

フロンティア医学研究所  
ゲノム医科学部門

○主な研究内容

- 1 ヒト癌の発生機序の解明
- 2 がん関連遺伝子の機能の解明
- 3 癌における細胞周期チェックポイント異常の解析
- 4 癌の遺伝子治療の基礎研究
- 5 ヒトゲノム情報活用基盤技術の確立
- 6 ヒトゲノム解析を利用した癌の遺伝子診断・治療への展開

○Pub Med 掲載論文 (2018 年)

1. Targeted next-generation sequencing of 50 cancer-related genes in Japanese patients with oral squamous cell carcinoma.

Nakagaki T, Tamura M, Kobashi K, Omori A, Koyama R, Idogawa M, Ogi K, Hiratsuka H, Tokino T, Sasaki Y.

Tumour Biol. 2018 Sep;40(9):1010428318800180. doi: 10.1177/1010428318800180.

PMID: 30226113

2. Mutational analysis of uterine cervical cancer that survived multiple rounds of radiotherapy.

Nuryadi E, Sasaki Y, Hagiwara Y, Permata TBM, Sato H, Komatsu S, Yoshimoto Y, Murata K, Ando K, Kubo N, Okonogi N, Takakusagi Y, Adachi A, Iwanaga M, Tsuchida K, Tamaki T, Noda SE, Hirota Y, Shibata A, Ohno T, Tokino T, Oike T, Nakano T.

Oncotarget. 2018 Aug 24;9(66):32642-32652. doi: 10.18632/oncotarget.25982. eCollection 2018 Aug 24.

PMID: 30220971 Free PMC Article

3. DOT1L inhibition blocks multiple myeloma cell proliferation by suppressing IRF4-MYC signaling.

Ishiguro K, Kitajima H, Niinuma T, Ishida T, Maruyama R, Ikeda H, Hayashi T, Sasaki H, Wakasugi H, Nishiyama K, Shindo T, Yamamoto E, Kai M, Sasaki Y, Tokino T, Nakase H, Suzuki H.

Haematologica. 2018 Aug 31. pii: haematol.2018.191262. doi: 10.3324/haematol.2018.191262. [Epub ahead of print]

PMID: 30171029 Free Article

4. Screening for long noncoding RNAs associated with oral squamous cell carcinoma reveals the potentially oncogenic actions of DLEU1.

Nishiyama K, Maruyama R, Niinuma T, Kai M, Kitajima H, Toyota M, Hatanaka Y, Igarashi T, Kobayashi JI, Ogi K, Dehari H, Miyazaki A, Yoroazu A, Yamamoto E, Idogawa M, Sasaki Y, Sugai T, Tokino T, Hiratsuka H, Suzuki H.

Cell Death Dis. 2018 Aug 1;9(8):826. doi: 10.1038/s41419-018-0893-2.

PMID: 30069008 Free PMC Article

5. Dysregulation of miRNA in chronic hepatitis B is associated with hepatocellular carcinoma risk after nucleos(t)ide analogue treatment.

Wakasugi H, Takahashi H, Niinuma T, Kitajima H, Oikawa R, Matsumoto N, Takeba Y, Otsubo T, Takagi M, Ariizumi Y, Suzuki M, Okuse C, Iwabuchi S, Nakano M, Akutsu N, Kang JH, Matsui T, Yamada N, Sasaki H, Yamamoto E, Kai M, Sasaki Y, Sasaki S, Tanaka Y, Yotsuyanagi H, Tsutsumi T, Yamamoto H, Tokino T, Nakase H, Suzuki H, Itoh F.

Cancer Lett. 2018 Oct 10;434:91-100. doi: 10.1016/j.canlet.2018.07.019. Epub 2018 Jul 17.

PMID: 30026054

6. Surface microstructures are associated with mutational intratumoral heterogeneity in colorectal tumors.

Harada T, Yamamoto E, Yamano HO, Aoki H, Matsushita HO, Yoshikawa K, Takagi R, Harada E, Tanaka Y, Yoshida Y, Eizuka M, Yorozu A, Sudo G, Kitajima H, Niinuma T, Kai M, Sasaki Y, Tokino T, Sugai T, Nakase H, Suzuki H.

J Gastroenterol. 2018 Dec;53(12):1241-1252. doi: 10.1007/s00535-018-1481-z. Epub 2018 Jun 11.

PMID: 29948303

7. Target amplicon exome-sequencing identifies promising diagnosis and prognostic markers involved in RTK-RAS and PI3K-AKT signaling as central oncopathways in primary central nervous system lymphoma.

Takashima Y, Sasaki Y, Hayano A, Homma J, Fukai J, Iwadata Y, Kajiwara K, Ishizawa S, Hondoh H, Tokino T, Yamanaka R.

Oncotarget. 2018 Jun 8;9(44):27471-27486. doi: 10.18632/oncotarget.25463. eCollection 2018 Jun 8.

PMID: 29937999 Free PMC Article

8. Epigenetic silencing of miR-200b is associated with cisplatin resistance in bladder cancer.

Shindo T, Niinuma T, Nishiyama N, Shinkai N, Kitajima H, Kai M, Maruyama R, Tokino T, Masumori N, Suzuki H.

Oncotarget. 2018 May 11;9(36):24457-24469. doi: 10.18632/oncotarget.25326. eCollection 2018 May 11.

PMID: 29849953 Free PMC Article

9. Targeted sequencing reveals genetic variants associated with sensitivity of 79 human cancer xenografts to anticancer drugs.

Udagawa C, Sasaki Y, Suemizu H, Ohnishi Y, Ohnishi H, Tokino T, Zembutsu H.

Exp Ther Med. 2018 Feb;15(2):1339-1359. doi: 10.3892/etm.2017.5533. Epub 2017 Nov 21.

PMID: 29434720 Free PMC Article



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○Pub Med 掲載論文 (2017 年)

1. Downregulation of miR-186 is associated with metastatic recurrence of gastrointestinal stromal tumors.

Niinuma T, Kai M, Kitajima H, Yamamoto E, Harada T, Maruyama R, Nobuoka T, Nishida T, Kanda T, Hasegawa T, Tokino T, Sugai T, Shinomura Y, Nakase H, Suzuki H.  
Oncol Lett. 2017 Nov;14(5):5703-5710. doi: 10.3892/ol.2017.6911. Epub 2017 Sep 8.  
PMID:291131981.

2. Identification and characterization of a metastatic suppressor BRMS1L as a target gene of p53.

Koyama R, Tamura M, Nakagaki T, Ohashi T, Idogawa M, Suzuki H, Tokino T, Sasaki Y.  
Cancer Sci. 2017 Oct 13. doi: 10.1111/cas.13420. [Epub ahead of print]  
PMID: 29030916 Free Article

3. Profiling cancer-related gene mutations in oral squamous cell carcinoma from Japanese patients by targeted amplicon sequencing.

Nakagaki T, Tamura M, Kobashi K, Koyama R, Fukushima H, Ohashi T, Idogawa M, Ogi K, Hiratsuka H, Tokino T, Sasaki Y.  
Oncotarget. 2017 Jul 15;8(35):59113-59122. doi: 10.18632/oncotarget.19262. eCollection 2017 Aug 29.  
PMID: 28938622

4. Fledglings in p53 signaling network.

Tokino T, Idogawa M, Sasaki Y.  
Oncotarget. 2017 Jul 14;8(34):55768-55769. doi: 10.18632/oncotarget.19229. eCollection 2017 Aug 22. No abstract available.  
PMID: 28925413

5. Assessment of the quality of DNA from various formalin-fixed paraffin-embedded (FFPE) tissues and the use of this DNA for next-generation sequencing (NGS) with no artifactual mutation.

Einaga N, Yoshida A, Noda H, Suemitsu M, Nakayama Y, Sakurada A, Kawaji Y, Yamaguchi H, Sasaki Y, Tokino T, Esumi M.  
PLoS One. 2017 May 12;12(5):e0176280. doi: 10.1371/journal.pone.0176280. eCollection 2017.  
PMID: 28498833

6. Long non-coding RNA NEAT1 is a transcriptional target of p53 and modulates p53-induced transactivation and tumor-suppressor function.

Idogawa M, Ohashi T, Sasaki Y, Nakase H, Tokino T.  
Int J Cancer. 2017 Jun 15;140(12):2785-2791. doi: 10.1002/ijc.30689. Epub 2017 Mar 27.  
PMID: 28295289

7. p53 mediates the suppression of cancer cell invasion by inducing LIMA1/EPLIN.

Ohashi T, Idogawa M, Sasaki Y, Tokino T.  
Cancer Lett. 2017 Apr 1;390:58-66. doi: 10.1016/j.canlet.2016.12.034. Epub 2017 Jan 13.  
PMID: 28093207

8. The effect of forced expression of mutated K-RAS gene on gastrointestinal cancer cell lines and the IGF-1R targeting therapy.

Matsunaga Y, Adachi Y, Sasaki Y, Koide H, Motoya M, Noshio K, Takagi H, Yamamoto H, Sasaki S, Arimura Y, Tokino T, Carbone DP, Imai K, Shinomura Y.  
Mol Carcinog. 2017 Feb;56(2):515-526. doi: 10.1002/mc.22513. Epub 2016 Jun 23.  
PMID:27312358

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○Pub Med 掲載論文 (2016 年)

1. Identification and characterization of the intercellular adhesion molecule-2 gene as a novel p53 target.

Sasaki Y, Tamura M, Takeda K, Ogi K, Nakagaki T, Koyama R, Idogawa M, Hiratsuka H, Tokino T. *Oncotarget*. 2016 Aug 18. doi: 10.18632/oncotarget.11366. [Epub ahead of print]  
PMID: 27556181 Free Article

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

Saijo H, Hirohashi Y, Torigoe T, Horibe R, Takaya A, Murai A, Kubo T, Kajiwara T, Tanaka T, Shionoya Y, Yamamoto E, Maruyama R, Nakatsugawa M, Kanaseki T, Tsukahara T, Tamura Y, Sasaki Y, Tokino T, Suzuki H, Kondo T, Takahashi H, Sato N. *Oncotarget*. 2016 Jul 13. doi: 10.18632/oncotarget.10571. [Epub ahead of print]  
PMID: 27418136

3. The effect of forced expression of mutated K-RAS gene on gastrointestinal cancer cell lines and the IGF-1R targeting therapy.

Matsunaga Y, Adachi Y, Sasaki Y, Koide H, Motoya M, Nosho K, Takagi H, Yamamoto H, Sasaki S, Arimura Y, Tokino T, Carbone DP, Imai K, Shinomura Y. *Mol Carcinog*. 2016 Jun 17. doi: 10.1002/mc.22513. [Epub ahead of print]

4. A genomic screen for long noncoding RNA genes epigenetically silenced by aberrant DNA methylation in colorectal cancer.

Kumegawa K, Maruyama R, Yamamoto E, Ashida M, Kitajima H, Tsuyada A, Niinuma T, Kai M, Yamano HO, Sugai T, Tokino T, Shinomura Y, Imai K, Suzuki H. *Sci Rep*. 2016 May 24;6:26699. doi: 10.1038/srep26699.  
PMID: 27215978 Free PMC Article  
PMID: 27312358

5 . Genomic characterization of esophageal squamous cell carcinoma: Insights from next-generation sequencing.

Sasaki Y, Tamura M, Koyama R, Nakagaki T, Adachi Y, Tokino T.

World J Gastroenterol. 2016 Feb 21;22(7):2284-93. doi: 10.3748/wjg.v22.i7.2284. Review.

PMID: 26900290 Free PMC Article

6 . Systemic Prophylactic Antibiotics for the Modified Introducer Method for Percutaneous Endoscopic Gastrostomy: A Prospective, Randomized, Double-Blind Study.

Adachi Y, Akino K, Mita H, Kikuchi T, Yamashita K, Sasaki Y, Arimura Y, Endo T.

J Clin Gastroenterol. 2016 Oct;50(9):727-32. doi: 10.1097/MCG.0000000000000470.

PMID: 26756107

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○Pub Med 掲載論文 (2015 年)

1. Tamura M, Sasaki Y, Kobashi K, Takeda K, Nakagaki T, Idogawa M, Tokino T.  
CRKL oncogene is downregulated by p53 through miR-200s.  
Cancer Sci. 2015 Aug;106(8):1033-40. doi: 10.1111/cas.12713. Epub 2015 Jul 14.
2. Kamimae S, Yamamoto E, Kai M, Niinuma T, Yamano HO, Nojima M, Yoshikawa K, Kimura T, Takagi R, Harada E, Harada T, Maruyama R, Sasaki Y, Tokino T, Shinomura Y, Sugai T, Imai K, Suzuki H.  
Epigenetic silencing of NTSR1 is associated with lateral and noninvasive growth of colorectal tumors.  
Oncotarget. 2015 Aug 17. [Epub ahead of print]
3. Mitsuhashi K, Yamamoto I, Kurihara H, Kanno S, Ito M, Igarashi H, Ishigami K, Sukawa Y, Tachibana M, Takahashi H, Tokino T, Maruyama R, Suzuki H, Imai K, Shinomura Y, Yamamoto H, Noshio K.  
Analysis of the molecular features of rectal carcinoid tumors to identify new biomarkers that predict biological malignancy.  
Oncotarget. 2015 Sep 8;6(26):22114-25.
4. Murata A, Ito Y, Kashima R, Kanbayashi S, Nanatani K, Igarashi C, Okumura M, Inaba K, Tokino T, Takahashi S, Kamagata K.  
One-Dimensional Sliding of p53 Along DNA Is Accelerated in the Presence of Ca(2+) or Mg(2+) at Millimolar Concentrations.  
J Mol Biol. 2015 Aug 14;427(16):2663-78. doi: 10.1016/j.jmb.2015.06.016. Epub 2015 Jul 2.
5. Isosaka M, Niinuma T, Nojima M, Kai M, Yamamoto E, Maruyama R, Nobuoka T, Nishida T, Kanda T, Taguchi T, Hasegawa T, Tokino T, Hirata K, Suzuki H, Shinomura Y.  
A Screen for Epigenetically Silenced microRNA Genes in Gastrointestinal Stromal Tumors.  
PLoS One. 2015 Jul 27;10(7):e0133754. doi: 10.1371/journal.pone.0133754. eCollection 2015.
6. Someya M, Yamamoto H, Nojima M, Hori M, Tateoka K, Nakata K, Takagi M, Saito M, Hirokawa N, Tokino T, Sakata K.  
Relation between Ku80 and microRNA-99a expression and late rectal bleeding after radiotherapy for prostate cancer.  
Radiother Oncol. 2015 May;115(2):235-9. doi: 10.1016/j.radonc.2015.04.008. Epub 2015 Apr 30.



7. Nakagaki S, Arimura Y, Nagaishi K, Isshiki H, Nasuno M, Watanabe S, Idogawa M, Yamashita K, Naishiro Y, Adachi Y, Suzuki H, Fujimiya M, Imai K, Shinomura Y.

Contextual niche signals towards colorectal tumor progression by mesenchymal stem cell in the mouse xenograft model.

J Gastroenterol. 2015 Sep;50(9):962-74. doi: 10.1007/s00535-015-1049-0. Epub 2015 Feb 14.

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○Pub Med 掲載論文 (2014 年)

1. Idogawa M<sup>1</sup>, Ohashi T<sup>1</sup>, Sugisaka J<sup>2</sup>, Sasaki Y<sup>2</sup>, Suzuki H<sup>3</sup>, Tokino T<sup>2</sup>.  
Array-based genome-wide RNAi screening to identify shRNAs that enhance p53-related apoptosis in human cancer cells.  
Oncotarget. 2014 Sep 15;5(17):7540-8.
2. Tamura M<sup>1</sup>, Sasaki Y<sup>1</sup>, Koyama R<sup>1</sup>, Takeda K<sup>1</sup>, Idogawa M<sup>1</sup>, Tokino T<sup>1</sup>.  
Forkhead transcription factor FOXF1 is a novel target gene of the p53 family and regulates cancer cell migration and invasiveness.  
Oncogene. 2014 Oct 2;33(40):4837-46. doi: 10.1038/onc.2013.427. Epub 2013 Nov 4.
3. Ito M, Mitsunashi K, Igarashi H, Nosho K, Naito T, Yoshii S, Takahashi H, Fujita M, Sukawa Y, Yamamoto E, Takahashi T, Adachi Y, Nojima M, Sasaki Y, Tokino T, Baba Y, Maruyama R, Suzuki H, Imai K, Yamamoto H, Shinomura Y.  
MicroRNA-31 expression in relation to BRAF mutation, CpG island methylation and colorectal continuum in serrated lesions.  
Int J Cancer. 2014 Dec 1;135(11):2507-15. doi: 10.1002/ijc.28920. Epub 2014 Apr 30.
4. Idogawa M<sup>1</sup>, Ohashi T, Sasaki Y, Maruyama R, Kashima L, Suzuki H, Tokino T.  
Identification and analysis of large intergenic non-coding RNAs regulated by p53 family members through a genome-wide analysis of p53-binding sites.  
Hum Mol Genet. 2014 Jun 1;23(11):2847-57. doi: 10.1093/hmg/ddt673. Epub 2014 Jan 8.

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○Pub Med 掲載論文 (2013 年)

1. Ohashi T, Idogawa M, Sasaki Y, Suzuki H, Tokino T.  
AKR1B10, a transcriptional target of p53, is Downregulated in Colorectal Cancers Associated with Poor Prognosis.  
Mol Cancer Res. 2013 Oct 18. [Epub ahead of print]
2. Aoki Y, Nojima M, Suzuki H, Yasui H, Maruyama R, Yamamoto E, Ashida M, Itagaki M, Asaoku H, Ikeda H, Hayashi T, Imai K, Mori M, Tokino T, Ishida T, Toyota M, Shinomura Y.  
Correction: Genomic vulnerability to LINE-1 hypomethylation is a potential determinant of the clinicogenetic features of multiple myeloma.  
Genome Med. 2013 Oct 11;5(10):88. [Epub ahead of print]
3. Shimizu T, Suzuki H, Nojima M, Kitamura H, Yamamoto E, Maruyama R, Ashida M, Hatahira T, Kai M, Masumori N, Tokino T, Imai K, Tsukamoto T, Toyota M.  
Methylation of a panel of microRNA genes is a novel biomarker for detection of bladder cancer.  
Eur Urol. 2013 Jun;63(6):1091-100. doi: 10.1016/j.eururo.2012.11.030. Epub 2012 Nov 23.
4. Morita R, Hirohashi Y, Suzuki H, Takahashi A, Tamura Y, Kanaseki T, Asanuma H, Inoda S, Kondo T, Hashino S, Hasegawa T, Tokino T, Toyota M, Asaka M, Torigoe T, Sato N.  
DNA methyltransferase 1 is essential for initiation of the colon cancers.  
Exp Mol Pathol. 2013 Apr;94(2):322-9. doi:10.1016/j.yexmp.2012.10.004. Epub 2012 Oct 9.
5. Adachi Y, Ohashi H, Imsumran A, Yamamoto H, Matsunaga Y, Taniguchi H, Nosho K, Suzuki H, Sasaki Y, Arimura Y, Carbone DP, Imai K, Shinomura Y.  
The effect of IGF-I receptor blockade for human esophageal squamous cell carcinoma and adenocarcinoma.  
Tumour Biol. 2013 Sep 13. [Epub ahead of print]
6. Tamura M, Sasaki Y, Koyama R, Takeda K, Idogawa M, Tokino T.  
Forkhead transcription factor FOXF1 is a novel target gene of the p53 family and regulates cancer cell migration and invasiveness.  
Oncogene. 2013 Nov 4. doi: 10.1038/onc.2013.427. [Epub ahead of print]