

フェローシップ及びSPRING支援学生・指導教員の交流会

EEPD1 enhances malignant phenotypes and mediates 5-FU resistance by regulating ABCA1 expression in colorectal cancer



MIE UNIVERSITY MIE UNIVERSITY MIE UNIVERSITY MIE UNIVERSITY MIE UNIVERSITY MIE UNIVERSITY MIE UNIVERSITY MIE UNIVERSITY

MA RUIYA (マ リヤ)

三重大学大学院生命医科学専攻

三重大学大学院医学系研究科 消化管・小児外科学



GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

Innovative Surgery and Surgical Techniques Development
Gastrointestinal and Pediatric Surgery

Background

- ✓ Exonuclease/Endonuclease/Phosphatase Domain-1 (EPPD1) is a structure-specific nuclease that mediates DNA repair function and is a potential target for cancer therapy. EPPD1 promotes cellular cholesterol efflux by controlling cellular levels and activity of ATP-binding cassette transporter A1 (ABCA1).
- ✓ ABCA1 is an oncogene in colorectal cancer (CRC) and is also associated with acquired tumor chemoresistance.
- ✓ However, no studies have been performed the function of EPPD1 and the regulatory relationship between EPPD1 and ABCA1 in CRC have not been evaluated.
- ✓ Furthermore, the functions and mechanisms of chemotherapeutic efficacy and drug resistance of EPPD1 in CRC have not been fully delineated..



Purpose

- ✓ To evaluate the expression and clinical prognostic significance of EEPD1 in CRC.
- ✓ To elucidate the role of EEPD1 in the regulation of CRC progression.
- ✓ To identify the role of the regulatory relationship between EEPD1 and ABCA1 in CRC 5-FU resistance.

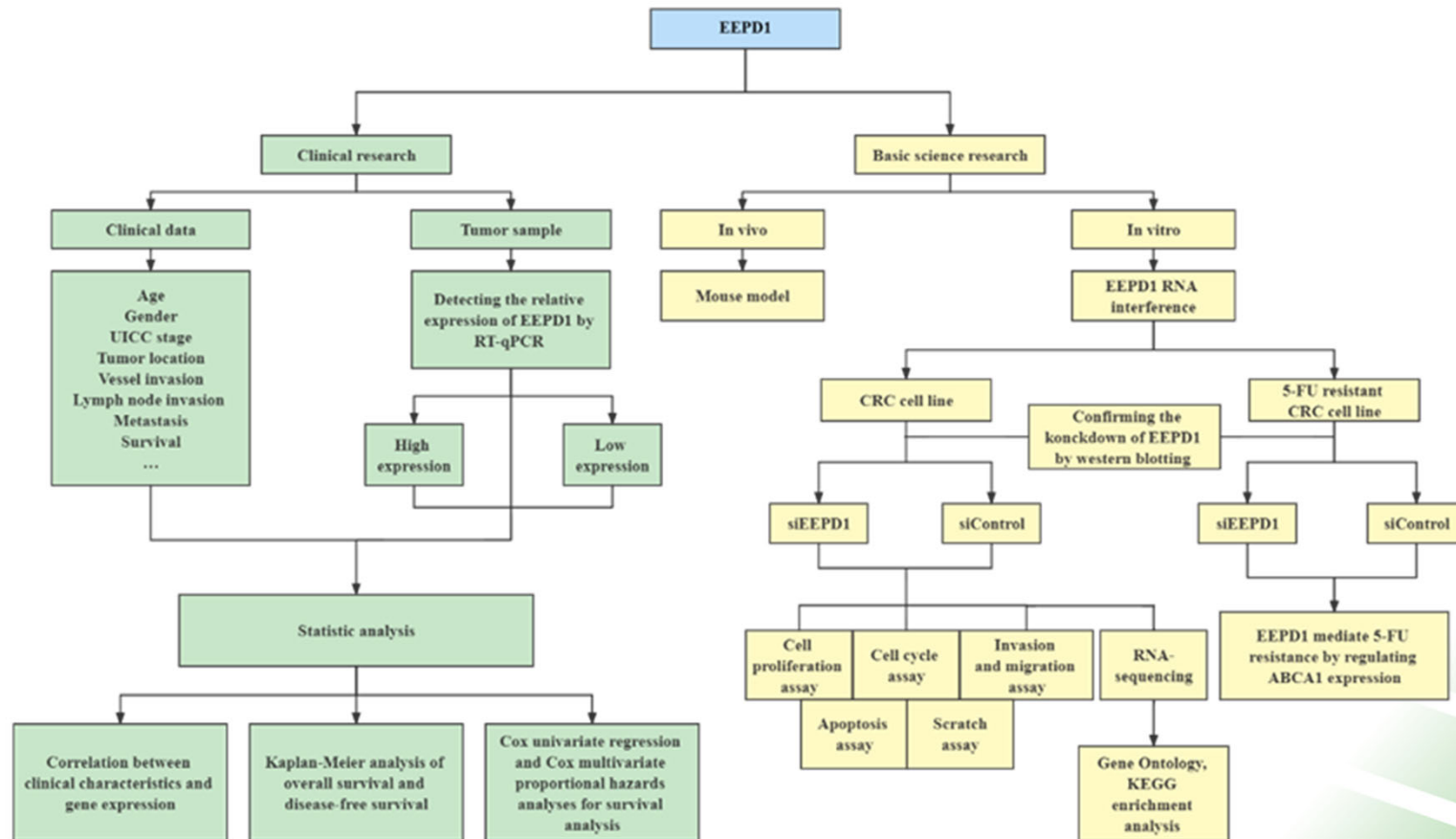


GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

پیشرفت در جراحی گوارش و کودکان و توسعه تکنیک‌های جراحی نوین

Experimental works



Summary of current research

- ✓ The study is conducted in patients with CRC who underwent curative resection at Mie University Hospital from 2011 to 2015. We quantified the relative expression levels of EEPD1 in CRC tissues and tumor-adjacent normal tissues by qPCR, and then analyzed the associations between clinical features, prognosis and EEPD1 expression.
- ✓ The present study has up to now investigated a series of in vitro experiments (cell proliferation, colony formation and apoptosis assays) to elucidate the anti-tumor potential and mechanism of EEPD1 on CRC cells.



GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

胃腸肝胆臓器と小児科手術の最先端医療の発展と
創傷外科手術の発展と

Introduction

三重大学大学院医学系研究科 消化管・小児外科学



GIPS and DIS
Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

消化管・小児外科
消化管・小児外科

Introduction

- ✓ Our department conducts clinical and basic research to identify problems through detailed analysis of clinical results and to develop or improve diagnostic, therapeutic, and preventive methods necessary to improve treatment outcomes. By carrying out this clinical research and bridging research, we hope to establish biomarkers and new treatment methods that can change new treatment strategies, fulfill the mission of a university hospital as an academic institution, and contribute to medicine by disseminating evidence originating from Mie University to the world.



GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

胃腸外科と小児外科の革新的な手術技術の開発
Gastrointestinal and Pediatric Surgery, Innovative Surgery and Surgical Techniques Development

Introduction



- ✓ MA RUIYA (マ リヤ)
 - ✓ Inner Mongolia, China
 - ✓ Mie University
 - ✓ Clinical Medical Sciences
 - ✓ Gastrointestinal and Pediatric Surgery
-
- ✓ 2012.09-2017.07 Inner Mongolia University of Science & Technology Baotou Medical College B.Med
 - ✓ 2018.09-2021.06 North China University of Science and Technology M.D.
 - ✓ 2022.10 Admission Mie University Graduate School of Medicine PhD program



GIPS and DIS

Gastrintestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

胃腸病、小児外科、手術技術の発展
革新的な手術技術の開発

Introduction

ONCOLOGY LETTERS 22: 523, 2021

Antitumor effects of Andrographis via ferroptosis-associated genes in gastric cancer

RUIYA MA^{1,2*}, TADANOBU SHIMURA^{1*}, CHENGZENG YIN^{1*}, YOSHINAGA OKUGAWA³,
TAKAHITO KITAJIMA¹, YUHKI KOIKE¹, YOSHIKI OKITA¹, MASAKI OHI¹, KEIICHI UCHIDA¹,
AJAY GOEL⁴, LI YAO⁵, XUEMING ZHANG² and YUJI TOIYAMA¹

¹Department of Gastrointestinal and Pediatric Surgery, Institute of Life Sciences, Mie University Graduate School of Medicine, Tsu, Mie 514-8507, Japan; ²Department of Colorectal Surgery, Tangshan Gongren Hospital, Tangshan, Hebei 063000, P.R. China; ³Department of Genomic Medicine, Mie University Hospital, Tsu, Mie 514-8507, Japan; ⁴Department of Molecular Diagnostics and Experimental Therapeutics, Beckman Research Institute, City of Hope Comprehensive Cancer Center, Duarte, CA 91016, USA; ⁵Department of Surgery, China-Japan Friendship Hospital, Beijing 100029, P.R. China

Received February 14, 2021; Accepted March 31, 2021

DOI: 10.3892/ol.2021.12784



GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

胃腸病科と小児外科の革新的な手術技術の開発

Introduction

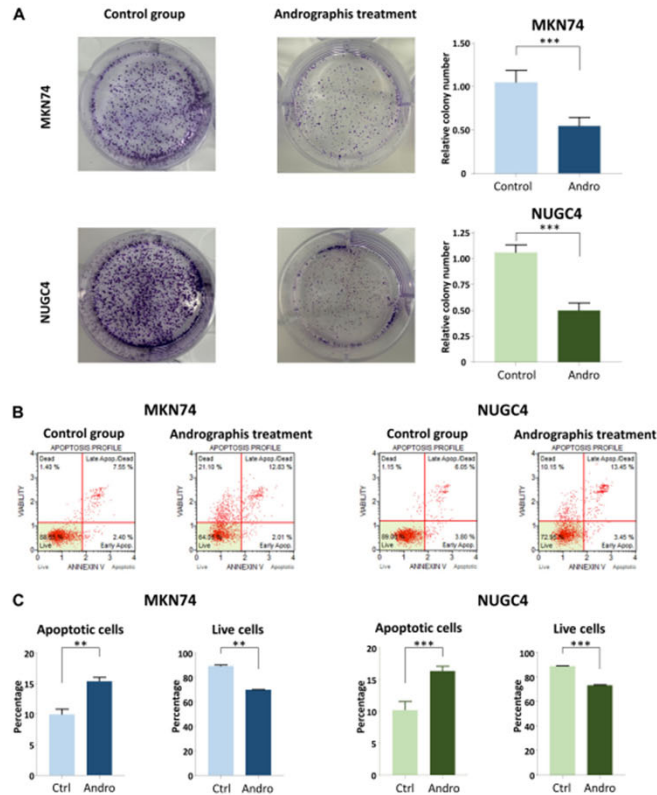


Figure 2. Inhibition of colony formation and enhancement of apoptotic activity induced by Andrographis in gastric cancer cells. (A) Colony formation assay to assess clonogenicity in MKN74 and NUGC4 cells following treatment with Andrographis. (B) Representative images illustrating the percentage of MKN74 and NUGC4 cells undergoing apoptosis, as indicated by positive staining for Annexin V. (C) Bar graphs showing the percentage of live and apoptotic cells in each treatment group in the apoptosis assay. * $P < 0.01$ and *** $P < 0.001$ (two-tailed Student's *t*-test). Andro, Andrographis treatment group; Ctrl, Control group; Apop, apoptosis.

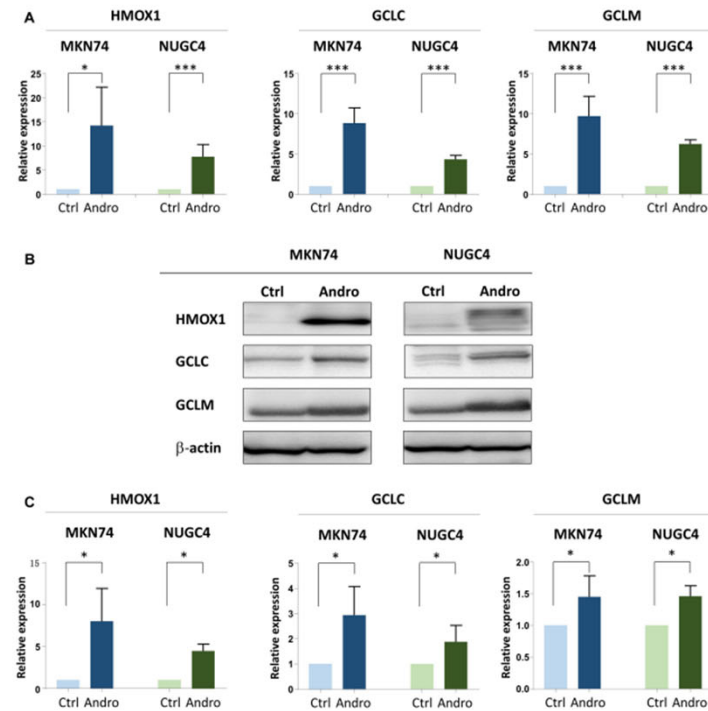


Figure 3. Altered mRNA and protein expression levels of the ferroptosis-associated targets *HMOX1*, *GCLC* and *GCLM* after Andrographis treatment in gastric cancer cells. (A) Changes in *HMOX1*, *GCLC* and *GCLM* mRNA expression after Andrographis treatment in MKN74 and NUGC4 cells. (B) Representative image of immunoblotting assays for each group in MKN74 and NUGC4 cells. (C) Changes in HMOX-1, GCLC and GCLM protein expression after andrographis treatment in MKN74 and NUGC4 cells. * $P < 0.05$ and *** $P < 0.001$ (two-tailed Student's *t*-test). GCLC, glutamate-cysteine ligase catalytic; GCLM, glutamate-cysteine ligase modifier; HMOX1, heme oxygenase-1; Andro, Andrographis treatment group; Ctrl, Control group.



GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

რეპროდუქციის უფლება არის შეზღუდული და გამოიყენება მხოლოდ
ცენტრის ოფიციალურ ვებ-გვერდზე.



Thank you very much!



GIPS and DIS

Gastrointestinal and Pediatric Surgery,
Innovative Surgery and Surgical Techniques Development

Гиперплазия эндометрия и дисплазия шейки матки
определяются при гистологическом исследовании

