

ヒト胃上皮組織幹細胞オルガノイド増殖培養技術

プロジェクト
責任者

奈良先端科学技術大学院大学 先端科学技術研究科

教授 栗崎 晃、助教 高田 仁実

プロジェクト概要

胃癌で胃を全摘出すると、胃の内分泌機能の低下や内因子の減少による巨赤芽球性貧血、消化吸収障害や体重減少などが起こり、多くの患者が胃切除症候群を発症する。胃切除術後には、食物を一時的に貯えるため、小腸の一部を利用して胃の再建が行われるが、胃の機能を再建する方法は開発されていない。

我々はこれまでに世界で初めてマウスES細胞から機能的な胃袋を作製することに成功し¹、マウス胃上皮幹細胞を増殖させる方法を開発して²特許申請しており³、これを応用して、胃再建のための様々な胃の機能性細胞への分化能を持つヒト胃上皮幹細胞増殖方法を開発中である。

1. Nat Cell Biol. 2015, 17(8):984-993. 2. Nat Commun. 2023, 14(1):3750. 3. 特願2023-99622

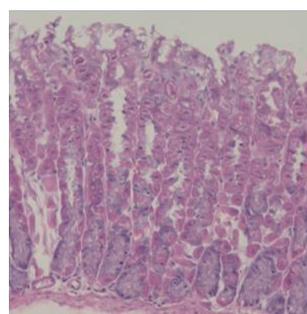


図1. 正常胃上皮組織

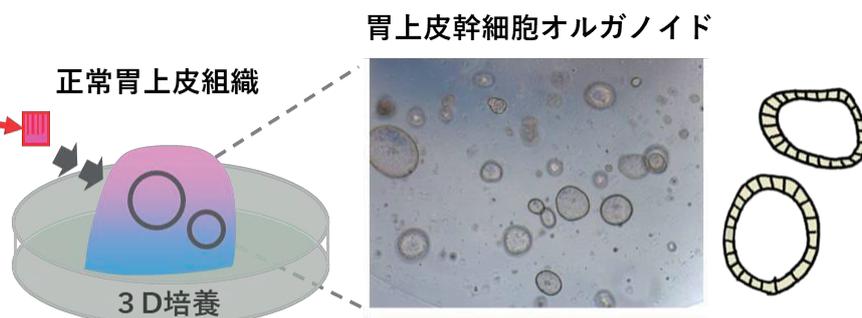
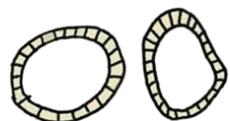
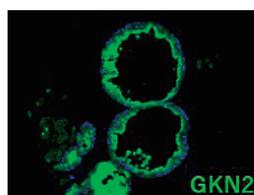
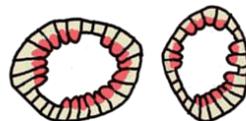


図2. 増殖中の胃上皮幹細胞オルガノイド



分化
7日



胃幹細胞オルガノイド

胃粘膜細胞

図3. 胃幹細胞オルガノイドから胃粘膜細胞を作製

開発中の技術

- ・ヒト胃上皮幹細胞を増殖方法
- ・ヒトの胃の機能性細胞分化培地
胃酸分泌細胞
消化酵素分泌細胞
胃粘液分泌細胞

対象疾患：胃癌

特許情報：特願2023-99622

技術の特徴：胃の様々な機能性細胞に分化できる胃上皮幹細胞オルガノイドの増殖技術、増殖培地、分化培地。

市場性、開発における課題：日本では毎年1万人以上が胃全摘出手術を受ける。効率的な拡大培養技術の開発が必要。

希望する企業連携の内容：共同研究開発の後に、ライセンスアウトを希望。

Human Gastric Tissue Epithelial Stem Cell Organoid Expansion Culture Technology

Principal Investigator

Graduate School of Science and Technology,
Nara Institute of Science and Technology (NAIST)

Professor Akira KURISAKI, Assistant Professor Hitomi TAKADA

Project Outline

When the stomach is entirely removed due to gastric cancer, the decrease in gastric endocrine function and intrinsic factor leads to megaloblastic anemia, along with digestive and absorption disorders and weight loss. Many patients develop post-gastrectomy syndrome. After gastrectomy, the stomach is reconstructed using part of the small intestine to temporarily store food, but no method has been developed to restore the stomach's functions.

We previously succeeded in creating a mini functional stomach tissue from mouse embryonic stem (ES) cells for the first time in the world¹. Additionally, we developed a method for propagating mouse gastric epithelial stem cells^{2,3}. Building on these achievements, we are currently developing a method to propagate human gastric epithelial stem cells with the ability to differentiate into various functional gastric cell types for stomach tissue regeneration.

1. Nat Cell Biol. 2015, 17(8):984-993. 2. Nat Commun. 2023, 14(1):3750. 3. Japanese Patent Application No. 2023-99622

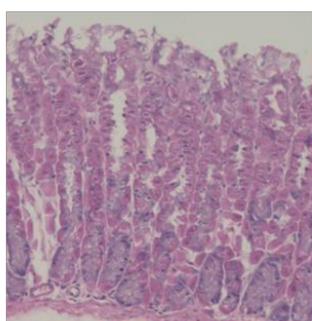


Fig. 1 Gastric tissue

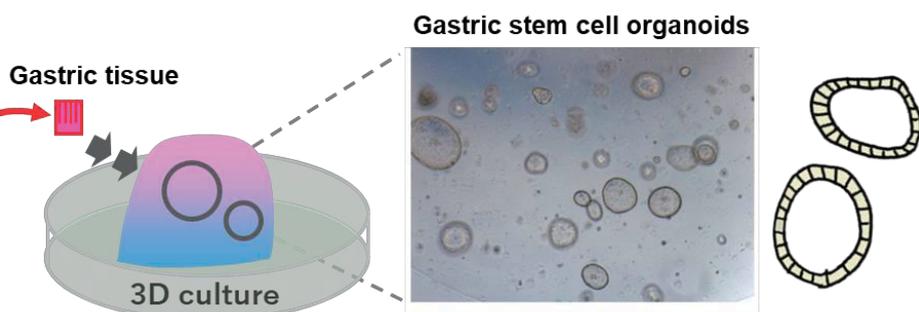
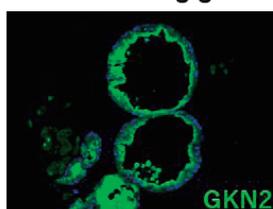
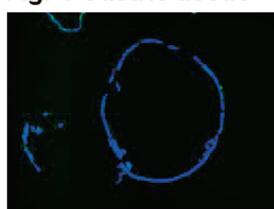


Fig. 2 Proliferating gastric stem cell organoids in 3D culture



Gastric stem cell organoid

Mucus-secreting pit cells

Fig. 3 Mucus-secreting pit cells differentiated from gastric stem cells

Technologies under development

- Method for propagating human gastric stem cells
- Culture media for differentiating human functional gastric cells:

Gastric acid-secreting cells
Digestive enzyme-secreting cells
Gastric mucus-secreting cells

Target Disease: Gastric Cancer.

Japanese Patent application: No. 2023-99622

Technical Features: Propagation technology for human gastric epithelial stem cell organoids capable of differentiating into various functional gastric cells. Growth media and differentiation media for human gastric organoids.

- **Market Potential:** In Japan, over 100,000 people are diagnosed gastric cancer and 10-20% of them undergo total gastrectomy.
- **Challenges:** Development of efficient and scalable production systems for stem cell-derived functional gastric cells.
- **Desired Corporate Collaboration:** Collaboration Model: Joint research and development, followed by licensing-out.