

# 学位論文 全文要約

Molecular biological analysis of 5-FU-resistant gastric cancer organoids; KHDRBS3 contributes to the attainment of features of cancer stem cell  
(5-FU 耐性胃癌オルガノイドの分子生物学的解析；KHDRBS3 は癌幹細胞性の獲得に寄与する)

主指導教員: 安井 弥教授  
(医系科学研究科 分子病理学)  
副指導教員: 武島 幸男教授  
(医系科学研究科 病理学)  
副指導教員: 大上 直秀准教授  
(医系科学研究科 分子病理学)

学位申請者 鵜飼 翔一  
(医歯薬保健学研究科 医歯薬学専攻)

## 全文要約 (Abstract)

5-FU is one of the key drugs in the treatment of gastric cancer (GC). Much evidence has shown that cancer stem cells (CSCs) play a key role in the acquisition of drug resistance. The organoid is a novel 3D cell culture system technology that sustains stem-cell-driven formation of near-physiological, self-renewing tissues using specific niche factors in a dish. In this study, we established GC organoids (GCOs) and gradually treated them with higher concentrations of 5-FU. We successfully harvested four 5-FU-resistant GCOs, which were supported by significant changes in the expression of molecules related to 5-FU metabolism. We then performed microarray analysis using three normal gastric organoids and three pairs of 5-FU-resistant and parental GCOs. Through the comparison of expression profiles and further validation, we chose KHDRBS3 as a target gene. We found KHDRBS3 to be an independent prognostic factor in GC patients, especially in GC patients treated with 5-FU chemotherapy. We also determined that KHDRBS3 might play an important role in the acquisition of stem cell-like features, such as multi-drug resistance and organoid formation, by regulating CD44 variant expression. We found KHDRBS3, which is thought to play an important role in the acquisition of characteristics of CSCs in GC, to be a promising candidate marker for predicting therapeutic effect and prognosis in GC patients.

Material from : Ukai, S., Honma, R., Sakamoto, N. et al. Molecular biological analysis of 5-FU-resistant gastric cancer organoids; KHDRBS3 contributes to the attainment of features of cancer stem cell. *Oncogene* 39, 7265–7278 (2020).

<https://doi.org/10.1038/s41388-020-01492-9>

<https://www.nature.com/articles/s41388-020-01492-9>