Press Release

Keio University

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# Identifying Antifungal Drugs as a Potential Therapeutic Agent for Biliary Tract Carcinoma

Scientists successfully establish and maintain long-term culture of "organoids" derived from biliary tract carcinoma and have identified antifungal drugs as a potential therapeutic agent for biliary tract carcinoma.

## 1. Main Points of Research

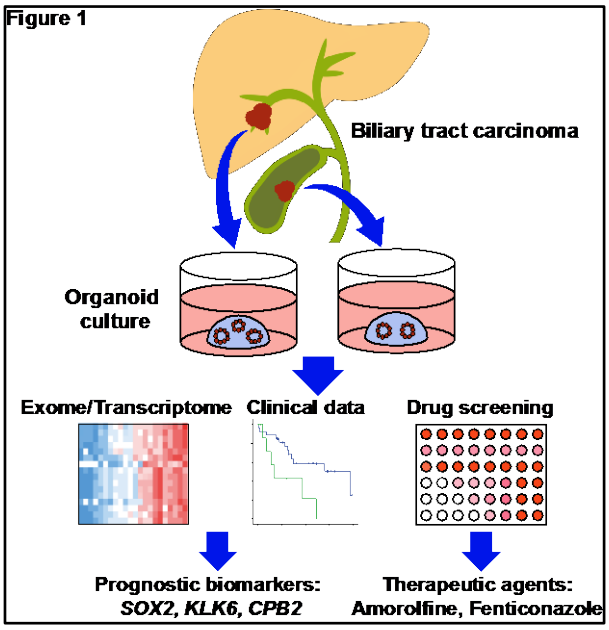
- Establishment of organoids derived from biliary tract carcinoma (BTC) patients
- Biological similarity between the primary BTC tissues and established organoids
- Identification of SOX2, KLK6, and CPB2 as prognostic biomarkers for BTC patients
- Drug screening identified antifungal drugs as potential therapeutic agents for BTC

## 2. Background of Research

Biliary tract carcinomas (BTCs) are epithelial malignancies arising in the region between the intrahepatic bile ducts and the ampulla of Vater. Patients with inoperable BTC generally receive a chemotherapy regimen of gemcitabine and cisplatin. However, the effect of these drugs is limited, and the 5-year survival rate of patients is very low. The lack of *in vitro* models that can reproduce the properties of human BTC has hindered understanding of its molecular pathogenesis and development of more effective therapeutic drugs. In recent years, the development of the new 3D culture system known as "organoid culture" has enabled long-term expansion of tissue stem cells into cyst-like structures (organoids) resembling the properties of original tissues.

## 3. Content of Research and Results

In the current study, a group led by Yoshimasa Saito of Keio University successfully established organoids derived from BTC patients. These BTC organoids were cultured stably for over one year and closely recapitulated the histopathology, gene expression, and genetic alterations evident in the primary tumors. Gene expression profiling of the organoids and clinical data of patients revealed that *SOX2*, *KLK6*, and *CPB2* could be a potential prognostic biomarker for patients with BTC. Moreover, they performed a drug screening with a compound library consisting of drugs employed clinically for their ability to suppress BTC organoids as a "drug repositioning" strategy. They discovered that the antifungal drugs amorolfine and fenticonalzole significantly suppressed the growth of BTC organoids (see Figure 1).




4. Future Developments

"Antifungal drugs including amorolfine and fenticonalzole could be potentially applied for the prevention and treatment of BTC patients," says Saito. "Patient-derived organoids may be a powerful preclinical model for clarification of molecular pathogenesis and discovery of biomarkers and therapeutic drugs for refractory cancers."

5. Details of Journal Article

Saito Y. et al., Establishment of patient-derived organoids and drug screening for biliary tract carcinoma. *Cell Reports*, April 23, 2019.

6. Funding information

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*Please direct any requests or inquires to the contact information provided below.

・Inquiries about research
Associate Professor Yoshimasa Saito
Division of Pharmacotherapeutics, Keio University Faculty of Pharmacy
Tel: +81- 3-5400-2692 Fax: +81- 3-5400-2692 E-mail: saito-ys@pha.keio.ac.jp
http://www.pha.keio.ac.jp/en/research/index.html
・Inquiries about press release
Keio University Office of Communications and Public Relations (Ms.Toyoda)
Tel: +81-3-5427-1541 Fax: +81-3-5441-7640 Email: m-pr@adst.keio.ac.jp
https://www.keio.ac.jp/