T	Candidate markers for stem and early progenitor cells, Musashi-1 and Hes1, are expressed in crypt base columnar cells of mouse small intestine	FEBS Lett	535	131-135	2003
Tonchev AB, Zhao L, Yamashima T, Okano H	Differential proliferative response in the postischemic hippocampus, temporal cortex and olfactory bulb of adult primates.	Glia	42	209-224	2003
Tonchev AB, Yamashima T, Zhao L, Okano HJ, Okano H	Increased proliferation of neural progenitors and neurogenesis in the postischemic brain of young adult primates.	Mol Cell Neurosci	23	292-301	2003
Kuo H-C, Pau FKY, Yeoman RR, Mitalipov SM, Okano H , Wolf DP	Differentiation of monkey embryonic stem cells into neural lineages.	Biology of Reproduction	68	1727-1735	2003
Kokuzawa J, Yoshimura S, Kitajima H, Shinoda J, Kaku Y, Iwama T, Morishita R, Shimazaki T, Okano H , Kunisada T, Sakai N	Hepatocyte growth factor promotes proliferation and neural differentiation of neural stem cells from mouse embryos.	Mol Cell Neurosci	24	190-197	2003
Ishizuya-Oka A, Shimizu K, Sakakibara SI, Okano H , Ueda S	Thyroid hormone-upregulated expression of Musashi-1 is specific for progenitor cells of the adult epithelium during amphibian gastrointestinal remodeling.	J Cell Sci,	116	3157-64	2003
Kanuka H, Kuranaga E, Hiratou T, Igaki T, Nelson B, Okano H , Miura M	Translocon complex mediates neural cell death and degeneration implicated for polyglutamine toxicity.	Proc Natl Acad Sci USA,	100	11723-8	2003
Baker H, Kobayashi K, Okano H , Saino-Saito S	Cortical and striatal expression of tyrosine hydroxylase mRNA in neonatal and adult mice.	Cell Mol Neurobiol	23	503-18	2003

Tamaki T, Akatsuka A, Okada Y, Matsuzaki Y, Okano H , Kimura M	Growth and differentiation ability of main- and side-population cells derived from skeletal muscle CD34+/45- fraction.	Exp Cell Res	291	83-90	2003
Miyanomori Y, Kobayashi H, Watanabe M, Nagata T, Imai T, Uesugi S, Okano H , Katahira M	Origin of higher affinity to RNA of the N-terminal RNA-binding domain than the C-terminal one of a mouse neural protein, Musashi1, as revealed by NMR spectroscopy.	J Biol Chem	278	41309-15	2003
Yoshida T, Tokunaga A, Nakao K, Okano H	Expression of a splicing isoform of mNumb is downregulated during endocrine differentiation in pancreas.	Differentiation	71	486-495	2003
Hu QD., Ang BT, Karsak M, Hu WP, Cui XY, Duka T, Takeda Y, Chia W, Natesan S, Ng YK, Ling EA, Israel A, Maciag T, Small D, Trifonova R, Kopan R, Okano H , Nakafuku M, Chiba S, Hirai H, Schachner M, Pallen CJ, Watanabe K and Xiao ZC	F3/Contactin acts as a functional ligand for Notch during oligodendrocyte maturation.	Cell	115	163-175	2003
Okada S, Nakamura M, Mikami Y, Ohsugi Y, Yoshizaki K, Kishimoto T, Toyama Y, Okano H	Blockade of interleukin-6 receptor ameliorates functional recovery in spinal cord injury.	J Neurosci Res			In press
Yamashima T, Tonchev BA, Seki T, Sawamoto K, Okano H	Vascular adventitia generates neuronal progenitors in monkey hippocampus after ischemia.	Hippocampus			In press
Takahashi R, Mizukawa Y, Yamazaki Y, Hayakawa K, Hayakawa J, Kudo A, Shiohara T.	In vitro differentiation from naive to mature e-selectin binding CD4 T cells: acquisition of skin-homing properties occurs independently of cutaneous lymphocyte antigen expression.	J Immunol.	171	5769-77	2003

Nori M, Iwata S, Munakata Y, Kobayashi H, Kobayashi S, Umezawa Y, Hosono O, Kawasaki H, Dang NH, Tanaka H, Shiohara T , Morimoto C	Ebastine inhibits T cell migration, production of Th2-type cytokines and proinflammatory cytokines.	Clin Exp Allergy	33	1544-54	
Teraki Y, Shiohara T .	IFN-gamma-producing effector CD8+ T cells and IL-10-producing regulatory CD4+ T cells in fixed drug eruption.	J Allergy Clin Immunol	112	609-15	2003
Shiohara T , Mizukawa Y	Recall phenomenon: some skin-resident cells remember previous insults.	Dermatology	207	127-9	2003
Inoue Y, Isobe M, Shiohara T , Hayashi H	Inhibitory activity of CX-659S, a novel diaminouracil derivative, against the rebound phenomenon following withdrawal of corticosteroid therapy for chronic contact hypersensitivity responses.	Int Arch Allergy Immunol	131	143-52	2003
Jin G-b, Nakayama H, Shmyhlo M, Inoue S, Kondo M, Ikezawa Z , Ouchi Y, Cyong J-C:	High positive frequency of antibodies to metallothionein and heat shock protein 70 in sera of patients with metal allergy.	Clin Exp Immunol	131	275-9	2003
Hamada Y, Nagashima Y, Shiomi K, Shimojo N, Kohno Y, Shibata R, Nishima S, Ohsuna H, Ikezawa Z :	Reactivity of IgE in fish-allergic patients to fish muscle collagen.	Allergology International	52	139-47	2003
Katsuno M, Aihara M, Kojima M, Osuna H, Hosoi J, Nakamura M, Toyoda M, Matsuda H, Ikezawa Z	Neuropeptides concentrations in the skin of a murine (NC/Nga mice) model of atopic dermatitis.	J Dermatol Sci	33	55-65	2003,
Kobayashi K, Kishimoto J , Hattori S, Wachi H, Shinkai H, Burgeson RE	Matrix metalloproteinase-9 expression is coordinately modulated by the KRE-M9 and TPA responsive elements.	J Invest Dermatol			In press

Botchkarev VA, <u>Kishimoto J</u>	Molecular control of epithelial-mesenchymal interactions during hair follicle cycling.	J Invest Dermatol	8	46s-55s	2003
Nitta H, <u>Kishimoto J</u> , Grogan TM	Application of automated mRNA In Situ hybridization for formalin-fixed, paraffin-embedded mouse skin sections: effects of heat and enzyme pretreatment on mRNA signal detection.	Appl Immunohistochem Mol Morphol	11	183-7	2003
Kondo M, Suzuki H, Takehara K, Miyazono K, and <u>Kato M</u> .	Transforming growth factor- β signaling is differentially inhibited by Smad2D450E and Smad3D407E.	Cancer Sci	95	12-17	2004
Sasaki T, Suzuki H, Yagi K, Furuhashi M, Yao R, Susa S, Noda T, Arai Y, Miyazono K, and <u>Kato M</u> .	Lymphoid enhancer factor 1 makes cells resistant to transforming growth factor- β -induced repression of <i>c-myc</i> .	Cancer Res	63	801-806	2003
Nakayama K, Tamura Y, Suzawa M, Harada S, Fukumoto S, <u>Kato M</u> , Miyazono K, Rodan G A, Takeuchi Y, Fujita T.	Receptor tyrosine kinases inhibit bone morphogenetic protein-Smad responsive promoter activity and differentiation of murine MC3T3-E1 osteoblast-like cells.	J Bone Miner Res	18	827-835	2003

研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
藤山幹子、 <u>橋本公二</u>	薬剤誘発性過敏症症候群	medicina	40	997-9	2003
藤山幹子、 <u>橋本公二</u>	drug-induced hypersensitivity syndrome と HHV-6	臨床免疫	40	219-21	2003
<u>橋本公二</u>	D I H S の経緯と診断基準	医学のあゆみ	205	951-4	2003
<u>橋本公二</u>	D I H S とはなにか	アレルギー・免疫	10	811-5	2003
山崎研志、白方裕司、佐山浩二、 <u>橋本公二</u>	角化細胞の幹細胞	再生医学	40	218-225	2003
藤山幹子、 <u>橋本公二</u>	薬剤誘発性過敏症症候群	アレルギー科	15	381-6	2003
白方裕司、 <u>橋本公二</u>	培養皮膚の臨床応用	臨床皮膚	46	173-180	2004
<u>大河内仁志</u>	皮膚の幹細胞と再生医療	最新医学	58s	789-796	2003

<u>大河内仁志</u>	毛髪の再生医療	遺伝子医学	別冊	173-177	2003
<u>大河内仁志</u>	皮膚と再生医療	日皮会誌	113	247-251	2003
<u>大河内仁志</u>	毛髪の再生にむけて	臨床現場での再生医療の最前線	羊土社	84-88	2003
<u>大河内仁志</u>	皮膚にある幹細胞と再生医療への応用	BIO Clinica	18	76-80	2003
<u>玉井克人</u>	先天性表皮水疱症	今日の小児疾患治療指針	13	576	2003
<u>玉井克人</u>	先天性表皮水疱症を治す	皮膚病診療プラクティス	15	238	2003
<u>塩原哲夫</u>	DIHS (Drug-induced hypersensitivity syndrome) の治療	アレルギー・免疫	10	836-843	2003
<u>塩原哲夫</u>	DIHS をめぐる重症薬疹アレルギーの新展開 DIHS を中心にした重症薬疹の病態とそのとらえ方	医学のあゆみ	205	960-964	2003
<u>塩原哲夫</u>	診断の指針 治療の指針 中毒疹と薬疹の鑑別	総合臨床	52	1765-1766	2003
<u>塩原哲夫</u>	薬疹をめぐる諸問題 薬疹とは	アレルギー科	15	375-380	2003

平原和久、 狩野葉子、 塩原哲夫	カルバマゼピンによる drug-induced hypersensitivity syndrome の1例	臨皮	58	1069-1072	2003
水川良子、 塩原哲夫	限局性のかゆみ 陰部へ ルペスと診断されていた 固定薬疹	Visual Dermatology	2	908-909	2003
塩原哲夫	ウィルス感染と薬疹	日本小児皮膚 科学会誌	22	59-64	2003
飯島正文	薬物アレルギー防止と早 期発見における薬剤師へ の期待	月刊薬事	45	2333-5	in pres s
北見 周、 飯島正文	DIHS の臨床的特徴と 診断基準。	アレルギー・免 疫	10	830-3	2003
鈴木寛丈、 飯島正文	Hypersensitivity syndrome	BIO Clinica	18	787	2003
北見 周、 鈴木寛丈、 飯島正文	TEN に進展する発疹	Medicina	40	993-995	2003
浅古佳子、三谷 直子、山田正 子、掛水夏恵、 山川有子、相原 道子、日比 潔、安藤大作、 安田 元、 池澤善郎	血漿交換療法が奏効した オメプラゾールによる TEN 型薬疹の1例	日本皮膚アレ ルギー学会雜 誌	11	27-33	2003

三谷直子、杉山朝美、相原道子、 <u>池澤善郎</u>	少量のプレドニゾロン内服で軽快した塩酸メキシレチンによる drug-induced hypersensitivity syndrome の1例；塩酸メキシレチンによる drug-induced hypersensitivity syndrome の文献的検討	日本皮膚アレルギー学会雑誌、	11	71-77	2003
山口絢子、山川有子、相原道子、牧万里子、佐々木哲雄、柳浩正、 <u>池澤善郎</u>	ヒト免疫グロブリンが奏功した TEN 型薬疹の1例	日本皮膚アレルギー学会雑誌、	11	87-93	2003
<u>岸本治郎</u>	毛包の再生。	日本農芸化学会誌	77	12-15	2003
<u>加藤光保</u>	三次元培養モデルを用いた癌の浸潤能の解析。	Medical Science Digest	29	4-5	2003
<u>加藤光保</u>	トランスフォーミング増殖因子 β による転写制御	蛋白質核酸酵素	48	2247-2253	2003