

厚生労働科学研究費補助金（肝炎等克服緊急対策研究事業）
分担研究報告書（平成 22～24 年度）

ウイルス性肝炎に対する応答性を規定する宿主因子も含めた情報の
データベース構築・治療応用に関する研究

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分担研究課題：ウイルス性肝炎に対する応答性を既定する宿主因子も含めた情報の
データベース構築

研究要旨：ウイルス性肝炎に関して、宿主(ヒト)側とウイルス側双方の要因のデータを収集し、患者より得られた臨床情報を加えて多次元的に構成されたデータベースを構築し、継続的に臨床情報の拡充を遂行した。その成果を基に、遺伝子発現情報の導入、宿主側因子より IFN/RBV 治療効果を予測するシステムの構築、班員外の一般研究者への情報公開を念頭に置いた新たな利用者インターフェースの構築を遂行した。

A. 研究目的

本研究では、ウイルス性肝炎を特徴付けるプロファイルを構築し、それがテラーメイド医療の分野で利用されることを目的としている。その実現のために構築されたデータベースの宿主側因子の情報を拡充し、また、班員のニーズを実現した解析機能を追加する。併せて、一般研究者への情報公開を目的とした機能を追加する。

B. 研究方法

これまでに収集した SNP 情報および臨床情報を参照し、ある宿主側因子を持つ患者の IFN/RBV 治療の治療効果を予測するシステムを構築する。五條掘班員の提言に基づき、宿主側因子情報として遺伝子発現情報を導入する。両件の実現に必要なデータベーススキーマ改訂、解析モジュール、利用者インターフェースを構築する。また、一般研究者への情報公開を目的として新たな利用者インターフェースを構築する。

C. 研究結果

治療効果予測システムは、患者 SNP、ウイルス情報、臨床情報をパラメータとして SVR+TR および NR+Null の頻度を推定する機能を有し、既報の治療効果は再現された。遺伝子発現情報は、臨床情報、SNP 情報と相互参照できる形式でシステム化され、さらに発現情報間相互比較も実現された。一般研究者向け利用者インターフェースは、班員向けのそれとシステムを共有し、対象のみ既報データに限定する形式に構築した。

D. 考察

治療効果予測システム、遺伝子発現情報、一般向け利用者インターフェースにより、本データベースの利用上の有用性が向上したと考えられる。

E. 結論

本データベースの有用性向上、および今後の情報および機能追加の枠組みの準備が実現できた。

F. 研究発表

1. 論文発表

なし

2. 学会発表

なし

G. 知的所得権の所得状況

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

III. 研究成果の刊行一覧

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
平成 22 年度							
渡辺久剛、斎藤貴史、西瀬雄子、邵力、佐藤智佳子、石井里佳、芳賀弘明、奥本和夫、斎藤孝治、富樫整、新沢陽英、河田純男	HCV コホート研究による持続感染者の自然経過	佐田通夫・新沢陽英・斎藤貴史	HCV 感染の natural course を探る：わが国におけるコホート研究	山形大学出版	山形	2011	45-50
平成 23 年度							
渡邊綱正、 <u>田中靖人</u>	HCV 感染と IL28B	小俣政男	2012-2013 肝疾患 Review	日本メディカルセンター	東京都千代田区	2012	96-101
平成 24 年度							
渡邊綱正、 <u>田中靖人</u>	HCV 感染と IL28B	小俣政男	2012-2013 肝疾患 Review	日本メディカルセンター	東京都千代田区	2012	96-101
渡邊綱正.	慢性肝炎・肝硬変	日本臨床検査医学会ガイドライン作成委員会	臨床検査のガイドライン JSLM2012 検査値アプローチ／症候／疾患	株式会社 宇宙堂八木書店	東京都千代田区	2012	279-283

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
平成 22 年度					
Kurbanov F, <u>Tanaka Y,</u> Matsuura K, <u>Sugauchi F,</u> Elkady A, Khan A, Hasegawa I, Ohno T, Tokuda H, <u>Mizokami M.</u>	Positive selection of core 70Q variant genotype 1b hepatitis C virus strains induced by pegylated interferon and ribavirin.	J Infect Dis.	201(11)	1663-1671	2010

* <u>Tanaka Y,</u> Nishida N, Sugiyama M, Tokunaga K, Mizokami M.	lambda-Interferons and the single nucleotide polymorphisms: A milestone to tailor-made therapy for chronic hepatitis C.	Hepatol Res.	40(5)	449-460	2010
Akkarathamrongsin S, Sugiyama M, Matsuura K, Kurbanov F, Poovorawan Y, <u>Tanaka Y,</u> Mizokami M.	High sensitivity assay using serum sample for IL28B genotyping to predict treatment response in chronic hepatitis C patients.	Hepatol Res.	40(10)	956-962	2010
Elkady A, <u>Tanaka Y,</u> Kurbanov F, <u>Sugauchi F,</u> Sugiyama M, Khan A, Ali EM, Mouhamed L, Abou el-fetouh S, AbdEl-Hameed AR, <u>Mizokami M.</u>	Performance of two Real-Time RT-PCR assays for quantitation of hepatitis C virus RNA: evaluation on HCV genotypes 1-4.	J of Med Virol.	82	1878-88	2010
Afdhal NH, McHutchison JG, Zeuzem S, Mangia A, Pawlotsky JM, Murray JS, Shianna KV, <u>Tanaka Y,</u> Thomas DL, Booth DR, Goldstein DB; Pharmacogenetics and Hepatitis C Meeting Participants.	Hepatitis C pharmacogenetics: state of the art in 2010.	Hepatology	53(1)	336-345	2011

Sugiyama M, <u>Tanaka Y,</u> Nakanishi M, <u>Mizokami M.</u>	Novel Findings for the Development of Drug Therapy for Various Liver Diseases: Genetic Variation in IL-28B Is Associated With Response to the Therapy for Chronic Hepatitis C.	J Pharmacol Sci.	115	263-269	2011
Ito K, Higami K, Masaki N, Sugiyama M, Mukaide M, Saito H, Aoki Y, Sato Y, Imamura M, Murata K, Nomura H, Hige S, Adachi H, Hino K, <u>Yatsuhashi H,</u> Orito E, Kani S, <u>Tanaka Y,</u> <u>Mizokami M.</u>	The rs8099917 Polymorphism, Determined by a Suitable Genotyping Method, is a Better Predictor for Response to Pegylated Interferon- α /Ribavirin Therapy in Japanese Patients than Other SNPs Associated with IL28B.	J Clin Microbiol.	49(5)	1853-60	2011
<u>田中靖人</u>	GWAS から同定された C 型肝炎の治療効果に関連する遺伝子多型	実験医学	28(18)	2955-2960	2010
<u>田中靖人</u>	IL28B 遺伝子多型に基づいた C 型肝炎診療の展望	Schneller	76	4-9	2010
<u>田中靖人、溝上雅史</u>	IL28B 遺伝子検査に基づいた C 型慢性肝炎の個別化医療	ISRL 宝函	31(3)	33-39	2010
<u>徳永勝士</u>	ゲノムワイド関連解析による疾患感受性遺伝子・薬剤応答性遺伝子の探索	ファルマシア	46(5)	421-431	2010
Tateyama M, <u>Yatsuhashi H,</u> Taura N, Motoyoshi Y, Nagaoka S, Yanagi K, Abiru S, Yano K, Komori A, Migita K, Nakamura M, Nagahama H, Sasaki Y, Miyakawa Y, Ishibashi H.	Alpha-fetoprotein above normal levels as a risk factor for the development of hepatocellular carcinoma in patients infected with hepatitis C virus.	J Gastroenterol.	46(1)	92-100	2011

* <u>Kurosaki M</u> , <u>Tanaka Y</u> , Nishida N, <u>Sakamoto N</u> , Enomoto N, <u>Honda M</u> , Sugiyama M, Matsuura K, <u>Sugauchi F</u> , Asahina Y, Nakagawa M, Watanabe M, Sakamoto M, Maekawa S, Sakai A, Kaneko S, Ito K, Masaki N, <u>Tokunaga K</u> , Izumi N, <u>Mizokami M</u> .	Pretreatment Prediction of Response to Pegylated-Interferon Plus Ribavirin for Chronic Hepatitis C using Genetic Polymorphism in <i>IL28B</i> and Viral Factors.	J Hepatol.	54(3)	439-448	2011
* <u>Watanabe H</u> , Wells F, Major ME.	Clearance of hepatitis C in chimpanzees is associated with intrahepatic T-cell perforin expression during late acute phase.	J Viral Hepat.	17(4)	245-253	2010
Sanjo M, Saito T, Nishise Y, Haga H, Okumoto K, Ito J, <u>Watanabe H</u> , Saito K, Togashi H, Fukuda K, Imai Y, El Shamy A, Deng L, Shoji I, Hotta H, Kawata S.	Secondary structure of the amino-terminal region of HCV NS3 and virological response to pegylated interferon plus ribavirin therapy for chronic hepatitis C.	J Med Virol.	82(8)	1364-1370	2010
Nishise Y, Saito T, Makino N, Okumoto K, Ito JI, <u>Watanabe H</u> , Saito K, Togashi H, Ikeda C, Kubota I, Daimon M, Kato T, Fukao A, Kawata S.	Relationship between alcohol consumption and serum adiponectin levels: the Takahata study- a cross-sectional study of a healthy Japanese population.	J Clin Endocrinol Metab.	95	3828-3835	2010

Hattori E, Shu HJ, Saito T, Okumoto K, Haga H, Yokozawa J, Ito J, <u>Watanabe H</u> , Saito K, Togashi H, Kawata S.	Expression of the RNA-binding protein Musashil1 in adult liver stem-like cells.	Hepatol Res	40(4)	432-437	2010
* <u>Sakamoto N</u> , <u>Tanaka Y</u> , Nakagawa M, <u>Yatsuhashi H</u> , Nishiguchi S, Enomoto N, Azuma S, Nishimura-Sakurai Y, Kakinuma S, Nishida N, <u>Tokunaga K</u> , <u>Honda M</u> , Ito K, <u>Mizokami M</u> , Watanabe M.	ITPA gene variant protects against anemia induced by pegylated interferon- α and ribavirin therapy for Japanese patients with chronic hepatitis C.	Hepatol Res.	40(11)	1063-1071	2010
Suda G, <u>Sakamoto N</u> , Itsui Y, Nakagawa M, Tasaka-Fujita M, Funaoka Y, Watanabe T, Nitta S, Kiyohashi K, Azuma S, Kakinuma S, Tsuchiya K, Imamura M, Hiraga N, Chayama K, Watanabe M.	IL-6-mediated intersubgenotypic variation of interferon sensitivity in hepatitis C virus genotype 2a/2b chimeric clones.	Virology	407(1)	80-90	2010
Nakagawa M, <u>Sakamoto N</u> , Ueyama M, Mogushi K, Nagaie S, Itsui Y, Azuma S, Kakinuma S, Tanaka H, Enomoto N, Watanabe M.	Mutations in the Interferon Sensitivity Determining Region and virological response to combination therapy with Pegylated-interferon alpha 2b plus ribavirin in patients with chronic hepatitis C-1b infection.	J Gastroenterol.	45(6)	656-665	2010

Mizui T, Yamashina S, Tanida I, Takei Y, Ueno T, Sakamoto N , Ikejima K, Kitamura T, Enomoto N, Sakai T, Kominami E, Watanabe S.	Inhibition of hepatitis C virus replication by chloroquine targeting virus-associated autophagy.	J Gastroenterol.	45(2)	195-203	2010
Kurosaki M , Sakamoto N , Iwasaki M, Sakamoto M, Suzuki Y, Hiramatsu N, Sugauchi F , Tamori A, Nakagawa M, Izumi N.	Sequences in the interferon sensitivity-determining region and core region of hepatitis C virus impact pretreatment prediction of response to PEG-interferon plus ribavirin: data mining analysis.	J Med Virol.	83(3)	445-452	2011
* Sakamoto N , Nakagawa M, Tanaka Y , Sekine-Osajima Y, Ueyama M, Kurosaki M , Nishida N, Tamori A, Nishimura-Sakurai Y, Itsui Y, Azuma S, Kakinuma S, Hige S, Ito Y, Tanaka E, Hiasa Y, Izumi N, Tokunaga K , Mizokami M , Watanabe M	Association of IL28B variants with response to pegylated-interferon alpha plus ribavirin combination therapy reveals intersubgenotypic differences between genotypes 2a and 2b.	J Med Virol.	83(5)	871-878	2011
篠島裕子、中川美 奈、 坂本直哉	C型肝炎の日常診療:治療 の適応、選択の実際	medicina	47(3)	2010-2103	2010
坂本直哉	新規治療薬の開発動向	最新医学	65(9)	1919-1924	2010
坂本直哉	STAT-C (Specifically Targeted Antiviral Therapy for hepatitis C) 開発の動向	肝胆膵	2010 増刊号	204-208	2010
坂本直哉 、中川美 奈、渡辺守	肝疾患における血液生化 学検査、肝炎ウイルスマ ーカー、腫瘍マーカーの 見方 IL28B	肝胆膵	60(4)	657-660	2010

植山真由美、中川 美奈、 <u>坂本直哉</u> 、 渡辺守	IL-6 と肝炎・肝発癌.	肝胆膵	60(5)	849-856	2010
<u>坂本直哉</u>	新しいインターフェロン 製剤:PEG インターフェロ ンλを中心	肝胆膵	61(6)	955-958	2011
笈島裕子、中川美 奈、 <u>坂本直哉</u>	HCV の複製・増殖機構と遺 伝子型・遺伝子変異	日本臨床	69 卷増刊 4	52-58	2011
<u>坂本直哉</u>	インターロイキン 28-29 (IL-28・IL-29) -インタ ーフェロンλ.	臨床免疫・アレル ギー科	57 卷 Suppl.21	184-187	2012
* <u>Honda M</u> , Nakamura M, Tateno M, Sakai A, Shimakami T, Shirasaki T, Yamashita T, Arai K, Yamashita T, Sakai Y, Kaneko S.	Differential interferon signaling in liver lobule and portal area cells under treatment for chronic hepatitis C.	J Hepatol.	53(5)	817-826	2010
Shirasaki T, <u>Honda M</u> , Mizuno H, Shimakami T, Okada H, Sakai Y, Murakami S, Wakita T, Kaneko S.	La protein required for internal ribosome entry site-directed translation is a potential therapeutic target for hepatitis C virus replication.	J Infect Dis.	202(1)	75-85	2010
Yamashita T, <u>Honda M</u> , Nio K, Nakamoto Y, Yamashita T, Takamura H, Tani T, Zen Y, Kaneko S.	Oncostatin m renders epithelial cell adhesion molecule-positive liver cancer stem cells sensitive to 5-Fluorouracil by inducing hepatocytic differentiation.	Cancer Res.	70(11)	4687-4697	2010
<u>Honda M</u> , Sakai Y, Yamashita T, Yamashita T, Sakai A, Mizukoshi E, Nakamoto Y, Tatsumi I, Miyazaki Y, Tanno H, Kaneko S; Hokuriku Liver Study Group.	Differential gene expression profiling in blood from patients with digestive system cancers.	Biochem Biophys Res Commun.	400(1)	7-15	2010

* <u>Honda M</u> , Sakai A, Yamashita T, Nakamoto Y, Mizukoshi E, Sakai Y, Yamashita T, Nakamura M, Shirasaki T, Horimoto K, <u>Tanaka Y</u> , <u>Tokunaga K</u> , <u>Mizokami M</u> , Kaneko S; Hokuriku Liver Study Group.	Hepatic ISG expression is associated with genetic variation in interleukin 28B and the outcome of IFN therapy for chronic hepatitis C.	Gastroenterology	139(2)	499-509	2010
Hodo Y, Hashimoto S, <u>Honda M</u> , Yamashita T, Suzuki Y, Sugano S, Kaneko S, Matsushima K.	Comprehensive gene expression analysis of 5'-end of mRNA identified novel intronic transcripts associated with hepatocellular carcinoma.	Genomics.	95(4)	217-223	2010
Mizukoshi E, Nakamoto Y, Arai K, Yamashita T, Sakai A, Sakai Y, Kagaya T, Yamashita T, <u>Honda M</u> , Kaneko S.	Comparative analysis of various tumor-associated antigen-specific T cell responses in patients with hepatocellular carcinoma.	Hepatology	53(4)	1206-16	2011
Nakamura Y, Komiyama T, Furue M, <u>Gojobori T</u> , Akiyama Y.	CIG-DB: The database for human or mouse immunoglobulin and T cell receptor genes available for cancer studies.	BMC Bioinformatics	11(398)	1-9	2010
Gaudet P, Bairoch A, Field D, <u>Gojobori T</u> , White O, Yamasaki C. et al.	Towards BioDBcore: a community-defined information specification for biological databases.	Nucleic Acids Res.	39	D7-D10	2011
平成 23 年度					
渡邊綱正、 <u>田中靖人</u>	C型肝炎治療効果に影響する IL28B 遺伝子多型	肝胆膵.	63(6)	1079-1086	2011

* <u>Tanaka Y,</u> <u>Kurosaki M,</u> Nishida N, Sugiyama M, Matsuura K, <u>Sakamoto N,</u> Enomoto N, <u>Yatsuhashi H,</u> Nishiguchi S, Hino K, Hige S, Itoh Y, Tanaka E, Mochida S, <u>Honda M,</u> Hiasa Y, Koike A, <u>Sugauchi F,</u> Kaneko S, Izumi N, <u>Tokunaga K,</u> <u>Mizokami M.</u>	Genome-wide association study identified ITPA/DDRGK1 variants reflecting thrombocytopenia in pegylated interferon and ribavirin therapy for chronic hepatitis C.	Hum Mol Genet.	20(17)	3507-3516	2011
*Sugiyama M, <u>Tanaka Y,</u> Wakita T, Nakanishi M, <u>Mizokami M.</u>	Genetic Variation of the IL-28B Promoter Affecting Gene Expression.	PLoS One.	6(10)	e26620	2011
<u>Kurosaki M,</u> <u>Tanaka Y,</u> Tanaka K, Suzuki Y, Hoshioka Y, Tamaki N, Kato T, Yasui Y, Hosokawa T, Ueda K, Tsuchiya K, Kuzuya T, Nakanishi H, Itakura J, Takahashi Y, Asahina Y, Matsuura K, <u>Sugauchi F,</u> Enomoto N, Nishida N, <u>Tokunaga K,</u> <u>Mizokami M,</u> Izumi N.	Relationship between polymorphisms of the inosine triphosphatase gene and anaemia or outcome after treatment with pegylated interferon and ribavirin.	Antivir Ther.	16(5)	685-694	2011
Seto WK, <u>Tanaka</u> <u>Y,</u> Liu K, Lai CL, Yuen MF.	The Effects of IL-28B and ITPA Polymorphisms on Treatment of Hepatitis C Virus Genotype 6.	Am J Gastroenterol.	106(5)	1007-1008	2011

Matsuura K, <u>Tanaka Y,</u> Kusakabe A, Hige S, Inoue J, Komatsu M, Kuramitsu T, Hirano K, Ohno T, Hasegawa I, Kobashi H, Hino K, Hiasa Y, Nomura H, <u>Sugauchi F</u> , Nogiri S, Joh T, <u>Mizokami M.</u>	Recommendation of lamivudine-to-entecavir switching treatment in chronic hepatitis B responders: Randomized controlled trial.	Hepatol Res.	41(6)	505-511	2011
Tamori A, Kioka K, Kurai O, Sakaguchi H, Enomoto M, Fujii H, Kobayashi S, Iwai S, Morikawa H, Yamaguchi S, Kawasaki Y, Oka H, <u>Tanaka Y</u> , Kawada N.	Favorable factors for re-treatment with pegylated interferon α 2a plus ribavirin in patients with high viral loads of genotype 1 hepatitis C virus.	Hepatol Res.	41(12)	1169-1177	2011
Miyaaki H, Ichikawa T, <u>Yatsuhashi H</u> , Taura N, Miura S, Usui T, Mori S, Kamihiro S, <u>Tanaka Y</u> , <u>Mizokami M</u> , Nakao K.	Suppressor of cytokine signal 3 and IL28 genetic variation predict the viral response to peginterferon and ribavirin.	Hepatol Res.	41(12)	1216-1222	2011
Raghwanji J, Thomas XV, Koekkoek SM, Schinkel J, Molenkamp R, van de Laar TJ, Takebe Y, <u>Tanaka Y</u> , <u>Mizokami M</u> , Rambaut A, Pybus OG.	Origin and evolution of the unique hepatitis C virus circulating recombinant form 2k/1b.	J Virol.	86(4)	2212-2220	2012
<u>Tanaka Y</u> .	Interleukin28B and Inosine Triphosphatase Help to Personalize Hepatitis C Treatment.	Digestion.	84 Suppl 1	50-55	2011

*Nishida N, Mawatari Y, Sageshima M, <u>Tokunaga K.</u>	Highly Parallel and Short-Acting Amplification with Locus-Specific Primers to Detect Single Nucleotide Polymorphisms by the DigiTag2 Assay.	PLoS One.	7(1)	e29967	2012
* <u>Kurosaki M,</u> <u>Sakamoto N,</u> Iwasaki M, Sakamoto M, Suzuki Y, Hiramatsu N, <u>Sugauchi F,</u> <u>Yatsuhashi H,</u> Izumi N.	Pretreatment prediction of response to peginterferon plus ribavirin therapy in genotype 1 chronic hepatitis C using data mining analysis.	J Gastroenterol.	46(3)	401-409	2011
<u>Kurosaki M,</u> <u>Sakamoto N,</u> Iwasaki M, Sakamoto M, Suzuki Y, Hiramatsu N, <u>Sugauchi F,</u> Tamori A, Nakagawa M, Izumi N.	Sequences in the Interferon Sensitivity Determining Region and Core Region of Hepatitis C Virus Impact Pretreatment Prediction of Response to Peg-interferon Plus Ribavirin: Data Mining Analysis.	J Med Virol.	83 (3)	445-452	2011
<u>Kurosaki M,</u> Hiramatsu N, Sakamoto M, Suzuki Y, Iwasaki M, Tamori A, Matsuura K, Kakinuma S, <u>Sugauchi F,</u> <u>Sakamoto N,</u> Nakagawa M, <u>Yatsuhashi H,</u> Izumi N.	Age and total ribavirin dose is an independent predictor of relapse among early virological responders to peg-interferon plus ribavirin therapy in chronic hepatitis C revealed by data mining analysis.	Antivir Ther.	17(1)	35-43	2012
<u>Kurosaki M,</u> Izumi N.	Decision model incorporating IL28B genotype and ISDR could identify patients with high probability of SVR among patients who failed to achieve RVR.	J Hepatol.	55(5)	1164-1166	2011

Kurosaki M, Hiramatsu N, Sakamoto M, Suzuki Y, Iwasaki M, Tamori A, Matsuura K, Kakinuma S, Sugauchi F, Sakamoto N, Nakagawa M, Izumi N.	Data mining model using simple and readily available factors could identify patients at high risk for hepatocellular carcinoma in chronic hepatitis C.	J Hepatol.	56(3)	602-608	2012
Sasayama M, Shoji I, Adianti M, Jiang DP, Deng L, Saito T, Watanabe H. Kawata S, Aoki C, Hotta H.	A point mutation at Asn-534 that disrupts a conserved N-Glycosylation motif of the E2 glycoprotein of hepatitis C virus markedly enhances the sensitivity to antibody neutralization.	J Med Virol.	84(2)	229-234	2012
Soga T, Sugimoto M, Honma M, Mori M, Igarashi K, Kashikura K, Ikeda S, Hirayama A, Yamamoto T, Yoshida H, Otsuka M, Tsuji S, Yatomi Y, Sakuragawa T, Watanabe H. Nihei K, Saito T, Kawata S, Suzuki H, Tomita M, Suematsu M.	Serum metabolomics reveals γ -glutamyl dipeptides as biomarkers for discrimination among different forms of liver disease.	J Hepatol.	55(4)	896-905	2011
El-Shamy A, Shoji I, Saito T, Watanabe H. , Ide YH, Deng L, Kawata S, Hotta H.	Sequence heterogeneity of NS5A and core proteins of hepatitis C virus and virological responses to pegylated-interferon/ribavirin in combination therapy.	Microbiol Immunol.	55(6)	418-426	2011

Kusano-Kitazume A, Sakamoto N , Okuno Y, Sekine-Osajima Y, Nakagawa M, Kakinuma S, Kiyonashi K, Nitta S, Murakawa M, Azuma S, Nishimura-Sakurai Y, Hagiwara M, Watanabe M.	Identification of novel N-(morpholine-4-carbonylox y) amidine compounds as potent inhibitors against hepatitis C virus replication.	Antimicrob Agent Chemother.	56(3)	1315-1323	2012
Asahina Y, Tsuchiya K, Muraoka M, Tanaka K, Suzuki Y, Tamaki N, Hoshioka Y, Yasui Y, Katoh T, Hosokawa T, Ueda K, Nakanishi H, Itakura J, Takahashi Y, Kurosaki M , Enomoto N, Nitta S, Sakamoto N , Izumi N.	Association of gene expression involving innate immunity and genetic variation in IL28B with antiviral response.	Hepatology.	55(1)	20-29	2012
Kadokura M, Maekawa S, Sueki R, Miura M, Komase K, Shindo H, Amemiya F, Uetake T, Inoue T, Sakamoto M, Nakagawa M, Sakamoto N , Watanabe M, Enomoto N.	Analysis of the complete open reading frame of genotype 2b hepatitis C virus in association with the response to peginterferon and ribavirin therapy.	PLoS One.	6 (9)	e24514	2011
Funaoka Y, Sakamoto N , Suda G, Itsui Y, Nakagawa M, Kakinuma S, Watanabe T, Mishima K, Ueyama M, Onozuka I, Nitta S, Kitazume A, Kiyohashi K, Murakawa M, Azuma S, Tsuchiya K, Watanabe M.	Analysis of interferon signaling by infectious hepatitis C virus clones with substitutions of core amino acids 70 and 91.	J Virol.	85(12)	5986-5994	2011

Watanabe T, Sakamoto N , Nakagawa M, Kakinuma S, Itsui Y, Nishimura-Sakurai Y, Ueyama M, Funaoka Y, Kitazume A, Nitta S, Kiyohashi K, Murakawa M, Azuma S, Tsuchiya K, Oooka S, Watanabe M.	Inhibitory effect of a triterpenoid compound, with or without alpha interferon, on hepatitis C virus infection.	Antimicrob Agents Chemother.	55(6)	2537-2545	2011
Sato Y, Ren XS, Harada K, Sasaki M, Morikawa H, Shiomi S, Honda M , Kaneko S, Nakanuma Y.	Induction of elastin expression in vascular endothelial cells relates to hepatoportal sclerosis in idiopathic portal hypertension: possible link to serum anti-endothelial cell antibodies.	Clin Exp Immunol.	167(3)	532-542	2012
Nakamura S, Kawai K, Takeshita Y, Honda M , Takamura T, Kaneko S, Matoba R, Matsubara K.	Identification of blood biomarkers of aging by transcript profiling of whole blood.	Biochem Biophys Res Commun.	418(2)	313-318	2012
Yamashita T, Arai K, Sunagozaka H, Ueda T, Terashima T, Yamashita T, Mizukoshi E, Sakai A, Nakamoto Y, Honda M , Kaneko S.	Randomized, Phase II Study Comparing Interferon Combined with Hepatic Arterial Infusion of Fluorouracil plus Cisplatin and Fluorouracil Alone in Patients with Advanced Hepatocellular Carcinoma.	Oncology.	81(5-6)	281-290	2011
Mizukoshi E, Nakamoto Y, Arai K, Yamashita T, Sakai A, Sakai Y, Kagaya T, Yamashita T, Honda M , Kaneko S.	Comparative analysis of various tumor-associated antigen-specific t-cell responses in patients with hepatocellular carcinoma.	Hepatology	53(4)	1206-1216	2011

Shindo H, Maekawa S, Komase K, Sueki R, Miura M, Kadokura M, Shindo K, Amemiya F, Kitamura T, Nakayama Y, Inoue T, Sakamoto M, Okada SI, Asahina Y, Izumi N, <u>Honda M.</u> , Kaneko S, Enomoto N.	Characterization of naturally occurring protease inhibitor-resistance mutations in genotype 1b hepatitis C virus patients.	Hepatol Int.	in press.		2011
Yamashita T, <u>Honda M.</u> , Kaneko S.	Molecular mechanisms of hepatocarcinogenesis in chronic hepatitis C virus infection.	J Gastroenterol Hepatol.	26(6)	960-964	2011
Sunagozaka H, <u>Honda M.</u> , Yamashita T, Nishino R, Takatori H, Arai K, Yamashita T, Sakai Y, Kaneko S.	Identification of a secretory protein c19orf10 activated in hepatocellular carcinoma.	Int J Cancer.	129(7)	1576-1585	2011
Takayama K, Tsutsumi S, Katayama S, Okayama T, Horie-Inoue K, Ikeda K, Urano T, Kawazu C, Hasegawa A, Ikeo K, <u>Gojobori T.</u> , Ouchi Y, Hayashizaki Y, Aburatani H, Inoue S.	Integration of cap analysis of gene expression and chromatin immunoprecipitation analysis on array reveals genome-wide androgen receptor signaling in prostate cancer cells.	Oncogene.	30(5)	619-630	2011
Bousquet J, Anto J, Sterk P, Adcock I, Brahmachari S, Roca J, Agusti A, <u>Gjojobori T.</u> , Auffray C. et al.	Systems medicine and integrated care to combat chronic noncommunicable diseases.	Genome Medicine.	3 (43)	1-12	2011

Taniya T, Tanaka S, Yamaguchi-Kabata Y, Imanishi T, <u>Gojobori T.</u>	A prioritization analysis of disease association by data-mining of functional annotation of human genes.	Genomics.	99(1)	1-9	2012
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Kumar V, Yi Lo PH, Sawai H, Kato N, Takahashi A, Deng Z, Urabe Y, Mbarek H, <u>Tokunaga K,</u> <u>Tanaka Y,</u> Sugiyama M, <u>Mizokami M,</u> Muroyama R, Tateishi R, Omata M, Koike K, Tanikawa C, Kamatani N, Kubo M, Nakamura Y, Matsuda K.	Soluble MICA and a MICA variation as possible prognostic biomarkers for HBV-induced hepatocellular carcinoma.	PLoS One.	7(9)	e44743	2012
*Nishida N, Sawai H, Matsuura K, Sugiyama M, Ahn SH, Park JY, Hige S, Kang JH, Suzuki K, <u>Kurosaki M,</u> Asahina Y, Mochida S, Watanabe M, Tanaka E, <u>Honda M,</u> Kaneko S, Orito E, Itoh Y, Mita E, Tamori A, Murawaki Y, Hiasa Y, Sakaida I, Korenaga M, Hino K, Ide T, Kawashima M, Mawatari Y, Sageshima M, Ogasawara Y, Koike A, Izumi N, Han KH, <u>Tanaka Y, Tokunaga K, Mizokami M.</u>	Genome-wide association study confirming association of HLA-DP with protection against chronic hepatitis B and viral clearance in Japanese and Korean.	PLoS One.	7(6)	e39175	2012

Sawai H, Nishida N, Mbarek H, Matsuda K, Mawatari Y, Yamaoka M, Hige S, Kang JH, Abe K, Mochida S, Watanabe M, Kurosaki M , Asahina Y, Izumi N, Honda M , Kaneko S, Tanaka E, Matsuura K, Itoh Y, Mita E, Korenaga M, Hino K, Murawaki Y, Hiasa Y, Ide T, Ito K, Sugiyama M, Ahn SH, Han KH, Park JY, Yuen MF, Nakamura Y, Tanaka Y , Mizokami M , Tokunaga K .	No association for Chinese HBV-related hepatocellular carcinoma susceptibility SNP in other East Asian populations.	BMC Med Genet.	13	47	2012
Michikawa T, Inoue M, Sawada N, Iwasaki M, Tanaka Y , Shimazu T, Sasazuki S, Yamaji T, Mizokami M , Tsugane S; Japan Public Health Center-based Prospective Study Group.	Development of a prediction model for 10-year risk of hepatocellular carcinoma in middle-aged Japanese: the Japan Public Health Center-based Prospective Study Cohort II.	Prev Med.	55(2)	137-143	2012
Kani S, Tanaka Y , Matsuura K, Watanabe T , Yatsuhashi H , Orito E, Inose K, Motojuku N, Wakimoto Y, Mizokami M .	Development of new IL28B genotyping method using Invader Plus assay.	Microbiol Immunol.	56(5)	318-323	2012
Kim SR, El-Shamy A, Imoto S, Kim KI, Ide YH, Deng L, Shoji I, Tanaka Y , Hasegawa Y, Ota M, Hotta H.	Prediction of response to pegylated interferon/ribavirin combination therapy for chronic hepatitis C genotype 1b and high viral load.	J Gastroenterol.	47(10)	1143-1151	2012