

Cover:

Designed by Dr KWOK Ka Ki, in memory of Dr BEH Swan Lip, Philip

College Secretary:

Ms Dilly Yip

Tel: 2871 8756 Fax: 2871 8755

Email: hkcpath@hkcpath.org

Homepage:

http://www.hkcpath.org/



Address: College Chamber, Rm. 606, 6/F, HKAM Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong.

Facebook:

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Message from the President

As I reach the midpoint of my term of presidency, I wish to take a moment to reflect on our progress and share some of our priorities and upcoming initiatives. This is a time for us to celebrate our achievements and to look ahead with renewed focus.

First of all, following the return of normalcy in Hong Kong, the College has now reestablished connections with overseas sister Colleges and professional bodies through the platform of the International Liaison of Pathology Presidents (ILPP) and the Hong Kong Academy of Medicine (HKAM). This year, we will continue to collaborate with overseas sister Colleges of Pathologists and professional bodies, to share the difficulties and challenges ahead and to foster a collaborative effort in managing the turbulence in our profession.

Apart from the regular educational activities and the annual examination, I would like to highlight two initiatives newly introduced by the College: the electronic examination platform and the well-being programmes.

The introduction of the electronic examination platform aligns with the initiatives first presented in the last President's speech at the Conferment Ceremony, namely, Green Pathology. As we step into 2025, the College is committed to evolving the landscape of our examination. I am excited to share our dedication to enhancing the examination experience through the adoption of the electronic examination format. This transition represents not only a technology advancement in examinations, but also a significant step toward fostering a more inclusive and efficient learning environment.



We understand that transitioning to an electronic examination format may present challenges, but we are committed to providing the necessary support and resources. Development of training sessions will be considered for our candidates and examiners to ensure everyone is comfortable with the new system. We encourage open communication and feedback throughout this process, as your valuable input is essential to the success of this initiative. A pilot scheme will be rolled out this year, and the experience will be shared in an appropriate platform to facilitate the phased implementation of the electronic examination platform across various specialties.

Furthermore, the College is also committed to enhancing the mental health of our Fellows, Members and Associates via introducing well-being programmes. The first programme is a complimentary hand building pottery workshop offered to our members. I would like to take this opportunity to thank the Chairman and the members of the Professional & General Affairs Committee (PGAC). Without their invaluable contributions, the successful organization of this workshop would not have been possible. I hope the participants will find this well-being activity enjoyable and rewarding.

As we move forward, I encourage each of you to stay engaged and share your ideas. Your feedback on both the electronic examination platform and the well-being programmes is essential to motivate us. I look forward to seeing you all at upcoming well-being programmes, educational activities and the College's annual event.



Dr MAK Siu Ming President June 2025

President's Activities



President's duty visiting Kuala Lumpur for International Liaison of Pathology Presidents (ILPP) 2025 from 21 – 23 July 2025



HKCPath dinner with RCPA in the evening on 17 July 2025

From left to right (sitting): Dr Trishe LEONG (RCPA President), Dr MAK Siu Ming (HKCPath President), Dr Linda ILES (RCPA Visiting Professor), Dr Daniel OWENS (RCPA Vice President)

President's Hong Kong Academy of Medicine activities



Inaugural Ceremony for the Establishment of Jockey Club Institute for Medical Education and Development (JCIMED) on 27 November 2024



31st Annual General Meeting on 6 December 2024



31st Annual Fellowship Conferment Ceremony and 2024 David Todd Oration on 6 December 2024



Media Spring Luncheon on 11 February 2025



Strategic Planning Retreat on 1 March 2025

President's Local Activities

Career Talk on 2025/26 HA Resident Training Program on 30 November 2024





Sharing by
President in
Implementation
of Digital
Pathology in
Hong Kong:
Where are we?
on 17 January
2025

A Seminar on Sudden Infant Death by Professor Roger BYARD on 16 May 2025





Mindful Creations: A Handbuilding Pottery Workshop on 22 June 2025



HKAM Officers visiting HKCPath Council on 30 June 2025

Obituary

Dr Philip Beh

Dear Fellows, Members and Associates,

We are deeply saddened to inform you of the passing of Dr BEH Swan Lip, one of our College's Founder Fellows and a towering figure in Forensic Pathology in Hong Kong.

Dr Beh was born in Malaysia in 1957. He graduated from The University of Hong Kong in 1981, obtained his Diploma in Medical Jurisprudence (Clinical and Pathology) in 1988, and was admitted Founder Fellow in Forensic Pathology of the College in 1991. After working as Forensic Pathologist and Senior Forensic Pathologist in the Department of Health, Dr Beh joined the Department of Pathology, The University of Hong Kong in 1995, where he taught for three decades and inspired many generations of medical students with his passion in forensic medicine.

Beyond academia, Dr Beh was a visionary advocate for vulnerable communities. He established RainLily, Hong Kong's first crisis centre to provide support services for female victims of sexual violence. Professionally, he was a distinguished forensic pathologist and served as expert witness in many challenging cases. He also worked with international organizations including International Red Cross and United Nations Office of Drugs and Crime.

Dr Beh served numerous positions in the College, including Chief Examiner in Forensic Pathology, member of the Credentials and Appeals Committee, Professional and General Affairs Committee, Specialty Board in Forensic Pathology, as well as the Laboratory Inspection Team in Forensic Pathology. He also held prestigious positions including President of the World Police Medical Officers, Vice-President of the International Association of Forensic Sciences, President of the Hong Kong Forensic Science Society, and others.

Despite his distinguished professional accomplishments, Dr Beh has an easy-going and generous personality. Many of us still vividly remember his humorous lectures and workshops in the medical school, his charismatic media interviews, as well as an experienced connoisseur of fine wines.

Dr Beh is survived by his wife and two sons. He will be deeply missed by the medical profession and beyond, and may we honour Dr Beh's legacy by continuing his mission of medical education and serving the marginalized in our community. The College offers our heartfelt condolences to his family.

Dr MAK Siu Ming President The Hong Kong College of Pathologists



Dr Beh delivering a talk on development of Forensic Pathology in Hong Kong



Dr Beh serving as an examiner in Forensic Pathology during COVID-19 pandemic



Dr Beh serving as an examiner in Forensic Pathology



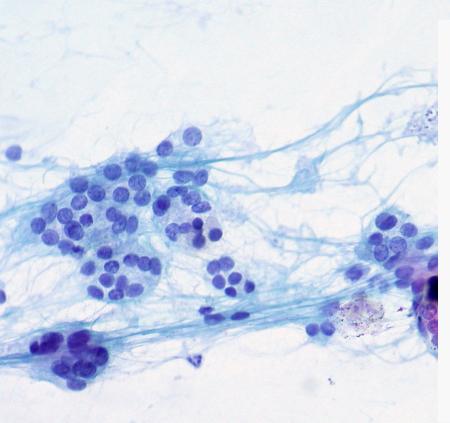
Dr Beh's trainee days in England



Dr Beh enjoying food with his friends/colleagues



Dr Beh and RainLily team



Editorial note:

With the release of the 5th edition of the WHO Classification of Tumours of Endocrine and Neuroendocrine Tumours and 3rd edition of the Bethesda System for Reporting Thyroid Cytopathology, major changes have been made in thyroid pathology and cytopathology. This topical update provides a review on selected new entities and changes in terminology in thyroid pathology, and updates to the Bethesda reporting system. We welcome any feedback or suggestions. Please direct them to <u>Dr Angela</u> Zaneta CHAN of Education Committee, the Kong College of Pathologists. Opinions expressed are those of the authors named individuals, and are necessarily those of the Hong Kong College of Pathologists.

Topical Update: Updates from the Thyroid WHO Classification and Bethesda System

Volume 20, Issue 1, Jan 2025 *The Hong Kong College of Pathologists, Incorporated in Hong Kong with Limited Liability*

Dr Angela Zaneta CHAN

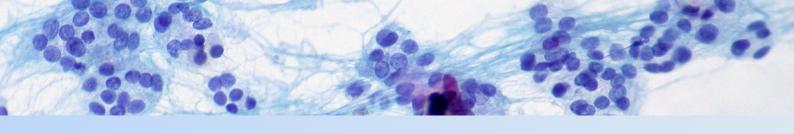
Department of Anatomical & Cellular Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong

All volumes of the WHO 5th edition have undergone major changes in terminology and volume structure, with an emphasis placed on taxonomy and cytogenesis. The thyroid gland represents the largest chapter in the latest 5th edition of the WHO classification of Endocrine and Neuroendocrine Tumours (2022). Thyroid tumours have been placed into several new categories to allow better understanding of the cell of origin, pathologic or molecular features, and biological behaviour. Newly recognized tumour types, subtypes and a grading system are included.

A third edition of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was released in 2023 and contains only minor updates, mainly to the AUS category and updated implied risk of malignancy (ROMs).

Follicular cell-derived neoplasms <u>Benign neoplasms</u>

In the 4th edition, follicular adenoma was the only single entity included under the "benign" category. The new classification now includes thyroid follicular nodular disease, follicular adenoma, follicular adenoma with papillary architecture, and oncocytic adenomas.



Thyroid follicular nodular disease (TFND)

This newly included entity corresponds to the multifocal hyperplastic/neoplastic lesions that commonly occur in the clinical setting of "multinodular goitre". Some studies have shown these nodules to be clonal, while some are hyperplastic [1-3]. The term TFND achieved consensus as the best to describe this enigmatic entity, and avoids defining this lesion as hyperplastic or neoplastic, in contrast to prior names such as "colloid nodules", "hyperplasia", "adenomatoid nodule", or the contradictory "adenomatous hyperplasia".

Follicular adenoma with papillary architecture

This was previously classified as hyperfunctioning adenoma within the category follicular adenoma, and is now a separate entity. These tumours are usually well-delineated and may have a distinct capsule. Histologic features include cystic change, intrafollicular complex papillary infoldings and formation of subfollicles within follicles. The lining cells lack nuclear features of papillary thyroid carcinoma (PTC). They are generally negative for HBME-1, Galectin-3 and BRAF p.V600E immunostains. There are often associated with TSHR (up to 70%) [4-6], GNAS and/or EZH1 mutations [7,8], unlike follicular adenomas which harbour RAS mutations.

Oncocytic adenoma of the thyroid

This is now a distinct entity in the latest classification and requires encapsulation, follicular-patterned tumours with >75% oncocytic cytology and lack of capsular or vascular invasion for diagnosis. The term "Hurthle cell" is discouraged as it is a misnomer. These tumours have distinct genomic alterations in the mitochondrial genome (mtDNA) [9,10].

Low-risk neoplasms

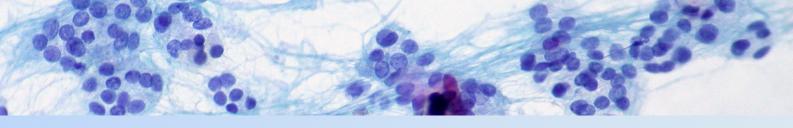
This new category was introduced in the latest classification. These are borderline tumours that are morphologically and clinically intermediate between benign and malignant tumours with an extremely low rate of metastasis. Three tumours fall into this category, namely non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), thyroid tumours of uncertain malignant potential (UMP) and hyalinizing trabecular tumour (HTT).

Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

The original criterion [11] of allowing less than 1% of true papillae from the 2017 WHO classification remains unchanged in the absence of BRAF V600E mutation [12], although there was debate about the percentage (0% vs 1%) of true papillae allowed. Previously, tumours \leq 1 cm and oncocytic tumours that fulfilled the histologic criteria of NIFTP were diagnosed as subtypes of PTC. They are now considered subtypes of NIFTP, as they behave similarly to NIFTP and show negligible risk of tumour recurrence and lymph node metastasis. A diagnosis of oncocytic NIFTP requires at least 75% oncocytic cells [13].

Thyroid tumours of uncertain malignant potential (UMP)

The definition of tumors of UMP remains unchanged, which is "well-differentiated thyroid tumors with follicular architecture that are encapsulated or unencapsulated but well-circumscribed, in which invasion remains questionable after thorough sampling and exhaustive examination".



There are 2 subtypes: (1) Follicular tumour of uncertain malignant potential (FT-UMP), which lacks PTC-like nuclear features (nuclear score of 0-1), and (2) Well-differentiated tumour of uncertain malignant potential (WDT-UMP), which has more pronounced nuclear features of PTC (nuclear scores of 2-3). If invasion has been thoroughly excluded, the term NIFTP should be used. The term "atypical adenoma" is not recommended.

Malignant neoplasms

Follicular thyroid carcinoma (FTC)

Diagnosis requires presence of capsular and/or vascular invasion. Apart from the lack of nuclear features of PTC, emphasis is placed on the lack of high-grade features and necrosis. When an FTC has areas of solid or trabecular growth, it is important to examine the mitotic count and presence of necrosis to exclude a diagnosis of poorly differentiated thyroid carcinoma (see section on PDTC). When an FTC with entirely follicular architecture has a mitotic count ≥ 5 per 2 mm², the tumor should be diagnosed as differentiated high-grade thyroid carcinoma (see section on DHGTC).

Invasive encapsulated follicular variant of papillary thyroid carcinoma (IEFVPTC)

This is distinguished from NIFTP solely by the presence of capsular and/or vascular invasion. Distinction from FTC is solely based on presence of nuclear features of PTC in IEFVPTC. Like FTC, it is subclassified into 3 groups: (i) minimally invasive (capsular invasion only), (ii) encapsulated angioinvasive (venous invasion +/-capsular penetration) and (iii) widely invasive. Encapsulated angioinvasive tumours are further divided into those with limited (<4 foci) or extensive (4 or more foci) vascular invasion. IEFVPTC has an identical genomic profile (RAS-like) and clinical behaviour to FTC [14,15].

Papillary thyroid carcinoma and subtypes

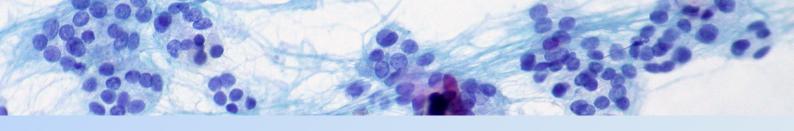
In the latest edition, molecular signature takes precedence over PTC nuclear features for diagnosis, and therefore only BRAF-like tumours are included in this category. IEFVPTC has been removed from this category and is now a distinct entity due to presence of RAS-like mutations [16].

The term "variant" has been replaced by "subtype" to remain consistent with other WHO tumour classification schemes, and to avoid confusion with the molecular diagnostic term "genetic variant(s)".

There are 13 histologic subtypes in total: classic, encapsulated classic, infiltrative follicular, diffuse sclerosing, solid/trabecular, tall cell, columnar cell, hobnail, clear cell, spindle cell, Warthin-like, oncocytic, and PTC with fibromatosis/fasciitis-like/desmoid-type stroma. Aggressive histologic subtypes include tall cell, columnar cell and hobnail PTCs.

Key points or changes of selected subtypes are highlighted as below:

- Infiltrative follicular: This is now the only PTC subtype with a follicular pattern. The "macrofollicular" variant is no longer considered a subtype.
- Tall cell: This is defined as cells whose height is at least three times their width (unlike two to three times in the previous edition), as well as having abundant eosinophilic cytoplasm and a prominent cell membrane. Tall cells should represent at least 30% or more of the PTC cells for diagnosis.
- Solid/trabecular: >50% solid, trabecular or nested growth pattern is required for diagnosis, unlike the "all or nearly all" cutoff in the previous edition.
- Diffuse-sclerosing: This subtype is no longer considered aggressive.



Previous subtypes/ variants that are no longer considered a subtype are:

- Macrofollicular: No longer considered a subtype.
- Cribriform-morular: No longer considered a subtype, and is listed under tumours of uncertain histogenesis.
- Papillary microcarcinoma: No longer considered a subtype, but should instead be subtyped by the histological pattern (such as classic papillary microcarcinoma, tall cell papillary microcarcinoma, etc.) as they can also display aggressive pathologic features and clinical behaviours [17-19].

High-grade follicular cell-derived non-anaplastic thyroid carcinoma

In the new classification, there are 2 groups of high-grade follicular cell-derived non-anaplastic thyroid carcinomas that have intermediate prognosis between well-differentiated carcinomas of follicular cells (papillary, follicular and oncocytic thyroid carcinoma) and anaplastic carcinoma. About 50% of these tumours will not take up radioactive iodine [20] and systemic therapy may be needed.

Poorly differentiated thyroid carcinoma (PDTC)

The diagnosis is based on Turin consensus criteria [21]: (i) presence of a solid/trabecular/insular pattern of growth in a tumour diagnosed as malignant based on invasive properties; (ii) absence of conventional nuclear features of papillary carcinoma; (iii) presence of at least one of the following: convoluted nuclei, mitotic count ≥ 3 per 2 mm², and tumour necrosis.

Differentiated high-grade thyroid carcinoma (DHGTC)

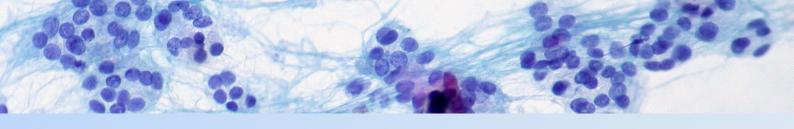
This new category includes follicular cell-derived carcinomas that are not poorly differentiated histologically but have high-grade features and the lack of anaplastic foci. By definition, the mitotic count must be ≥ 5 per 2 mm² ("hot spot" mitotic counting). Tumour necrosis is defined by karyorrhectic nuclear debris or ghost contours of dead tumour cells [22]. Tumour necrosis must be distinguished from infarct-type necrosis resulting from fine needle aspiration or regressive changes, as in the case of oncocytic tumours. Vascular, lymphatic, perineural and extrathyroidal invasions are commonly found. DHGTC should be subclassified according to their dominant histotypes, the majority of which are aggressive subtypes of PTC such as tall cell, hobnail or columnar cell [23, 24].

Anaplastic Thyroid Carcinoma (ATC)

ATC is composed of undifferentiated cells which may have focal features of thyroid follicular differentiation and/or a previous differentiated thyroid carcinoma. Primary squamous cell carcinoma (SCC) was considered a separate entity from ATC in previous WHO classifications; it is now recognized as a morphological pattern of ATC. Pure SCC without a differentiated thyroid carcinoma component carries BRAF V600E mutations in 60% of cases and has a similar outcome to ATC [25]. The majority express PAX8, confirming their follicular cell origin [26]. BRAF V600E detection by immunostaining and/or genotyping should be performed as the combination of BRAF and MEK inhibitors was found to be active against BRAF V600E-mutated anaplastic carcinoma [27].

Medullary thyroid carcinoma (MTC)

A two-tiered grading scheme for MTC has been introduced in this WHO edition. High-grade MTCs are defined as tumours with at least one of the following three features: mitotic count ≥5 per 2 mm2, Ki67 proliferation index ≥5%, and/or tumour necrosis [28]. Grading of biopsies is not recommended as tumour necrosis can be focal. Mitotic count and Ki67 index should be based on the area of tumour with highest proliferative activity.



Thyroid tumours of uncertain histogenesis

This new category is introduced and includes sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) and cribriform-morular thyroid carcinoma (CMTC).

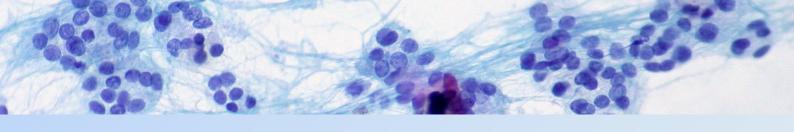
SMECE is a rare tumour (< 60 reported cases) and was previously considered as a subtype of salivary gland-type carcinomas of the thyroid gland. The morphology partially overlaps with MEC, along with a marked infiltration of lymphocytes and eosinophils in a background of marked stromal sclerosis [7,29]. Its origin still remains under debate, is but is favoured to be ultimobranchial body remnants [30]. It lacks the characteristic MAML2 rearrangement of mucoepidermoid carcinoma [31]. Reported genetic alterations include MET hyperploidy and point mutations in APC, NTRK3 and NF1 [32].

CMTC was previously classified as a variant/subtype of PTC, and is now a distinct entity. Almost all tumours have genetic alterations in the Wnt/beta-catenin pathway [33] which is distinct from BRAF V600E mutations in PTC [34]. Up to 53% are associated with familial adenomatous polyposis (FAP) [35]. They show nuclear expression of beta-catenin, estrogen receptor and progesterone receptor, and are often negative for markers of thyroid follicular cell differentiation (thyroglobulin and PAX8). The cribriform component is positive for TTF-1 [36].

Biomarkers

The current classification also emphasizes the value of biomarkers that may aid diagnosis and provide prognostic information.

Surrogate immunostains that can act as screening tools include: mutation-specific BRAF antibody (clone VE1) to screen for V600E mutations, pan-RAS Q61R (clone SP174) to detect HRAS/NRAS/KRAS Q61R mutations, pan-TRK for NTRK1/3 fusions, and 5A4 and D5F3 antibodies for ALK fusions.



2023 Bethesda System for Reporting Thyroid Cytopathology

A 3rd edition of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was released in July 2023 and contains only minor updates [37].

The new system assigns only a single distinct name for each of its six diagnostic categories: (I) nondiagnostic; (II) benign; (III) atypia of undetermined significance; (IV) follicular neoplasm; (V) suspicious for malignancy; and (VI) malignant. The use of the corresponding category number after the category name is optional.

Alternate names for 3 of the diagnostic categories: (I) "unsatisfactory", (III) "follicular lesion of undetermined significance", and (IV) "suspicious for a follicular neoplasm" have been discontinued to avoid confusion.

An implied risk of malignancy (ROM) for each of the six categories has been updated (Table 1) based on extensively published data since the 2nd edition of the TBSRTC in 2017 (Table 2); clinical management algorithms for each category have also been revised. A revised ROM for each category when excluding NIFTP is also included (Table 3). Paediatric ROMs and management algorithms are newly added for the same six reporting categories (Table 4).

AUS category is now subcategorized into 2 groups: "nuclear" and "other", with different implied ROM and molecular profile. AUS-nuclear atypia carries a significantly higher implied ROM (59%) than AUS associated with other patterns, especially architectural or oncocytic atypia (6.5%) [38]. AUS-other includes cases with architectural atypia, oncocytic atypia, and lymphocytic atypia. Cases with both mild nuclear and architectural alterations are grouped with aspirates exhibiting only nuclear atypia, since the ROM is similar regardless of presence or absence of coexisting architectural atypia.

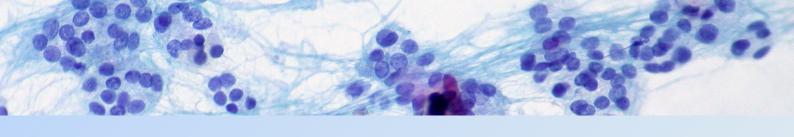


Table 1. The Bethesda System for Reporting Thyroid Cytopathology (2023): implied risk of malignancy (ROM) with expected ranges based on follow-up of surgically resected nodules with recommended clinical management

ROM	Usual management
Mean% (range)	
13 (5-20)	Repeat FNA with ultrasound guidance
4 (2-7)	Clinical and sonographic follow-up
22 (13–30)	Repeat FNA, molecular testing, diagnostic lobectomy,
	or surveillance
30 (23-34)	Molecular testing, diagnostic lobectomy
74 (67–83)	Molecular testing, lobectomy or near-total
	thyroidectomy
97 (97–100)	Lobectomy or near-total thyroidectomy
	Mean% (range) 13 (5-20) 4 (2-7) 22 (13-30) 30 (23-34) 74 (67-83)

Table 2. The Bethesda System for Reporting Thyroid Cytopathology (2017): implied risk of malignancy and recommended clinical management

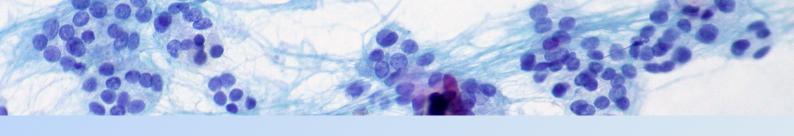
Diagnostic category	ROM (%)	Usual management	
Nondiagnostic or Unsatisfactory	5-10	Repeat FNA with ultrasound guidance	
Benign	0-3	Clinical and sonographic follow-up	
Atypia of Undetermined Significance			
or Follicular Lesion of Undetermined	~10-30	Repeat FNA, molecular testing, or lobectomy	
Significance			
Follicular Neoplasm or Suspicious for	25-40	Molecular testing, lobectomy	
a Follicular Neoplasm	23-40		
Suspicious for Malignancy	50-75	Near-total thyroidectomy or lobectomy	
Malignant	97-99	Near-total thyroidectomy or lobectomy	

Table 3. Reported decreases in the risk of malignancy (ROM) of TBSRTC (2023) diagnostic categories if excluding nodules diagnosed on surgical pathology to be "Noninvasive Follicular Thyroid Neoplasm with Papillary Like Nuclear Features (NIFTP)"

Diagnostic category	% Decrease in ROM if excluding NIFTP Mean% (range)	Estimated final ROM if excluding NIFTP
Nondiagnostic	1.3 (0-2)	12
Benign	2.4 (0-4)	2
Atypia of Undetermined Significance	6.4 (6-20)	16
Follicular Neoplasm	7.1 (0.2–30)	23
Suspicious for Malignancy	9.1 (0-40)	65
Malignant	2.6 (0-13)	94

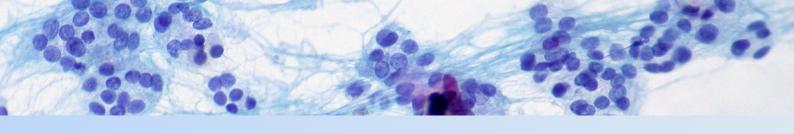
Table 4. The Bethesda System for Reporting Thyroid Cytopathology (2023) in Pediatric Patients with implied risk of malignancy (ROM) and possible management recommendations

Diagnostic category	ROM	Possible management
	Mean% (range)	recommendations
Nondiagnostic	14 (0-33)	Repeat FNA with ultrasound guidance
Benign	6 (0-27)	Clinical and sonographic follow-up
Atypia of Undetermined Significance	28 (11–54)	Repeat FNA or surgical resection
Follicular Neoplasm	50 (28-100)	Surgical resection
Suspicious for Malignancy	81 (40–100)	Surgical resection
Malignant	98 (86–100)	Surgical resection

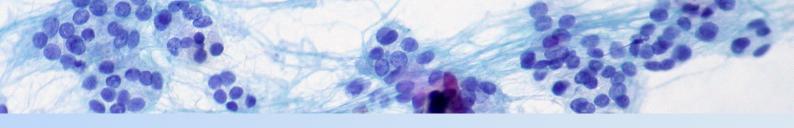


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- thyroid carcinomas. Histopathology 2021; 79:427-436
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The 20th Trainee Presentation Session

The 20th Trainee Presentation Session proceeded successfully on 16th November 2024. Twenty six trainees presented on the stage with good performance achieved. We would like to thank our four judges: Dr LUK Shik, Kristine (Microbiology, PMH), Dr WONG Chi Kin, Felix (Chemical Pathology, QMH), Dr WONG Ching Ching, Alice (Haematology, TMH) and Prof Peter SCHIRMACHER (Histopathology, Heidelberg University Hospital) for spending their precious time with us and giving the trainees invaluable comments for their improvement and future growth. The best trainee presentation was awarded to Dr CHOY Lok Yee on the topic "Genomic origin, fragmentomics and transcriptional properties of long cell-free DNA molecules in human plasma." Congratulations to Dr CHOY and everyone!

Dr YAU Tsz Wai Vice-Chairman of Education Committee









Our esteemed judges attentively evaluate the innovative research and projects presented by our talented trainees, offering valuable feedback and insight

























Trainees
showcasing their
hard work and
dedication as
they present
their projects



The winning presentation

My current research interest lies in the biology of cell-free DNA and their applications to the development of novel molecular diagnostics. I was eager to join the HKCPath Trainee Presentation Session as I thought it would be a great opportunity to learn from esteemed pathologists and other trainee doctors.

Existing studies in the field of liquid biopsy mainly utilized next-generation sequencing platforms for cell-free DNA (cfDNA) analysis. However, current research efforts focused on cfDNA molecules that are shorter than 600 bp due to the technical constraints of next-generation sequencing platforms. In the past few years, with the use of third-generation sequencing platforms, our team has demonstrated that long cfDNA molecules exists in the plasma of pregnant women, healthy subjects and cancer patients and have potential clinical utilities in prenatal and cancer testing. However, the origin and biological properties of long cfDNA molecules remain to be elucidated.

In the current project, we tried to understand more about the biological properties of long cfDNA molecules by analyzing the genomic representation, molecule abundance and cleavage profile surrounding CpG sites of the cfDNA molecules from third-generation sequencing data of cancer patients, pregnant women and healthy subjects. We observed that long cfDNA molecules are preferentially originate from the transcriptionally active regions of the genome and exhibit a distinctive cleavage profile surrounding CpG sites. Based on these observations, several tools could be developed to distinguish patients with and without cancer. By analyzing the plasma DNA molecules from nuclease-knockout mice, we observed that the characteristic distribution of long cfDNA in the genome is related to DNA fragmentation factor subunit beta (DFFB) activity. The enhanced understanding on the biology of long cfDNA generation may open new possibilities for biomarker discovery.

During the presentation session, I got the precious opportunity to learn about the exciting research work of the doctors from other pathology subspecialties. The presentation session was filled with fascinating research findings and interesting cases. It was an eye-opening experience for me and I was glad to learn that there are many trainee doctors who are dedicated to advancing patient care through research and innovation. Also, I received valuable advice from the panel of judges. This experience has enhanced my communication skills which would be conducive to my future career.

I was delighted when I learned that I was privileged to be awarded the Best Presentation Prize. I am immensely grateful to my supervisor, Prof Dennis LO, and to other seniors and colleagues for their guidance and support. Also, I would like to thank the College for organizing this meaningful event. Looking forward to seeing more trainees of our College to participate for the exchange of new ideas.

Dr CHOY Lok Yee, Lois Clinical Lecturer, Department of Chemical Pathology, The Chinese University of Hong Kong Honorary Resident, Department of Chemical Pathology, Prince of Wales Hospital





Abstract of winning presentation

Genomic origin, fragmentomics and transcriptional properties of long cell-free DNA molecules in human plasma



Huiwen Che^{1,2,3}, Peiyong Jiang^{1,2,3,4}, L.Y. Lois Choy^{1,2,3,4}, Suk Hang Cheng^{1,2,3}, Wenlei Peng^{1,2,3}, Rebecca W.Y. Chan^{1,2,3}, Jing Liu^{1,2,3}, Qing Zhou^{1,2,3}, W.K. Jacky Lam^{1,2,3,4}, Stephanie C.Y. Yu^{1,2,3}, So Ling Lau⁵, Tak Y. Leung⁵, John Wong⁶, Vincent Wai-Sun Wong⁷, Grace L.H. Wong⁷, Stephen L. Chan^{4,8}, K.C. Allen Chan^{1,2,3,4}, Y.M. Dennis Lo^{1,2,3,4}, #

AFFILIATIONS

- ¹ Centre for Novostics, Hong Kong Science Park, Pak Shek Kok, Hong Kong SAR, China.
- ² Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- ³ Department of Chemical Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- ⁴ State Key Laboratory of Translational Oncology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- ⁵ Department of Obstetrics and Gynaecology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- ⁶ Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- ⁷ Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- ⁸ Department of Clinical Oncology, Sir Y.K. Pao Centre for Cancer, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China.
- * Corresponding author

Abstract:

Recent studies have revealed an unexplored population of long cell-free DNA (cfDNA) molecules in human plasma using long-read sequencing technologies. However, the biological properties of long cfDNA molecules (>500 bp) remain largely unknown. To this end, we have investigated the origins of long cfDNA molecules from different genomic elements. Analysis of plasma cfDNA using long-read sequencing reveals an uneven distribution of long molecules from across the genome. Long cfDNA molecules show overrepresentation in euchromatic regions of the genome, in sharp contrast to short DNA molecules. We observe a stronger relationship between the abundance of long molecules and mRNA gene expression levels, compared with short molecules (Pearson's r = 0.71 vs. -0.14). Moreover, long and short molecules show distinct fragmentation patterns surrounding CpG sites. Leveraging the cleavage preferences surrounding CpG sites, the combined cleavage ratios of long and short molecules can differentiate patients with hepatocellular carcinoma (HCC) from non-HCC subjects (AUC = 0.87). We also investigated knockout mice in which selected nuclease genes had been inactivated in comparison with wild-type mice. The proportion of long molecules originating from transcription start sites are lower in Dffb-deficient mice but higher in Dnase1I3-deficient mice compared with that of wild-type mice. This work thus provides new insights into the biological properties and potential clinical applications of long cfDNA molecules.

The 33rd Annual General Meeting

The 33rd Annual General Meeting (AGM) was held in the afternoon of 16th November 2024. Six Councillors were elected. Four of them were in previous Council 2023/24: Dr LAI Koon Chi, Christopher was reelected as Vice-President; Dr CHEONG Renee Constance Yue-Kew was reelected as Honorary Treasurer; Dr WONG Lap Gate, Michael was elected as Council Member; while Dr Siddharth SRIDHAR was reelected as Council Member. Two new Council Members were elected: Dr CHIAO Wing Fu and Dr LAM Winwhole Larry Ruey Si. We would like to take this opportunity to thank outgoing outgoing Council Members Dr NG Hoi Yan, Joshua and Dr POON Wai Ming for their contributions to College Council.









Members of College Council 2024/25



Front row from left to right:

- 1. Dr CHENG Shui Ying (Deputy Registrar)
- 2. Dr CHEONG Renee Constance Yue-Kew (Honorary Treasurer)
- 3. Dr LEUNG Yuk Yan, Rock (Vice-President)
- 4. Dr MAK Siu Ming (President)
- 5. Dr LAI Koon Chi, Christopher (Vice-President)
- 6. Dr AU YEUNG Kwok Him, Rex (Registrar)
- 7. Dr FUNG Ngai Sheung

Back row from left to right:

- 1. Dr CHIAO Wing Fu
- 2. Dr WONG Lap Gate, Michael
- 3. Dr Siddharth SRIDHAR
- 4. Dr WONG Chi Kin, Felix
- 5. Dr CHEN Pak Lam, Sammy
- 6. Dr LAM Winwhole Larry Ruey Si
- 7. Dr LEUNG Ying Kit

Absent:



The 32nd Conferment Ceremony

Fellows and Members admitted to the College in 2024 AGM were invited to this Conferment Ceremony. In 2024 AGM, 14 Fellows and 13 Members were admitted to the College. Two Fellows passed the Fellowship Assessment in Genetic and Genomic Pathology in 2024.

Honourable guests included Prof LEUNG Ka Kit, Gilberto, President, Hong Kong Academy of Medicine; Prof LO Chung Mau, Secretary for Health, Health Bureau, HKSAR; Dr TO May Kei, Liza, Assistant Director of Health (Health Sciences & Technology), Department of Health, HKSAR; Dr Hon LAM Tzit Yuen, David, Legislative Councillor (Medical and Health Services), Legislative Council, HKSAR; Dr LAW Chun Bon, Cluster Chief Executive, Kowloon West, Hospital Authority, HKSAR; Prof Peter SCHIRMACHER, President, European Society of Pathology; and Dr Raed AL DIERI, Chief Executive Officer, European Society of Pathology.





A wonderful gathering
of honourable guests
celebrating the joy
and pride of our new
Fellows and Members
during the Conferment
Ceremony











Honourable guests join us
to celebrate the
achievements of our new
Fellows and Members,
marking a significant
milestone in their
professional journey





















Surrounded by esteemed

guests, our new Fellows and

Members proudly celebrate

their achievements during

this memorable Conferment

Ceremony

35





Prof Peter SCHIRMACHER



CHAN Chun Hei, Toby



CHENG Shui Kuen



CHOW Kin Yi



FONG Nga Yee



HO Cheuk Lam



LI Po Yin



LUI Yin Wing



WU Wing Gi



YEUNG Ka Pik, Vivian



FU Man Chi, Eric



LEE Pascoe Ao Ting TANG Cheuk Yin





YEUNG Pak Kwan



LI Ting Hon, Stanford

Congratulations to all newly admitted Members and Fellows!



We would like to express our gratitude to our College Secretary Ms Dilly YIP for her support in organizing the event. A big thank you to Dr Victoria TSE for being the Mistress of Ceremonies at the AGM and Conferment Ceremony. We would also like to thank our photographer Mr K K LAU for his professional work, and our helpers Ms YEUNG Yuen Mei, Ms NG Wing Ka and Ms IP Ka Fun for their help.

The 32nd T.B. Teoh Foundation Lecture





The 32nd T.B. Teoh Foundation Lecture was delivered by Professor Peter SCHIRMACHER, President of the European Society of Pathology and Honorary Fellow of the College on the topic "Third Generation Molecular Pathology – From Research to Diagnostic Implementation". During the lecture, Professor Schirmacher shared his experiences in the development of molecular diagnostics in tumour biopsies, upcoming challenges of applying genomic techniques to cancer diagnostics, features of the Diagnostic Trial Centre in Heidelberg, Germany, and his vision in comprehensive molecular pathology reporting for personalized medicine in the future. The lecture was very informative, and emphasized the importance of delivering genetic and genomic pathology services that are meaningful and helpful to patients and clinicians.





College Dinner 2024 - Photos































International Pathology Day Workshop 2024

On December 14, 2024, the International Pathology Day Workshop was successfully held at the student laboratory of Prince of Wales Hospital. The event commenced with an opening speech by Dr Christopher LAI, Vice President of the Hong Kong College of Pathologists, who emphasized the importance of pathology in understanding diseases and improving patient care.

The workshop featured six engaging stations, each designed to introduce secondary school students to various aspects of pathology. The first station focused on anatomical pathology, where participants explored organ blocks and uncovered the mysteries of human anatomy. This hands-on approach captivated the students, allowing them to appreciate the complexities of the human body.

The second station, led by the chemical pathology team, utilized test papers to demonstrate urinalysis and kidney pathology. Students learned how chemical tests can reveal important information about a patient's health, sparking their interest in laboratory diagnostics.

At the haematology station, participants delved into the fascinating world of blood groups. They discovered the significance of blood types in transfusions and how haematologists play a crucial role in patient treatment. The interactive discussions encouraged students to ask questions and engage with the material actively.

The forensic pathology station offered a unique glimpse into the daily work of forensic pathologists. Students were shown photos that illustrated the real-life applications of forensic science in solving crimes. This station highlighted the intersection of pathology and law, revealing the vital role pathologists play in the justice system.

In the microbiology session, the speakers provided insights into microorganisms and the importance of handwashing in infection control. Through demonstrations and discussions, students learned how microbiologists study pathogens and contribute to public health.

Lastly, the immunology station focused on the principles of allergy, educating students about the immune system's responses to allergens. This segment provided valuable knowledge about common allergic reactions and the significance of immunologists in diagnosing and treating these conditions.

Overall, the workshop was a resounding success, with approximately 110 secondary school students participating. They enjoyed a hands-on learning experience that fostered curiosity about the field of pathology. A heartfelt thank you goes out to all the volunteers, educators, and staff who made this event possible. Your dedication and enthusiasm greatly contributed to the students' enrichment and understanding of pathology.









Young Fellows Chapter Mainland Exchange and Study Trip to Shanghai 2025

The 'Shanghai-Hong Kong-Shenzhen Young Specialists' Study and Exchange Summit' jointly organised by the Shanghai Medical Doctor Association, the Shenzhen Medical Doctor Association and the SZ-HK Medical Specialist Training Centre was successfully held in Shanghai in March 2025. As Hong Kong pathology representatives, Dr Johann LOK (Chairman of Young Fellows Chapter, HKCPath) and I joined the exchange trip together with other Young Fellows Chapter representatives from other Colleges under the HKAM. Grateful to the organizing committee for this meaningful event.

This opportunity for exchange with mainland doctors has been an eye opening experience for us. The chance of visiting different departments of different hospitals, commercial imaging centers and out-patient clinics was really invaluable. It was the first time that I saw how the smooth infusion of traditional Chinese medicine into the Western medicine could take place. Before, they appeared to be extremes of the same spectrum to me. Yet, the old Chinese wisdom can push the scientific knowledge to another level, benefiting our patients. Besides, the visit to the imaging centre had been a fantastic experience. To be exact, it was not only a centre for providing imaging service, it was also the birthplace of the most up-to-date imaging devices, which provided services locally and internationally. Through different networking activities, we have more opportunities to communicate with colleagues from different Colleges, as well as those from Shanghai and Shenzhen. In our daily work, we don't have much chance to interact with colleagues from other hospitals. It was so nice catching up with them, discussing ways we could further collaborate for our patients clinically and academically. Besides, we also chatted with a Shanghai anatomical pathologist who was planning to work in Hong Kong! So nice to have the opportunity to meet our potential future colleagues. After all, we belong to the big family of healthcare, which is without border.

Will definitely look forward to future exchange opportunities and invaluable learning experiences.

Dr LAM Ki Vice-Chairman Young Fellows Chapter



Visit to imaging center with tour on advanced imaging machines





Sharing session on medical education and medical specialist training in China



Dr LAM Ki and Dr Johann LOK, Young Fellows Chapter representatives from our College



Visit to the Oriental Pearl Tower



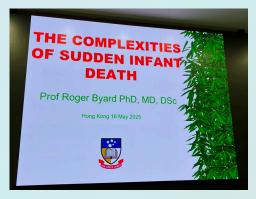
Visit to the Bund with beautiful nightview

Seminar by Prof Roger Byard on Sudden Infant Death





We are happy to share that a seminar on "Sudden Infant Death" by Professor Roger BYARD, Emeritus Professor, School of Biomedicine, Faculty of Health Medical Sciences, University of Adelaide, Australia, was a resounding success! This was jointly organised by The Hong Kong College of The Department Pathologists, of Health and Pathology, School of Clinical Department of Medicine, HKUMed, and was held on May 16, 2025, at the Lecture Theatre, Block T, Queen Mary Hospital. The event attracted many enthusiastic attendees. The session provided valuable insights into forensic pathology, and we appreciate everyone who participated. A special thanks to Professor BYARD for sharing his expertise.









Mindful Creations: A Handbuilding Pottery Workshop on 22 June 2025

We are pleased to announce that our Mindful Creations: A Handbuilding Pottery Workshop was successfully held on June 22, 2025. With 15 enthusiastic participants from The Hong Kong College of Pathologists, the workshop provided a wonderful opportunity for members and fellows to engage in meaningful conversations and connect with their inner creativity.

Under the guidance of our talented instructor, Mr. Ng Ka Ho, participants created unique pottery pieces, fostering personal expression and enhancing their mental well-being. This workshop aligns with the Hong Kong Academy of Medicine's initiative to promote doctors' well-being, offering a supportive environment for reflection and creativity.

A big thank you to everyone who joined us for this enriching experience! We look forward to more activities that support our members' well-being.

Dr Karen YUEN Secretary Professional and General Affairs Committee



Organized by The Hong Kong College of Pathologists

22nd June 2025 (Sun) 2:30 pm to 5:30 pm Studio in Kowloon Bay



Free of charge for Associates, Members and Fellows

Mindful Creations: A Handbuilding Pottery Workshop

Enhance your creativity and well-being

Join us for a mindful pottery workshop experience. Please refer to email for enrollment.







Panel of Examiners 2025



Anatomical Pathology - Membership Viva

Back row (from left to right):
Dr WONG Wing Cheuk, Dr LEUNG Ying Kit (Deputy Chief Examiner), Dr
CHAN Kui Fat

Front row (from left to right):

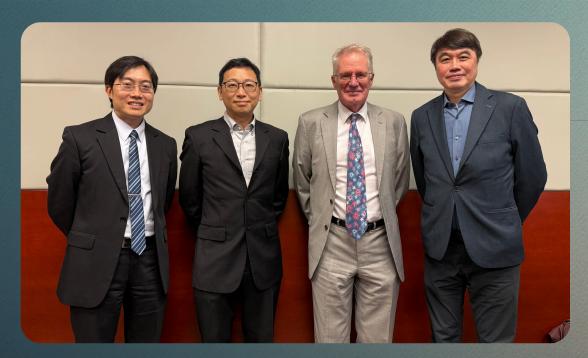
Dr CHEUNG Ho Kwan, Alvin, Dr KAN Nim Chi, Amanda, Prof TO Ka Fai (Chief Examiner), Prof Ian ELLIS (External Examiner)



<u> Anatomical Pathology - Fellowship Viva</u>

Back row (from left to right):
Dr CHAN Bik Wan, Dr CHAU Kwok Fung, Tony, Dr LO Wing Ip, Anthony,
Dr CHEONG Renee Constance Yue-Kew, Dr MAK Siu Ming

Front row (from left to right):
Dr LEUNG Ying Kit, Prof TO Ka Fai, Prof lan ELLIS



Anatomical Pathology - Fellowship Assessment in Genetic and Genomic Pathology Viva

From left to right:

Dr LEUNG Ying Kit (Deputy Chief Examiner), Dr LO Wing Ip, Anthony, Prof TO Ka Fai (Chief Examiner), Prof Ian ELLIS (External Examiner)



Chemical Pathology

Back row (from left to right):

Dr CHENG Hua Tse, Timothy, Dr CHONG Yeow Kuan, Dr MAK Miu, Dr CHING Chor Kwan, Doris, Dr LEUNG Mei Tik, Dr WONG Chi Kin, Felix (Deputy Chief Examiner) and Dr LEE Han Chih, Hencher

Front row (from left to right):

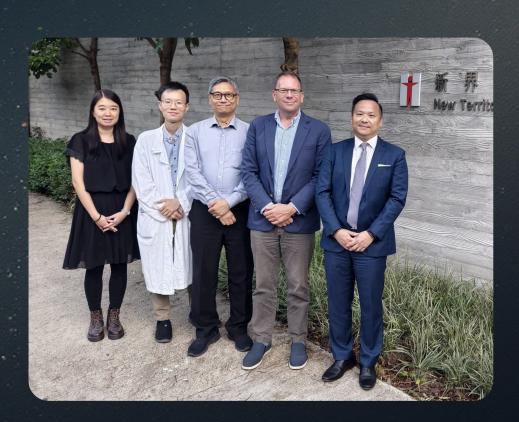
Dr SHEK Chi Chung, Dr YUEN Yuet Ping, Dr CHEN Pak Lam, Sammy (Chief Examiner), Dr LU Zhong Xian (External Examiner) and Dr TAI Hok Leung, Morris



Clinical Microbiology and Infection

Back row (from left to right):
Prof CHAN Fuk Woo, Jasper, Dr LUK Shik, Kristine, Dr LUNG David
Christopher, Dr LAI Koon Chi, Christopher, Dr LAM Yiu Wing
Front row (from left to right):
Dr LEE Kin Ping, Dr TSE Wing Sze, Cindy (Chief Examiner), Dr HO Pak Leung

[Absent in photo: Robert NORTON (External Examiner)]



Forensic Pathology

From left to right:
Dr KWOK Ka Ki, Dr FOO
Ka Chung, Dr LAI Sai
Chak (Chief Examiner),
Prof Michael POLLANEN
(External Examiner), Dr
LAM Wai Kwok



Haematology

Back row (from left to right):

Dr WONG Hung Fan, Dr LEUNG Fung Shan, Kate, Dr WONG Wai Shan, Dr YIP Sze Fai, Dr WONG Ching Ching, Alice

Front row (from left to right):

Dr LEUNG Yuk Yan, Rock, Dr IP Ho Wan (Chief Examiner), A/Prof Merrole COLE-SINCLAIR (External Examiner), Dr MA Shiu Kwan, Edmond, Dr CHOW Yu De, Eudora, Dr SO Chi Chiu, Jason



We are pleased to announce that the following candidates have passed the Fellowship Assessment or Membership Examination in 2025. Congratulations!

Fellowship Assessment - Anatomical Pathology

CHAN Hoi Tung FU Man Chi Eric LU Jianlin YUEN Wing Nam

Fellowship Assessment - Chemical Pathology

CHEUNG Yee Ting
TSEUNG Sik Bit Jeremiah

Fellowship Assessment – Clinical Microbiology and Infection

LEE Pascoe Ao Ting

Fellowship Assessment - Haematology

CHEUNG Tsz Long HOU Hei Wan LI Chung Hin

Fellowship Assessment - Genetic and Genomic Pathology

LEE Wai Kwan LING Tsz Ki LAM Wing Kit

Membership Examination - Anatomical Pathology

CHENG Tsz Fan
CHENG Tung
CHEUK Tsun Leung
CHEUNG Man Hin
CHIU Yuen Kei
HO Lok Lun
KWAN Sui Chun Sampson
LEUNG Cheuk Hei
NGAI Ching Yee
TSE Lik Ka Jenny
YUEN Ka Choi

Membership Examination – Forensic Pathology

WONG Ho Yan

Membership Examination - Haematology

MAK Hiu Chun

Cheetah

KEY FACTS

By Dr LO Hui Yin

TERMINOLOGY

- 獵豹
- Acinonyx jubatus
- Acinonyx: "immobile nails" in Greek, as cheetahs cannot fully retract their claws
- Jubatus: "crested" in Latin Cheetah: derived from "painted" in old Hindu language

PHYLOGENY

- Cheetahs belong to the subfamily Felinae (small cats). They can pur but not roar like big cats.
- Their closest relatives are the puma (or cougar; Puma concolor) and the jaguarundi (Herpailurus yagouaroundi)

SUBSPECIES

- Southeast African Cheetah
- Northeast African Cheetah
- Northwest African Cheetah
- Asiatic Cheetah: central Iran

BEHAVIOUR ECOLOGY AND CONSERVATION STATUS

- Usually solitary, some males might stay in groups (coalitions)

- Fastest land animal
- Up to 98km/h or more
- They can go from 0-97km/h in less than 3 seconds
- Relatively friendly with humans
- Tamed and kept as pets or hunting companions in Ancient Egypt
- Similar records observed in the Middle East, China, and Mongol empire
- No documented fatal attacks on humans by wild cheetahs
- Lifespan: in average 8-12 years and up to 15 years in the wild, more in captivity
- Conservation status: Vulnerable

MACROSCOPIC

- Body length 112-150cm, tail length 66-84cm
- Body weight 21-65kg
- Black tear marks from corners of eyes down to side of nose
- Tawny coat with solid black spots around 3-5 cm in diameter
- Chin, throat and belly are white

DIFFERENTIAL DIAGNOSES

- Leopard (in Africa, and selected parks in India with re-introduced cheetahs)
- Serval (in Africa)
- Honey badgers (of cubs)

(left) Cheetah has solid black spots, a slender body and a long tail. (right) Cheetahs hunt mostly in the daytime, utilising their good vision and high running speed. They often climb up on rocks or termite mounds to get a better view of potential preys.





Cheetah

(left) Cheetah has black tear marks. (right) Leopard does not have tear marks. Leopard has rosettes rather than solid spots.





(left) Serval also has solid black spots. Serval is smaller (Body length 67-100cm and weight 9-18kg) and has bigger ears. (right) Female cheetah gives birth to a litter of usually 3-4 cubs (up to 8) after 3 months of gestation. Only around <10% of cubs survive to adulthood. Cubs stay with their mothers for 1.5-2 years before gaining independence.





(left) Cheetah cubs have a silvery mantle of fur on their necks and backs, said to be resembling honey badgers ("Batesian mimicry"). This camouflage helps to protect them from predators. (right) Honey badgers are known to be aggressive and fierce. Predators including lions often avoid them.





<u>Programme of the 34th Annual General Meeting</u> <u>15 November 2025 (Saturday)</u>

Pao Yue Kong Auditorium, G/F, Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen Hong Kong

10:00 - 14:30 Th	e 21st Trainee	Presentation	Session
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Title: Between Slides and Soul: Finding Fulfilment at the Intersection of Practicing Histopathologist and Translational Researcher

Speaker: Professor TO Ka Fai Professor, Department of Anatomical and Cellular Pathology The Chinese University of Hong Kong

19:00 – 21:00 Chinese Banquet Dinner