Ⅲ. 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
Sugawara N, Yasui-Furukori N, Sato Y, Saito M, Furukori H, Nakagami T, Kudo S, Kaneko S	Body mass index and quality of life among outpatients with schizophrenia in Japan	BMC Psychiatry	13	108	2013
Yasui-Furukori N, Hashimoto K, Kubo K, Tomita T	Interaction between paliperidone extended-release and TS-1, an oral anticancer drug containing a 5-fluorouracil derivative in a schizophrenic patient Neuropsychiat Dis Treat	Neuropsychiat Dis Treat	9	317-9	2013
Takahiro Joudoi, Yudai Shichiri, Nobuto Kamizono, Takaaki Akaike, Tomohiro Sawa, Jun Yoshitake, Naotaka Yamada, and Sumio Iwai.	Nitrated cyclic GMP modulates guard cell signaling in Arabidopsis.	Plant Cell.		in press	2013
Yuki Kurauchi, Akinori Hisatsune, Yoichiro Isohama, Tomohiro Sawa, Takaaki Akaike, and Hiroshi Katsuki.	Nitric oxide/soluble guanylyl cyclase signaling mediates depolarization-induced protection of rat mesencephalic dopaminergic neurons from MPP(+) cytotoxicity.	Neuroscience	231	206-215	2013
Shigemoto Fujii and Takaaki Akaike.	Redox signaling by 8-nitro-cyclic guanosine monophosphate: nitric oxide- and reactive oxygen species-derived electrophilic messenger.	Antioxid Redox Signal.		in press	2013

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Takaaki Akaike, Motohiro Nishida, and Shigemoto Fujii.	Regulation of redox signalling by an electrophilic cyclic nucleotide.	J Biochem	153	131-138	2013
Md. Mizanur Rahaman, Tomohiro Sawa, Ahmed Khandaker Ahtesham, Shahzada Khan, Hirofumi Inoue, Atsuhi Irie, Shigemoto Fujii, and Takaaki Akaike.	S-Guanylation proteomics for redox-based mitochondrial signaling.	Antioxid Redox Signal		in press	2013
Kaori Watanabe, Yu Ishima, Takaaki Akaike, Tomohiro Sawa, Teruo Kuroda, Wakano Ogawa, Hiroshi Watanabe, Ayaka Suenaga, Toshiya Kai, Masaki Otagiri, and Toru Maruyana.	S-nitrosated α-1-acid glycoprotein kills drug-resistant bacteria and aids survival in sepsis.	FASEB J.	27	391-398	2013
Yamada S, Shiohira H, Yasui-Furukori N, Tateishi T, Akamine Y, Uno T	The (R)-omeprazole hydroxylation index reflects CYP2C19 activity in healthy Japanese volunteers	Eur J Clin Pharmacol	69	1423-1428	2013
Tuchimine S, Yasui-Furukori N, Kaneda A, Kaneko S	The CLOCK C3111T Polymorphism Is Associated with Reward Dependence in Healthy Japanese Subjects	Neuropsychobiology	67(1)	1-5	2013
Yoshifumi Sato, Mitsutoki Hatta, Md. Fazlul Karim, Tomohiro Sawa, Fan-Yan Wei, Shoki	Anks4b, a novel target of HNF4α interacts with GRP78 and regulates endoplasmic reticulum stress-induced apoptosis	J Biol Chem	287	23236-23245	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Sato, Mark A. Magnuson, Frank J. Gonzalez, Kazuhito Tomizawa, Takaaki Akaike, Tatsuya Yoshizawa, and Kazuya Yamagata.	in pancreatic β-cells.				
Yasui-Furukori N, Tsuchimine S, Kaneda A, Kaneko S.	Association between plasma brain-derived neurotrophic factor levels and personality trait in healthy Japanese subjects.	Psychiatr Res		in press	2012
Tsuchimine S, Yasui-Furukori N, Sugawara N, Sasaki K, Kaneda A, Yoshida S, Kaneko S	Association between the dopamine D2 receptor (DRD2) polymorphism and the personality traits of healthy Japanese participants	Prog Neuropsychopharmacol Biol Psychiatry	38	190-3	2012
Sugawara N, Yasui-Furukori N, Tsuchimine S, Fujii A, Umeda T, Sato Y, Saito M, Nakaji S, Kaneko S	Body composition in patients with schizophrenia: Comparison with healthy controls	Ann Gen Psychiatry	11	11	2012
Sugawara N, Yasui-Furukori N, Tsuchimine S, Fujii A, Umeda T, Sato Y, Saito M, Nakaji S, Kaneko S	Body composition in patients with schizophrenia: Comparison with healthy controls	Ann Gen Psychiatry	11	11	2012
Akamine Y,* Miura M,* Yasui-Furukori N, * Kojima M, Uno T.	Carbamazepine Differentially Affects the Pharmacokinetics of Fexofenadine Enantiomers.	Br J Clin Pharmacol	73	478-81	2012
Akamine Y,* Miura M,* Yasui-Furukori N,* Kojima M, Uno T.	Carbamazepine Differentially Affects the Pharmacokinetics of Fexofenadine Enantiomers.	Br J Clin Pharmacol	73	478-81	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Takatsugu Goto, Yoshitoshi Ogura, Hideki Hirakawa, Junko Tomida, Yuji Morita, Takaaki Akaike, Tetsuya Hayashi, and Yoshiaki Kawamura.	Complete genome sequence of Helicobacter cinaedi strain PAGU611, isolated in a case of human bacteremia.	J Bacteriol	194	3744-3745	2012
Sugawara N, Yasui-Furukori N, Sasaki G, Tanaka O, Umeda T, Takahashi I, Danjo K, Matsusaki M, Kaneko S, Nakaji S	Coping behaviors in relation to depressive symptoms and suicidal ideation among middle-aged workers in Japan	J Affect Disord	142	264-8	2012
Saruwatari J,* Yasui-Furukori N,* Niioka T, Akamine Y, Takashima A, Uno T	Different Effects of the Selective Serotonin Reuptake Inhibitors Fluvoxamine, Paroxetine, and Sertraline on the Pharmacokinetics of Fexofenadine	J Clin Psychopharmacol	32	195-99	2012
Saruwatari J,* Yasui-Furukori N,* Niioka T, Akamine Y, Takashima A, Uno T.	Different Effects of the Selective Serotonin Reuptake Inhibitors Fluvoxamine, Paroxetine, and Sertraline on the Pharmacokinetics of Fexofenadine.	J Clin Psychopharmacol	32	195-99	2012
Tsuchimine S, Yasui-Furukori N, Nakagami T, Sato Y, Kaneko S	DRD3 genotype, but not the BDNF genotype, affects treatment response to paroxetine in major depressive disorder: A Preliminary Study	J Clin Psychopharmacol	32	724-6	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Yasui-Furukori N, Kaneda A, Sugawara N, Tomita T, Kaneko S	Effect of adjunctive treatment with aripiprazole to atypical antipsychotics on cognitive function in schizophrenia patients	J Psychopharmacology	26	806-12	2012
Sugawara N, Yasui-Furukori N, Umeda T, Tsuchimine S, Fujii A, Sato Y, Saito M, Furukori H, Danjo K, Matsuzaka M, Takahashi I, Kaneko S.	Effect of age and disease on bone mass in Japanese patients with schizophrenia.	Ann Gen Psychiatry	11	5	2012
Sugawara N, Yasui-Furukori N, Umeda T, Tsuchimine S, Fujii A, Sato Y, Saito M, Furukori H, Danjo K, Matsuzaka M, Takahashi I, Kaneko S.	Effect of age and disease on bone mass in Japanese patients with schizophrenia.	Ann Gen Psychiatry	11	5	2012
Kusuhara H, Miura M, Yasui-Furukori N, Yoshida K, Akamine Y, Yokochi M, Fukizawa S, Ikejiri K, Kanamitsu K, Uno T, Sugiyama Y	Effect of Coadministration of Single and Multiple Doses of Rifampicin on the Pharmacokinetics of Fexofenadine Enantiomers in Healthy Subjects	Drug Metab Dispos	41(1)	206-13	2012
Sugawara N, Yasui-Furukori N, Kaneda A, Sato Y, Tsuchimine S, Fujii A, Danjo K, Takahash, I Matsuzaka M, Kaneko S	Factor structure of the Liebowitz Social Anxiety Scale for a community-dwelling population in Japan	Psychiatr Clin Neurosci	66	525-8	2012
Shang Guoguo, Takaaki Akaike, Jiang Tao, Chen Qi, Zhang Nong, and Li Hui.	HGF-mediated inhibition of oxidative stress by 8-nitro-cGMP in high glucose-treated rat	Free Radic Res	46	1238-1248	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
	mesangial cells.				
Motohiro Nishida, Tomohiro Sawa, Naoyuki Kitajima, Katsuhiko Ono, Hirofumi Inoue, Hideshi Ihara, Hozumi Motohashi, Masayuki Yamamoto, Makoto Suematsu, Hitoshi Kurose, Albert van der Vliet, Bruce A Freeman, Takahiro Shibata, Koji Uchida, Yoshito Kumagai, and Takaaki Akaike.	Hydrogen sulfide anion regulates redox signaling via electrophile sulfhydration.	Nat Chem Biol	8	714-72 4	2012
Shiohira H,* Yasui-Furukori N,* Yamada S,* Akamine Y, Tateishi T, Uno T	Hydroxylation of R(+)- and S(-)-omeprazole after racemic dosing are different among the CYP2C19 genotypes	Pharmaceutical Res	29	2310-6	2012
Kohta Oyama, Shahzada Khan, Tatsuya Okamoto, Shigemoto Fujii, Katsuhiko Ono, Tetsuro Matsunaga, Jun Yoshitake, Tomohiro Sawa, Junko, Tomida, Yoshiaki Kawamura, and Takaaki Akaike.	Identification of and screening for human Helicobacter cinaedi infections and carriers via nested PCR.	J Clin Microbiol	50	3893-3 900	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Yoshida A, Yamamoto N, Kinoshita M, Hiroi N, Hiramoto T, Kang G, Trimble WS, Tanigaki K, Nakagawa T, Ito J.	Localization of septin proteins in the mouse cochlea.	Hear Res	289 (1-2)	40-51	2012
Harper KM, Hiramoto T, Tanigaki K, Kang G, Suzuki G, Trimble W, Hiroi N.	lterations of social interaction through genetic and environmental manipulation of the 22q11.2 gene Sept5 in the mouse brain.	Hum Mol Genet	1;21 (15)	3489-99	2012
Saruwatari J, Deguchi M, Yoshimori Y, Noai M, Abe T, Nakagawa T, Yoshida S, Yasui-Furukori N, Kaneko S, Ishitsu T, Nakagawa K	Mitochondorial superoxide dismutase 2 polymorphisms as a risk factor for elevated alanine aminotransferase among Japanese patients treated with valproic acid	Epilepsy Res	99	183-6	2012
Yohei Saito, Tomohiro Sawa, Jun Yoshitake, Chisato Ito, Shigemoto Fujii, Takaaki Akaike, and Hirokazu Arimoto.	Nitric oxide promotes recycling of 8-nitro-cGMP, a cytoprotective mediator, into intact cGMP in cells.	Mol Biosyst	8	2909-2915	2012
Sugawara N, Yasui-Furukori N, Tsuchimine S, Kaneda A, Tsuruga K, Iwane K, Okubo N, Takahashi I, Kaneko S	No association between dietary patterns and depressive symptoms among a community-dwelling population in Japan	Ann Gen Psychiatry	11	24	2012
Yasui-Furukori N, Fujii A, Sugawara N, Tsuchimine S, Saito M, Hashimoto K, Kaneko S.	No association between hormonal abnormality and sexual dysfunction in Japanese patients with schizophrenia treated with antipsychotics.	Hum Psychopharmacology	27	82-89	2012
Yasui-Furukori N, Fujii A, Sugawara N, Tsuchimine S, Saito M, Hashimoto K, Kaneko	No association between hormonal abnormality and sexual dysfunction in Japanese patients with	Hum Psychopharmacology	27	82-89	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
S.	schizophrenia treated with antipsychotics.				
Yasui-Furukori N, Sato Y, Kato H, Kaneko S.	Paroxetine-associated hypereosinophilia may clinically resemble a panic attack	Clin Neuropharmacol	35	47-48	2012
Khan S, Okamoto T, Enomoto K, Sakashita N, Oyama K, Fujii S, Sawa T, Takeya M, Ogawa H, Yamabe H, Akaike T.	Potential association of Helicobacter cinaedi with atrial arrhythmias and atherosclerosis.	Microbiol Immunol.	56	145-54	2012
Akamine Y, Yasui-Furukori N, Ieiri I, Uno T	Psychotropic drug-drug interactions involving P-glycoprotein	CNS Drugs	26	959-73	2012
Sugawara N, Yasui-Furukori N, Sasaki G, Umeda T, Takahashi I, Danjo K, Matsuzaka M, Kaneko S, Nakaji S.	Relationships between suicidal ideation and the dimensions of depressive symptoms among middle-aged population in Japan.	J Affect Disord	136	819-23	2012
Sugawara N, Yasui-Furukori N, Sasaki G, Umeda T, Takahashi I, Danjo K, Matsuzaka M, Kaneko S, Nakaji S.	Relationships between suicidal ideation and the dimensions of depressive symptoms among middle-aged population in Japan.	J Affect Disord	136	819-823	2012
澤　智裕、赤池孝章.	ROS・親電子リガンドとガス状分子のシグナルネットワーク.	実験医学増刊	30	2740-2745	2012
Kimoto S, Muraki K, Toritsuka M, Mugikura S, Kajiwara K, Kishimoto T, Illingworth E, Tanigaki K.	Selective overexpression of Comt in prefrontal cortex rescues schizophrenia-like phenotypes in a mouse model of 22q11 deletion syndrome.	Transl Psychiatry	7;2	e146	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Yu Ishima, Hitomi Hoshino, Takuya Shinagawa, Kaori Watanabe, Takaaki Akaike, Tomohiro Sawa, Ulrich Kragh-hansen, Toshiya Kai, Hiroshi Watanabe, Toru Maruyama, and Masaki Otagiri.	S-guanylation of human serum albumin is a unique posttranslational modification and results in a novel class of antibacterial agents.	J Pharm Sc	101	3222-3229	2012
Tomita T, Yasui-Furukori N, Nakagami T, Kaneda A, Kaneko S.	The association between sunshine duration and paroxetine response time in patients with major depressive disorder.	J Affect Disord	136	1067-71	2012
Tomita T, Yasui-Furukori N, Nakagami T, Kaneda A, Kaneko S.	The association between sunshine duration and paroxetine response time in patients with major depressive disorder.	J Affect Disord	136	1067-71.	2012
藤井重元,赤池孝章.	ニトロ化環状ヌクレオチドによるタンパク質S-グアニル化を介する酸化ストレス適応応答の分子機序.	生化学	84	124-28	2012
赤池孝章.	概論：活性酸素によるレドックス制御の新たなパラダイム転換に迫る.	実験医学増刊	30	2690-2696	2012
赤池孝章.	新・活性酸素中毒学	ファルマシア	48	1	2012
赤池孝章.	特集「活性酸素シグナル制御とレドックスホメオスタシス」監修：赤池孝章.	細胞工学	31	134-37	2012
藤井重元、赤池孝章.	硫化水素と炎症.	感染・炎症・免疫	42	235-237	2012

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Sugawara N, Yasui-Furukori N, Umeda T, Kaneda A, Sato Y, Takahashi I, Matsuzaka M, Danjo K, Nakaji S, Kaneko S	Ankle brachial pressure index as a marker of apathy in a community-dwelling population	Int J Geriatr Psychiatry	65	109-11	2011
Sawa T, Ihara H, Akaike T.	Antioxidant effect of a nitrated cyclic nucleotide functioning as an endogenous electrophile.	Curr Top Med Chem.	11	1854-60	2011
Yasui-Furukori N, Tsuchimine S, Nakagami T, Sato Y, Inoue Y, Kaneko S	Association between plasma paroxetine concentration and changes in BDNF levels in patients with major depression disorder	Hum Psychopharmaco	26	194-200	2011
Ishima Y, Yoshida F, Kragh-Hansen U, Watanabe K, Katayama N, Nakajou K, Akaike T, Kai T, Maruyama T, Otagiri M.	Cellular uptake mechanisms and responses to NO transferred from mono- and poly-S-nitrosated human serum albumin.	Free Radic Res.	45	1196-206	2011
Shiohira H, Yasui-Furukori N, Tateishi T, Uno T	Chiral assay of omeprazole and metabolites and its application to a pharmacokinetics related to CYP2C19 genotypes	J Chromatogr B Analyt Technol Biomed Life Sci	879	2465-70	2011
Odagiri G, Sugawara N, Kikuchi A, Takahashi I, Umeda T, Saitoh H, Yasui-Furukori N, Kaneko S.	Cognitive function among hemodialysis patients in Japan.	Ann Gen Psychiatry	10	20	2011

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Yasui-Furukori, N. Tsuchimine S, Saito M, Nakagami T, Sugawara N, Fujii A, Kaneko	Comparing the influence of dopamine D2 polymorphisms and plasma drug concentrations on clinical response to risperidone.	J Clin Psychopharmacol	31	633-7	2011
Sugawara N, Yasui-Furukori N, Sato Y, Kishida I, Yamashita H, Saito M, Furukori H, Nakagami T, Hatakeyama M, Kaneko S.	Comparison of prevalence of metabolic syndrome in hospital and community-based Japanese patients with schizophrenia.	Ann Gen Psychiatry	10	21	2011
Kitagawa E, Yasui-Furukori N, Tsushima T, Kaneko S, Fukuda I	Depression increases the length of hospitalization for patients undergoing thoracic surgery: a preliminary study	Psychosomatics	52	428-32	2011
Yoshida E, Toyama T, Shinkai Y, Sawa T, Akaike T, Kumagai Y.	Detoxification of methylmercury by hydrogen sulfide-producing enzyme in Mammalian cells.	Chem Res Toxicol	24	1633-5	2011
Akaike T, van der Vliet A, Eaton P.	Frontiers in nitric oxide and redox signaling.	Nitric Oxide.	25	57-8	2011
Sugawara N, Sasaki A, Yasui-Furukori N, Kakehata S, Umeda T, Numba A, Makaji S, Shinkawa H, Kaneko S.	Hearing impairment and mental correlates among a community-dwelling population in Japan.	Ann Gen Psychiatry	10	27	2011
Kawase S, Imai T, Miyauchi-Hara C, Yaguchi K, Nishimoto Y, Fukami SI, Matsuzaki Y, Miyawaki A, Itohara S,	Identification of a Novel Intronic Enhancer Responsible for the Transcriptional Regulation of Musashi1 in Neural	Mol Brain.	4	14	2011

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Okano H.	Stem/Progenitor Cells.				
Hideshi Ihara, Ahmed Khandaker Ahtesham, Tomoaki Ida, Shingo Kasamatsu, Kouhei Kunieda, Tatsuya Okamoto, Tomohiro Sawa, Takaaki Akaike.	Methodological proof of immunochemistry for specific identification of 8-nitroguanosine 3',5'-cyclic monophosphate formed in glia cells.	Nitric Oxide	25	169-175	2011
Yuki Kurauchi, Akinori Hisatsune, Yoichiro Isohama, Tomohiro Sawa, Takaaki Akaike, Koichi Shudo, Hiroshi Katsuki.	Midbrain dopaminergic neurons utilize nitric oxide/cyclic GMP signaling to recruit ERK that links retinoic acid receptor stimulation to up-regulation of BDNF.	J Neurochem	116	323-333	2011
Sugawara N, Yasui-Furukori N, Fujii A, Saito M, Sato Y, Nakagami T, Tsuchimine S, Kaneko S.	No association between bone mass and prolactin levels among patients with schizophrenia.	Hum Psychopharmacol	26	596-691	2011
Ishifune C, Maekawa Y, Nishida J, Kitamura A, Tanigaki K, Yagita H, Yasutomo K.	Notch signaling regulates the development of a novel type of Thy 1-expressing dendritic cell in the thymus.	Eur J Immunol.	41	1309-20	2011
Ishifune C, Maekawa Y, Nishida J, Kitamura A, Tanigaki K	Notch signaling regulates the development of a novel type of Thy1-expressing dendritic cell in the thymus.	Eur J Immunol.	41	1309-20	2011
Hideshi Ihara, Tomohiro Sawa, Yusaku Nakabeppu, Takaaki Akaike.	Nucleotides function as endogenous chemical sensors for oxidative stress signaling.	J Clin Biochem Nutr	48	1-7	2011
Yasui-Furukori N, Nakagami T, Kaneda A, Inoue Y, Suzuki A,	nverse correlation between clinical response to paroxetine and plasma	Hum Psychopharmacol	26	602-608	2011

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Otani K, Kaneko S.	drug concentration in patients with major depressive disorders.				
Ahmed KA, Sawa T, Akaike T.	Protein cysteine S-guanylation and electrophilic signal transduction by endogenous nitro-nucleotides.	Amino Acids	41	123-30	2011
Ahmed KA, Sawa T, Ihara H, Kasamatsu S, Yoshitake J, Rahaman MM, Okamoto T, Fujii S, Akaike T.	Regulation by mitochondrial superoxide and NADPH oxidase of cellular formation of nitrated cyclic GMP: potential implications for ROS signalling.	Biochem J	441	719-30	2011
Ohta C, Yasui-Furukori N, Furukori H, Tsuchimine S, Saito M, Nakagami T, Yoshizawa K, Kaneko S	The effect of smoking status on the plasma concentration of prolactin already elevated by risperidone treatment in schizophrenia patients	Prog Neuropsychopharmacol Biol Psychiatry	35	573-6	2011
Kaneda A, Yasui-Furukori N, Nakagami T, Sato Y, Kaneko S.	The influence of personality factors on paroxetine response time in patients with major depression.	J Affect Disord.	135	321-5	2011
Tokutomi Y, Kataoka K, Yamamoto E, Nakamura T, Fukuda M, Nako H, Toyama K, Dong YF, Ahmed KA, Sawa T, Akaike T, Kim-Mitsuyama S.	Vascular responses to 8-nitro-cyclic GMP in non-diabetic and diabetic mice.	Br J Pharmacol.	162	1884-93	2011
Yoshiko Tokutomi, Keiichiro Kataoka,	Vascular responses to 8-nitro-cyclic GMP in	J Pharmacol	162	1884-1893	2011

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Eiichiro Yamamoto, Taishi Nakamura, Masaya Fukuda, Hisato Nako, Kensuke Toyama, Yi-Fei Dong, Ahmed Khandaker Ahtesham, Tomohiro Sawa, Takaaki Akaike, Shokei Kim-Mitsuyama.	nondiabetic and diabetic mice.				
澤 智裕, 小野勝彦, 赤池孝章.	活性酸素・一酸化窒素によるニトロ化シグナルと抗炎症作用.	感染・炎症・免疫.	41	12-19	2011
澤智裕, 小野勝彦, 赤池孝章	活性酸素・一酸化窒素によるニトロ化シグナルと抗炎症作用.	感染・炎症・免疫	41	12-19	2011
岡本竜哉, 居原秀, 赤池孝章.	喫煙と酸化ストレス: Oxidative stress induced by cigarette smoking.	最新精神医学	16	431-39	2011
今吉理恵子, 岡本竜哉, 永尾潤一, 長環, 松永勝政, 赤池孝章, 上西秀則.	植物精油 citral のインフルエンザウイルス感染能抑制効果について.	医学と生物学	155	489-94	2011
橋本和典, 岸本年史.	精神障害と喫煙・禁煙.	最新精神医学	16	409-14	2011
橋本和典, 岸本年史.	精神障害と禁煙.	奈良県医師会医学会年報	21	26-33	2011
橋本和典、岸本年史.	統合失調症と喫煙.	日本社会精神医学雑誌	21	89-93	2011
藤井重元, 澤 智裕, 赤池孝章	8-Nitro-cGMP の発見と生理機能の解明.	化学と生物	48	22-27	2010
Tatsuya Okamoto, Shahzada Khan, Kohta Oyama, Shigemoto Fujii, Tomohiro Sawa, Takaaki Akaike.	A new paradigm for antimicrobial host defense mediated by a nitrated cyclic nucleotide.	J Clin Biochem Nutr	46	14-19	2010
Takaaki Akaike, Tatsuya Okamoto, Shigemoto Fujii, Tomohiro Sawa,	Cellular signaling mediated by nitrated cyclic nucleotides.	Nitric Oxide	23	166-174	2010

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Hirokazu Arimoto.					
Sato T, Shimazaki T, Naka H, Fukami S, Satoh Y, Okano H, Lax I, Schlessinger J, Gotoh N.	FRS2α regulates Erk levels to control a self-renewal target Hes1 and proliferation of FGF-responsive neural stem/progenitor cells.	Stem Cells	28	1661-1673	2010
岡本竜哉，澤智裕，赤池孝章	Nitric oxide（NO）およびNO関連物質	日本臨床増刊号広範囲血液・尿化学検査，免疫学的検査-4	982	839-842	2010
Yu Ishima, Shuichi Hiroyama, Ulrich Kragh-Hansen, Toru Maruyama, Tomohiro Sawa, Takaaki Akaike, Toshiya Kai, and Masaki Otagiri.	One-step preparation of S-nitrosated human serum albumin with high biological activities.	Nitric Oxide	23	121-127	2010
Tomohiro Sawa, Hirokazu Arimoto, Takaaki Akaike.	Regulation of redox signaling involving chemical conjugation of protein thiols by nitric oxide and electrophiles.	Bioconjugate Chemistry	21	1121-1129	2010
Shigemoto Fujii, Tomohiro Sawa, Hideshi Ihara, Kit I. Tong, Tomoaki Ida, Tatsuya Okamoto, Ahmed Khandaker Ahtesham, Yu Ishima, Hozumi Motohashi, Masayuki Yamamoto, Takaaki Akaike.	The critical role of nitric oxide signaling, via protein S-guanylation and nitrated cyclic GMP, in the antioxidant adaptive response.	J Biol Chem	285	23970-23984	2010
Tanigaki K, Honjo T.	Two opposing roles of RBP-J in Notch signaling.	Curr Top Dev Biol	92	231-52	2010
橋本和典，岸本年史	禁煙に伴う抑うつとその対策	呼吸器内科	17	494-498	2010

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
岡本竜哉，赤池孝章	呼吸器疾患における酸化ストレスと制御シグナルの分子基盤: Molecular mechanisms of nitric oxide- and reactive oxygen species-mediated signalings in the respiratory diseases.	呼吸	29	859-866	2010
澤 智裕，赤池孝章	毒性説から脱した活性酸素研究 -シグナル分子としての活躍-	現代化学	469	34-38	2010
Sugawara N, Yasui-Furukori N, Sasaki G, Tanaka O, Umeda T, Takahashi I, Danjo K, Matsuzaka M, Kaneko S, Nakaji S	Gender Differences in Factors Associated with Suicidal Ideation and Depressive Symptoms among Middle-Aged Workers in Japan	Ind Health		in press	
Yasui-Furukori N, Kubo K, Ishioka M Inoue Y	Interaction between paliperidone and carbamazepine	Ther Drug Monit	22	481-485	
Ishioka M, Hashimoto K, Sugawara N, Yasui-Furukori N	Neuroleptic malignant syndrome induced by lamotorigine	Clin Neuropharmacol		in press	
Yasui-Furukori N, Fujii A	Worsened hypertension control induced by aripiprazole	Neuropsychiat Dis Treat		in press	

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
藤井重元、赤池孝章.	NO シグナリング NO signaling.	山本 雅, 仙波憲太郎, 山梨裕司	イラストで徹底理解するシグナル伝達キーワード事典	羊土社	東京都	2012	67-69

Ⅲ. 研究成果の別刷

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A New Paradigm for Antimicrobial Host Defense Mediated by a Nitrated Cyclic Nucleotide

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Summary **Nitric oxide (NO), produced by inducible NO synthase (iNOS) during infection, plays a crucial role in host defense mechanisms. *Salmonella typhimurium* infection in mice is associated with excessive production of NO from iNOS as a host defense response. An important cytoprotective and antimicrobial function of NO is mediated by induction of heme oxygenase (HO)-1. The signaling mechanism of NO-dependent HO-1 induction has remained unclear, however. We recently discovered a nitrated cyclic nucleotide, 8-nitroguanosine 3',5'-cyclic monophosphate (8-nitro-cGMP), which is formed via guanine nitration with NO and reactive oxygen species. iNOS-dependent 8-nitro-cGMP formation and HO-1 induction were identified in *Salmonella*-infected mice. Extensive apoptosis observed with iNOS-deficient macrophages infected with *Salmonella* was remarkably suppressed via HO-1 induced by 8-nitro-cGMP formed in cells. This cytoprotective signaling appears to be mediated by the reaction of 8-nitro-cGMP with protein sulfhydryls to generate a novel post-translational modification named protein *S*-guanylation. We also found that 8-nitro-cGMP specifically *S*-guanylates Keap1, a negative regulator of transcription factor Nrf2, which in turn up-regulates transcription of HO-1. Here, we discuss the unique mechanism of NO-mediated host defense that operates via formation of a novel signaling molecule - 8-nitro-cGMP - during microbial infections.**

***Key Words*: nitric oxide, host defense, 8-nitro-cGMP, heme oxygenase-1, protein *S*-guanylation**

Introduction

Nitric oxide (NO) plays a crucial role in innate host defense mechanisms against microbial infection. Regardless of the type of pathogen, whether bacteria, viruses, or fungi, an inducible NO synthase (iNOS) is induced almost universally during the infection process. This induction occurs in various cells after recognition by host cells of microbial structural components (e.g., lipopolysaccharides, lipoteichoic acid, peptidoglycans, and fungal polysaccharides) and nucleic acid components (such as dsRNA, ssRNA, and CpG DNA) via pattern recognition receptors including Toll-like receptors [*1*]. iNOS induction is synergistically enhanced by inflammatory cytokines and interferon produced during infection [*2*]. NO produced by iNOS reportedly reacts with simultaneously generated reactive oxygen species (ROS), is converted to reactive nitrogen species (RNS), such as per-

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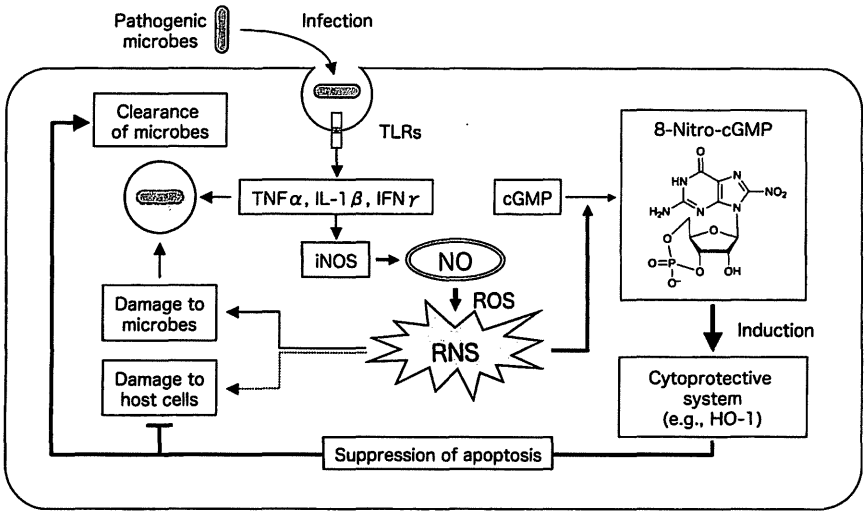

Fig. 1. iNOS induction and NO-mediated host defense mechanism against microbial infection. NO overproduced by iNOS induced during microbial infection is converted to reactive nitrogen species (RNS) via reaction with reactive oxygen species (ROS). RNS have two opposite biological effects: potent bactericidal activity contributing to host defense and damage of cells and tissues of the host. 8-Nitro-cGMP may function as a signaling molecule mediating oxidative stress responses, such as HO-1 induction, and it may play a crucial role in the innate host immunity.

oxynitrite ($ONOO^-$) and nitrogen dioxide (NO_2), and may demonstrate direct antimicrobial activities (Fig. 1) [*3–5*]. In fact, infection with *Salmonella typhimurium*, a facultative intracellular bacterium, causes excessive production of NO via iNOS induction, along with microabscess formation, in the liver in mice. A comparative experiment with iNOS-deficient ($iNOS^{-/-}$) and wild-type mice demonstrated that the bacterial growth in the liver and mortality in $iNOS^{-/-}$ mice were significantly higher than those in wild-type mice. This finding indicates that NO from iNOS participates in host defense against infection, possibly by means of antimicrobial activity [*3*].

In contrast, NO and ROS also reportedly damage host cells and tissues, which causes oxidative stress. In a murine influenza virus-infected pneumonia model, iNOS expression increased in infected lungs, especially in the respiratory epithelium and alveolar macrophages, with resultant excessive production of NO [*6, 7*]. However, unlike progression of *Salmonella* infection, progression of pneumonia is well correlated with iNOS induction; pneumonia was less severe and mortality was lower in $iNOS^{-/-}$ mice than in wild-type mice [*6, 8*]. In general, NO and ROS show antibacterial activity, but because they have no effective antiviral activity, they cause nonspecific damage of host cells and tissues. Therefore, the role of NO in the pathogenesis of infection is known as a double-edged sword (Fig. 1) [*6, 8*].

Recently, much attention has focused on the signaling functions of NO and ROS. NO can suppress apoptosis of host cells caused by infection, and it is involved, together with ROS, in responses to oxidative stress [*9–11*] (Fig. 1). Here, we reexamine the role of NO and ROS in host defense against infection, with a focus on a unique signaling function of the nitrated cyclic nucleotide 8-nitroguanosine 3',5'-cyclic monophosphate (8-nitro-cGMP), which mediates cytoprotective oxidative stress responses occurring during infections.

NO- and ROS-dependent Formation of 8-Nitro-cGMP

NO was initially discovered as a signaling molecule regulating vascular tone and neuronal systems [*12, 13*]. These functions are mainly mediated through a guanosine 3',5'-cyclic monophosphate (cGMP)-dependent mechanism, but other pathways that are not directly related to cGMP appear to be responsible for many aspects of NO signaling [*14–16*]. Although NO has diverse pathophysiological functions, NO itself is an inert molecule. Much of its chemical reactivity depends on RNS generated through the reaction with ROS produced together with in various cells. The reaction of NO with O_2 and superoxide (O_2^-), and the reaction of nitrite (NO_2^-) with the H_2O_2-peroxidase system lead to the generation of RNS [*17–19*]. NO- and ROS-derived RNS have strong nitration potentials for various biological molecules such as proteins, lipids, and nucleic acids, and they possess cGMP-independent signaling functions, as mentioned above.

In fact, nitrated guanine derivatives, such as 8-nitroguanine and 8-nitroguanosine, are known to be formed by RNS, and their formation was identified in various cultured cells and in tissues from influenza virus-infected mice with viral pneumonia and humans with lung disease [*8, 20, 21*]. We recently clarified the NO- and ROS-dependent formation of