HGVT

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PARAFFINALIA NEWSLETTER

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The HGVT aims to provide a dynamic continuing education program in which all persons with an interest in Histology and Histotechnology are freely invited to participate.

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Committee Page

The members of the Histology Group of Victoria and Tasmania 2020 are:

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President's Report – Behind the Bench

Greetings from behind the bench!

We are back.!!!!!

After 3 long years the HGVT held our first face to face meeting. Big thanks to Peter Mac for hosting us, David for the technical support ,Sam from our committee, for her unwavering energy and of course our wonderful young speakers who shared their cases with us.. It was lovely to see your faces. We had audience onsite and online, as we prepare to build educational momentum towards a state conference later in the year.
It was fantastic to see the latest news has the toy of the year as a microscope. It warms my heart that a new generation can fall in love with the smallest details, not seen with the naked eye. Relating structure to function, is a game that I have played my whole life and it still surprises and excites me.
There is not a Histo department that isn't incredibly under the pump currently, so please work safely and may your tissue be well fixed, blocks cold, blades sharp, slides of good quality and your stains as expected.

Kerrie Scott
(Leica/ Dorevitch Pathology)
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UNDER THE MICROSCOPE
with Kate Wilson

What is your current job?
Complex Cut Up Medical Scientist for Monash Health.

How long have you been working in Histology?
I started my career as a Lab Assistant at Histolab back in 2016 whilst in my second year of my studies. I then completed a bursary year at The Alfred and continued to work in Histology after graduating which would add up to 6-7 years.

What piece of advice would you give to people starting in Histology?
Listen to advice, ask questions, take initiative, learn to be able to work independently and with others, keep up with continuing education and never become complacent.

What's a goal you have for this year?
It's a bit of an odd one but I'd really love to rediscover my passion for reading and collecting comic books again.

What music is on your playlist at the moment?
BLACKPINK, BTS, Ed Sheeran, Little Big and My Chemical Romance (I'm seeing 3 of these artists this year!).

Other than histology, what is another scientific topic that interests you?
Paleontology. Besides loving dinosaurs since I was a kid; I'm a massive nerd, you hear stories of The Kraken, Megalodon and many other creatures and I've always wanted to know more.

What movie or TV show do you think everyone should watch?
Arcane on Netflix!

If you could live anywhere in the world for a year, where would you pick?
Seoul, South Korea. I love technology and gaming; it's been a dream of mine to see an E-Sports tournament in South Korea.

If you could choose two famous people, past or present, to have dinner with, who would it be?
Ryan Reynolds and Gal Gadot (I'd say the entire cast of Red Notice if I could). They say laughter is the best medicine ☺.

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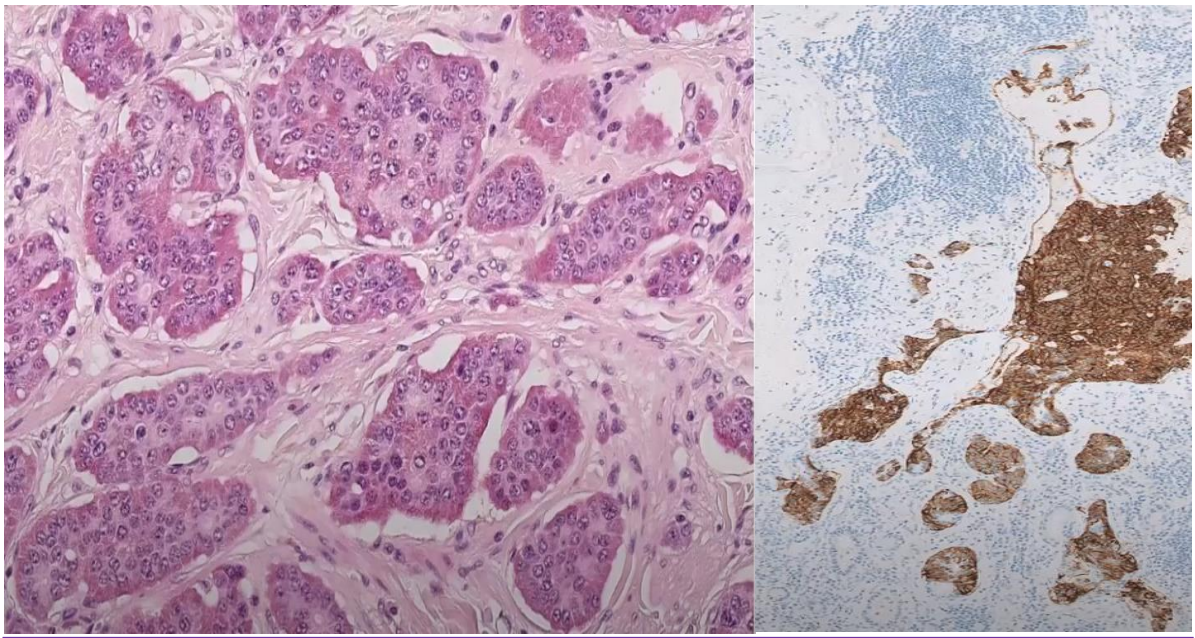
HGVT Scientific Meeting Review February 23rd: "Short Cases Presentations"

On the 23rd of February the HGVT were excited to resume face to face scientific meetings. Arriving at 6:30, we were welcomed by a not quite foreign yet not fully familiar sight of Histopathology professionals conversing on work, life and the presentations yet to come. The feeling was not strange for long and it was great to see people interacting like old friends and certainly primed a level of enthusiasm and anticipation for the night.

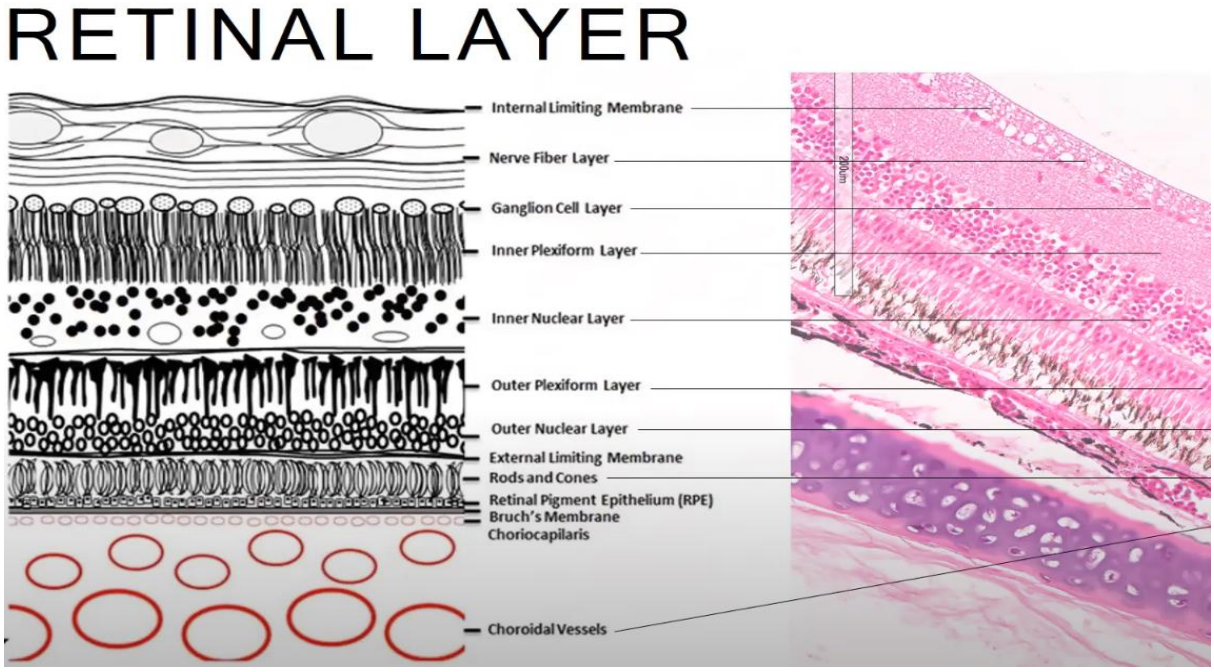
We were fortunate enough to be treated to a stacked line up of student presentations. Personally, these are always are engaging as they offer an insight into the next generation of scientists and colleagues joining us at the benches, so it's interesting to see their perspectives on what topics intrigue them and get a preview of the personality behind the professional. All the images you will see below have been sourced directly from the presentations themselves, there will be a link at the bottom to go watch the full context if you were unable to attend on the night.

Starting us off strong was Michelle Kong with a series of visually engaging case studies on carcinoid. For those not familiar with them, carcinoid tumours are a type of slow-growing neuroendocrine tumour typically found in the bowel, respiratory tract and other tissues. Michelle informed the group that they can sometimes be difficult to visualize with a H&E stain so neuroendocrine IHC markers and others are used to help identify including chromogranin A, CD56 and Ki67.

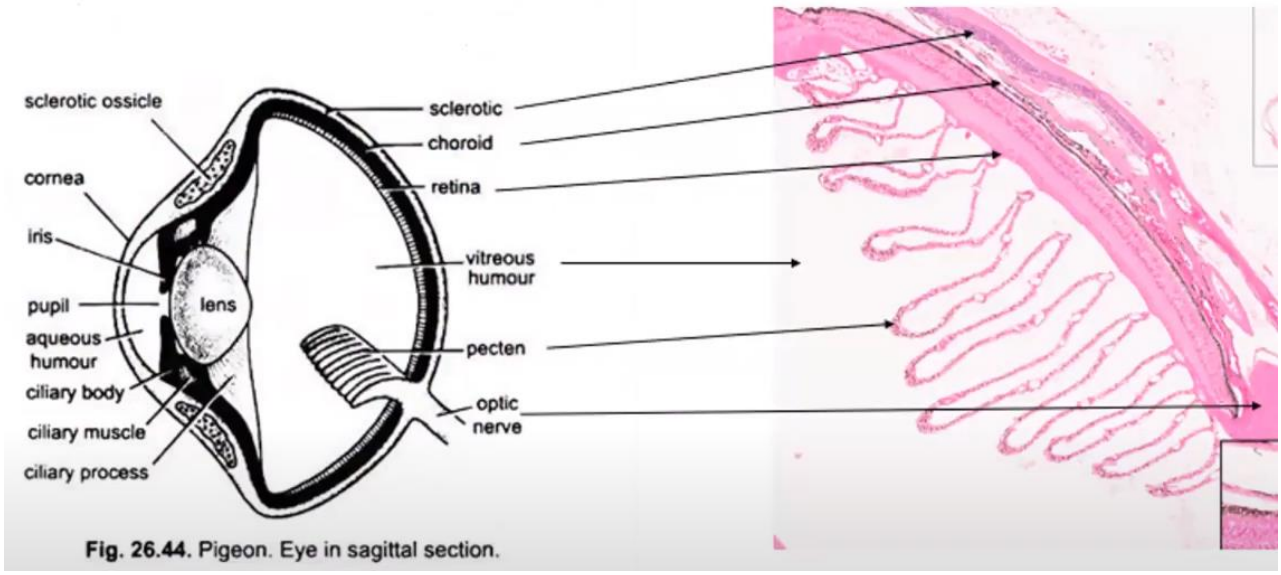


(Left image) Michelle's H&E of a carcinoid tumour.
Note, the round nuclei with stippled/salt and pepper chromatin pattern as well as the finely granular cytoplasm.
(Right image) Example of carcinoid sample stained with IHC targeting chromogranin

Following Michelle we were exposed to the infrequently considered but highly important world of animal histology with ‘A Bird Eye View of Histology’ from Julachai Yonterng and Ramanjeet Kaur. The initating event that spurred this talk was the presentation of multiple avian speices from Healsville Sanctuary suspected of having Psittacine Beak and Feather Disease (PBFT). However, our two speakers were also able to provide a crash course in the histology of different avian eyes and how these differences confer different evolutionary characteristics in theior respective ecosystems. Out of the flat, round and tubular eyes discussed, the tubular eye (seen in owls) was a personal favourtie simply due to the unexpected complexity of the structure.

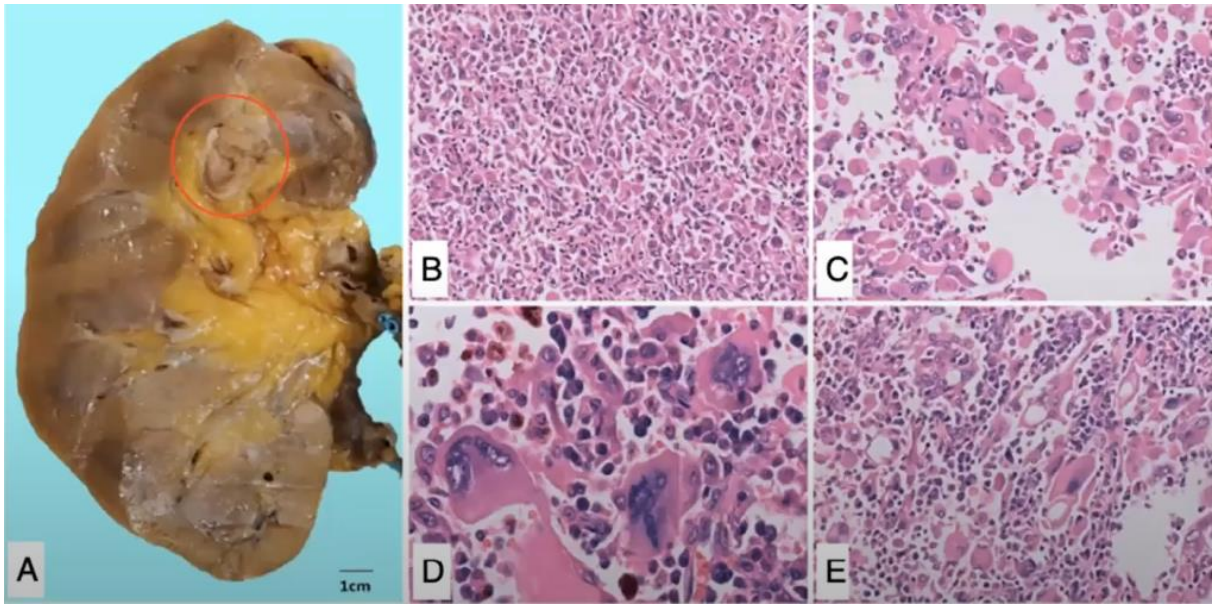


One other notable physical feature discussed, unique to avian eyes (and some reptiles) is the pecten, a comb-like structure of tightly knit blood vessels. This reduces the vascularization of the retina, aiding the sharp eyesight of birds. In mammals blood vessels in front of the retina can partially obscure the image. In addition, it is thought that the pecten functions to provide the retina with the nutrients it requires. One last point of interest is that the structure is pigmented which is believed to offer some protection from ultraviolet light.
Overall it allowed a new appreciation of how different the architecture can be in species other than humans.

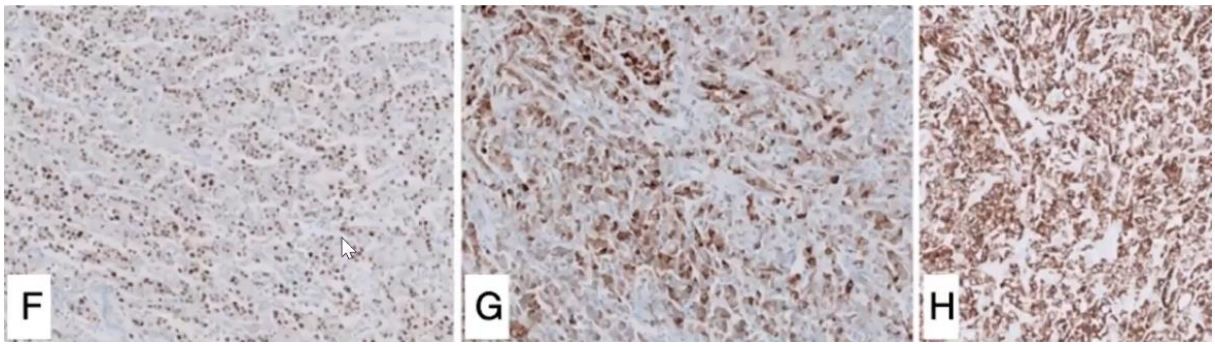


Cross-section of bird eye demonstrating the pecten (H&E)

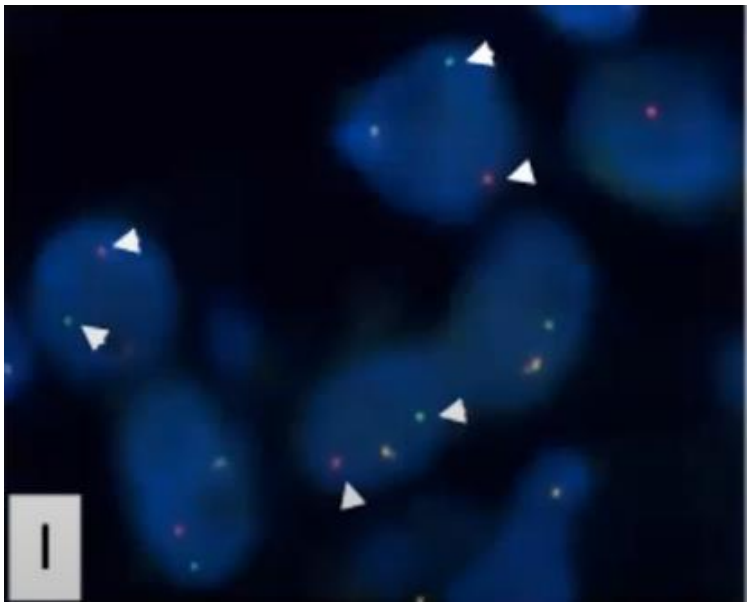
Haley Chen was next up, providing a unique insight into an uncommon form of Renal Cell Carcinoma with her presentation ‘ALK-Rearrangement of Renal Cell Carcinoma with TPM3’. Haley began describing the disease, which begins with a rearrangement of the ALK gene with various other fusion partner genes. The consequence of this she described was the ‘formation of various oncogenic chimeric proteins’ which lead to ALK activation. Given the rarity of the disease, Haley was able to break down the nuances well, providing a case study to aid her descriptions.



Gross and morphological fgindings of the tumour. (A) Gross image, (B)-(E) Microscopic image. Adaptive from Galea LA et al., 2022



IHC staining: (F) PAX8, (G) CK7 and (H) ALK



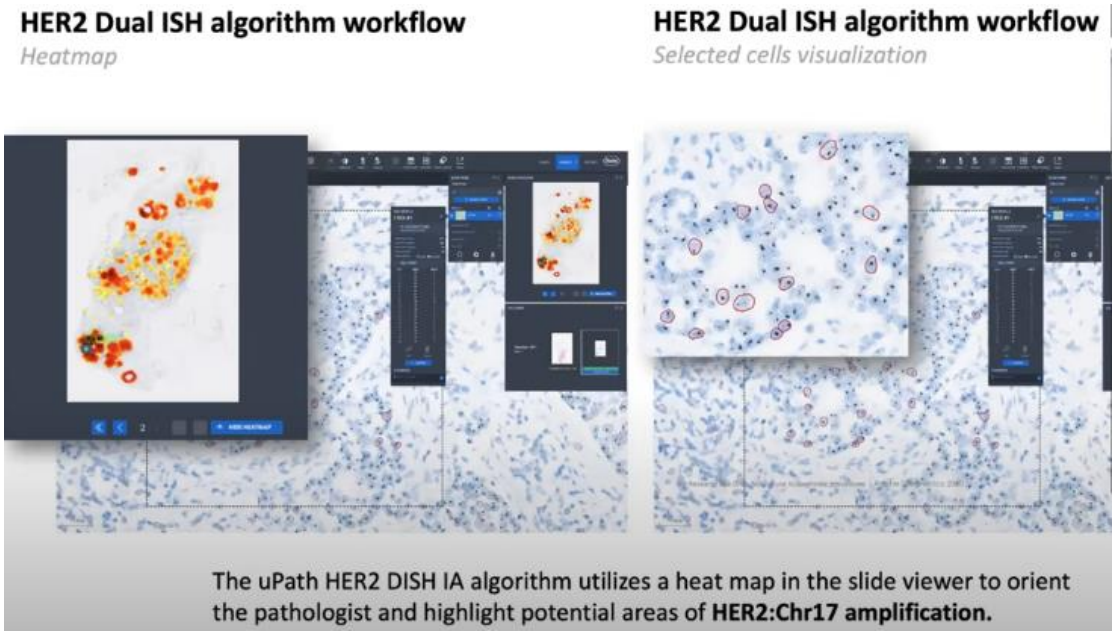
FISH staining: Note the significant split signals of ALK shown by the arrows.

The case study was a great example of how H&E, IHC, FISH and even RNA sequencing can work together to help classify a pathology presentation, even one that is seldom seen.

Finally, to round off an already interesting medley of presentations was Madeleine Gough who discussed the progress and application of digital pathology in ‘Digital Pathology: improving HER2 cancer”

The world of digital pathology has come a long way and is only having greeater presence over time in laboratories so it is always an intriguing topic for discussion.

Specifically, Madeline presented a study on applying algorithm-assisted assessment of HER2 in situ hybridization to reduce interobserver variability in difficult cases. One early engaging point of information was that there are different requirements around the world to gauge eligibility for HER2 targetted therapy. Specifically to Australia, Madeline explained that patients needed to demonstrate evidence of HER2 gene amplification to be eligible meaning that 2+/3+ protein expression cases need to have a reflex ISH assay to confirm the gene amplification.
The study looked back at previously reported HER2 cases using freshly cut and stained sections to compare interobserver variability of pathologists to that of the image analysis algorithm.



The findings from this study indicated that for less common patterns of HER 2 ISH staining, interobserver variability is reduced with the assistance of the digital algorithm with one of the key takeaways being that there is the potential to use the algorithm m in the future to potentially improve patient selection for HER2-targerted therapies. .

Overall the night was a party mix of different topics and a vibrant return to face to face meetings. I was grateful to learn something from each of our speakers and it left me (and hopefully you) excited to see what follows next time!

The above is only a brief insight into each of the speaker’s topics and I would highly encourage those interested in the above, but were unable to attend to go and listen to the full recording available here: (https://drive.google.com/file/d/1hdoAM3WHn8BU9dC8aXNaVH7FfdWfVzv-/view)

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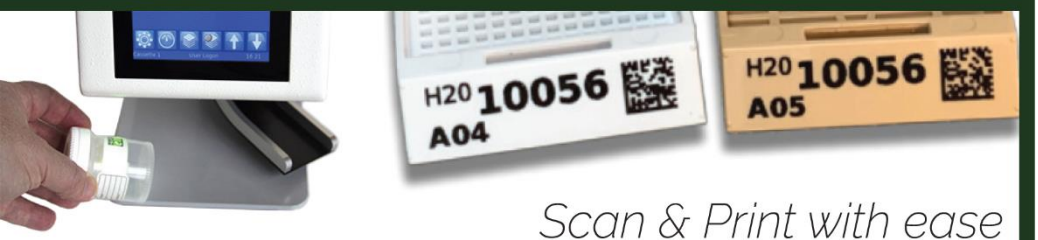

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Hello Histo group! The HGVT is interested in promoting Histology into the public eye more (to show off of course!) and want to see pictures from our community to develop an Instagram (or Histo-gram, for the pun-minded). Above is some artistic inspo of the already incredible potential our discipline offers, however, anything related to Histology, your lab or your team is more than welcome!

Send all pictures to: editor@hgvt.org.au

Best regards!

Links to above art:
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WOMEN IN PATHOLOGY

BY MARK BROMLEY

According to the World Health Organisation, 70% of people working in healthcare around the world are female. And in Australia it is much the same, women predominate. There are more than 24,000 women working in the Australian pathology sector, making a massive difference to healthcare. Without them, Australian Healthcare simply wouldn't function the way it does.

Since out last newsletter came out, we've seen International Day of Women and Girls in Science on February 11th, and more recently International Women's Day on March 8th, so in honour of the women currently holding the torch of Australian pathology, we are going to look back at just a few of the influential women throughout history who have contributed to medicine and pathology, usually with far less fanfare or recognition than their male counterparts.

Let's kick off with **Myrtelle May Canavan**, who was born in Greenbush Township in Michigan on the 24th of June, 1879.

She received her M.D. from the Women's Medical College of Pennsylvania in 1905, and after developing an interest in neuropathology, she became one of the first female pathologists in the world, taking a residency portion in Boston State Hospital in 1910.

She became Associate Professor of Neuropathology at Boston University and curated the Warren Anatomical Museum at Harvard Medical School. However, despite adding over 1500 specimens to the collection, discarding all of the damaged ones and vastly improving the institutions record keeping, she was always referred to as "assistant curator" because of objections to a woman heading the museum. She is best known for her published description of a neurological degenerative disease in 1931, which became known as Canavan Disease in her name.

Next we have the Spitz nevus. Anyone who has worked in a lab that does dermatopathology will have heard the name, but not many would know that it was **Dr Sophie Spitz** who published a paper in the American Journal of Pathology in 1948, detailing these lesions which now bear her name.

Born in Nashville, Tennessee on February 4th, 1910, she had a passion for music in her youth, and especially enjoyed the violin. She earned her M.D. from Vanderbilt University in 1932, and after World War II and her appointment with the Army Institute of Pathology, she took a position at the Memorial Sloan Kettering Cancer Centre where she came across twelve cases of what was then known as juvenile melanoma and recognised that these lesions have benign behaviour despite their resemblance to melanoma.

She is also recognised for her other contributions to pathology, especially for advocating the use of the pap smear when it first came on the scene.

For all of us who have done some biochemistry at uni, the name "Menten" will likely cause palpitations as it invokes memories of Michaelis- Menten enzyme kinetics, but few would realise that Menten's first name was Maud, and that she was... well, a she!

Born on March 20th, 1879 in Ontario, Canada, **Maud Menten** was to become a physician and a chemist. She studied in the University of Toronto, earning a B.A. in 1904, a Masters in 1907 and an M.D in 1911, to become one of the first women in Canada to earn a medical degree.

However, women were not allowed to participate in research in Canada at that time, so she moved to Berlin in 1912 where she worked with Leonor Michaelis and co-authored their seminal work on enzyme kinetics.

After completing her work in Berlin, she earned a PhD from the University of Chicago in 1916 with a dissertation entitled "The Alkalinity of the Blood in Malignancy and Other Pathological Conditions; Together with Observations on the Relation of the Alkalinity of the Blood to Barometric Pressure".

She went on to make significant contributions to biochemistry and in histochemistry. Her extensive work on alkaline phosphatase lead to her inventing the azo-dye coupling reaction still in use in histo labs today. It was referred to in Pearse's "Histochemistry: Theoretical and Applied", a major text book in its day, as "It is not too much to say that the use of this principle was a stroke of genius"

Upon her death in 1960, an obituary was published in *Nature* describing her as "untiring in her efforts on behalf of sick children. She was an inspiring teacher who stimulated medical students, resident physicians, and research associates to their best efforts. She will long be remembered by her associates for her keen mind, for a certain dignity of manner, for unobtrusive modesty, for her wit, and above all for her enthusiasm for research."

For the cytologists among the readers of this, I give you **Priscilla Taft**. She was born in Budapest, Hungary in 1917, she and her family emigrated to the US at the age of 5. After obtaining an undergraduate degree, she had hoped to study medicine and train to become a physician at Harvard, but the medical school denied her admission because she was a woman. Described as "feisty and determined", she did not let this stop her, and eventually secured admission to Yale, and trained as a pathologist in Massachusetts General after her graduation, where she eventually became director of the cytology laboratory, but not before arguing for pay equal to that of her male colleagues. Dr. Priscilla Dienes Taft was the first pathologist to practice cytopathology exclusively and directed Cytopathology at Mass General for over 30 years.

One of the classic texts of neuro-oncology, Russell and Rubinstein's *Pathology of Tumours of the Nervous System*, has a place on the bookshelves of most neuropathologists. There was, however, nothing commonplace about either author, and certainly not the Russell half of the partnership- **Dorothy Russell**, the first woman to be appointed to a pathology chair in Western Europe.
She was born in Sydney in 1895. Her father died of a chest infection when she was three. She then then moved to Queensland with her mother who married again, but a few years later died herself, from measles. Dorothy and her sister were sent to England to live with their late father's sister.
She excelled at school, and went to Girton College, Cambridge, obtaining a first in Zoology with the top mark among her peers. However despite her result, as a woman she was not entitled to be rewarded a degree.
She was, however, determined to study medicine. Towards the end of the First World War, medical schools where reluctantly beginning to open their doors to women to overcome the shortage of qualified doctors and medical students, and in 1919 she secured a place at The London Hospital Medical College, a notably male-oriented and culturally inbred establishment. Despite being viewed as second class reportedly ignored in lectures, she excelled, and was awarded an undergraduate prize in pathology. After graduating, she entered the Institute of Pathology and then obtained a three year research attachment. Her interest focussed on Neuropathology, and years later in 1946 she became professor of morbid anatomy and Director of the Institute of Pathology, the first female to be appointed a pathology chair in Western Europe.

Last but by no means least, let's meet **Elizabeth Stern**. She was a Canadian born (1915) American pathologist. After receiving her medical degree from the University of Toronto in 1939, she migrated to the US and became a naturalised citizen in 1943. After becoming certified by the American Board of Pathology, she became interested in the progression of cervical cancer, and published her first papers on the subject. She was a driving force in defining dysplasia as the earliest sign of cervical cancer development, and her breakthrough studies changed the disease from fatal to one of the most easily diagnosed and treated cancers there is. She also published a paper in Science in 1977 demonstrating the link between oral contraceptive pills and cervical cancer.

It is because of Dr Stern's findings that Pap smears were adopted routinely and can identify cervical cancer early in its development. Her work has had a lasting impact on women's healthcare, improving cervical cancer diagnosis and promoting the inclusion and protection of all women against disease.

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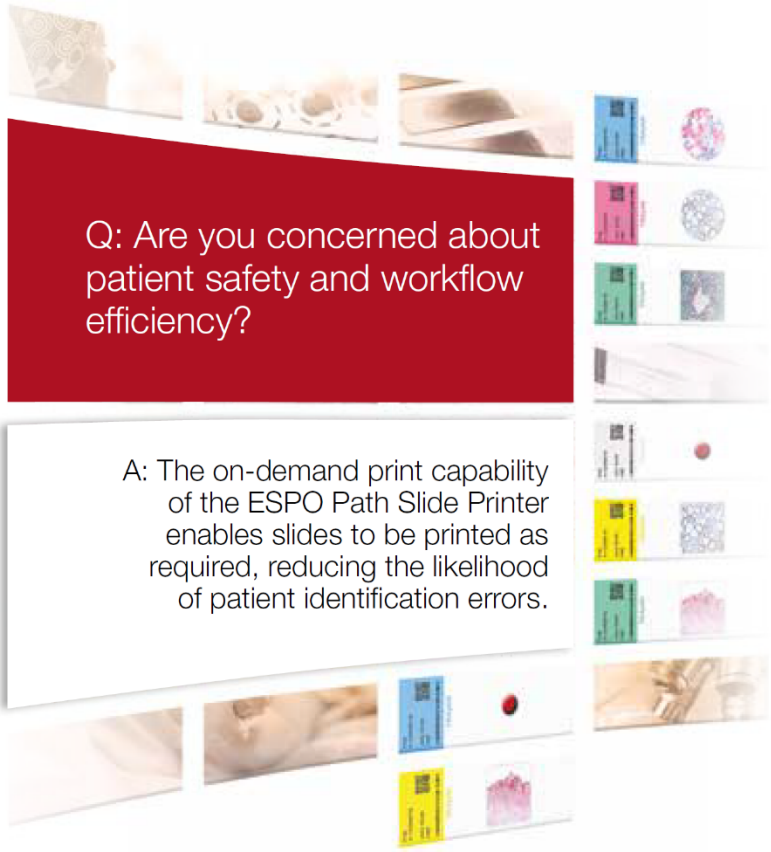

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- Double-width slide capacity (optional)
- Flexible Priority/STAT slide position allocation
- Parallel operation: slide loading and preview in parallel with scanning
- Three individual objectives exchangeable automatically during scanning
- Multilayer (Z-stack) and Extended Focus scanning (optional)
- 1D and 2D barcode reading and parsing
- Automated tissue detection and coverslip detection

[1]Actual scanning time dependent on slide quality, local server speed and other factors

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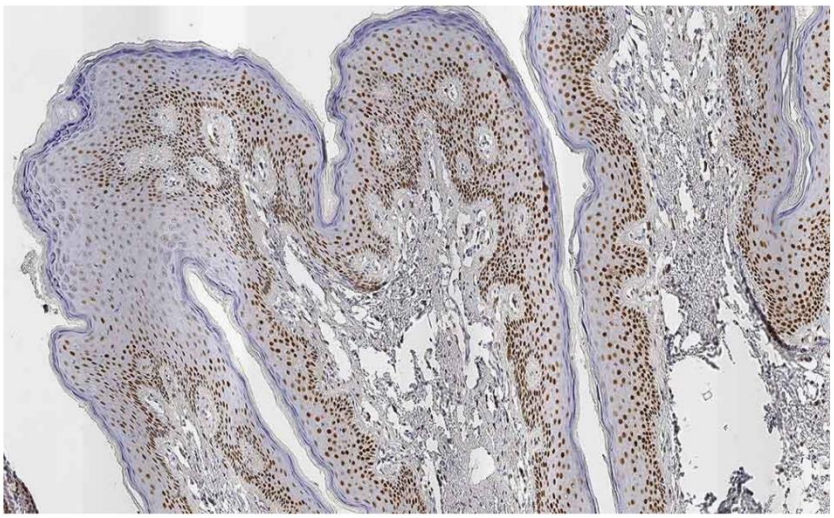
IHC ANTIBODY SPOTLIGHT:

Androgen Receptor

The androgen receptor (AR) is a member of the superfamily of ligand responsive transcription regulators. The androgen receptor is in the nucleus where it is believed to act as a transcriptional regulator mediating the action of male sex hormones (androgens). The androgen receptor has wide distribution across several tissue types e.g. prostate, skin, and oral mucosa. Androgen receptor has been reported in a diverse range of human tumors e.g. osteosarcoma.[1] The receptors are present in many of the body's tissues. The resulting androgen-receptor complex then binds to DNA and regulates the activity of androgen-responsive genes. By turning the genes on or off as necessary, the androgen receptor helps direct the development of male sexual characteristics.



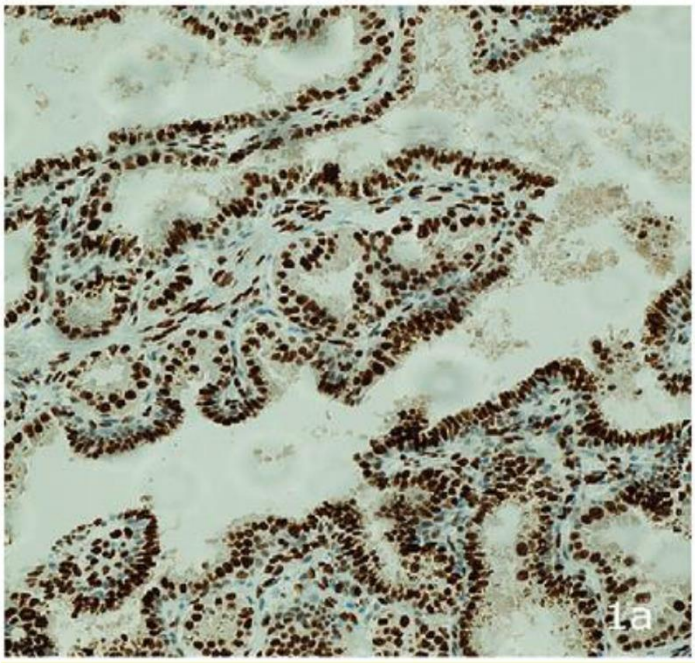
Human skin: immunohistochemical staining for Androgen Receptor. Note the nuclear staining of the epithelial cells. Androgen Receptor: clone AR27 [1]

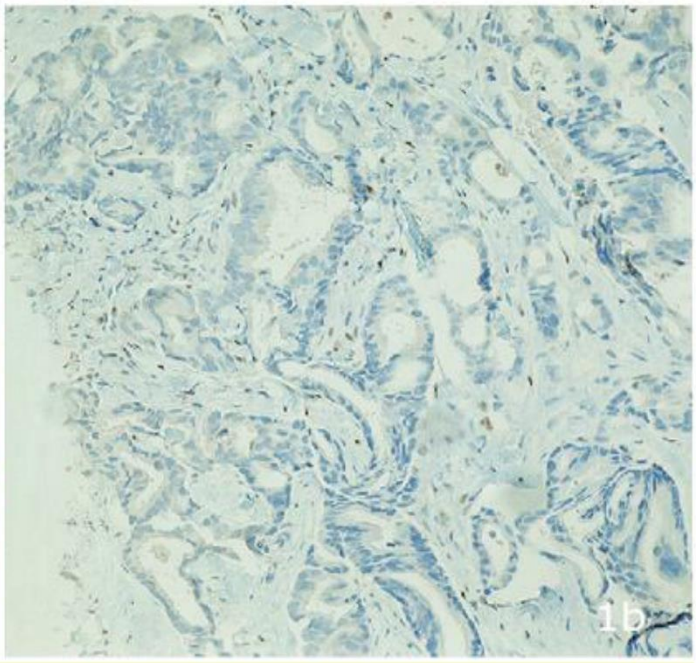
Sourced from: https://shop.leicabiosystems.com/en-au/ihc-ish/ihc-primary-antibodies/pid-androgen-receptor

AR signaling may also be involved in the development of tumors in the prostate, bladder, liver, kidney and lung.[2] Several diseases, such as androgen insensitivity syndrome (AIS) and prostate cancer, are associated with alterations in AR functions.[3]

Introducing drugs that prevent the production of androgens and/or block the action of the AR, inhibits prostate cancer growth. However, it should be noted that resistance to these drugs often occurs after 2–3 years as the patients develop castration-resistant prostate cancer (CRPC).[3] In CRPC, a functional AR remains a key regulator. To briefly elaborate, there are four possible mechanisms of CRPC development: 1) Increased sensitivity of the AR to its agonists, 2) AR mutations that render the receptor responsive to alternate, non-androgen ligands, 3) ligand-independent AR activation, and 4) AR-independent mechanisms. CRPC patients are usually treated with chemotherapy.

More recently, the androgen receptor has been investigated as a potential factor in the pathogenesis of breast cancer. AR is expressed in 60–80% of breast cancers, with higher prevalence among estrogen receptor-positive (ER+) tumors.[4] AR antagonists are also being investigated in preclinical and clinical studies. Currently available AR inhibitors are being widely used to treat prostate cancer and are showing encouraging results in several clinical trials in breast cancer. A phase II clinical trial evaluating bicalutamide, a first-generation AR antagonist, in AR-positive/ERα-negative/PgR-negative advanced breast cancers, showed a clinical benefit rate of 19% at 6 months and a median progression-free survival duration of 12 weeks.[5] The value of AR as a biomarker and therapeutic target in breast cancer is still unclear at this time. There are contradictory results, due to the heterogeneity of the disease, as well as to the fact that there is no well-defined cut-off value of AR positivity. The dual role of AR as either a suppressor or inducer of tumor progression enables both androgens and antiandrogens to be used in potential therapeutic regiments. For further information I would highly recommend reading references 4 to 6, that look at the androgen receptor in breast cancer and provide more detail to this brief overview.





Left image (1a): Androgen receptor positive breast cancer. Stained androgen receptor in breast cancer tissue (DAB);

Right image (1b): Androgen receptor staining on negative breast cancer. Note, no DAB staining in androgen receptor negative breast cancer tissue.[6]

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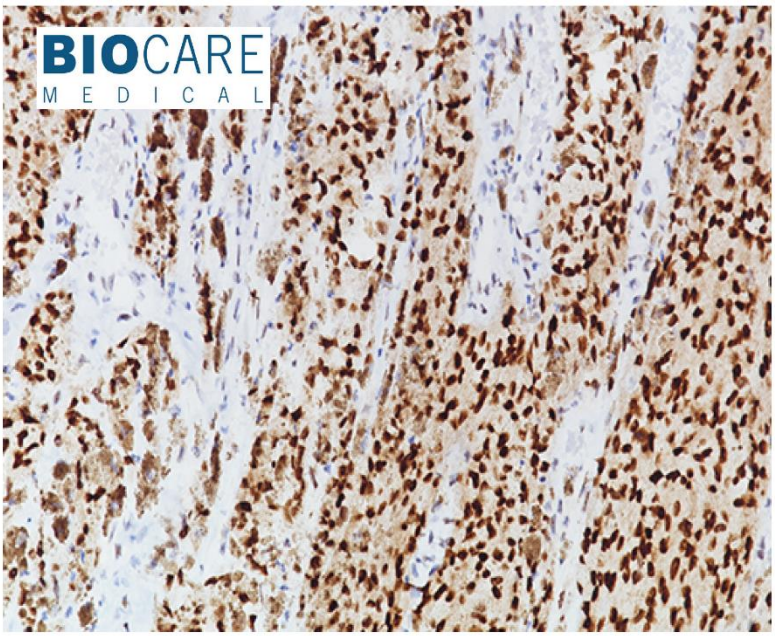

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*Lezcano, C et al. PRAME Expression in Melanocytic Tumors. Am J Surg Pathol. 2018 Nov; 42(11): 1456–1465.

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Future Events: 2022

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HGVT Scientific Meeting

Topic: Green Lab **Venue:** Peter Mac (Level 7) (Recorded virtually via Zoom)

Date: 29th June, 2023

HGVT Scientific Meeting

Topic: Prostate Cut Up **Venue:** Peter Mac (Level 7) (Recorded virtually via Zoom)

Date: July/August, 2023

Trivia Night

Venue: TBA

Date: 15th September, 2023

HGVT Scientific Meeting

Topic: TBA Venue: Peter Mac (Level 7) (Recorded virtually via Zoom)

Date: October, 2023

One Day Seminar/Workshop

Venue: TBA