

病理学第一講座

○主な研究内容

- 1 腫瘍免疫分子機構、ヒト癌ワクチン臨床研究
- 2 腫瘍の免疫学的エスケープの分子機構
- 3 分子シャペロン、特に熱ショック蛋白と免疫、癌、神経変性疾患
- 4 アポトーシスの分子機構
- 5 細胞周期と細胞癌化機構
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- 7 白血病、悪性リンパ種の分子遺伝学
- 8 遺伝子診断と分子病理
- 9 寄生虫病と分子病理
- 10 重力医学、宇宙医学、時間医学
- 11 光工学と医療技術、がん光線療法
- 12 機能的食品開発研究

○Pub Med 掲載論文 (2018 年)

1. Rechallenge With Nivolumab After Vemurafenib Treatment of Initially Nivolumab-Resistant Advanced Melanoma.

Kato J, Hida T, Kamiya T, Sato S, Takahashi H, Torigoe T, Uhara H.
J Immunol Methods. 454:89. 2018.

2. The Antigen ASB4 on Cancer Stem Cells Serves as a Target for CTL Immunotherapy of Colorectal Cancer.

Miyamoto S, Kochin V, Kanaseki T, Hongo A, Tokita S, Kikuchi Y, Takaya A, Hirohashi Y, Tsukahara T, Terui T, Ishitani K, Hata F, Takemasa I, Miyazaki A, Hiratsuka H, Sato N, Torigoe T.
Cancer Immunol Res. 2018 Jan 25. doi: 10.1158/2326-6066.CIR-17-0518. [Epub ahead of print]

3. Cellular stress induces cancer stem-like cells through expression of DNAJB8 by activation of heat shock factor 1.

Kusumoto H, Hirohashi Y, Nishizawa S, Yamashita M, Yasuda K, Murai A, Takaya A, Mori T, Kubo T, Nakatsugawa M, Kanaseki T, Tsukahara T, Kondo T, Sato N, Hara I, Torigoe T.
Cancer Sci. 109(3):741-750. 2018.

4. LpMab-23-recognizing cancer-type podoplanin is a novel predictor for a poor prognosis of early stage tongue cancer.

Miyazaki A, Nakai H, Sonoda T, Hirohashi Y, Kaneko MK, Kato Y, Sawa Y, Hiratsuka H.
Oncotarget. 9(30):21156-21165. 2018.

5. Mechanisms underlying the lack of endogenous processing and CLIP-mediated binding of the invariant chain by HLA-DP84Gly.

Anczurowski M, Yamashita Y, Nakatsugawa M, Ochi T, Kagoya Y, Guo T, Wang CH, Rahman MA, Saso K, Butler MO, Hirano N.
Sci Rep. 8(1):4804. 2018.

6. Image analysis is an excellent tool for quantifying Ki-67 to predict the prognosis of gastrointestinal stromal tumor patients.

Sugita S, Hirano H, Hatanaka Y, Fujita H, Kubo T, Kikuchi N, Ito Y, Sugawara T, Segawa K, Hisai H, Yamashita K, Nobuoka T, Matsuno Y, Hasegawa T.
Pathol Int. 68(1):7-11. 2018.

7. Type 2 innate lymphoid cells disrupt bronchial epithelial barrier integrity by targeting tight junctions through IL-13 in asthmatic patients.

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Baldauf MC, Gerke JS, Kirschner A, Blaeschke F, Effenberger M, Schober K, Rubio RA, Kanaseki T, Kiran MM, Dallmayer M, Musa J, Akpolat N, Akatli AN, Rosman FC, Özen Ö, Sugita S, Hasegawa T, Sugimura H, Baumhoer D, Knott MML, Sannino G, Marchetto A, Li J, Busch DH, Feuchtinger T, Ohmura S, Orth MF, Thiel U, Kirchner T, Grünewald TGP.
Oncoimmunology. 23:7(9):e1481558. 2018.

9. Comparison of HPV genotyping and cytology triage, COMPACT-Study: Design, methods and baseline results in 14,642 women.

Aoyama-Kikawa S, Fujita H, Hanley SJB, Kasamo M, Kikuchi K, Torigoe T, Matsuno Y, Tamakoshi A, Sasaki T, Matsuura M, Kato Y, Dong P, Watari H, Saito T, Sengoku K, Sakuragi N.
Cancer Sci. 109(6):2003-2012. 2018.

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Pagès F, Mlecnik B, Marliot F, Bindea G, Ou FS, Bifulco C, Lugli A, Zlobec I, Rau TT, Berger MD, Nagtegaal ID, Vink-Börger E, Hartmann A, Geppert C, Kolwelter J, Merkel S, Grützmann R, Van den Eynde M, Jouret-Mourin A, Kartheuser A, Léonard D, Remue C, Wang JY, Bavi P, Roehrl MHA, Ohashi PS, Nguyen LT, Han S, MacGregor HL, Hafezi-Bakhtari S, Wouters BG, Masucci GV, Andersson EK, Zavadova E, Vocka M, Spacek J, Petruzella L, Konopasek B, Dundr P, Skalova H, Nemejcova K, Botti G, Tatangelo F, Delrio P, Ciliberto G, Maio M, Laghi L, Grizzi F, Fredriksen T, Buttard B, Angelova M, Vasaturo A, Maby P, Church SE, Angell HK, Lafontaine L, Bruni D, El Sissy C, Haicheur N, Kirilovsky A, Berger A, Lagorce C, Meyers JP, Paustian C, Feng Z, Ballesteros-Merino C, Dijkstra J, van de Water C, van Lent-van Vliet S, Knijn N, Muşină AM, Scripcariu DV, Popivanova B, Xu M,

- Fujita T, Hazama S, Suzuki N, Nagano H, Okuno K, Torigoe T, Sato N, Furuhashi T, Takemasa I, Itoh K, Patel PS, Vora HH, Shah B, Patel JB, Rajvik KN, Pandya SJ, Shukla SN, Wang Y, Zhang G, Kawakami Y, Marincola FM, Ascierto PA, Sargent DJ, Fox BA, Galon J. *Lancet*. 391(10135):2128–2139. 2018.
11. Development of a TCR multimer with high avidity for detecting a naturally presented tumor-associated antigen on osteosarcoma cells.
- Watanabe K, Tsukahara T, Toji S, Saitoh S, Hirohashi Y, Nakatsugawa M, Kubo T, Kanaseki T, Kameshima H, Terui T, Sato N, Torigoe T. *Cancer Sci*. 2018 Oct 30. doi: 10.1111/cas.13854. [Epub ahead of print]
12. Differential bronchial epithelial response regulated by $\Delta Np63$: a functional understanding of the epithelial shedding found in asthma.
- Kubo T, Tsujiwaki M, Hirohashi Y, Tsukahara T, Kanaseki T, Nakatsugawa M, Hasegawa T, Torigoe T. *Lab Invest*. 2018 Sep 25. doi: 10.1038/s41374-018-0132-6. [Epub ahead of print]
13. Influence of PD-L1 expression in immune cells on the response to radiation therapy in patients with oropharyngeal squamous cell carcinoma.
- Fukushima Y, Someya M, Nakata K, Hori M, Kitagawa M, Hasegawa T, Tsuchiya T, Gocho T, Ikeda H, Hirohashi Y, Torigoe T, Sugita S, Hasegawa T, Himi T, Sakata KI. *Radiother Oncol*. S0167-8140(18)33463-7. 2018.
14. Association between PD-L1 expression and lymph node metastasis in cutaneous squamous cell carcinoma.
- Kamiya S, Kato J, Kamiya T, Yamashita T, Sumikawa Y, Hida T, Horimoto K, Sato S, Takahashi H, Sawada M, Kubo T, Torigoe T, Uhara H. *Asia Pac J Clin Oncol*. 2018 Nov 8. doi: 10.1111/ajco.13102. [Epub ahead of print]
15. Clonal analysis revealed functional heterogeneity in cancer stem-like cell phenotypes in uterine endometrioid adenocarcinoma.
- Tabuchi Y, Hirohashi Y, Hashimoto S, Mariya T, Asano T, Ikeo K, Kuroda T, Mizuuchi M, Murai A, Uno S, Kawai N, Kubo T, Nakatsugawa M, Kanaseki T, Tsukahara T, Saito T, Torigoe T. *Exp Mol Pathol*. 30:106:78–88. 2018.
16. Cancer stem cells as targets for immunotherapy. *Immunology*.
- Codd AS, Kanaseki T, Torigoe T, Tabi Z. *Immunology*. 153(3):304–314. 2018.
17. Hepatic portal venous gas due to polystyrene sulfonate-induced enteritis.
- Kubo T, Yamashita K, Yokoyama Y, Hirayama D, Shirata T, Mitsuhashi K, Onodera K, Yamamoto E, Nosho K, Yamano H, Kubo T, Sugita S, Hasegawa T, Nakase H.

Clin J Gastroenterol. 11(3):220-223. 2018.

18. Occult ovarian clear-cell carcinoma diagnosed as primary adenocarcinoma of the lung: A case report of a diagnostic pitfall for clinicians and pathologists.

Kubo T, Hirohashi Y, Fujita H, Sugita S, Kikuchi Y, Shinkawa T, Nakatsugawa M, Tsujiwaki M, Sudo Y, Asai Y, Umeda Y, Takahashi H, Hasegawa T, Torigoe T.
Respir Med Case Rep. 18:25:306-308. 2018.

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Shima H, Kutomi G, Satomi F, Imamura M, Kimura Y, Mizuguchi T, Watanabe K, Takahashi A, Murai A, Tsukahara T, Kanaseki T, Hirohashi Y, Iwayama Y, Tsuruma T, Kameshima H, Sato N, Torigoe T, Takemasa I.
Cancer Immunol Immunother. 67(10):1603-1609. 2018.

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- 1 久保輝文, 廣橋良彦, 鳥越俊彦、腫瘍免疫と免疫チェックポイント阻害剤、病理と臨床、36(1):10-20. 2018.
- 2 金関貴幸、宮本 昇、鳥越俊彦、がん幹細胞特異的抗原 ASB4 を利用したがん免疫治療、臨床免疫・アレルギー科、69(5):499-504、2018.
- 3 廣橋良彦、鳥越俊彦、免疫療法の標的としてのがん幹細胞、病理と臨床、36(12):1193-1199, 2018.
- 4 菊池泰弘、久保輝文、鳥越俊彦、免疫チェックポイント阻害剤の免疫学的基盤と免疫関連副作用、内分泌・糖尿病・代謝内科、47(5):387-394, 2018.
- 5 菊池泰弘、鳥越俊彦、複合免疫療法: 1. 複合免疫療法とは: 複合免疫療法のコンセプトと種類、分子機序、開発研究、がん免疫療法、2(1):56-59. 2018.

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- 12 機能的食品開発研究

○Pub Med 掲載論文 (2017 年)

1. Cancer-associated oxidoreductase ERO1- α promotes immune escape through up-regulation of PD-L1 in human breast cancer. *Oncotarget*. 8(15):24706–24718. 2017

Tanaka T, Kutomi G, Kajiwara T, Kukita K, Kochin V, Kanaseki T, Tsukahara T, Hirohashi Y, Torigoe T, Okamoto Y, Hirata K, Sato N, Tamura Y.

2. Identification and functional analysis of variants of a cancer/testis antigen LEMD1 in colorectal cancer stem-like cells. *Biochem Biophys Res Commun*. 485(3):651–657. 2017.

Takeda R, Hirohashi Y, Shen M, Wang L, Ogawa T, Murai A, Yamamoto E, Kubo T, Nakatsugawa M, Kanaseki T, Tsukahara T, Nishidate T, Okita K, Kutomi G, Sato N, Takemasa I, Torigoe T.

3. LY6/PLAUR domain containing 3 has a role in the maintenance of colorectal cancer stem-like cells. *Biochem Biophys Res Commun*. 486(2):232–238. 2017

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4. Brother of the regulator of the imprinted site (BORIS) variant subfamily 6 is a novel target of lung cancer stem-like cell immunotherapy. *PLoS One*. 12(3):e0171460. 2017

Horibe R, Hirohashi Y, Asano T, Mariya T, Suzuki T, Takaya A, Saijo H, Shionoya Y, Kubo T, Nakatsugawa M, Kanaseki T, Tsukahara T, Watanabe K, Atsuyama E, Toji S, Hirano H, Hasegawa T, Takahashi H, Sato N, Torigoe T.

5. Mismatch Repair Protein Deficiency Is a Risk Factor for Aberrant Expression of HLA Class

I Molecules: A Putative "Adaptive Immune Escape" Phenomenon. *Anticancer Res.* 37(3):1289–1295. 2017

6. Loss of tapasin in human lung and colon cancer cells and escape from tumor-associated antigen-specific CTL recognition. *Oncoimmunology.* 6(2):e1274476. 2017

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Kubo T, Hirohashi Y, Matsuo K, Sonoda T, Sakamoto H, Furumura K, Tsukahara T, Kanaseki T, Nakatsugawa M, Hirano H, Furuhashi T, Takemasa I, Hasegawa T, Torigoe T.

7. HLA-A24 ligandome analysis of colon and lung cancer cells identifies a novel cancer-testis antigen and a neoantigen that elicits specific and strong CTL responses. *Oncoimmunology.* 6(4):e1293214. 2017

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Takahashi D, Fujihara M, Miyazaki T, Matsubayashi K, Sato S, Azuma H, Kato T, Kino S, Ikeda H, Takamoto S, Sato N, Torigoe T.

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10. GRIK2 has a role in the maintenance of urothelial carcinoma stem-like cells, and its expression is associated with poorer prognosis. *Oncotarget.* 8(17):28826–28839. 2017

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14. Elevated expression of JAM-A promotes neoplastic properties of lung adenocarcinoma. *Cancer Sci.* 108(11):2306–2314. 2017

Magara K, Takasawa A, Osanai M, Ota M, Tagami Y, Ono Y, Takasawa K, Murata M, Hirohashi Y, Miyajima M, Yamada G, Hasegawa T, Sawada N.

15. Claudin-18 coupled with EGFR/ERK signaling contributes to the malignant potentials of bile duct cancer.

Takasawa K, Takasawa A, Osanai M, Aoyama T, Ono Y, Kono T, Hirohashi Y, Murata M, Sawada N. *Cancer Lett.* 403:66–73. 2017.

16. Identification of antigenic peptides from novel renal cancer stem-like cell antigen, DNAJB8. *Biochem Biophys Res Commun.* 494(3–4):693–699. 2017.

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17. Comprehensive single-cell transcriptome analysis reveals heterogeneity in endometrioid adenocarcinoma tissues. *Sci Rep.* 7(1):14225. 2017

Hashimoto S, Tabuchi Y, Yurino H, Hirohashi Y, Deshimaru S, Asano T, Mariya T, Oshima K, Takamura Y, Ukita Y, Ametani A, Kondo N, Monma N, Takeda T, Misu S, Okayama T, Ikeo K, Saito T, Kaneko S, Suzuki Y, Hattori M, Matsushima K, Torigoe T.

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19. Immune-related adverse events of immune checkpoint inhibitors. *Nihon Rinsho Meneki Gakkai Kaishi.* 40(2):102–108. 2017.

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Miyamoto S, Kanaseki T, Hirohashi Y, Tsukahara T, Kikuchi Y, Sato N, Torigoe T.

21. Cancer stem cells as targets for immunotherapy. *Immunology*.
Codd AS, Kanaseki T, Torigo T, Tabi Z.
2017 Nov 18. doi: 10.1111/imm.12866. [Epub ahead of print]

○その他の論文 (2017)

480 王利明、廣橋良彦、鳥越俊彦、 がん細胞亜集団（がん幹細胞、EMT）とがん免疫、炎症と免疫 25(4):63-67. 2017.

481 塚原智英, 廣橋良彦, 鳥越俊彦. 次世代がんペプチドワクチン療法の開発. *日本臨牀* 2017; 75: 275-279.

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- 4 胸腺上皮による免疫寛容誘導機構
- 5 リンパ球抗原と機能
- 6 移植片拒絶の制御機構
- 7 分子シャペロンと神経細胞変性機構
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- 11 白血病、悪性リンパ種の分子遺伝学
- 12 遺伝子診断と分子病理
- 13 寄生虫病と分子病理
- 14 海洋生物産生物質と癌、免疫、医学
- 15 重力医学、宇宙医学

○Pub Med 掲載論文 (2016 年)

1. Hypoxia augments MHC class I antigen presentation via facilitation of ERO1- α -mediated oxidative folding in murine tumor cells.

Kajiwara T1, Tanaka T1, Kukita K2, Kutomi G2, Saito K2, Okuya K2, Takaya A1, Kochin V1, Kanaseki T1, Tsukahara T1, Hirohashi Y1, Torigoe T1, Hirata K2, Sato N1, Tamura Y3.

Eur J Immunol. 2016 Sep 26. doi: 10.1002/eji.201646525. [Epub ahead of print]

PMID: 27667124

2. Identification of a novel human memory T-cell population with the characteristics of stem-like chemo-resistance.

Murata K1, Tsukahara T2, Emori M3, Shibayama Y1, Mizushima E1, Matsumiya H4, Yamashita K4, Kaya M3, Hirohashi Y2, Kanaseki T2, Kubo T2, Himi T4, Ichimiya S5, Yamashita T3, Sato N2, Torigoe T2.

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PMID: 2743514

4. Non-neoplastic Fallopian Tube Epithelium Carrying Gene Mutations of a Novel SOX2

Repressor Region is Soil of High-grade Serous Ovarian Cancer.

Hirohashi Y1, Torigoe T2.

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5. Plasticity of lung cancer stem-like cells is regulated by the transcription factor HOXA5 that is induced by oxidative stress.

Saijo H1,2, Hirohashi Y1, Torigoe T1, Horibe R1,2, Takaya A1, Murai A1, Kubo T1, Kajiwara T1, Tanaka T1, Shionoya Y1,2, Yamamoto E1, Maruyama R3, Nakatsugawa M1, Kanaseki T1, Tsukahara T1, Tamura Y1,4, Sasaki Y5, Tokino T5, Suzuki H3, Kondo T6, Takahashi H2, Sato N1. Oncotarget. 2016 Jul 13. doi: 10.18632/oncotarget.10571. [Epub ahead of print]

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6. Establishment and Analysis of Cancer Stem-Like and Non-Cancer Stem-Like Clone Cells from the Human Colon Cancer Cell Line SW480.

Takaya A1, Hirohashi Y1, Murai A1, Morita R1, Saijo H1,2, Yamamoto E1, Kubo T1, Nakatsugawa M1, Kanaseki T1, Tsukahara T1, Tamura Y3, Takemasa I4, Kondo T5, Sato N1, Torigoe T1.

PLoS One. 2016 Jul 14;11(7):e0158903. doi: 10.1371/journal.pone.0158903. eCollection 2016.

PMID: 27415781 Free PMC Article

7. SOX2 and ALDH1 as Predictors of Operable Breast Cancer.

Shima H1, Kutomi G2, Satomi F2, Maeda H2, Hirohashi Y3, Hasegawa T4, Mori M5, Torigoe T3, Takemasa I2.

Anticancer Res. 2016 Jun;36(6):2945-53.

PMID: 27272809

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Murata K1, Tsukahara T, Torigoe T.

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PMID: 27181230 Free Article

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Tsukahara T1, Emori M2, Murata K1,2, Mizushima E1,2, Shibayama Y1,2, Kubo T1, Kanaseki T1, Hirohashi Y1, Yamashita T2, Sato N1, Torigoe T1.

Expert Opin Biol Ther. 2016 Aug;16(8):1049-57. doi: 10.1080/14712598.2016.1188075. Epub 2016 May 27.

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○主な研究内容

- 1 腫瘍免疫分子機構、ヒト癌ワクチン開発
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病理学第一講座

○主な研究内容

- 1 腫瘍免疫分子機構、ヒト癌ワクチン開発
- 2 腫瘍の免疫学的エスケープの分子機構
- 3 分子シャペロン、特に熱ショック蛋白と免疫、熱ショック蛋白質と癌
- 4 胸腺上皮による免疫寛容誘導機構
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- 9 細胞周期、細胞癌化機構、特にセントロゾーム異常と癌
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- 11 白血病、悪性リンパ種の分子遺伝学
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- 14 海洋生物産生物質と癌、免疫、医学
- 15 重力医学、宇宙医学

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