

- Mycobacterium bovis* bacillus Calmette-Guérin (BCG) and replication-deficient vaccinia virus DIs- based HIV vaccine. 14th Joint Meeting of AIDS Panels, Japan-US CMSP, Mar.5-7, 2003, Okinawa, Japan.
- 2) Nakasone T, Izumi Y, Matsuo K, Ami Y, Someya K, Kanekiyo M, Hamano T, Horibata S, Yoshino N, Hara T, Takizawa M, Kawahara M, Kaizu M, Hamatake M, Sakai K, Shinohara K, Yamazaki S, Yamamoto N, Honda M. Prime-boost vaccination with recombinant *Mycobacterium bovis* bacillus Calmette-Guérin in and vaccinia strain DIs elicits protective immunity against pathogenic SHIV infection in macaques. Japan-U.S. Cooperative Medical Science Program 14th Joint Meeting of AIDS Panel (March 5-7, 2003, Okinawa)
- 3) Nakasone T, Izumi Y, Matsuo K, Ami Y, Someya K, Kanekiyo M, Hamano T, Horibata S, Yoshino N, Hara T, Takizawa M, Kawahara M, Kaizu M, Hamatake M, Sakai K, Shinohara K, Yamazaki S, Yamamoto N, Honda M. Prime-boost vaccination with recombinant *Mycobacterium bovis* bacillus Calmette-Guérin in and vaccinia strain DIs elicits protective immunity against pathogenic SHIV infection in macaques. International Symposium on “Research and Development of Recombinant BCG and Vaccinia Virus-Based HIV Vaccine” (Feb 5-6, 2003, Tokyo)
- 4) Nakasone T, Yamamoto N, Izumi Y, Matsuo K, Ami Y, Yamazaki S, Honda M. Prime-boost vaccination with recombinant *Mycobacterium bovis* bacillus Calmette-Guérin in and vaccinia strain DIs elicits protective immunity against pathogenic SHIV infection in macaques. 10th Conference on Retroviruses and Opportunistic Infections (Feb 10-14, 2003, Boston, USA)
- 5) 浜野隆一、岡本尚、野内英樹、日比悠里名、高橋なを子、原敬志、山本直樹、山崎修道、本多三男、松尾和浩 Gag p17 遺伝子変異による HIV-1 CRF01_AE 複製の制御 第 17 回日本エイズ学会総会 (11/27-29, 2003, 神戸)
- H. 知的財産権の出願・登録状況（予定を含む。）
- 1) 特許取得 無し
 - 2) 実用新案登録 無し
 - 3) その他 無し

図 1

Investigator Brochure

<p>THAI AIDS VACCINE EVALUATION GROUP- SIRARA(TAVEG-SIRIRAJ)</p> <p>Guideline CLINICAL INVESTIGATOR BROCHURE</p> <p>1. INTRODUCTION</p> <p>2. AIMS OF PROPOSED CLINICAL PROGRAM</p> <p>3. PRODUCT DESCRIPTION</p> <p style="padding-left: 20px;">Name Active substance / Adjuvant / Descriptions</p> <p style="padding-left: 20px;">Investigation product</p> <p style="padding-left: 40px;">Formulation and presentation</p> <p style="padding-left: 40px;">Stability Test on the finished product</p> <p>4. PRECLINICAL IMMUNOGENICITY STUDIES</p> <p style="padding-left: 20px;">Experiment description</p> <p style="padding-left: 40px;">Animal Study Design</p> <p style="padding-left: 40px;">Product</p> <p style="padding-left: 40px;">Inoculation</p> <p style="padding-left: 40px;">Administration</p> <p style="padding-left: 40px;">Results</p> <p style="padding-left: 60px;">Clinical Observation</p> <p style="padding-left: 60px;">Serological Results</p>	<p>5. PRECLINICAL SAFETY STUDIES</p> <p style="padding-left: 20px;">Toxicology</p> <p style="padding-left: 20px;">Teratogenicity</p> <p style="padding-left: 20px;">General safety</p> <p style="padding-left: 20px;">Pyrogenicity</p> <p>6. PREVIOUS HUMAN EXPERIENCE</p> <p style="padding-left: 20px;">Clinical trials</p> <p style="padding-left: 40px;">Designs / Objectives</p> <p style="padding-left: 40px;">Safety / Reactogenicity results</p> <p style="padding-left: 40px;">Immunogenicity results</p> <p style="padding-left: 40px;">Conclusions</p> <p style="padding-left: 20px;">Case of HIV infections</p> <p style="padding-left: 20px;">General conclusion</p> <p style="padding-left: 20px;">Additional Experience</p> <p>7. ADDITIONAL GUIDANCE FOR THE INVESTIGATOR</p> <p>8. REFERENCE</p> <p>9. LIST OF FIGURES</p> <p>10. LIST OF ABBREVIATIONS</p>
---	--

図 2

rDIs-gag治療薬製造に必要な主な作業項目とスケジュール

分類	項目	スケジュール				
		2003 7-12	2004 1-6	2004 7-12	2005 1-6	2005 7-12
作業準備	実験開始手続き	→				
	設備・機器の整備	→				
培養法検討	技術移管	→				
	培養法の最適化	→	→			
精製法検討	技術移管	→				
	精製法の最適化	→	→			
ウイルスバンク作	ウイルスバンクの作製			→		
	ウイルスバンクの試験			→		
規格及び試験方法	試験項目設定及び試験方法の確立	→	→			
	分析法バリデーション			→		
	規格値の設定				→	
製剤化検討	製剤設計	→				
	添加剤の検討		→	→		
非臨床試験	非臨床試験機体の製造			→		
	非臨床試験機体の品質試験				→	
	非臨床試験機体の実施					→
治療薬製造	治療薬GMP等類等の整備・手続き				→	→
	治療薬製造に関するペリフィケーション				→	
	治療薬の製造					→
	治療薬の品質試験					→

III. 業績一覽

研究成果の刊行に関する一覧表

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
<u>Nakasone T.</u> <u>Hara T.</u> <u>Yoshino N.</u> <u>Honda M.</u>	Update on HIV/AIDS in Japan, 2003	Lu Y, Essex M	AIDS in ASIA		U.S.A.	2004	73-81
<u>Matsuo K.</u> <u>Puthavathana P.</u> <u>Promkhatkaew D.</u> <u>Balachandra K.</u> <u>Ruxrungtham K.</u> <u>Hamano T.</u> <u>Sutthent R.</u> <u>Sittisombut N.</u> <u>Butraporn R.</u> <u>Sriwanthana B.</u> <u>Boonlong J.</u> <u>Izumi Y.</u> <u>Yamazaki S.</u> <u>Yamamoto N.</u> <u>Warachit P.</u> <u>Honda M.</u>	Japan's collaboration with Thailand in the development of an HIV/AIDS vaccine	Lu Y, Essex M	AIDS in ASIA		U.S.A.	2004	561-569
<u>Tetsuka, T.</u> <u>Okamoto, T.</u>	Oxidative stress and signal transduction pathway of redox sensor protein.	Eds. R. G. Cutler and H. Rodriguez	Critical Reviews of Oxidative Stress and Aging.	World Scientific Publishing Co. Pte. Ltd	U.S.A.	2003	112-127

雑誌

発表者氏名	論文タイトル	発表誌名	巻号	ページ	出版年
<u>Nakao R.</u> <u>Hanada N.</u> <u>Asano T.</u> <u>Hara T.</u> <u>Salam Md A.</u> <u>Matin K.</u> <u>Shimazu Y.</u> <u>Nakasone T.</u> <u>Horibata S.</u> <u>Aoba T.</u> <u>Honda M.</u> <u>Amagasa T.</u> <u>Senpuku H.</u>	Assesment of oral transmission using cell-free HIV-1 in mice reconstituted with human peripheral blood leucocytes.	Immunology.	109	271-282	2003

Sakaue G, Hiroi T, Nakagawa Y, Someya K, Iwatani K, Sawa Y, <u>Takahashi H,</u> <u>Honda M,</u> Kunisawa J, Kiyono H.	HIV mucosal vaccine: nasal immunization with gp160-encapsulated hemagglutinating virus of Japan-liposome induces antigen-specific CTLs and neutralizing antibody responses.	J Immunol.	170	495-502	2003.
Kaizu M., Sato H., <u>Ami Y.,</u> Izumi Y., <u>Nakasone T.,</u> Tomita Y., Someya K., Takebe Y., Kitamura K., Tochikubo O. <u>Honda M.</u>	Infection of macaques with an R5-tropic SHIV bearing a chimeric envelope carrying subtype E V3 loop among subtype B framework.	Arch. Virol	148	973-988	2003
Takizawa M, Chiba J, Haga S, Asano T, <u>Yamamoto N,</u> <u>Honda M.</u>	Fractionation of guinea pig leukocyte by flow cytometry using a novel MIL4/SSC parameter.	Cytometry Research	13	25-32	2003
Kaizu M., <u>Ami Y.,</u> <u>Nakasone T.,</u> Sasaki Y., Izumi Y., Sato H., Takahashi E., Sakai K., Shinohara K., Nakanishi K. <u>Honda M.</u>	Higher levels of IL-18 circulate during primary infection of monkeys with a pathogenic SHIV than with a nonpathogenic SHIV.	Virology	313	8-12	2003.
Gzyl J, Bolesta E, Wierzbicki A, Kmieciak D, Naito T, Kaneko Y, <u>Honda M,</u> <u>Komuro K,</u> Kozbor D.	Effect of partial and complete variable loop deletions of the Human Immunodeficiency virus type 1 envelope glycoprotein and the breadth of gp160-specific immune responses.	Virology	318	493-506	2004
Izumi Y., <u>Ami Y.,</u> <u>Matsuo K.,</u> Someya K.,	Intravenous inoculation of replication-deficient recombinant Vaccinia DIs expressing SIV Gag controls	J. Virol.	77	13248-13256	2003

<u>Sata T.</u> <u>Yamamoto N.</u> <u>Honda M.</u>	highly pathogenic SHIV in monkeys.				
Hamano T, Sawanpanyalert P, Yanai H, Piyaworawong S, Hara T, Sapsutthipas S, Phromjai J, <u>Yamazaki S.</u> <u>Yamamoto N.</u> Warachit P, <u>Honda M.</u> <u>Matsuo K.</u>	Determination of HIV-1 CRF01_AE gag p17 and env-V3 consensus sequences for HIV/AIDS vaccine design.	AIDS Res. Hum. Retroviruses	20	337-340	2004
Takizawa M, Chiba J, Haga S, Asano T, <u>Yamamoto N.</u> <u>Honda M.</u>	The normalization of guinea pig leukocyte fractions and lymphocyte subsets in blood and lymphoid tissues using a flow cytometric procedure.	Experimental Animals		in press	2004
Takeda S, Shiosaki K, Kaneda Y, Nakasatomi T, Yoshizaki H, Someya K, Konno Y, Eda Y, Kino Y, <u>Yamamoto N.</u> <u>Honda M.</u>	Hemagglutinating Virus of Japan (HVJ) Protein is Efficient for Induction of CD4 ⁺ T-cell response by a Hepatitis B core Particle-Based HIV Vaccine	Clin. Immunol.		in press	2004
Takahashi N, Kobayashi S, Jiang X, Kitagori K, Imai K, Hibi Y, <u>Okamoto T.</u>	Expression of 53BP2 and ASPP2 proteins from TP53BP2 gene by alternative splicing.	Biochem Biophys Commun Res	315(2):	434-8	2004
Tozawa, K., Kawai, N., Hayashi, Y., Sasaki, S., Kohri K <u>Okamoto, T.</u>	Gold compounds inhibit adhesion of human cancer cells to vascular endothelial cells.	Cancer Lett.	196	93-100	2003
Ando, K., Kanazawa, S., Tetsuka, T., Ohta, S., Jiang, X.,	Induction of Notch signaling by tumor necrosis factor in rheumatoid synovial fibroblasts.	Oncogene	22	7796-7803	2003

Tada, T., Kobayashi, M., Matsui, N., Okamoto, T.					
Torigoe, T., Izumi, H., Yoshida, Y., Ishiguchi, H., Okamoto, T., Itoh, H., Kohnno, K.	Low pH enhances Sp1 DNA binding activity and interaction with TBP.	Nucleic Acids Res.	31	1-8	2003
Kanazawa, S., Soucek, L., Evan, G., Okamoto, T., Peterlin, B. M.	c-Myc recruits P-TEFb for transcription, cellular proliferation and apoptosis.	Oncogene	22	5705-5711	2003
Asamitsu, K., Kanazawa, S., Tetsuka, T., Okamoto, T.	RING finger protein AO7 supports the NF-kB-mediated transcription by interacting with the transactivation domain of p65 subunit.	J. Biol. Chem.	278	26879-26887	2003
Teranishi, F., Liu, Z.-Q., Kunimatsu, M., Imai, K., Takeyama, H., Manabe, T., Sasaki, M., Okamoto, T.	Calpain is involved in the HIV replication from the latently-infected OM10.1 cells.	Biochem. Biophys. Res. Commun.	303	940-949	2003
Ohata, H., Tetsuka, T., Hayashi, H., Onozaki, K., Okamoto, T.	3-Methylcholanthrene activates human immunodeficiency virus type 1 replication via aryl hydrocarbon receptor.	Microbiol. Immunol.	45	363-370	2003
Okano, A., Usuda, N., Furihata, K., Nakayama, K., Tian, Q B., Okamoto, T., Suzuki, T.	Huntingtin-interacting protein-1-related protein of rat (rHIP1R) is localized in the postsynaptic regions.	Brain Res.	967	210-225	2003
Matsumura, T., Degawa, T., Takii, T., Hayashi, H., Okamoto, T., Inoue, J., Onozaki, K.	TRAF6-NF-kB pathway is essential for IL-1-induced TLR2 expression and its functional response to TLR2 ligand in murine hepatocytes.	Immunology	109	127-136	2003

Jiang, X., Takahashi, N., Ando, K., Otsuka, T., Tetsuka, T., Okamoto, T.	NF- κ B p65 transactivation domain is involved in the NF- κ B-inducing kinase (NIK) pathway.	Biochem. Biophys. Res. Commun.	301	583-590	2003
Jiang, X., Takahashi, N., Matsui, N., Tetsuka, T., Okamoto, T.	The NF- κ B activation in the lymphotoxin beta receptor signaling depends on the phosphorylation of p65 at serine 536.	J. Biol. Chem.	278	919-926	2003
Saito K, Ohara N, Hotokezaka H, Fukumoto S, Yuasa K, Naito M, Fujiwara T, Nakayama K.	Infection-induced upregulation of the costimulatory molecule 4-1BB in osteoblastic cells and its inhibitory effect on M-CSF/RANKL-induced in vitro osteoclastogenesis	J Biol Chem		in press	2004
Kitaura H, Nakao N, Yoshida N, Yamada T.	Induced sensitization to nickel in guinea pigs immunized with mycobacteria by injection of purified protein derivative with nickel.	New Microbiol.	26	101-108	2003
Lee J-S, Ohara N, Kamijo K, Kitamura T, Miki T.	MgcRacGAP regulates membrane blebbing through RhoA during cytokinesis.	Exp. Cell. Res.		in press	2004
Saito SI, Liu X-F, Kamijo K, Razziudin R, Tatsumoto T, Okamoto I, Chen X, Lee C-C, Lorenzi MV, Ohara N, Miki T.	Deregulation and mislocalization of the cytokinesis regulator ECT2 activate the Rho signaling pathways leading to malignant transformation.	J. Biol. Chem.		in press	2004
Kojima A., Yasuda, A., Asanuma, H., Ishikawa, T., Takamizawa, A., Yasui, K., Kurata, T.	Stable high-producer cell clone expressing virus-like particles of the Japanese encephalitis virus E protein for a second-generation subunit vaccine.	J. Virol.	77	8745-8755	2003
Yokomaku, Y., Miura, H.,	Impaired processing and presentation of cytotoxic T-lymphocyte (CTL) epitopes	J. Virol.	78(3):	1324-32.	2004

Tomiyama, H., Kawana-Tachikawa, A., <u>Takiguchi, M.</u> <u>Kojima, A.</u> Nagai, Y., Iwamoto, A., Matsuda, Z. Ariyoshi, K.	lymphocyte (CTL) epitopes are major escape mechanisms from CTL immune pressure in human immunodeficiency virus type 1 infection.				
Aoki, Y., Saint-Germain N., Gyda M., Magner-Fink E. K., Lee Y-H, Credidio C., Saint-Jeannet, J-P.	The transcription factor Sox9 is required for cranial neural crest development in Xenopus. Development.	Developmental Biology.	259(1):	19-33,	2003
Park EJ, Takahashi I, Ikeda J, Kawahara K, <u>Okamoto T.</u> Kweon MN, Fukuyama S, Groh V, Spies T, Obata Y, Miyazaki J, <u>Kiyono H.</u>	Clonal expansion of double-positive intraepithelial lymphocytes by MHC class I-related chain a expressed in mouse small intestinal epithelium.	J. Immunol	171	4131-4139	2003
Kobayashi M, Kweon MN, Kuwata H, Schreiber RD, Kiyono H, Takeda K, Akira S.	Toll-like receptor-dependent production of IL-12p40 causes chronic enterocolitis in myeloid cell-specific Stat3-deficient mice.	J. Clin Invest	111	1297-1308	2003.
Jang MH, Kweon MN, Hiroi T, Yamamoto M, Takahashi I, <u>Kiyono H.</u>	Induction of cytotoxic T lymphocyte responses by cholera toxin-treated bone marrow-derived dendritic cells.	Vaccin	21	1613-1619	2003
Hagiwara Y, McGhee JR, Fujihashi K, Kobayashi R, Yoshino N, Kataoka K, Etani Y, Kweon MN, Tamura S, Kurata T,	Protective mucosal immunity in aging is associated with functional CD4 ⁺ T cells in nasopharyngeal-associated lymphoreticular tissue.	J. Immunol	170	1754-1762	2003

Takeda Y, Kiyono H, Fujihashi K.					
Okuda Y, Takahashi I, Kim JK, Ohta N, Iwatani K, Iijima H, Kai Y, Tamagawa H, Hiroi T, Kweon MN, Kawano S, Takeda K, Akira S, Sasaki Y, Hori M, Kiyono H.	Development of colitis in signal transducers and activators of transcription 6-deficient T-cell receptor alpha-deficient mice: a potential role of signal transducers and activators of transcription 6-independent interleukin-4 signaling for the generation of Th2-biased pathological CD4 ⁺ beta beta T cells.	Am J Pathol.	162	263-271	2003
Boyaka PN, Ohmura M, Fujihashi K, Koga T, Yamamoto M, Kweon MN, Takeda Y, Jackson RJ, Kiyono H, Yuki Y, McGhee JR.	Chimeras of labile toxin one and cholera toxin retain mucosal adjuvanticity and direct Th cell subsets via their B subunit.	J. Immunol	170	454-462	2003
Shinya, E., Hidaka, C., Owaki, A., Shimizu, M., Li, Y., Watanabe, K., Watari, E., Hayami, M., Klatzmann, D., Takahashi, H.	Effect of Nef-deleted pseudotyped HIV virions bearing an enhanced green fluorescent protein gene in the env on HIV-sensitive transformed T cells.	Biomed. Res	24	59-69	2003
Kawashima, T., Norose, Y., Watanabe, Y., Enomoto, Y., Narazaki, H., Watari, E., Tanaka, S., Takahashi, H., Yano, I., Brenner, M., Sugita, M.	Major CD8 T cell response to live bacillus Calmette-Guérin is mediated by CD1 molecules.	J. Immunol	170	5345-5348	2003

Akahata, W., Ido, E., Akiyama, H., Uesaka, H., Enose, Y., Horiuchi, R., Kuwata, T., Goto, T., <u>Takahashi, H.</u> , Hayami, M.	DNA vaccination of macaques by a full-genome simian/human immunodeficiency virus type 1 plasmid chimera that produces non-infectious virus particles.	J. Gen. Virol	84	2237-2244	2003
Takeuchi, J., Watari, E., Shinya, E., Norose, Y., Matsumoto, M., Seya, T., Sugita, M., Kawana, S., <u>Takahashi, H.</u>	Down-regulation of Toll-like receptor expression in monocyte-derived Langerhans cell-like cells: implications of low-responsiveness to bacterial components in the epidermal Langerhans cells.	BBRC	306	674-679	2003
<u>Takahashi, H.</u>	Antigen presentation in vaccine development.	Comp. Immunol. & Microbiol. Infect. Dis.	26,	309-328	2003
高橋めぐみ, 中川洋子, <u>高橋秀実</u>	エピトープペプチドによるキラーT細胞の特異的活性抑制と細胞死の誘導.	炎症と免疫	11	249-255	2003
Hossain MS., Tomiyama H., Inagawa T., Ida S., Oka S., <u>Takiguchi M.</u>	Identification and characterization of HLA-A*3303-restricted, HIV-1 Pol- and Gag-derived cytotoxic T cell epitopes.	AIDS Res. Huma. Retroviruses.	19	503-510	2003
Ueno, T., Tomiyama, H., Fujiwara, M., Oka, S., <u>Takiguchi, M.</u>	HLA class I-restricted recognition of an HIV-derived epitope peptide by a human T cell receptor α chain having a V ₁ variable segment.	Eur. J. Immunol.	33	2910-2916	2003
杉本正信 大石和恵 木所穂 橋爪壮	国産天然痘ワクチンの新たな役割 バイオテロ対策およびベクターとしての利用	蛋白質核酸酵素	48	1693-1701	2003
Ohmori, H., Makita, Y., F unamizu, M., Chiba, S., Ohtani, K., Suzuki, Y., <u>Wakamiya, N.</u>	Haplotype analysis of human collectin placenta 1 (hCL-P1) gene.	J. Hum. Genet.	48	82-85	2003

Hata, A.					
Suzutani T, Ishioka K, De Clercq E, Ishibashi K, Kaneko H, Kira T, Hashimoto KI, Ogasawara M, Ohtani K, <u>Wakamiya N</u> , Saijo M	Differential Mutation Patterns in Thymidine Kinase and DNA Polymerase Genes of Herpes Simplex Virus Type 1 Clones Passaged in the Presence of Acyclovir or Penciclovir.	Antimicrob. Agents Chemother.	47(5)	1707-1713	2003
Saito, T., Fukuzawa, J., Osaki, J., Sakuragi, H., Yao, N., Haneda, T., Fujino, T., <u>Wakamiya, N.</u> , Kikuchi, K., Hasebe, N	Roles of calcineurin and calcium/calmodulin-dependent protein kinase II in pressure overload-induced cardiac hypertrophy.	J. Molecular and Cellular Cardiology.	35(9)	1153-1160	2003