Histologic subtyping of ampullary carcinoma for targeted therapy

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Carcinomas of the ampulla of Vater, or ampullary carcinomas, are a rare form of gastrointestinal tract cancer in Korea. Of the many histologic subtypes of ampullary carcinomas, the vast majority are tubular adenocarcinomas of the intestinal type, pancreatobiliary type, or mixed type. There are no well-established adjuvant chemotherapy protocols for treating advancedstage ampullary cancer, and most of the currently used chemotherapeutic regimens are either extrapolated from pancreatic, biliary, and colorectal cancers or derived from retrospective studies from high-volume institutions [1].

In this issue of the Journal of Pathology and Translational Medicine, Kumari et al. [2] report the whole-exome sequencing results of ampullary carcinomas. Their observations confirmed the commonly mutated genes identified by next-generation sequencing of ampullary carcinomas, which included KRAS, TP53, APC, ELF3, SMAD4, CTNN1B, MUC4, ERBB2, and CDKN2A [3-6]. The authors also found that the mutation patterns of several genes were different according to the histologic subtype: KRAS, TP53, and CDH10 mutations were more frequently found in the pancreatobiliary type, which shares mutations commonly observed in pancreatic ductal adenocarcinomas. In contrast, APC, ACVR2A, SOX9, and EPHA6 genes were more frequently mutated in the intestinal type ampullary carcinomas, which were commonly mutated in colorectal cancers [3-5]. This suggests that gemcitabine-based regimens could be particularly useful in patients with pancreatobiliary type ampullary carcinomas, and 5-fluorouracil-based regimens could be beneficial for those with intestinal type ampullary carcinomas. Therefore, providing information regarding the histologic subtypes in surgical pathologic reports

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Ethics Statement

Not applicable.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

Code Availability

Not applicable.

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Conflicts of Interest

The authors declare that they have no potential conflicts of interest.

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References

- Regalla DK, Jacob R, Manne A, Paluri RK. Therapeutic options for ampullary carcinomas: a review. Oncol Rev 2019; 13: 440.
- Kumari N, Singh RK, Mishra SK, Krishnani N, Mohindra S, L R. Identification of PI3K-AKT signaling as the dominant altered pathway in intestinal type ampullary cancers through whole-exome sequencing. J Pathol Tansl Med 2021; 55: 192-201.
- Hechtman JF, Liu W, Sadowska J, et al. Sequencing of 279 cancer genes in ampullary carcinoma reveals trends relating to histologic subtypes and frequent amplification and overexpression of ERBB2 (HER2). Mod Pathol 2015; 28: 1123-9.
- Gingras MC, Covington KR, Chang DK, et al. Ampullary cancers harbor ELF3 tumor suppressor gene mutations and exhibit frequent WNT dysregulation. Cell Rep 2016; 14: 907-19.
- 5. Yachida S, Wood LD, Suzuki M, et al. Genomic sequencing identifies ELF3 as a driver of ampullary carcinoma. Cancer Cell 2016; 29: 229-40.
- Kwon MJ, Kim JW, Jung JP, et al. Low incidence of KRAS, BRAF, and PIK3CA mutations in adenocarcinomas of the ampulla of Vater and their prognostic value. Hum Pathol 2016; 50: 90-100.