

# ASIP 2018 Journal CME Programs

## JMD 2018 CME Program in Molecular Diagnostics

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### CME January Questions # 1-12

An article and associated Commentary on tubulocystic renal cell carcinoma and an article and Commentary on telomere diagnostics for pancreatic disorders were selected for the **January 2018 JMD CME Program in Molecular Diagnostics**. The authors of the referenced articles, the planning committee members, and staff have no relevant financial relationships with commercial interests to disclose.

Questions #1-5 are based on: Lawrie CH, Armesto M, Fernandez-Mercado M, Arestín M, Manterola L, Goicoechea I, Larrea E, Caffarel MM, Araujo AM, Sole C, Sperga M, Alvarado-Cabrero I, Michal M, Hes O, López JI: Noncoding RNA expression and targeted next-generation sequencing distinguish tubulocystic renal cell carcinoma (TC-RCC) from other renal neoplasms. *J Mol Diagn* 2018, 20:34-45; <http://dx.doi.org/10.1016/j.jmoldx.2017.09.002> and associated Commentary by Ding Y, Miyamoto H, Rothberg PG: Is tubulocystic renal cell carcinoma real? *J Mol Diagn* 2018, 20:28-30; <http://dx.doi.org/10.1016/j.jmoldx.2017.10.004>

Questions #6-12 are based on: Hata T, Molin MD, McGregor-Das A, Song TJ, Wolfgang C, Eshleman JR, Hruban RH, Goggins M: Simple detection of telomere fusions in pancreatic cancer, intraductal papillary mucinous neoplasm, and pancreatic cyst fluid. *J Mol Diagn* 2018, 20:46-55; <http://dx.doi.org/10.1016/j.jmoldx.2017.09.006> and associated Commentary by Joseph L: Telomere diagnostics for pancreatic neoplasms and cysts. *J Mol Diagn* 2018, 20:31-33; <http://dx.doi.org/10.1016/j.jmoldx.2017.11.001>

Upon completion of this month's journal-based CME activity, you will be able to:

- Describe tubulocystic renal cell carcinoma (TC-RCC) and other subtypes of RCC.
- Understand the molecular basis of distinguishing TC-RCC from other renal neoplasms.
- Describe the miRNA profile of TC-RCC.
- Describe the noncoding RNA (ncRNA) profile of TC-RCC.
- Understand telomeres and define telomeric repeat sequences.
- Explain the role of telomeric fusions in cancers and precursor lesions.
- Understand the importance of characterizing pancreatic cysts.

**1. Renal cell carcinoma (RCC) is a common urinary tract malignancy in adults. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See *J Mol Diagn* 2018, 20:34-45 and *J Mol Diagn* 2018, 20:28-30.]

- a. The most prevalent histologic subtype is chromophobe RCC (ChRCC).
- b. In 2016, 47,200 deaths from kidney and renal pelvis cancer were estimated to occur in the United States.
- c. The prevalence of clear cell RCC (CCRCC) is 70%.
- d. The prevalence of papillary RCC (PRCC) is 5%.

**2. Tubulocystic RCC (TC-RCC) has a distinctive morphology and has been recognized by the International Society of Urological Pathology and the World Health Organization (WHO) as a distinct renal tumor entity. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See *J Mol Diagn* 2018, 20:34-45 and *J Mol Diagn* 2018, 20:28-30.]

- a. TC-RCC malignancies have a circumscribed multicystic gross appearance.
- b. TC-RCC are found more commonly in women.
- c. TC-RCC have a high propensity for recurrence and metastasis.
- d. Immunohistochemically, TC-RCC are indistinguishable from ChRCC.

**3. Studies of noncoding (nc) RNA expression have been useful in classifying and understanding the pathogenesis of RCC. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:34-45 and J Mol Diagn 2018, 20:28-30.]

- a. The expression of mature miRNAs in TC-RCC cases was similar to that of CCRCC and PRCC cases.
- b. The expression of pre-miRNAs in TC-RCC cases clustered distinctly from CCRCC, clear cell papillary RCC (CCPRCC), and PRCC.
- c. The pattern of small nucleolar RNAs in TC-RCC was indistinguishable from CCRCC.
- d. The pattern of small Cajal body-specific RNAs was similar among TC-RCC, PRCC, CCRCC, and ChRCC.

**4. Genetic studies suggesting a relationship between TC-RCC and other RCC subtypes remain controversial. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:34-45 and J Mol Diagn 2018, 20:28-30.]

- a. TC-RCC and PRCC consistently show gains in chromosomes 7 and 17, proving a close relationship between the two RCC subtypes.
- b. Loss of the Y chromosome in ChRCC was found by microarray analysis.
- c. The most common mutations in PRCC are in the *MET*, *SETD2*, *PBRM1*, and *BAP1* genes.
- d. TC-RCCs frequently had nonsense mutations in the *ABL1* and *PDGFRA* genes.

**5. Targeted next-generation sequencing of TC-RCC cases identified mutations in 14 genes. Based on the referenced article, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:34-45.]

- a. Tumor cell load was correlated with variant allele frequencies of the TC-RCC mutations.
- b. The majority of the 27 identified TC-RCC mutations were synonymous, suggesting that the mutations had no effect on biological processes.
- c. The identified *ABL1* mutations were found scattered throughout the gene.
- d. The three *PDGFRA* mutations identified in TC-RCC patients were nonsynonymous and affected amino acids located within the kinase domain of the protein.

**6. Telomeres are structures present at all chromosomal ends. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. Telomeric repeat sequences (TTAGGG) prevent the fusion of chromosomal ends.
- b. In general, telomere lengthening is the main mechanism that contributes to the progression of precancerous neoplasms to invasive cancers.
- c. The most common mechanism for neoplastic cells with critically shortened telomeres to overcome cell death is the alternate length telomere pathway.
- d. Rarely, neoplastic cells with short telomeres overcome cell death by activating telomerase.

**7. Advances in imaging of the pancreas have led to an increase in the frequency of presymptomatic detection of lesions. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. Early detection of pancreatic ductal adenocarcinoma (PDAC) has a good prognosis.
- b. PDAC lesions characteristically have both a solid and a cystic component.
- c. Most lesions found incidentally do not represent PDAC, but several classes of neoplasms have an increased risk of progression to PDAC.
- d. Most cysts have sufficient exfoliated cells for cytopathology assessment.

**8. Pancreatic intraepithelial neoplasia is a microscopy-based finding. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. Pancreatic intraepithelial neoplasia has been found in up to 55% of pancreases with PDAC.
- b. Pancreatic intraepithelial neoplasia has not been detected in apparently normal pancreases.
- c. Pancreatic intraepithelial neoplasia lesions are, by definition, <0.25 cm.
- d. Pancreatic intraepithelial neoplasia is widely held to be the earliest stage in pancreatic neoplasms.

**9. Imaging can detect precursor lesions of PDAC. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. Pseudocysts resulting from regenerative changes after pancreatitis account for 25% of cysts.
- b. Mucinous cystic neoplasms (MCNs) have a high risk of progression to cancer.
- c. Intraductal papillary mucinous neoplasms (IPMNs) have a low risk of progression to cancer.
- d. Several classes of neoplasms can have cystic components: IPMNs, MCNs, serous cystadenomas, and solid-pseudopapillary neoplasms.

**10. IPMNs are the most common type of neoplastic cyst. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. IPMNs are characterized by the papillary proliferation of serous-producing epithelial cells.
- b. IPMNs with low-grade dysplasia have the same poor prognosis as IPMNs with high-grade dysplasia.
- c. Approximately 35% of IPMNs have *KRAS* mutations.
- d. Given the morbidity and risks related to pancreatic surgery, watchful observation is generally recommended for patients with IPMNs with low-grade and intermediate-grade dysplasia.

**11. Better characterization of pancreatic cysts may allow more patients with worrisome cysts to continue with surveillance. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. The authors of the referenced article examined telomere length, telomerase activity, and the presence of telomeric fusions in PDACs (cell lines and xenografts), IPMNs, and IPMN cystic fluids.
- b. DNA recovered from cyst fluid showed less size degradation than that seen in paraffin sections, increasing the ability to detect longer fusions.
- c. Telomere length was measured by multiplex PCR that provided information about the distribution of telomere lengths.
- d. Telomere fusions were found in normal human pancreatic tissue as well as in pancreatic cancer xenografts.

**12. Prospective studies are needed to evaluate the diagnostic utility of using telomere fusion detection for patients undergoing endoscopic ultrasound evaluation and pancreatic cyst fluid sampling. Based on the referenced article and associated Commentary, select the ONE best TRUE statement:** [See J Mol Diagn 2018, 20:46-55 and J Mol Diagn 2018, 20:31-33.]

- a. Data indicate that telomere fusions may serve as a biomarker for predicting the presence of low-grade dysplastic lesions within a cyst.
- b. The results of the referenced study cannot be directly applied to patients who undergo surveillance without surgical resection.
- c. Telomeric fusion events did not predict the grade of dysplasia of IPMNs.
- d. The supplemental data showed a significant correlation of telomeric fusion status with survival.