

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. Seimiya H, Nagasawa K, Shin-Ya K. Chemical targeting of G-quadruplexes in telomeres and beyond for molecular cancer therapeutics. **J. Antibiot.**, 74:617-628, 2021.
2. 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 1 α . **Bioorg. Med. Chem.**, 30:115949, 2021.
3. 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.

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. Shimizu Y, Okada K, Adachi J, Abe Y, Narumi R, Uchibori K, Yanagitani N, Koike S, Takagi S, Nishio M, Fujita N, Katayama R. GSK3 inhibition circumvents and overcomes acquired lorlatinib resistance in ALK-rearranged non-small-cell lung cancer. **NPJ Precis. Onc.**, 6:16, 2022.
2. Sagawa R, Sakata S, Gong B, Seto Y, Takemoto A, Takagi S, Ninomiya H, Yanagitani N, Nakao M, Mun M, Uchibori K, Nishio M, Miyazaki Y, Shiraishi Y, Ogawa S, Kataoka K, Fujita N, Takeuchi K, Katayama R. Soluble PD-L1 through alternative polyadenylation works as a decoy in lung cancer immunotherapy. **JCI Insight**, 7(1):e153323, 2022.
3. 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 Precis. Onc., 5:32, 2021.

4. 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.**, 112(6):2371-2380, 2021.
5. 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.
6. Iwao Y, Okamoto Y, Shirahama H, Tsukahara S, Tomida A. eIF4B enhances ATF4 expression and contributes to cellular adaptation to asparagine limitation in BRAF-mutated A375 melanoma. **Biochem. Biophys. Res. Commun.**, 573:93-99, 2021.

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. Takagi S, Sasaki Y, Koike S, Takemoto A, Seto Y, Haraguchi M, Ukaji T, Kawaguchi T, Sugawara M, Saito M, Funauchi Y, Ae K, Matsumoto S, Fujita N, Katayama R. Platelet-derived lysophosphatidic acid mediated LPAR1 activation as a therapeutic target for osteosarcoma metastasis. **Oncogene**, 40:5548-5558, 2021.
3. 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.**, 112(6):2299-2313, 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. Nishiya N, Oku Y, Ishikawa C, Fukuda T, Dan S, Mashima T, Ushijima M, Furukawa Y, Sasaki Y, Otsu K, Sakyō 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.**, 112:1963-1974, 2021.
2. 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 II α : Induction of G2 phase arrest in human gastric cancer cells. **Bioorg. Med. Chem.**, 30:115904, 2021.

3. 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.

4. 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.