事業成果物：

研究成果は、国内外の学会などに報告し、あるいは原著論文として論文発表を行った。学会発表などは省略し、英文原著論文のみを記載する。

研究１　腫瘍細胞社会の解析と阻害剤スクリーニング

1. Matsumoto K, Okamoto K, Okabe S, Fujii R, Ueda K, Ohashi K, Seimiya H. G-quadruplex-forming nucleic acids interact with splicing factor 3B subunit 2 and suppress innate immune gene expression.
   Genes Cells, 26: 65-82, 2021.
2. Yasuda M, Ma Y, Okabe S, Wakabayashi Y, Su D, Chang YT, Seimiya H, Tera M, Nagasawa K. Target identification of a macrocyclic hexaoxazole G-quadruplex ligand using post-target-binding visualization.
   Chem Commun, 56: 12905-12908, 2020.
3. Tomizawa F, Jang MK, Mashima T, Seimiya H. c-KIT regulates stability of cancer stemness in CD44-positive colorectal cancer cells.
   Biochem Biophys Res Commun, 527: 1014-1020, 2020.
4. Shimizu T, Takahashi N, Huber VJ, Asawa Y, Ueda H, Yoshimori A, Muramatsu Y, Seimiya H, Kouji H, Nakamura H, Oguri H. Design and synthesis of 14 and 15-membered macrocyclic scaffolds exhibiting inhibitory activities of hypoxia-inducible factor 1alpha.
   Bioorg Med Chem, 30: 115949, 2020.
5. Seimiya H. Crossroads of telomere biology and anticancer drug discovery.
   Cancer Sci, 111: 3089-3099, 2020.
6. Nakanishi C, Seimiya H. G-quadruplex in cancer biology and drug discovery.
   Biochem Biophys Res Commun, 531: 45-50, 2020.
7. Koi H, Takahashi N, Fuchi Y, Umeno T, Muramatsu Y, Seimiya H, Karasawa S, Oguri H. A fully synthetic 6-aza-artemisinin bearing an amphiphilic chain generates aggregates and exhibits anti-cancer activities.
   Org Biomol Chem, 18: 5339-5343, 2020.

研究２　治療薬耐性と微小環境適応に関わる腫瘍細胞社会ネットワークの解明

1. Yoshizawa T, Uchibori K, Araki M, Matsumoto S, Ma B, Kanada R, Seto Y, Oh-hara T, Koike S, Ariyasu R, Kitazono S, Ninomiya H, Takeuchi K, Yanagitani N, Takagi S, Kishi, K, Fujita N, Okuno Y, Nishio M, Katayama R. Microsecond-timescale MD simulation of EGFR minor mutation predicts the structural flexibility of EGFR kinase core that reflects EGFR inhibitor sensitivity.

NPJ Prec Oncol, in press, 2021.

2. Ariyasu R, Uchibori K, Sasaki T, Tsukahara M, Kiyotani K, Yoshida R, Ono Y, Kitazono S, Ninomiya H, Ishikawa Y, Mizukami Y, Yanagitani N, Fujita N, Nishio M, Katayama R. Monitoring EGFR C797S mutation in Japanese NSCLC patients with serial cell free DNA evaluation using digital droplet PCR.
   Cancer Sci, in press, 2021.
3. Mizuta H, Okada K, Araki M, Adachi J, Takemoto A, Kutkowska J, Maruyama K, Yanagitani N, Oh-Hara T, Watanabe K, Tamai K, Friboulet L, Katayama K, Ma B, Sasakura Y, Sagae Y, Kukimoto-Niino M, Shirouzu M, Takagi S, Simizu S, Nishio M, Okuno Y, Fujita N, Katayama R. Gilteritinib overcomes lorlatinib resistance in ALK-rearranged cancer.
   Nature Commun, 12: 1261, 2021.
4. Efficacy of EGFR tyrosine kinase inhibitors in patients having EGFR-activating mutations with or without BIM polymorphisms. Ariyasu R, Yanagitani N, Tadokoro K, Yamaguchi T, Uchibori K, Kitazono S, Fujita N, Katayama R, Nishio M.
   Cancer Chemother Pharmacol, 86: 517-525, 2020.
5. Papadopoulos KP, Borazanci E, Shaw AT, Katayama R, Shimizu Y, Zhu VW, Sun TY, Wakelee HA, Madison R, Schrock AB, Senaldi G, Nakao N, Hanzawa H, Tachibana M, Isoyama T, Nakamaru K, Deng C, Li M, Fan F, Zhao Q, Gao Y, Seto T, Jänne PA, Ou SI. U.S. phase I first-in-human study of taletrectinib (DS-6051b/AB-106), a ROS1/TRK inhibitor, in patients with advanced solid tumors.
   Clin Cancer Res, 26: 4785-4794, 2020.

研究２　治療薬耐性と微小環境適応に関わる腫瘍細胞社会ネットワークの解明

1. Nagasawa I, Koido M, Tani Y, Tsukahara S, Kunimasa K, Tomida A. Disrupting ATF4 expression mechanisms provides an effective strategy for BRAF-targeted melanoma therapy.
   iScience, 23: 101028, 2020.
2. Kato Y, Kunimasa K, Takahashi M, Harada A, Nagasawa I, Osawa M, Sugimoto Y, Tomida A. GZD824 inhibits GCN2 and sensitizes cancer cells to amino acid starvation stress.
   Mol Pharmacol, 98: 669-676, 2020.

研究３　腫瘍組織内におけるがん転移形質の獲得機構の解明と転移阻害薬の開発

1. Ukaji T, Takemoto A, Shibata H, Kakino M, Takagi S, Katayama R, Fujita N. Novel knock-in mouse model for the evaluation of therapeutic efficacy and toxicity of

human podoplanin-targeting agents.
Cancer Sci, In press, 2021.

研究４　腫瘍細胞社会ネットワークを標的にした抗がんリード化合物評価系の開発と整備

1. Matsusaka S, Hanna DL, Ning Y, Yang D, Cao S, Berger MD, Miyamoto Y, Suenaga M, Dan S, Mashima T, Seimiya H, Zhang W, Lenz HJ. Epidermal growth factor receptor mRNA expression: A potential molecular escape mechanism from regorafenib.
Cancer Sci, 111: 441-450, 2020.
2. Tsukada K, Shinki S, Kaneko A, Murakami K, Irie K, Murai M, Miyoshi H, Dan S, Kawaji K, Hayashi H, Kodama EN, Hori A, Salim E, Kuraishi T, Hirata N, Kanda Y, Asai T. Synthetic biology based construction of biological activity-related library of fungal decalin-containing diterpenoid pyrones.
Nature Commun, 11: 1830, 2020.
3. Suenaga M, Mashima T, Kawata N, Wakatsuki T, Dan S, Seimiya H, Yamaguchi K. Serum IL-8 level as a candidate prognostic marker of response to anti-angiogenic therapy for metastatic colorectal cancer.
Int J Colorectal Dis, 36: 131-139, 2021.
4. Gonda A, Takada K, Yanagita RC, Dan S, Irie K. Effects of side chain length of 10-methyl-aplog-1, a simplified analog of debromoaplysiatoxin, on PKC binding, anti-proliferative, and pro-inflammatory activities.
Biosci Biotechnol Biochem, 85: 168-180, 2021.
5. Hikita K, Yamakage Y, Okunaga H, Motoyama Y, Matsuyama H, Matsuoka K, Murata T, Nakayoshi T, Oda A, Kato K, Tanaka H, Asao N, Dan S, Kaneda N. *(S)*-Erypoegin K, an isoflavone isolated from Erythrina poeppigiana, is a novel inhibitor of topoisomerase IIα: Induction of G2 phase arrest in human gastric cancer cells.
Bioorg Med Chem, 30:115904, 2021.
6. Nishiya N, Oku Y, Ishikawa C, Fukuda T, Dan S, Mashima T, Ushijima M, Furukawa Y, Sasaki Y, Otsu K, Sakyo T, Abe M, Yonezawa H, Ishibashi F, Matsuura M, Tomida A, Seimiya H, Yamori T, Iwao M, Uehara Y. Lamellarin 14, a derivative of marine alkaloids, inhibits the T790M/C797S mutant epidermal growth factor receptor.
Cancer Sci, In press, 2021.

以上