

齊郷 智恵美

Chiemi SAIGO

所属 Affiliation

岐阜大学大学院連合創薬医療情報研究科・准教授

(医療情報学専攻・生体制御研究領域)

United Graduate School of Drug Discovery and Medical Information Sciences, Gifu University (Field of Biofunctional Control, Medical Information Sciences Division) ; Associate Professor

専門 Research Area	病理学 Pathology
研究課題 代表的な研究	<p>がん代謝阻害剤とオートファジー阻害薬の併用による悪性腫瘍制御の試み</p> <p>100 年以上前から、がん細胞は、正常細胞にはない解糖系エネルギー代謝経路を利用することが提唱されてきた(1924 年 Otto Heinrich Warburg)。現在では、がん細胞は好気状況下でもミトコンドリアの酸化的リン酸化よりも、解糖系で ATP を産生しエネルギーを確保することが、広く知られており、この、がん細胞に特異的な代謝性要求を阻害する薬剤開発が、試みられている。われわれは、淡明細胞肉腫をがん代謝経路阻害剤 CPI-613® (devimistat) に暴露させると、この肉腫細胞は、細胞質内に蓄えていた豊富なグリコーゲンをオートファジーで処理し、増殖のエネルギーを確保しようとするを明らかにした。続けて、CPI-613 とオートファジー阻害剤であるクロロキンを併用することにより、淡明肉腫細胞は、グリコーゲンを処理できず、ネクローシスに陥ることを見出した。</p> <p>このCPI-613とクロロキンの併用に関して米国製薬企業 Rafael Pharmaceuticals, Inc. (現 Cornerstone Pharmaceuticals, Inc, NJ) と共同して国際特許、米国各国申請を行い、2021 年 9 月より再発・難治性淡明肉腫を対象に Phase I/II の臨床試験が、米国 6 施設で試行中である。</p> <p>病理組織学的知見に基づき、淡明肉腫に類似した生物学的態度をもつことが知られている悪性腫瘍を選び出し、がん代謝阻害剤とオートファジー阻害剤の併用による治療方法の適応拡大を試みている。</p>
Main Research Projects	<p>Combination of a cancer metabolism inhibitor and an autophagy inhibitor to control malignant tumors</p> <p>Nearly a century ago, it was proposed that cancer cells adopt a glycolytic pathway that is absent in normal cells for energy metabolism (Otto Heinrich Warburg, 1924). Now, it is widely accepted that cancer cells generate ATP through glycolysis rather than mitochondrial oxidative phosphorylation, even under aerobic conditions, and agents that could abrogate cancer cell prefer metabolic requirements are under development.</p> <p>We found that clear cell sarcoma, when exposed to CPI-613® (devimistat, an inhibitor of the metabolic pathway in cancer) use autophagic degradation of the abundant glycogen stock in the cytoplasm to secure energy for cell growth. We also found that use of CPI-613 in combination with chloroquine (an autophagy inhibitor) led clear cell sarcoma cells to necrosis by inhibiting their ability to use stocked glycogen.</p> <p>Together with the US pharmaceutical company Cornerstone Pharmaceuticals, Inc. (formerly Rafael Pharmaceuticals, Inc.), we have applied for international patents on the combination of CPI-613 and chloroquine in several countries. A phase I/II clinical study was launched in September 2021 to investigate the effectiveness of this approach for treatment of relapsed or refractory clear cell sarcoma and is currently underway at six facilities in the US.</p> <p>Based on histopathological findings, we plan to select malignant tumors having biological behaviors similar to that of clear cell sarcoma with the aim of expanding the indications for treatment using this approach to those tumors.</p>
研究業績 (過去 5 年)	<ol style="list-style-type: none">1. Hasegawa M, Hanamatsu Y, Saigo C, Kito Y, Takeuchi T. Tumor suppressor effect of an antibody on xenotransplanted sarcomatoid mesothelioma cells. Thoracic cancer. (IF:3.223, CS:3.1) In press 査読あり

2. Matsuo M, Saigo C, Takeuchi T, Onogi A, Watanabe N, Aikyo S, Toyoki H, Yanai H, Tanaka T. Ovarian Clear Cell Carcinoma and Mature Cystic Teratoma Transformed to PNET and Carcinosarcoma: A Case Report with an Immunohistochemical Investigation. *Biomedicines*. 2022 Feb 24;10(3):547. doi: 10.3390/biomedicines10030547. (IF:6.081, CS:3.0) 査読あり
3. Kito Y, Kawashima K, Saigo C, Hasegawa M, Nomura S, Mikamo T, Hanamatsu Y, Matsuo Y, Takeuchi T. Thoracic SMARCA4-deficient undifferentiated tumors with ganglioneuroma and enchondroma: implications for SLC7A11 and ARID1A expression: a case report. *Diagn Pathol*. 2022 Feb 12;17(1):29. doi: 10.1186/s13000-022-01205-8. (IF:2.644, CS:4.0) 査読あり
4. Kawase M, Nakane K, Namiki S, Takeuchi Y, Ueda S, Kawase K, Nakai C, Takeuchi S, Kato D, Takai M, Iinuma K, Fuwa M, Saigo C, Miyazaki T, Morita H, Koie T. A Case of Localized Prostate Cancer Associated with Polymyalgia Rheumatica with Marked Symptomatic Improvement after Robot-Assisted Radical Prostatectomy. *Case Rep Urol*. 2021 Oct 15;2021:8026883. doi: 10.1155/2021/8026883. eCollection 2021. (IF:-, CS:-) 査読あり
5. Takeuchi Y, Kato D, Nakane K, Kawase K, Takai M, Iinuma K, Saigo C, Miyazaki T, Koie T. Solitary Fibrous Tumor of the Prostate: A Case Report and Literature Review. *Medicina (Kaunas)*. 2021 Oct 23;57(11):1152. doi: 10.3390/medicina57111152. (IF:2.430, CS:2.7) 査読あり
6. Takeuchi S, Nakane K, Saigo C, Miyazaki T, Koie T. A Case of Muscle-Invasive Bladder Cancer With Pelvic Lymph Node Involvement Treated With Pembrolizumab and Subsequent Radical Cystectomy and Maintained No Evidence of Disease After Surgery. *Cureus*. 2021 Nov 8;13(11):e19375. doi: 10.7759/cureus.19375. eCollection 2021 Nov. (IF:-, CS:-) 査読あり
7. Hano K, Hatano K, Saigo C, Kito Y, Shibata T, Takeuchi T. Combination of Clptm1L and TMEM207 Expression as a Robust Prognostic Marker in Oral Squamous Cell Carcinoma. *Front Oral Health*. 2021 Mar 29;2:638213. doi: 10.3389/froh.2021.638213. eCollection 2021. (IF:-, CS:-) 査読あり
8. Saigo C, Hanamatsu Y, Hasegawa M, Nomura S, Mikamo T, Kito Y, Yasufuku I, Tanaka H, Yoshida K, Takeuchi T.: Submucosal tumor-like esophageal cancer mimicking a cutaneous sweat gland carcinoma: A case report. *Human Pathology : Case Reports*. 26(2021) 300551. (IF:-, CS:0.3) 査読あり
9. Saigo C, Kito Y, Hasegawa M, Nomura S, Mikamo T, Hanamatsu Y, Mori R, Futamura M, Yoshida K, Takeuchi T.: Incidental cytokeratin-positive interstitial reticulum cell tumor of the lymph node accompanied by breast cancer: Status of YAP/TAZ expression in tumor cells. *Human Pathology: Case Reports*. Available online 5 June 2021, 200526(2021). (IF:-, CS:0.3) 査読あり
10. Tanaka H, Saigo C, Iwata Y, Yasufuku I, Kito Y, Yoshida K, Takeuchi T.: Human colorectal cancer-associated carbohydrate antigen on annexin A2 protein. *J Mol Med (Berl)*. 2021 Aug;99(8):1115-1123. doi: 10.1007/s00109-021-02077-z. Epub 2021 Apr 27. PMID: 33904933 (2021). (IF:4.599, CS:7.7) 査読あり
11. Takao K, Tani A, Suwa T, Kuwabara-Ohmura Y, Nonomura K, Liu Y, Kato T, Mizuno M, Hirota T, Enya M, Iizuka K, Horikawa Y, Saigo C, Kito Y, Miyazaki T, Ohe N, Iwama T, Yabe D.: Diagnosis and treatment of primary central nervous system lymphoma with the primary lesion in the hypothalamus: a case report. *BMC Endocr Disord*. 2021 Jan 11;21(1):13. doi: 10.1186/s12902-020-00675-5. PMID: 33430828 (2021). (IF:2.763, CS:3.5) 査読あり
12. Iwata Y, Yasufuku I, Saigo C, Kito Y, Takeuchi T, Yoshida K.: Anti-fibrotic properties of an adiponectin paralog protein, C1q/TNF-related protein 6 (CTRP6), in diffuse gastric adenocarcinoma. *J Cancer*. 2021 Jan 1;12(4):1161-1168. doi: 10.7150/jca.46765. eCollection 2021. PMID: 33442414 (2021). (IF:4.207, CS:6.4) 査読あり
13. Hanamatsu Y, Saigo C, Kito Y, Takeuchi T.: An obstructive role of NK cells on metastatic growth of clear-cell sarcoma cells in a xenograft murine model. *Mol Clin Oncol*. 2021 Jan;14(1):9. doi:10.3892/mco.2020.2171. Epub 2020 Nov 12. PMID: 33262889 Free PMC article. (2021). (IF:0.693, CS:1.6) 査読あり
14. Yasufuku I, Saigo C, Kito Y, Yoshida K, Takeuchi T.: Prognostic significance of LDL receptor-related protein 1B in patients with gastric cancer. *J Mol Histol*. 2021 Jan 3. doi: 10.1007/s10735-020-09932-2. Online ahead of print. PMID: 33389427 (2021). (IF:2.611, CS:3.8) 査読あり
15. Sakuratani T, Takeuchi T, Yasufuku I, Iwata Y, Saigo C, Kito Y, Yoshida K.: Downregulation of ARID1A in gastric cancer cells: a putative protective molecular mechanism against the Harakiri-mediated apoptosis pathway. *Virchows Arch*. 2020 Aug 13. doi: 10.1007/s00428-020-02899-1. Online ahead of print. PMID: 32789692(2020). (IF:4.064, CS:6.5) 査読あり

16. Mizutani T, Araki H, Saigo C, Takada J, Kubota M, Ibuka T, Suzui N, Miyazaki T, Shimizu M.: Endoscopic and Pathological Characteristics of Helicobacter pylori Infection-Negative Early Gastric Cancer. *Dig Dis*. 2020;38(6):474-483. doi:10.1159/000506120. Epub 2020 Feb 11. PMID:32045929 (2020). (IF:2.404, CS:4.2) 査読あり
17. Hatano K, Saigo C, Kito Y, Shibata T, Takeuchi T. Overexpression of JAG2 is related to poor outcomes in oral squamous cell carcinoma. *Clin Exp Dent Res*. 6(2):174-180 (2020). (IF:1.45, CS:2.1) 査読あり
18. Kito Y, Hanamatsu Y, Kawashima K, Saigo C, Takeuchi T. A unique transgenic mouse model exhibiting a myeloproliferative disease-like phenotype. *Biol Open*. 2019 Nov 7. pii: bio.044438. doi: 10.1242/bio.044438. (IF:2.33, CS:4.6) 査読あり
19. Hanamatsu Y, Saigo C, Asano N, Kito Y, Nakada K, Takeda Y, Takeuchi T. A Case of Gastric Amphicrine Signet-Ring Cell Carcinoma. *Clin Pathol*. 2019 Oct 10;12:2632010X19880535. doi: 10.1177/2632010X19880535. (IF:1.16, CS:1.1) 査読あり
20. Hano K, Hatano K, Saigo C, Kito Y, Shibata T, Takeuchi T. An adiponectin paralog protein, CTRP6 decreased the proliferation and invasion activity of oral squamous cell carcinoma cells: possible interaction with laminin receptor pathway. *Mol Biol Rep*. 46(5):4967-4973. (2019) doi: 10.1007/s11033-019-04947-9. (IF:2.316, CS:3.3) 査読あり
21. Kawashima K, Saigo C, Kito Y, Hanamatsu Y, Egawa Y, Takeuchi T.: CD151 confers metastatic potential to clear cell sarcoma of the soft tissue in animal model. *Oncol Lett*. 17(6):4811-4818. (2019) doi: 10.3892/ol.2019.10164. (IF:2.967, CS:5.8) 査読あり
22. Asano Y, Saigo C, Kito Y, Iwata Y, Yoshida K, Takeuchi T. : Response to Yang et. al. *J Mol Med (Berl)*. doi:10.1007/s00109-019-01775-z, (2019). (IF:4.599, CS:7.7) 査読あり
23. Inoue K, Hatano K, Hanamatsu Y, Saigo C, Kito Y, Bunai K, Shibata T, Takeuchi T. : Pathobiological role of cleft palate transmembrane protein 1 family proteins in oral squamous cell carcinoma. *J Cancer Res Clin Oncol*. 145(4):851-859. doi: 10.1007/s00432-019-02843-0, (2019). (IF:4.553, CS:6.9) 査読あり
24. Asano Y, Takeuchi T, Okubo H, Saigo C, Kito Y, Iwata Y, Futamura M, Yoshida K. : Nuclear localization of LDL receptor-related protein 1B in mammary gland carcinogenesis. *J Mol Med*. 97(2):257-268. (2019). (IF:4.599, CS:7.7) 査読あり
25. Saigo C, Iinuma K, Kameyama K, Mizutani K, Nakano M, Kito Y, Takeuchi T. : Organ-confined plasmacytoid urothelial carcinoma: implication of the lack of expression of the receptor tyrosine kinase MET. *Int J Clin Exp Pathol*. 11(3):1754-1757, (2018). (IF:1.706, CS:2.1) 査読あり
26. Saigo C, Kito Y, Takeuchi T. : Cancerous Protein Network That Inhibits the Tumor Suppressor Function of WW Domain-Containing Oxidoreductase (WWOX) by Aberrantly Expressed Molecules. *Front Oncol*. 30(8):350. (2018). (IF:6.244, CS:4.5) 査読あり
27. Egawa Y, Saigo C, Kito Y, Moriki T, Takeuchi T. : Therapeutic potential of CPI-613 for targeting tumorous mitochondrial energy metabolism and inhibiting autophagy in clear cell sarcoma. *PLoS One*. 13(6):e0198940. (2018). (IF:3.240, CS:5.6) 査読あり
28. Bunai K, Okubo H, Hano K, Inoue K, Kito Y, Saigo C, Shibata T, Takeuchi T. : TMEM207 hinders the tumour suppressor function of WWOX in oral squamous cell carcinoma. *J Cell Mol Med*. 22(2):1026-1033. (2018). (IF:5.310, CS:7.6) 査読あり
29. Saigo C, Kito Y, Takeuchi T. : Immunoreactivity of a Monoclonal Antibody to SS18-SSX Fusion Gene Product in Formalin-fixed Paraffin-embedded Synovial Sarcoma Tissue Section. *Appl Immunohistochem Mol Morphol*. 26(3):206-211. (2018). (IF:1.71, CS:3.7) 査読あり
30. Mizutani K, Horie K, Nagai S, Tsuchiya T, Saigo C, Kobayashi K, Miyazaki T, Deguchi T. : Response to nivolumab in metastatic collecting duct carcinoma expressing PD-L1: A case report. *Mol Clin Oncol*. 7(6):988-990. (2017). (IF:1.78, CS:-) 査読あり
31. Kito Y, Saigo C, Takeuchi T. : Novel Transgenic Mouse Model of Polycystic Kidney Disease. *Am J Pathol*. 187(9):1916-1922. (2017). (IF:4.307, CS:8.6) 査読あり
32. Mori R, Futamura M, Morimitsu K, Saigo C, Miyazaki T, Yoshida K. : The diagnosis of a metastatic breast tumor from ovarian cancer by the succession of a p53 mutation: a case report. *World J Surg Oncol*. 29;15(1):117. (2017). (IF:2.477, CS:4.2) 査読あり

	<p>33. Kawashima K, Saigo C, Hanamatsu Y, Niwa A, Kito Y, Kawaura R, Kuze B, Takeuchi T. : Expression of transcription factor ZEB1 in sarcomatoid salivary duct carcinoma of the parotid gland. Int J Clin Exp Pathol. 10(5):5779-5783, (2017). (IF:1.706, CS:2.1) 査読あり</p> <p>34. Kawashima K, Maeda K, Saigo C, Kito Y, Yoshida K, Takeuchi T. : Adiponectin and Intelectin-1: Important Adipokine Players in Obesity-Related Colorectal Carcinogenesis. Int J Mol Sci.18(4). pii: E866. doi: 10.3390/ijms18040866. (2017). (IF:5.542, CS:6.9) 査読あり</p> <p>35. Takao C, Morikawa A, Ohkubo H, Kito Y, Saigo C, Sakuratani T, Futamura M, Takeuchi T, Yoshida K. : Downregulation of ARID1A, a component of the SWI/SNF chromatin remodeling complex, in breast cancer. J Cancer. 8(1):1-8. (2017). (IF:4.207, CS:6.4) 査読あり</p>
<p>外部資金 (過去 5 年)</p>	<p>1. 平成 29～30 年度 科学研究費助成事業(若手研究(B)) 課題番号 17K15642「内因性 2 分子間相互作用の腫瘍組織での可視化検討」</p>
<p>特許</p>	<p>国際特許 2 件 WIPO PCT WO2020/132395AI および PCT/JP2022/ 13783</p>
<p>略歴</p>	<p>平成 19 年 3 月 佐賀大学医学部医学科卒業 平成 19 年 4 月 岐阜大学医学部附属病院研修医 平成 21 年 4 月 同病理部医員 平成 26 年 4 月 岐阜大学大学院医学系研究科 形態機能病理学 助教 令和 2 年 3 月 同准教授 令和 4 年 1 月 岐阜大学大学院連合創薬医療情報研究科・准教授 現在に至る。</p>