Primary mucoepidermoid carcinoma of the intrahepatic bile duct: A case report

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Abstract
Mucoepidermoid carcinoma (MEC) is the most common salivary gland carcinoma; however, hepatobiliary MEC is extremely rare. A 74-year-old patient was diagnosed with hepatobiliary MEC after hepatectomy. We considered its origin could be the peribiliary glands. Its genome profile was similar to salivary MEC rather than standard biliary tract carcinoma.

KEYWORDS
cancer genome, companion diagnostic test, fusion gene analysis, hepatobiliary mucoepidermoid carcinoma, peribiliary gland

1 | BACKGROUND
Mucoepidermoid carcinoma (MEC) is a type of cancer, which is pathologically consisted of mucin-secreting cells, epithelioid cells, and intermitten cells.1 It is the most common malignant tumor in the salivary gland.2 It can arise from other structures such as the bronchi3; however, primary hepatobiliary MEC is rare.1 Although salivary gland MEC usually has low malignancy,4-7 hepatobiliary MEC tends to show poor prognosis.1,3 In addition, its pathogenesis mechanism has not been elucidated, and there are still no established therapeutic strategies for hepatobiliary MEC. Its genomic features are also unknown. We report a case of MEC diagnosed after hepatectomy and provide a brief literature review.

2 | CASE PRESENTATION
The patient was a 74-year-old man previously treated for hepatitis C with interferon therapy 10 years before. He achieved a sustained virological response (SVR). He had also undergone laparoscopic cholecystectomy for adenomyomatosis and gallbladder polyp 2 years before. During his follow-up after the SVR, a B2 localized intrahepatic bile duct dilatation was found on abdominal ultrasonography (US) (Figure 1). Computed tomography (CT) and magnetic resonance choangiopancreatography also showed a B2 dilatation and an S2 localized tumor, which appeared to obstruct B2 (Figure 1). During endoscopic retrograde choangiopancreatography (ERCP), brush cytology was performed at the B2 narrow point, and nasobiliary drainage was placed at
the B2 dilated segment (Figure 2). Brush cytology revealed some atypical cells with an enlarged, deeply stained nucleus. Intrahepatic cholangiocarcinoma was suspected, but an exact diagnosis could not be made. Fluorodeoxyglucose-positron emission tomography (FDG-PET) showed no abnormal FDG uptake other than the S2 tumor (maximum standardized uptake value: 13.69) (Figure 2).

Left lobe hepatectomy was performed for diagnosis and treatment. A pathological evaluation of the left hepatic duct stump during surgery was negative. The surgical time was 285 min. Blood volume was 1065 ml. The patient was in the intensive care unit until postoperative day (POD) 1. Oral intake was started on POD 3, and he was discharged on POD 11 with no major postoperative complications.

The size of the tumor was 45 × 25 × 25 mm (Figure 3). It had unclear margins and included necrotic tissue. Densely arranged mucous, intermediate, and epidermoid cells were seen on pathological examination (Figure 4). The patient was diagnosed with MEC. The pathological staging was pT3N0M0 pStageIII, based on the General Rules for the Clinical Pathological Study of Primary Liver Cancer. The mass existed under the B2 epithelium; no atypia was seen in the epithelium. This finding implied that the mass arose in the subepithelium of B2 (Figure 4). It invaded neural fibers, lymphatic vessels, and extrahepatic adipose tissue. Approximately 16 mitotic cells per 10 high-power fields were seen, and a cystic component was not included in the tumor tissue. Mucous cells were positive for periodic...
acid-Schiff (PAS) stain and Alcian blue stain (Figure 5). In addition, immunohistochemical staining was done (Figure 5). Mucous cells were positive for CK7; epidermoid cells were positive for CK5/6 and p40 and negative for CK7. This finding meant that these cells had traits of squamous cells. Intermittent cells were simultaneously positive for CK7 and p40, meaning that they had properties of both mucous and epidermoid cells. All cell types were negative for CK20 and CA19-9. The Ki-67 index was 40%.

After the pathological diagnosis was confirmed, an otorhinolaryngology examination was performed to search for another primary lesion, but no neoplasm was found. The patient was diagnosed with primary hepatobiliary MEC. Five months after surgical resection, CEA increased from 3.0 ng/ml 1 month after surgery to 6.0 ng/ml. A liver hilar lymph node recurrence was also detected on follow-up CT (Figure 6). Systemic chemotherapy (gemcitabine/cisplatin) was started. At the same time, a tissue-based companion diagnostic test (FoundationOne® CDx) was done. The result is shown in Table 1. He was eligible for BI 907828 (an MDM2–p53 antagonist) in a phase 1 trial (ClinicalTrials.gov ID: NCT03449381) since an MDM2 amplification was found. However, he could not participate because recruitment was temporarily terminated. There were no driver mutations, and no eligible clinical trials were available. Moreover, ribonucleic acid (RNA) sequencing was done for fusion gene analysis to search for CRTC1/3-MAML2 fusion. Multiple fusion genes including MDM2 were detected, which might reflect MDM2 amplification seen in the companion diagnostic test, but no significant findings including CRTC1/3-MAML2 fusion were found. The result is shown in Table 2. A follow-up CT revealed recurrent liver hilar lymph node enlargement and additional paraaortic lymph node metastasis 12 months after surgery. The chemotherapy regimen was changed to gemcitabine/S-1 therapy.

At this writing, 15 months after surgery, the patient is alive and continues gemcitabine/S-1 therapy.

3 | DISCUSSION

MEC is the most frequent histopathological type of salivary gland carcinoma.² It can arise from the lung, bronchus, esophagus, and thyroid gland,³ but liver MEC is
rare. Most salivary gland MECs have low malignancy, and their 5-year overall survival is 80%-90%. In contrast, liver and esophageal MECs typically demonstrate high malignancy. We reviewed previous case reports of hepatobiliary MEC and summarized them (Table 3). In previous case reports, all but two cases died within 1 year after admission or surgery. In this case, the tumor also relapsed early after surgery, and the prognosis appears poor.

Regarding the origin of MEC, the salivary gland is an exocrine organ rich in secretory glands. Other structures where MEC can arise, such as the bronchi and esophagus, also have exocrine glands. MEC from the pancreas, colon, and breast, as rare as hepatobiliary MEC, has been reported. They also have exocrine glands that can be the origin of MEC. MEC can also arise from the

| Nucleated tumor cell rate | 20% |
|----------------------------|-----|
| Purity                     | 22.6|
| Depth                      | 1086|
| TMB                        | 0.0 Muts/Mb |
| MSI-H                      | Not detected |
| Quality                    | PASS |
| Single nucleotide variance | STK11 F354L 59.3% (VUS) |
|                           | STK11 E199fs*88 19.2% |
| Copy number variance       | CDKN2A loss |
|                           | CDKN2B loss |
|                           | MDM2 amplification; copy number 16 |
|                           | MTA1 loss |
|                           | PTEN loss |
|                           | FAS loss |

**Detected fusion genes from RNA sequencing**

| Detected fusion genes from RNA sequencing |
|------------------------------------------|
| RNU5B−1RNA28SN5                           |
| MDM2-SMPD3                                |
| MDM2-CDC40                                |
| MDM2-ADA2                                 |
| MDM2-DPP10                                |
| MDM2-ZBTB7C                               |
| ARHGEF12-AGAP1                            |
| STK11 F354L 59.3% (VUS)                   |
| STK11 E199fs*88 19.2%                     |
| CDKN2A loss                               |
| CDKN2B loss                               |
| MDM2 amplification; copy number 16       |
| MTA1 loss                                 |
| PTEN loss                                 |
| FAS loss                                  |

Abbreviation: RNA, ribonucleic acid.
| Case | Year | Author | Age | Sex | Size (cm) | Location | Symptom | Metastasis | Treatment | Outcome |
|------|------|--------|-----|-----|-----------|----------|---------|------------|-----------|---------|
| 1    | 1971 | Pianzola | 44  | Male | 15        | Right lobe | Abdominal pain | None | Surgical excision | Died 45 days after surgery |
| 2    | 1980 | Ho      | 65  | Male | 8         | None       | Jaundice | Lymph nodes | Conservation | Died 14 days after laparotomy |
| 3    | 1980 | Ho      | 63  | Female | 6     | Right lobe | Abdominal pain, Jaundice | Pancreas, portal vein, lymph nodes | Conservation | Died 16 days after admission |
| 4    | 1982 | Koo     | 44  | Female | 12     | Left lobe | Epigastric pain | None | Surgical excision, Chemotherapy | Died 6 months after surgery |
| 5    | 1982 | Koo     | 66  | Male | 4         | Common hepatic duct | Jaundice | Gall bladder, lymph nodes, right hepatic artery | Surgical excision | Died 7 days after surgery |
| 6    | 1982 | Koo     | 62  | Male | 1.5       | Common hepatic duct | Jaundice | None | Surgical excision | Living 10 months after surgery |
| 7    | 1984 | Katsuda | 78  | Male | 11        | Left lobe | Abdominal discomfort | Lymph nodes, lung, kidney | Chemotherapy | Died 3 months after admission |
| 8    | 1986 | Lambrianides | 59  | Female | 18     | Right lobe | Abdominal pain | Right kidney | Conservation | Died 14 days after admission |
| 9    | 1987 | Hayashi | 46  | Female | 3      | Left lobe | Abdominal pain | None | Surgical excision | Died 11 months after surgery |
| 10   | 1992 | Di Palma | 66  | Female | 9.5    | Abdominal pain | Diaphragm, pericardium, portal vein | Surgical excision | Died 6 months after surgery |
| 11   | 2000 | Shuangshoti | 64  | Male | 5         | Jaundice | Lymph nodes, pancreas, portal vein | Conservation | Died 7 days after admission |
| 12   | 2003 | Kang    | 52  | Male | 9         | Abdominal pain | Diaphragm | TAE, surgical excision | Died 6 months after surgery |
| 13   | 2004 | Choi    | 69  | Female | 16     | Right lobe | Abdominal pain | Diaphragm | Surgical excision | Died 4 months after surgery |
| 14   | 2008 | Arakawa | 81  | Female | 10     | Right lobe | Fever | Lymph nodes, portal vein | Chemotherapy | Died 117 days after admission |
| 15   | 2013 | Moul    | 83  | Female | 2      | Common bile duct | Jaundice | Liver | Surgical excision, Chemotherapy | Died 13 months after surgery |
| 16   | 2014 | Guo     | 60  | Female | 8.5     | Jaundice, abdominal discomfort | Lymph nodes | Surgical excision, chemotherapy | Died 6 months after surgery |
| 17   | 2019 | Nallacheruvu | 50  | Male | 8        | Gall bladder | Liver | Surgical resection | Died 6 month after surgery |
| 18   | 2019 | Watanabe | 79  | Female | 5.3     | Left lobe | Abdominal pain | None | Surgical excision, chemotherapy | Living 10 years after surgery |
| 19   | 2021 | Hou     | 64  | Male | 10       | Left lobe | Abdominal distention | None | Surgical resection | Died 3 months after surgery |
| 20   | 2021 | present case | 74  | Male | 4.5      | Left lobe (B2) | None | Lymph nodes | Surgical excision, chemotherapy | Living 15 months after surgery |

Abbreviation: MEC, mucoepidermoid carcinoma
thyroid gland. It does not have to be an exocrine gland, but it is reported that thyroid gland MECs originate in solid cell nests (SCNs). SCNs are ultimobranchial body remnants that are found in the thyroid gland. They sometimes include mucus cells that can be the origin of MEC. In the hepatobiliary system, the extrahepatic bile duct, cystic duct, and intrahepatic large bile duct have secretory glands in the subepithelium called peribiliary glands. According to Table 3, obstructive jaundice was seen in 7 cases (35%), and some extrahepatic bile duct MECs were also reported. Although obstructive jaundice was not seen, MEC occurred in the subepithelium of the intrahepatic large bile duct and obstructed B2 in this case. We suggest that the origin of hepatobiliary MEC may be the peribiliary gland. Although it is difficult to explain why MEC can arise from gallbladder which has no peribiliary glands, that may be why the gallbladder MEC has ever been reported only one case in the world.

MEC is pathologically characterized by the coexistence of mucin-secreting, epithelioid, and intermediate cells. Goode made a pathological grading system of salivary gland MEC that classifies them into three grades (low, intermediate, and high). Their grading parameters consist of a cystic component, <20%, neural involvement, four or more mitotic figures per 10 high-power fields, necrosis, and anaplasia. This case meets these five criteria and is categorized as high-grade MEC. This result matches the unfavorable course of this case that relapsed early after surgery; however, it has been reported that the grading scheme for MEC of the salivary glands is not useful for hepatic MEC because those in the liver are always high grade.

Some driver mutations of biliary tract cancers have been reported by analyzing their genome. Reported driver mutations are shown in Table 4. On the contrary, frequently mutated genes in salivary gland MEC were also reported. Those that mutated in more than 10% of salivary gland MEC were CDKN2A (41.6%), TP53 (39.6%), CDKN2B (29.2%), BAP1 (20.8%), PIK3CA (20.8%), and HRAS (10.4%). Of these, CDKN2A loss and CDKN2B loss were seen in this case. The CDKN2A mutation is listed in both but was seen in only 5 out of 412 biliary tract cancer cases. It is a major driver mutation of salivary gland MEC than biliary tract cancer.

Furthermore, the CDKN2B mutation is listed in salivary MEC and biliary tract carcinoma. Its genome appears to be similar to salivary gland MEC rather than standard biliary tract cancer. In addition to that, MDM2 amplification was detected. MDM2 binds and inhibits p53, acting as an oncogene. Andrews et al. have reported that MDM2 is highly expressed in salivary MEC tissue and MDM2-p53

| Table 4 Reported driver mutations of biliary tract cancer |
|----------------------------------------------------------|
| **Nakamura et al.**                                       |
| Common bile duct                                         |
| TP53           | BRCA1  | BRCA2  | ERBB2  | PIK3CA |
| Common to intra- and extrahepatic bile duct              |
| KRAS           | SMAD4  | ARID1A | GNAS   |
| Intrahepatic bile duct                                  |
| FGFR2 fusion   | IDH1   | IDH2   | EPHA2a | BAP1   |
| Extrahepatic bile duct                                 |
| PRKACA fusiona | PRKACB fusiona | ELF3a | ARID1Ba  |
| Gallbladder                                             |
| EGFR           | ERBB3  | PTEN   | ARID2a | MLL2   |
| MLL3a          | TERT promoter |
| **Wardell et al.**                                       |
| TP53           | KRAS   | SMAD4  | NF1    | ARID1A |
| PBRM1          | KMT2D  | ATR    | PIK3CA | ERBB3  |
| KMT2Ca         | APC    | BAP1   | POLQa  | ARID2a |
| IDH1           | TET1a  | CTNNB1 | BRAF   | TGFB2R2|
| PTEN           | DNMT3A | FBXW7  | ELF3a  | CDKN2A |
| MSH6           | STK11  | RNF43  | NRAS   | MLH1   |
| TGFBR1a        |        |

*aNot included in FoundationOne® CDx.*
interaction inhibitor decreases MEC cancer stem cells.\textsuperscript{36} MDM2 amplification may be an important finding of hepatobiliary MEC, and although we could not access the MDM2–p53 antagonist clinical trial, MDM2 inhibition may be effective for MEC. In addition, TMB was 0.0 Muts/Mb, so a genomic mutation, in this case, appeared very little.

CRTC1/3-MAML2 fusion is sometimes seen in MEC, and it is considered a favorable prognostic factor of salivary gland MEC.\textsuperscript{37,38} A reported case of hepatobiliary MEC with CRTC1-MAML2 fusion presented a good prognosis without recurrence 10 years after surgery.\textsuperscript{23} CRTC1/3-MAML2 fusion was not detected in this case, and early systemic chemotherapy was administered according to the treatment protocol for unresectable recurrent biliary tract carcinoma. More studies and discussions are needed to define the therapeutic strategy since there is no established treatment for hepatobiliary MEC because of its rarity.

4 CONCLUSIONS

We report a primary hepatobiliary MEC with early recurrence after surgical resection. We believe that it originated from the peribiliary glands. Its genome profile was more similar to salivary MEC than biliary tract carcinoma.

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None.

CONFLICT OF INTEREST

All authors report no conflicts of interest.

AUTHOR CONTRIBUTIONS

Author 1 performed surgery, managed the perioperative course, and wrote the manuscript. Author 2 performed surgery, managed the perioperative course, followed up the patient and did chemotherapy, and mainly supervised the manuscript. Author 3 diagnosed with hepatobiliary MEC pathologically, considered its origin, and supervised pathological part of the manuscript. Author 4 considered the result of companion diagnostic test and fusion gene analysis and supervised oncogenical part of the manuscript. Author 5 did RNA sequencing for fusion gene analysis and considered the result. Author 6 supervised the patient surgical treatment and checked and approved the manuscript as a person responsible for the department of surgery. Author 7 supervised the patient surgical treatment and checked and approved the manuscript as a person responsible for the department of surgery.

ETHICAL APPROVAL

The present study was conducted in accordance with the ethical review board of our hospital.

CONSENT

Written informed consent for publication of this case report and any accompanying images was obtained from the patient.

DATA AVAILABILITY STATEMENT

The datasets used during the current report are available from the corresponding author on reasonable request.

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REFERENCES

1. Torbenson M, Zen Y, Yeh MM. Tumors of the liver: American Registry of Pathology. 2018. xv, 449 pp.
2. Boukheris H, Curtis RE, Land CE, Dores GM. Incidence of carcinoma of the major salivary glands according to the WHO classification, 1992 to 2006: a population-based study in the United States. Cancer Epidemiol Biomarkers Prev. 2009;18(11):2899-2906.
3. Goldblum JR, Lamp LW, McKenney JK, Myers JL. Rosai and Ackerman's surgical pathology. 11th ed. 2 v. Elsevier; 2018:xiv, 2142, 67 p.
4. Auclair PL, Goode RK, Ellis GL. Mucoepidermoid carcinoma of intraoral salivary glands. Evaluation and application of grading criteria in 143 cases. Cancer. 1992;69(8):2021-2030.
5. Brandwein MS, Ivanov K, Wallace DI, et al. Mucoepidermoid carcinoma: a clinicopathologic study of 80 patients with special reference to histological grading. Am J Surg Pathol. 2001;25(7):835-845.
6. Chen AM, Lau VH, Farwell DG, Luu Q, Donald PJ. Mucoepidermoid carcinoma of the parotid gland treated by surgery and postoperative radiation therapy: clinicopathologic correlates of outcome. Laryngoscope. 2013;123(12):3049-3055.
7. Goode RK, Auclair PL, Ellis GL. Mucoepidermoid carcinoma of the major salivary glands: clinical and histopathologic analysis of 234 cases with evaluation of grading criteria. Cancer. 1998;82(7):1217-1224.
8. Liver Cancer Study Group of Japan. General rules for the clinical and pathological study of primary liver cancer. 3rd English ed. Kanehara; 2010:94.
9. Pianzola LE, Drut R. Mucoepidermoid carcinoma of the liver. Am J Clin Pathol. 1971;56(6):758-761.
10. Ho JC. Two cases of mucoepidermoid carcinoma of the liver in Chinese. Pathology. 1980;12(1):123-128.
11. Koo J, Ho J, Wong J, Ong GB. Mucoepidermoid carcinoma of the bile duct. Ann Surg. 1982;196(2):140-148.
12. Katsuda S, Nakanishi I, Kajikawa K, Takabatake S. Mucoepidermoid carcinoma of the liver. Acta Pathol Jpn. 1984;34(1):153-157.
13. Lambricianides AL, Askew AR, Lefevre I. Thorotrust-associated mucoepidermoid carcinoma of the liver. Br J Radiol. 1986;59(704):791-792.
14. Hayashi I, Tomoda H, Tanimoto M, et al. Mucoepidermoid carcinoma arising from a preexisting cyst of the liver. J Surg Oncol. 1987;36(2):122-125.
15. Di Palma S, Andreola S, Audisio RA, Doci R, Lombardi L. Primary mucoepidermoid carcinoma of the liver: A case report. Tumori J. 1992;78(1):65-68.
16. Shuangshoti S Jr, Shuangshoti S. Primary mucoepidermoid carcinoma of the intrahepatic bile duct: a case report with review of literature. J Med Assoc Thai. 2000;83(2):197-203.
17. Kang H, Park YN, Kim SE, et al. Double primary mucoepidermoid carcinoma and hepatocellular carcinoma of the liver—a case report. Hepatogastroenterology. 2003;50(49):238-241.
18. Choi D, Kim H, Lee KS, Lee KG, Park CK. Mucoepidermoid carcinoma of the liver diagnosed as a liver abscess: report of a case. Surg Today. 2004;34(11):968-972.
19. Arakawa Y, Shimada M, Ikegami T, et al. Mucoepidermoid carcinoma of the liver: report of a rare case and review of the literature. Hepatol Res. 2008;38(7):736-742.
20. Moul AE, Bejarano PA, Casillas J, Levi JU, Garcia-Buitrago MT. Mucoepidermoid carcinoma of the intrapancreatic common bile duct: immunohistochemical profile, prognosis, and review of the literature. Case Rep Pathol. 2013;2013:192458.
21. Guo XQ, Li B, Li Y, Tian XY, Li Z. Unusual mucoepidermoid carcinoma of the liver misdiagnosed as squamous cell carcinoma by intraoperative histological examination. Diagn Pathol. 2014;9:24.
22. Nallacheruvu Y, Gaur K, Sakhija P, Agarwal AK, Srivastava S. Mucoepidermoid carcinoma of the gallbladder: a case-based study of an extremely rare tumor highlighting the role of immunohistochemical profiling. Int J Surg Pathol. 2019;27(4):418-422.
23. Watanabe J, Kai K, Tanikawa K, et al. Primary mucoepidermoid carcinoma of the liver with CRTC1-MAML2 fusion: a case report. Diagn Pathol. 2019;14(1):84.
24. Hou P, Su X, Cao W, et al. Whole-exome sequencing reveals the etiology of the rare primary hepatic mucoepidermoid carcinoma. Pathol Int. 2017;67(7):361-364.
25. Imazu N, Oe S, Tsuda Y, et al. Rapidly progressing anaplastic carcinoma of the pancreas with mucoepidermoid carcinoma: an autopsy case report. Intern Med. 2021;60:2235-2240.
26. Han F, Jiang H, Zhang S. Mucoepidermoid carcinoma of the transverse colon: a rare tumor entity with literature review. Pathol Int. 2017;67(7):361-364.
27. Ye RP, Liao YH, Xia T, Kuang R, Long HA, Xiao XL. Breast mucoepidermoid carcinoma: a case report and review of literature. Int J Clin Exp Pathol. 2020;13(12):3192-3199.
28. Ando M, Nakanishi Y, Asai M, Maeshima A, Matsuno Y. Mucoepidermoid carcinoma of the thyroid gland showing marked ciliation suggestive of its pathogenesis. Pathol Int. 2008;58(11):741-744.
29. Mizukami Y, Nomomura A, Michigishi T, et al. Solid cell nests of the thyroid. A histologic and immunohistochemical study. Am J Clin Pathol. 1994;101(2):186-191.
30. Nakamura Y, Hoso M, Sanzen T, Sasaki M. Microstructure and development of the normal and pathologic biliary tract in humans, including blood supply. Micros Res Tech. 1997;38(6):552-570.
31. de Jong IEM, van Leeuwen OB, Lisman T, Gouw ASH, Porte RJ. Repopulating the biliary tree from the peribiliary glands. Biochim Biophys Acta Mol Basis Dis. 2018;1864(4 Pt B):1524-1531.
32. Nakamura H, Arai Y, Totoki Y, et al. Genomic spectra of biliary tract cancer. Nat Genet. 2015;47(9):1003-1010.
33. Wardell CP, Fujita M, Yamada T, et al. Genomic characterization of biliary tract cancers identifies driver genes and predisposing mutations. J Hepatol. 2018;68(5):959-969.
34. Wang K, McDermott JD, Schrock AB, et al. Comprehensive genomic profiling of salivary mucoepidermoid carcinomas reveals frequent BAP1, PIK3CA, and other actionable genomic alterations. Ann Oncol. 2017;28(4):748-753.
35. Momand J, Zambetti GP, Olson DC, George D, Levine AJ. The mdm-2 oncogene product forms a complex with the p53 protein and inhibits p53-mediated transactivation. Cell. 1992;69(7):1237-1245.
36. Andrews A, Warner K, Rodriguez-Ramirez C, et al. Ablation of cancer stem cells by therapeutic inhibition of the MDM2-p53 interaction in mucoepidermoid carcinoma. Clin Cancer Res. 2019;25(5):1588-1600.
37. Okabe M, Miyabe S, Nagatsuka H, et al. MECT1-MAML2 fusion transcript defines a favorable subset of mucoepidermoid carcinoma. Clin Cancer Res. 2006;12(13):3902-3907.
38. Nakayama T, Miyabe S, Okabe M, et al. Clinicopathological significance of the CRTC3-MAML2 fusion transcript in mucoepidermoid carcinoma. Mod Pathol. 2009;22(12):1575-1581.

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