KOPANA 2018 Spring Seminar
Neuroendocrine Tumor of GI and Pancreas

March 17, 2018
The Sutton Place Hotel, Vancouver, Canada
Kee-Taek JANG
Department of Pathology, Samsung Medical Center
## NET in WHO 2010

<table>
<thead>
<tr>
<th></th>
<th>Mitoses (10 HPF)</th>
<th>Ki-67 index (%)</th>
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<tbody>
<tr>
<td>NET, G1</td>
<td>&lt;2</td>
<td>≤2</td>
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<tr>
<td>NET, G2</td>
<td>2-20</td>
<td>3-20</td>
</tr>
<tr>
<td>NEC, G3</td>
<td>&gt;20</td>
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If Ki-67 index of NET show 2.5%, is this G1? G2? Or G1.5?
Ki-67 index of NET

- 15% of PanNET fall within 2-3% range of Ki-67 proliferation index.

Calculation of the Ki67 index in pancreatic neuroendocrine tumors: a comparative analysis of four counting methodologies

Michelle D Rojai,1,2,3, Pelin Bagci,2,3, Nobuyuki Ohike,2, Burcu Saka,2, Ipek Erbatur Seven,2, Nevra Dursun,2, Serdar Balci,7, Hasan Guce,7, Kee-Tae Jung,7, Takuma Tajiri,7, Olca Basturk,10, So Yeon Kong,11, Michael Goodman,11, Gizem Akkas,11 and Volkan Adsay,1

1Department of Pathology, Emory University School of Medicine, Atlanta, GA, USA; 2Department of Pathology, Marmara University, Istanbul, Turkey; 3Department of Pathology, Showa University School of Medicine, Tokyo, Japan; 4Department of Pathology, Medipol University, Istanbul, Turkey; 5Department of Pathology, Istanbul Education and Training Hospital, Istanbul, Turkey; 6Department of Pathology, Yildirim Bayazit University, Ankara, Turkey; 7Department of Pathology, HKE University, Rio, Turkey; 8Department of Pathology, Samsung Medical Center, Seoul, Korea; 9Department of Pathology, Taksim University Hochschild Hospital, Tokyo, Japan; 10Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA and 11Department of Pathology, Department of Epidemiology, Emory University, Atlanta, GA, USA

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Pancrasic neuroendocrine tumors constitute a group of neoplasms with phenotypic and ultrastructural neuroendocrine differentiation. As studies with longer follow-up and better defined cohorts are published, it has become increasingly clear that pancreatic neuroendocrine tumors are low-grade malignancies. Stage of tumor, naturally, predicts the outcome of pancreatic neuroendocrine tumors; however, it has been difficult to predict which tumors are prone to recurrence and metastasis by pathologic examination alone.

Among a variety of potential prognostic parameters analyzed in numerous studies, proliferation index has consistently stood out as having strong prognostic value, along with mitotic count. Ki67 has
# Consensus Guidelines for the Management and Treatment of Neuroendocrine Tumors

*Pamela L. Kunz, MD,*+ Diane Reidy-Lagunes, MD, MS,† Lowell B. Anthony, MD,‡ Erin M. Bertino, MD,§ Kari Brendiro, BS,|| Jennifer A. Chan, MD,¶ Herbert Chen, MD,¶ Robert T. Jensen, MD,** Michelle Kang Kim, MD, MSc,†† David S. Klimstra, MD,¶¶ Matthew H. Kulke, MD, §§ Eric H. Liu, MD,|||| David C. Metz, MD,¶¶¶ Alexandria T. Phan, MD,## Rebecca S. Sippel, MD,# Jonathan R. Strosberg, MD,*** and James C. Yao, MD†††

## Pancreatic NET Pathology

Mitotic rate or Ki67 should be obtained. When both mitotic rate and Ki67 are obtained, the higher grade is assigned. If specimen is inadequate, repeat biopsy is recommended.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Recommend</th>
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<tbody>
<tr>
<td>Small cell, non–small cell (ie, large cell)</td>
<td>Recommend</td>
</tr>
<tr>
<td>Grading (proliferative rate)</td>
<td>Recommend</td>
</tr>
<tr>
<td>Mitotic rate</td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>&lt;2 mitoses/10 HPF*</td>
</tr>
<tr>
<td>G2</td>
<td>2–20 mitoses/10 HPF</td>
</tr>
<tr>
<td>G3</td>
<td>&gt;20 mitoses/10 HIFP</td>
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<tr>
<td>Ki 67</td>
<td></td>
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<tr>
<td>G1</td>
<td>&lt;3%</td>
</tr>
<tr>
<td>G2</td>
<td>3%–20%</td>
</tr>
<tr>
<td>G3</td>
<td>&gt;20%</td>
</tr>
<tr>
<td>Histology differentiation</td>
<td>Recommend</td>
</tr>
<tr>
<td>Poorly differentiated NECs (G3) are highly aggressive and need to be distinguished from other NETs</td>
<td></td>
</tr>
</tbody>
</table>
Ki-67 index of NET

The NANETS Consensus Guideline for the Diagnosis and Management of Neuroendocrine Tumors

Well-Differentiated Neuroendocrine Tumors of the Jejunum, Ileum, Appendix, and Cecum

J. Philip Boudreaux, MD,* David S. Klimstra, MD,† Manal M. Hassan, MD, PhD,‡ Eugene A. Woltering, MD,* Robert T. Jensen, MD,§ Stanley J. Goldsmith, MD,‖ Charles Nutting, DO,¶ David L. Bushnell, MD,∥ Martyn E. Caplin, MD,**, and James C. Yao, MD‡

TABLE 4. Grading Systems for Neuroendocrine Tumors of the Midgut

<table>
<thead>
<tr>
<th>Grade</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low grade (G1)</td>
<td>&lt;2 Mitoses/10 high-power fields,</td>
</tr>
<tr>
<td></td>
<td>and &lt;3% Ki-67 index</td>
</tr>
<tr>
<td>Intermediate grade (G2)</td>
<td>2–20 Mitoses/10 high-power fields,</td>
</tr>
<tr>
<td></td>
<td>or 3%–20% Ki-67 index</td>
</tr>
<tr>
<td>High grade (G3)</td>
<td>&gt;20 Mitoses/10 high-power fields</td>
</tr>
<tr>
<td></td>
<td>or &gt;20% Ki-67 index</td>
</tr>
</tbody>
</table>
Practical Issues in Grading of NET

• Hot spot interpretation: heterogeneity of mitotic count.

• Discordant mitotic rate and Ki-67 proliferation index: when the mitotic rate and Ki-67 index indicate different grades, it is recommended to assign the higher grade.

• How do you count?
Heterogeneity of Ki-67

1.4% vs. 21.5%

Am J Surg Pathol 2010;34:300–313
Problems with Ki-67 index: How do you count?

1. Eyeballing
2. Counting # of cells by live microscope
3. Counting # of cells by digital image analysis
4. Manual counting # of cells on a printed photomicrography
Eyeballing: is it reproducible?

Results of “eyeballing” of Ki-67 index by 18 observers in 45 cases illustrates striking inter-observer variability.

Problems with Ki-67 index: How do you count?

1. Eyeballing

- About 60% of the cases have an index close to the categorical cut-off index
- Only 5% are in the extremes (<1% and > 30%)

*Mod Pathol* 2015;28(5):686-694
Problems with Ki-67 index: How do you count?

1. Eyeballing
2. Counting # of cells by live microscope
Problems with Ki-67 index: How do you count?

1. Eyeballing
2. Counting # of cells by live microscope
3. Counting # of cells by digital image analysis

*Machine also counts*

*Lymphocytes, Endothelial cells, hemosiderin, etc...*
Problems with Ki-67 index:
How do you count?

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Modern Pathology (2015) 28, 686-694; doi:10.1038/modpathol.2014.156; published online 21 November 2014

Manual count on printed photomicrography is the most applicable approach (practical and accurate) in daily practice
Dual IHC of Synaptophysin & Ki-67

<table>
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<tr>
<th>Staining Method</th>
<th>Intraclass correlation (95% confidence interval)</th>
<th>P-value $^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ki67-only</td>
<td>0.51 (0.35-0.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Synaptophysin-Ki67</td>
<td>0.79 (0.69-0.85)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

$^+$ 2-sided vs. H$_0$:r=0
Heterogeneity of NEC

Are G3 ENETS neuroendocrine neoplasms heterogeneous?

The High-grade (WHO G3) Pancreatic Neuroendocrine Tumor Category Is Morphologically and Biologically Heterogenous and Includes Both Well Differentiated and Poorly Differentiated Neoplasms

A subset of well differentiated pancreatic neuroendocrine tumors (PanNETs) have an increased (>20%) Ki67 proliferation index
WD PanNET with high Ki-67 index

PanNETs with an increased Ki67 proliferation index
WD PanNET with high Ki-67 index

<table>
<thead>
<tr>
<th></th>
<th>G2 WDNETs (n=53)</th>
<th>WDNETs &gt;20% Ki67 (n=21)</th>
<th>PDNEC (n=44)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Small Cell</td>
<td>Large Cell</td>
</tr>
<tr>
<td>Average Mitotic Rate</td>
<td>3.5 (2-10)</td>
<td>7.6 (2-20)</td>
<td>51 (21-92)</td>
</tr>
<tr>
<td>(Per 10HPF)</td>
<td></td>
<td></td>
<td>37 (21-83)</td>
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<tr>
<td>Average Ki67 index (%)</td>
<td>8.1 (3-20)</td>
<td>40 (24-80)</td>
<td>74 (50-98)</td>
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<td></td>
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<td></td>
<td>66 (40-95)</td>
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WD PanNET with high Ki-67 index

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<tr>
<th></th>
<th>G2 WDNETs (n=53)</th>
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<th>PDNEC (n=43)</th>
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<tbody>
<tr>
<td>Median survival (mos)</td>
<td>68 (51.8-93.8)</td>
<td>54 (30.5-117.9)</td>
<td>11 (6-18)</td>
</tr>
</tbody>
</table>

WD PanNET with high Ki-67 index

Predictive and prognostic factors for treatment and survival in 305 patients with advanced gastrointestinal neuroendocrine carcinoma (WHO G3): The NORDIC NEC study


Grade 3 NECs that have <55%
  - Much worse (P<0.001) response to chemotherapy (cisplatin) but better (P<0.001) survival

Grade 3 NECs that have ≥55%
  - Better response to chemotherapy (cisplatin) but comes back quickly

Annals oncol 2013;24:152-160
WD PanNET with high Ki-67 index

Suggest the current G3 (>20% Ki-67 proliferation index) contains two distinct types of tumor and can be further separated into

- Well-differentiated PanNET with an increased proliferation index

- Poorly differentiated neuroendocrine carcinoma

WD PanNET with high Ki-67 index

Diagnosis: Well differentiated pancreatic neuroendocrine tumor with an increased (>20%) Ki67 proliferation index (See Note)

Note: A mitotic count reveals XX per mitoses /10 high-power fields and a Ki67 stain shows a proliferative rate of XX%. This proliferation rate would place the neuroendocrine tumor into the WHO 2010 Grade 3 (i.e. neuroendocrine carcinoma) category. However, morphologically, the tumor appears to be well differentiated. The overall appearance suggests that the tumor is best interpreted as a well differentiated neuroendocrine tumor with increased proliferative rate. Preliminary studies suggest that these tumors may be associated with more aggressive clinical behavior; however, are still not as aggressive as bona fide poorly differentiated neuroendocrine carcinomas (i.e. small cell or large cell neuroendocrine carcinoma as defined in the lung).

Genetics of WD PanNET

• Lack alterations in genes involved in ductal neoplasia: *KRAS, CDKN2A, SMAD4 mutation, p53*, etc...

• Alterations in chromatin remodeling genes; *MEN1 (44%), DAXX OR ATRX (43%)*, which culminate in loss of corresponding protein expression

*Science 2011;331(6021):1199-1203*
Genetics of WD PanNET

• MEN1 inactivation (44%)
  – Previously known

• DAXX/ATRX mutation (43%)
  – DAXX (death-domain-associated protein, Chr 6p)
  – ATRX: thalassemia/mental retardation syndrome X-linked
  – Together form a complex
  – Both required for H3.3 incorporation in telomeres

• mTOR pathway (15%): PTEN (7.3%), TSC2 (8.8%), PIK3CA (1.4%)
PD PanNEC (G3)

PanNECs

- Very rare
- Non syndromic
- Mean age = 59
- Usually located in the head
- Median size = 4 cm

PD PanNEC (G3)

(Poorly Differentiated) PanNECs

Small Cell Type

Large Cell Type
Ki-67 index of NEC

The average Ki67 index

Large cell: 66% (40-95)

Small cell: 75% (50-98)

PD PanNECs

- **Share** some of genotypic alterations of conventional pancreatic ductal adenocarcinoma including **KRAS, p16, p53, CDKN1A, and SMAD4**
- **Lack** alterations in **MEN1, DAXX, or ATRX**
- **Common** **RB1** gene mutations and associated loss of Rb protein expression (89% of small cell, 60% of large cell type)
Practical approach to classification of G3 tumor

<table>
<thead>
<tr>
<th>Consensus</th>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
<th>Reviewer 3</th>
<th>Specimen Type</th>
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</tbody>
</table>
Neuroendocrine neoplasm

Typical Morphology

Ambiguous Case
# High-grade Neuroendocrine Neoplasm of Pancreas

## Table 2: Classification of High-grade Pancreatic Neuroendocrine Neoplasms by Secondary Evidence

<table>
<thead>
<tr>
<th>Initial Consensus</th>
<th>IHC Abnormalities</th>
<th>Ki67%</th>
<th>Other Histologic Components</th>
<th>Confirmed Classification</th>
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<tbody>
<tr>
<td>WD-NET</td>
<td>DAXX</td>
<td>50</td>
<td>G1/G2 WD-NET</td>
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<tr>
<td>WD-NET</td>
<td>ATRX</td>
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<td>G1/G2 WD-NET</td>
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<tr>
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<td>DAXX</td>
<td>50</td>
<td>G1/G2 WD-NET</td>
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<tr>
<td>WD-NET</td>
<td>DAXX</td>
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<td>G1/G2 WD-NET</td>
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<td>WD-NET</td>
<td>DAXX</td>
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<td>WD-NET</td>
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<td>38</td>
<td>G1/G2 WD-NET</td>
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<td>60</td>
<td>G1/G2 WD-NET</td>
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<td>70</td>
<td>G1/G2 WD-NET</td>
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<tr>
<td>Ambiguous</td>
<td>p53/Rb</td>
<td>88</td>
<td>Ductal adenocarcinoma</td>
<td>PD-NEC</td>
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<tr>
<td>Ambiguous</td>
<td>p53/SMAD4</td>
<td>38</td>
<td>Ductal adenocarcinoma</td>
<td>PD-NEC</td>
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<tr>
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<td>70</td>
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<td>PD-NEC</td>
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<td>85</td>
<td>Ductal adenocarcinoma</td>
<td>PD-NEC</td>
</tr>
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<td>60</td>
<td>Ductal adenocarcinoma</td>
<td>PD-NEC</td>
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<td>p53</td>
<td>70</td>
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<td>PD-NEC-LCC</td>
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<tr>
<td>PD-NEC-LCC</td>
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<td>Ductal adenocarcinoma</td>
<td>PD-NEC</td>
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<td>PD-NEC</td>
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<td>PD-NEC-LCC</td>
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<td>PD-NEC-LCC</td>
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<td>90</td>
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<td>PD-NEC-LCC</td>
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<td>p53</td>
<td>88</td>
<td>Ductal adenocarcinoma</td>
<td>PD-NEC</td>
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</table>
Confidence Curve

Dunning-Kruger Effect

Unskilled and Unaware of It: How Difficulties in Recognizing One’s Own Incompetence Lead to Inflated Self-Assessment.

Nobel Prize Psychology 2000
IHC profile of G3

Loss of RB, SMAD4: PD PanNEC
Loss of ATRX/DAXX: WD PanNET

-Am J Surg Pathol 2016;40:1192-1202-
Diagnostic algorithm for Pancreatic high-grade neuroendocrine neoplasms

High grade features in a neuroendocrine neoplasm
(Tumor necrosis, increased mitotic activity >20/10 HPF, high Ki67 index >20%)

Thorough examination of additional pathology material

A component of lower grade (WHO G1/G2) WD-NET;
Prior lower grade WD-NET in another specimen

A component of conventional adenocarcinoma or
squamous cell carcinoma

Ancillary Immunohistochemical studies

Loss of DAXX or ATRX expression

Loss of Rb or abnormal p53 expression

WD-NET G3

PD-NEC

Clinical Information

Incidental finding without high grade malignancy associated symptoms
Elevated plasma neuroendocrine markers (Chromogranin-A)
Diffuse avidity on Octreotide Scintigraphy

High grade malignancy associated symptoms
Elevated plasma carcinoma markers (CEA, CA19.9, CA 125ect)
Negative or weak and focal activity on Octreotide Scintigraphy

## Pancreas Neuroendocrine Neoplasms

<table>
<thead>
<tr>
<th>WD PanNET</th>
<th>PD PanNEC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No</strong> KRAS, CDKN2A, SMAD4 mutations, except rare (~4%) p53</td>
<td><strong>KRAS, CDKN2A, SMAD4 and P53 mutation</strong></td>
</tr>
<tr>
<td>Often have MEN1, DAXX or ATRX mutations</td>
<td><strong>No</strong> MEN1, DAXX, ATRX mutations</td>
</tr>
<tr>
<td><strong>No</strong> RB1 mutation</td>
<td>Common RB1 mutation</td>
</tr>
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</table>
## WHO Neuroendocrine Neoplasm Grading Classifications

<table>
<thead>
<tr>
<th>WHO 2010</th>
<th>WHO 2017 (in press)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroendocrine tumor (NET) G1/G2</td>
<td>NET G1/G2/G3 (WD neuroendocrine neoplasm)</td>
</tr>
<tr>
<td>Neuroendocrine carcinoma (NEC) G3</td>
<td>NEC G3 (PD neuroendocrine carcinoma)</td>
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<tr>
<td>Mixed neuroendocrine carcinoma (MANEC)</td>
<td>Mixed neuroendocrine-nonneuroendocrine neoplasm (MiNEN)</td>
</tr>
</tbody>
</table>
Somatostain receptor in NET
Possible algorithm for treatment approach in patients with GEP-NETs

GEP NETs

Localized GEP NETs

Curative surgery

Follow-up ± adjuvant SSAs

Advanced GEP NETs

GEP NETs G3

Platinum-based Chemotherapy ± adjuvant SSAs

Progressive Disease

Temozolomide-based combinations, FOLFIRI, PRRT (7) etc.

GEP NETs G1&G2

Stable & Asymptomatic

Follow-up (3-6 m, with clinical, biochemical and radiological evaluation)

Progressive/Symptomatic Disease

Positive uptake on SRS/Ga68-DOTATOC/DOTATATE-PET-CT

SSAs + Follow-up every 3 m

Progressive Disease

Negative uptake on SRS/Ga68-DOTATOC/DOTATATE-PET-CT

SSAs (dose escalation; consider also in SRS negative patients); PLUS:
(based on tumor origin and characteristics)

Chemoembolisation, RFA
Liver debulking surgery (in patients with liver predominant disease)

Biological therapies (everolimus, sunitinib, bevacizumab, interferon, etc.), clinical trials

PRRT

Chemotherapy (SFU+STZ/CAPTEM)

Telotristat ethyl (in patients with uncontrolled carcinoid syndrome)
KOPANA

• Korean Pathologists Association of North America before USCAP

• Since 2001 (1st) ~ 2018 (17th)

• 1st day (Thu): Ice-Breaker

• 2nd day (Fri): Seminar (one day)

• 3rd day (Sat): Seminar (half-day) & Annual dinner
KOPANA Seminar

2001 (1st)

1st Spring Seminar of the Korean Pathologists Association of North America

with
Jae Y. Ro, MD
Professor
MD Anderson Cancer Center
Houston, Texas

1) Precursors and early detection of prostate cancer: Recent advances.
2) Distinguishing features of seminoma and non-seminomatous germ cell tumors.
3) Classification and prognostic factors of bladder cancers

March 1-3, 2001
Renaissance Pinesle Resort
Lake Lanier, Georgia

For Further Information
Kyu Y. Lee, MD
General Secretary / Treasurer
The Korean Pathologists Association of North America
Department of Pathology
The University of Kentucky
Lexington, KY 40539
Phone: 859-323-069, FAX: 859-323-0694, kyono@pop.uky.edu

2003 (2nd)

2nd Spring Seminar of the Korean Pathologists Association of North America

Soonyoung Park, MD, PhD
Director, Division of Pathology
National Surgical Adjuvant Breast Project (NSABP)

"Update on HER-2/neu testing and Herceptin clinical trials for breast cancer"

Sandra Shin, MD
Assistant Professor
Breast Consultation Service
Cornell University Hospital

"E-cadherin and lobular carcinoma of the breast"
"Uncommon lesions of the breast"
"Needle core biopsies of the breast"

Registration Fee: $100

March 20-22, 2003
Summerfield Suites by Wyndham Dulles
Herndon, Virginia

For Further Information
Kyu Y. Lee, MD
General Secretary / Treasurer
The Korean Pathologists Association of North America
Department of Pathology
The University of Kentucky
Lexington, KY 40539
Phone: 859-237-5419, FAX: 859-237-2094, kyono@uky.edu
KOPANA Seminar

2004 (3rd)

3rd Spring Seminar
of the
Korean Pathologists Association
of North America

Min Woo Lee, MD
Henry Ford Hospital

"Neuroendocrine tumor of lung"

Jae Yun Ro, MD, PhD
Joong Ang (Asan) Medical Center

"Practical update on lung cancer"
"New version of AJCC cancer staging system"

Eunhee Yi (Suh), MD
University of California, San Diego

"Practical update on non-neoplastic lung disease"

Megan Lim, MD, PhD
University of Utah Health Sciences Center

"Diagnostic approach of lymphoma for general surgical pathologists"

Registration Fee: $150

March 4-6, 2004
Vancouver Airport Conference Resort
Richmond, B.C., Canada

2005 (4th)

4th Spring Seminar
of the
Korean Pathologists Association
of North America

Dae Young Kang, MD, PhD
Chungnam National University

"Selected topics for liver pathology"

Grace Kim, MD
University of California, San Francisco

"Selected topics in GI and liver pathology"

Eun Young Lee, MD
University of Kentucky

"Selected topics in GI and liver pathology"

Registration Fee: $150

February 24-26, 2005
San Antonio Hawthorn Suites LTD
San Antonio, Texas
KOPANA Seminar

2006 (5th)

5th Spring Seminar of the Korean Pathologists Association of North America

Geung Hwan Ahn, MD
Samsung Medical Center
“Ovarian borderline tumors”
Kathleen R. Cho, MD
University of Michigan
“Molecular analysis of gynecological cancers”
Kyu Rae Kim, MD
Asan Medical Center
“Practical guideline of placental examination and its clinical relevance”
“Interpretation of non-neoplastic endometrial disease”

Registration Fee: $150
February 9-11, 2006
AmeriSuites Downtown
Atlanta, Georgia

2007 (6th)

6th Spring Seminar of the Korean Pathologists Association of North America

“Dermatopathology for General Pathologists”

Min Woo Lee, MD
Henry Ford Hospital, Detroit, Michigan
“Overview of rashes from pathologists perspective: Are they all same rashes with different names?”

Luke Chung, MD
AFIP, Washington, D.C.
“Cutaneous adnexal tumors: Cardinal dermatopathology, not adnexal dermatopathology”

Hee Kim, MD
Eastern Dermatology-Pathology, Greenville, North Carolina
“Melanocytic lesions: Searching for the light from darkness”

Albert Kim, MD
Kent Pathology Laboratory, Grand Rapids, Michigan
“Cutaneous spindle cells lesions: Do you know how to spin the spindle?”

Registration Fee: $150
March 22-24, 2007
The Bristol Hotel
San Diego, California
KOPANA Seminar

2008 (7th)

7th Spring Seminar
of the
Korean Pathologists Association
of North America

"Bone and Soft Tissue Tumors"

Jae Yun Ro, MD
Methodist Hospital, Houston, Texas
"General considerations of soft tissue sarcomas"

Joon Hyuk Choi, MD
Yeungnam University, Daegu, Korea
"Diagnostic approach of soft tissue tumors"

Yong Koo Park, MD
Kyung Hee University, Seoul, Korea
"Radiologic and pathologic correlation of the bone tumors and tumorous lesions"

Yeongju Dancer, MD
Methodist Hospital, Houston, Texas
"FNA of bone and soft tissue tumors"

Registration Fee: $150
February 28 – March 1, 2008
The Brown Palace Hotel
Denver, Colorado

2009 (8th)

8th Spring Seminar
of the
Korean Pathologists Association
of North America

"BREAST CANCER"

Soonmyung Paik, MD
Director of Pathology, NSABP, Pittsburgh, PA
"Prediction of response to systemic therapy for breast cancer"

Sandra Shin, MD
Weill Cornell Medical College, New York, NY
"Diagnosis and associated pitfalls in needle core biopsies of the breast"

Gyung Yub Gong, MD
Asan Medical Center, Seoul, Korea
"Prognostic and predictive factors in breast cancer"

Young Kyung Bai, MD
Yeonghnam University, Daegu, Korea
"Molecular classification of breast cancer"

"Special Lecture"

Eric E. Walk, MD
Senior VP & Chief Medical Officer, Ventana Medical Systems, Inc.
"The role of pathologists in the era of personalized medicine"

Registration Fee: $150
March 5-7, 2009
The Midtown Hotel
Boston, Massachusetts
KOPANA Seminar

2010 (9th)

9th Spring Seminar of the
Korean Pathologists Association of North America

“Gastrointestinal and Liver Tumors”

Young Nyun Park, MD, PhD
Yonsei University College of Medicine, Seoul, Korea
“Pathological diagnosis of dysplastic nodule and early RCC: new pathology criteria and molecular signatures”

Kyoung Mee Kim, MD, PhD
Sungkyunkwan University School of Medicine, Seoul, Korea
“Pathology and adenocarcinoma of gastroesophageal junction”

Gyeong Hoon Kang, MD, PhD
Seoul National University College of Medicine, Seoul, Korea
“Molecular classification of colon cancer”

Seung-Mo Hong, MD, PhD
Johns Hopkins Medical Institutions, Baltimore, Maryland
“Update on pancreatic cancer and precursor lesions”

Jason Y. Park, MD, PhD
Johns Hopkins Medical Institutions, Baltimore, Maryland
“Molecular testing in gastrointestinal and pancreatic cancer”

Registration Fee: $150
March 18-20, 2010

The Churchill Hotel
1914 Connecticut Avenue, NW
Washington, DC 20009
Tel: 202-797-2000, Fax: 202-328-1984

2011 (10th)

10th Spring Seminar of the
Korean Pathologists Association of North America

“Pulmonary Pathology”

Jae Y. Ro, MD, PhD
Methodist Hospital/Cornell University, Houston, Texas
“Pathologist’s role in multidisciplinary team approach on lung cancer”

Kun Young Kwon, MD, PhD
Keimyung University, Taegu, Korea
“Interpretation of lung biopsy”

Eun Hee Yi (Suh), MD
Mayo Clinic, Rochester, Minnesota
“Pathology of non-neoplastic lung lesions”

Seon Hee Jung, MD, PhD
Wonju College of Medicine, Yonsei University, Wonju, Korea
“Pathology of mesothelioma; recent advances”

Se Jin Jang, MD, PhD
Asan Medical Center/Ulsan University, Seoul, Korea
“Molecular pathology of lung cancer”

Registration Fee: $150
February 24-26, 2011

Hyatt Place San Antonio Riverwalk Hotel
601 S. St. Mary’s Street
San Antonio, TX 78205
Tel: 210-227-6854, Fax: 210-227-1247
KOPANA Seminar

2012 (11th)

11th Spring Seminar of the Korean Pathologists Association of North America

“GU Cancers”
Thomas Lee, MD, PhD
CellNetis Pathology, Seattle, Washington
“Recent Advances in prostate pathology and ISUP consensus”

Ghee Young Kwon, MD, PhD
Samsung Medical Center, Seoul, Korea
“Recent Advances in urinary bladder tumors”

Ghil Suk Yoon, MD, PhD
Kyungpook National University, Daegu, Korea
“Molecular pathology in GU tumors for general surgical pathologists”

Yong Mee Cho, MD, PhD
Asan Medical Center, Seoul, Korea
“Recent Advances in kidney tumors”

Jae Y. Ro, MD, PhD
Methodist Hospital/Cornell University, Houston, Texas
“Prognostic factors and pathologist’s role in modern targeted therapy for GU cancer”

Jeri Kim, MD
Department of Genitourinary Medical Oncology
MD Anderson Cancer Center, Houston, Texas
“What do clinicians need from pathologists?”

Registration Fee: $150
March 15-17, 2012
Days Inn Vancouver Downtown
921 West Pender Street
Vancouver, BC Canada V6C 1M2

2013 (12th)

12th Spring Seminar of the Korean Pathologists Association of North America

“GYN Pathology”
George G. Ahn, MD, PhD
University of San Francisco, California
“Practical Issues in Ovarian Pathology”

Kathleen R. Cho, MD
University of Michigan, Michigan
“Ovarian Cancer Pathogenesis: Insights from Morphology, Molecules, and Mice”

Sang Ran Hong, MD, PhD
Chul General Hospital & Women’s Health Care Center, Seoul, Korea
“Practical Issues in Endometrial Pathology”

Grace Kim, MD
University of San Francisco, California
“Diary of Intrauterine Life”

Insun Kim, MD, PhD
Korea University, Seoul, Korea
“Endometriosis-related Disorders”

Kyu-Rae Kim, MD, PhD
Asan Medical Center, Seoul, Korea
“Gestational Trophoblastic Diseases”

Kay J. Park, MD
Memorial Sloan Kettering Cancer Center, New York
“Cervical Adenocarcinoma, a Heterogenous Entity”

Registration Fee: $150
February 28 - March 2, 2013
Hampton Inn & Suites Baltimore Inner Harbor
131 East Redwood Street, Baltimore, MD 21202
KOPANA Seminar

2014 (13th)

13th Spring Seminar of the Korean Pathologists Association of North America

“Breast Pathology”
Sophia Apple, MD
University of California Los Angeles, Los Angeles
“Fibroepithelial lesions and stromal tumors of breast”

Gyung Yub Gong, MD, PhD
Asan Medical Center (University of Ulsan College of Medicine), Seoul
“In situ breast carcinomas (ductal and lobular)”

Woo Hee Jung, MD, PhD
Yonsei University, Seoul
“Invasive carcinomas and important variants”

Soomyung Paik, MD
NASBP, Pittsburgh & Yonsei University, Seoul
“Prognostic/predictive markers and cancer genome atlas (TCGA) in breast cancer”

Jae Y. Ro, MD, PhD
Methodist Hospital/Weill Medical School of Cornell University, Houston
& Ewha Womans University, Seoul
“Pathologist’s role in multidisciplinary team approach in breast cancer” and “Routines and beyond routines by pathologist”

Sandra Shin, MD
Weill Cornell Medical College, New York
“Benign mimics of malignancy in breast pathology”

Registration Fee: $150
February 27 - March 1, 2014
Hampton Inn San Diego Downtown
1531 Pacific Highway, San Diego, CA 92101

2015 (14th)

14th Spring Seminar of The Korean Pathologists Association of North America

“GI, Liver, & Pancreaticobiliary Pathology”
Seung-mo Hong, MD, PhD
Asan Medical Center, Seoul, Korea
“Recent updates of gastrointestinal and pancreaticobiliary neuroendocrine tumors”

Kee-Tae Jang, MD, PhD
Samsung Medical Center, Seoul, Korea
“The concept of tumoral intraepithelial neoplasia of biliary tract and gallbladder”

Gyeong-hoon Kang, MD, PhD
Seoul National University, Seoul, Korea
“Clinicopathological and prognostic features of CIMP and/or MSI-high colorectal cancer”

Grace Kim, MD
UC San Francisco, San Francisco, California
“Hepatic adenoma & FNH”

Hwa-jeong Lee, MD
Albany Medical College, Albany, New York
“Inflammatory bowel disease”

Do-young Park, MD, PhD
Pusan National University, Pusan, Korea
“Practical points in gastric pathology-cases and controversies”

Jason Park, MD, PhD
UT Southwestern, Dallas, Texas
“Advanced molecular diagnostics in gastrointestinal pathology”

Kunsil Yoo, MD, PhD
Asan Medical Center, Seoul, Korea
“Histopathological and molecular classification of hepatocellular carcinoma”

Registration Fee: $150
March 19-21, 2015
The Midtown Hotel
220 Huntington Avenue, Boston, MA 02115
# KOPANA Seminar

## 2016 (15th)

15th Spring Seminar of The Korean Pathologists Association of North America

**“Pulmonary Pathology”**

**Jae Y Ro**, MD, PhD
Methodist Hospital/Weill Medical School of Cornell University, Houston, TX
“Changing role of pathologists on lung cancer diagnosis”

**Mee-Sook Roh**, MD, PhD
Dong-A University College of Medicine, Busan, Korea
“What is new in 2015 WHO book on Lung Cancers?”

**Jin-Haeng Chung**, MD, PhD
Seoul National University Bundang Hospital, Bundang, Korea
“Approach to biomarker testing of lung cancers; IASLC recommendation”

**Chi Young Ok**, MD
MD Anderson Cancer Center, Houston, TX
“Introduction to NGS technique and its application in MDACC”

**Yoon-La Choi**, MD, PhD
Samsung Medical Center, Seoul, Korea
“Current status of molecular pathology in Korea”

**Michael Roh**, MD, PhD
University of Michigan Health System, Ann Arbor, MI
“The utilization of fine-needle aspirates of lung cancer for molecular diagnostic testing”

**Lucia Kim**, MD, PhD
Inha University Hospital, Incheon, Korea
“Thoracic epithelial tumors; update in 2016”

**Sunhee Chang**, MD, PhD
Inje University Injoo Paik Hospital, Goyang, Korea
“The role of immunohistochemistry in the diagnosis of malignant mesothelioma”

**Joanne Eunhee Suh Yi**, MD
Mayo Clinic, Rochester, MN
“Interstitial lung disease and pulmonary vasculitides: update in 2016 with vignette cases”

Registration Fee: $150
March 10-12, 2016
Springhill Suites Marriott Seattle Downtown

## 2017 (16th)

16th Spring Seminar of The Korean Pathologists Association of North America

**“Recently described, clinically relevant entities”**

**Sunhee Lee**, MD
Albert Einstein College of Medicine Hospital
“CNS tumors: the new 2016 WHO classification”

**Won Woo Shon**, MD
Cedars Sinai Hospital
“Recently characterized soft tissue tumors and tumor-like lesions”

**Geon-gook Lee**, MD, PhD
National Cancer Center, Ilsan, Korea
“Recently described, clinically relevant entities in the lung & mediastium”

**Han Kyoom Kim**, MD, PhD
Korea University Ansan Hospital, Ansan, Korea
“Mummies”

**Stephen Koh**, MD
Kaiser Permanente
“Immunohistochemistry on melanocytic lesions”

**Michael Roh**, MD, PhD
University of Michigan Health System, Ann Arbor, MI
“The utilization of fine-needle aspirates of lung cancer for molecular diagnostic testing”

**Thomas Lee**, MD
UC Irvine Health School of Medicine
“New and Old Clinically Significant Lesions in the Gastrointestinal Tract”

**Kyung-Ja Cho**, MD, PhD
Asan Medical Center, Seoul, Korea
“Recent changes of classification of squamous intraepithelial lesions of the head and neck”

**Soo-Jin Cho**, MD, PhD
UC San Francisco
“What’s Old is New Again in the GI Tract - From the Mundane to the Exotic”

**Sung Sik Shin**, MD
Kaiser Permanente
“2016 WHO Lymphoma Classification”

**Michael Roh**, MD, PhD
Mayo Clinic Rochester
“Serous tubal intraepithelial carcinoma and pelvic serous carcinogenesis”

Registration Fee: $150
March 2-4, 2017
Hyatt Place San Antonio Riverwalk
The 17th KOPANA Seminar 2018

- Title: Critical review and appraisal of the latest AJCC and/or WHO classification
- Time: March 15 ~17
- Place: The Sutton Place Hotel, Vancouver, Canada
- Speakers: Jae Y. Ro, Sophia Apple, Young Hyeh Ko, Chan Kwon Jung, Yong Mee Cho, Kyu Rae Kim, Joon Hyuk Choi, Maria Westterhoff, Won Tak Choi, Kee-Taek Jang, Jin Haeng Chung
- Trainee presentation: Christopher Bowman, Hayeon Kim, Sang Joon Choi
How about Japan & China?

Japan Night
IAP Japanese Division
USCAP Annual Meeting,
March 4-10 2017

Tuesday 7th March, 2017
17:30-19:30
Presidio C, Floor 3, Grand Hyatt San Antonio
San Antonio, TX, USA

Canapés/ Cash Bar: Entrance fee: $60.00
No reservation is required
For more information, please contact:
Tokyo Office, Japanese Division of the IAP
Tel: +81-50-5274-8683 Email: tokyo.office@iapjapan.org
On site contact: +81-90-9956-6576 (Dr. Matsubara)

CAPA eNewsletter
CHINESE AMERICAN PATHOLOGISTS ASSOCIATION
～全美华人病理学会～
VOLUME 5 ISSUE 1 2017

The President’s Message

Dear CAPA Members:

It is my great honor and privilege to serve you as the CAPA president for 2017-2018. Since its establishment in 1967, and with continuous and collective efforts from our past presidents, officers of all subcommittees, and all active members, CAPA has become a national and internationally recognized pathology organization with about 750 members today.

CAPA consists of a very broad membership as both academic and private practice, in both Anatomic Pathology and Clinical Pathology, with both “experienced” and “young” pathologists. As a group, we are extremely accomplished, with many nationally and internationally known pathologists and trained physicians in major medical centers. We have members serve as Department Chairs and Directors for academic pathology in top US/Canadian universities, directors for residency fellowship programs across the country, and directors/business owners in various settings of private practices.

The 95 members of CAPA is to serve our members. As we move forward, I will work with the past president Dr. Seng, the president-elect Dr. Gong, current and newly elected officers, EC members, all subcommittees, and all members towards the following goals and CAPA events for 2017-2018:

Education
1) The 1st CAPA Diagnostic Pathology Course (Chicago, August 19-20, 2017)
2) The 2nd CAPA Beijing Pathology Symposium (Beijing, September 2-3, 2017)
3) The third CAPA Companion Meeting at 2017 CAP (National Harbor, October 7-11, 2017)
4) The first CAPA Pathology Symposium in

Publication
1) To improve our website and create a member-only domain
2) To continue our quarterly newsletters with news from all of our members.

Other Messages
1) To re-organize CAPA subcommittees with special mentoring subcommittee for our junior members and chapters for each subcommittee.
2) To work with national and international pathology societies, including subspecialty pathology societies, and promote bigger role of our members in these societies.
3) To continue grow with new members and more sponsorships. Together, anything is possible. Let’s get to work.

Ping Ting, MD, PhD
CAPA President 2017-2018
Professor and Director of Hematopathology
University of Rochester Medical Center
Rochester, NY
The CAPA Annual Report 2016-2017 (Cont’d)

CAPA-Motic Best Abstracts Award

FIRST PLACE PRIZE
Shanmugaratnam et al. Peeking Union Medical College, Cancer Hospital, Chinese Academy of Medical Sciences, Beijing. The Use of a Molecular Hybridization Method Detecting Next Generation Sequencing

SECOND PLACE PRIZE
Jie Sun et al. Department of Pathology, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing. A Novel Method for the Detection of Colorectal Carcinoma

THIRD PLACE PRIZE
Jia Li et al. Department of Pathology, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing. The Use of a Novel Method for the Detection of Colorectal Carcinoma

Third China-US Pathology Symposium (Cont’d)

Hot Topics Session I
Moderators: Dr. Xi-Yun Du (Fudan University Cancer Center) Dr. Ping Tang (University of Rochester Medical Center)
8:35 - 9:00 Cardiac stem cells may lead to cardiac repair post myocardial infarction Dr. Guoping Wang (Tsinghua Medical College, HUST)
9:00 - 9:25 Infectious diseases: cancer-based presentation and review of immunohistochemistry Dr. Fang Liu (Genomics Medical Center)
9:25 - 9:50 Current status and progress of the basic and clinical research of colorectal cancer in China Dr. Li Liang (Southern Medical University)
9:50 - 10:15 IEC working algorithms for ENT pathology: a case-based approach Dr. Beverly Wang (UC Irvine)
10:15 - 10:30 Break

Hot Topics Session II
Moderators: Dr. Guoping Wang (Tsinghua Medical College, HUST) Dr. Ling Zhang (Princeton Healthcare System/Rutgers University)
10:30 - 10:55 Current status and problems of the pathology quality-control in China Dr. Zhi Chen (Peking Union Medical College)
10:55 - 11:20 Managing an academic department of pathology: How do young faculty prepare for it? Dr. Jiaping Huang (Duke University Medical Center)
11:20 - 11:45 Precise pathology guides next generation of pathology Dr. Xia-Wu Bian (Southeastern Hospital, Third Military Medical University)
11:45 - 12:10 Molecular / genomic alterations in lymphoma / leukemia - Brief review and practice applications Dr. Hsiung-Yun Wang (UC San Diego)
12:10 - 12:30 Break

Case Discussions (12:30-13:30)
Moderators: Dr. Ji Chen (Peking Union Medical College) Dr. Yan Gong (University of Texas MD Anderson Cancer Center)
Case #1: Peking Union Medical College, Chinese Academy of Medical Sciences
Case #2: Tsinghua Medical College, Huazhong University of Science & Technology
Case #3: Shanghai Cancer Center, Fudan University
Case #4: West China Hospital, Sichuan University
Case #5: Southeastern Hospital, Third Military Medical University

Program chairs: Drs. Xin-Wu Bian and Hsiung-Yun Wang
Executive chairs: Drs. Xi-Yun Du and Ling Zhang
Advisors: Drs. Ji Chen and Jiaping Liu
8:00 - 11:30 Registration (No registration fee)
11:30 - 11:45 Introduction and Welcome by Drs. Dr. Xin-Wu Bian (Southeastern Hospital, Third Military Medical University) and Hsiung-Yun Wang (University of Texas MD Anderson Cancer Center)

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CAPA AWARDs

CAPA Honorary Award: Dr. Lin is a well-known pathologist in China specialized in neoplastic pathology and molecular pathology. Dr. Lin successfully organized and served as the director of the First and Second joint CAPA-Beijing Pathology Seminars in Beijing and partially sponsored many CAPA speakers to three seminars in 2017 and 2016. Both meetings included many expert pathologists from China as speakers and provided a unique platform to promote the communications and collaborations between CAPA and the pathology community in China. Dr. Lin is currently planning for the 3rd CAPA Beijing Pathology Summit with CAPA, which will be held in Beijing in September, 2017.

The CAPA-ACD Distinguished Pathologist Award: Dr. Jinlian Guo and Dr. Qilin “Jim” Zhai are the recipients of this award. Congratulations to Dr. Guo and Dr. Zhai.

Dr. Jinlian Guo is a Professor and Chairman of the Department of Pathology at Peking University. He earned his medical degree from Anhui Medical University. Master degree from the Institute of Preventive Medicine in Beijing and PhD from New York University School of Medicine. Dr. Guo has been a Professor at the University of Rochester since 2007 and is the director of the Department of Pathology at the University of Rochester since 2012. Dr. Guo is a renowned pathologist with over 20 years of experience in the field of renal pathology. His research focuses on the molecular mechanisms of kidney disease and the development of new therapeutic approaches. He is also a member of the American Society of Nephrology and the American Society for Investigative Pathology. Dr. Guo is the recipient of several prestigious awards, including the National Institutes of Health (NIH) Merit Award and the American Society for Investigative Pathology (ASIP) Distinguished Scientist Award. He has published over 200 research papers and is a highly cited researcher in the field of kidney disease.

Dr. Qilin “Jim” Zhai is a professor of pathology, consultant pathologist and director of the Pathology Laboratory in Mayo Clinic Florida. He completed his pathology residency at Mayo Clinic Rochester (1982) followed by an oncology pathology fellowship at MD Anderson Cancer Center (2002-2003). He joined BayCare Health System as assistant professor (2003), then Houston Methodist Hospital/Cornell University as associate professor (2004-2009), and was recruited to University of California in 2010. He has a broad range of interests in molecular pathology and is currently the director of the Pathology and Immunology core of the Cancer Research Institute.

The CAPA-Ben-Gas Outstanding Service Award

Dr. Likuan Qin is the winner of this traditional award. Dr. Qin is a staff pathologist at Northwest Arkansas Pathology and Laboratory Associates. He is the director of the Douthro Microscope WeChat group, which has 173 active members and serves as a popular online community for the Chinese pathologists in North America. Dr. Qin served as a member of the CAPA Executive Committee and chaired the CAPA-ACD Regional Meeting in 2015. He has also served as the chair of the CAPA annual dinner and the dinners during both pathology courses, which have been outstanding events for CAPA. Congratulations to Dr. Qin!
Summary

• Neuroendocrine neoplasms of GI and pancreas
  ➢ Mitosis and/or Ki-67 index are important but still limitation of interobserver variability/reproducibility
  ➢ Manual count in printed photo may be practical (cost-effective)
  ➢ WD neuroendocrine tumor may show G3
  ➢ IHC panel: p53, Rb, DAXX, ATRX
  ➢ Molecular profiles of WD vs. PD PanNEC are different
Thanks for Attention!