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TURN
what if...
INTO
WHAT IS

Stop wondering
“**what if**” and
find out
“**what is**” by
understanding your
patients’ individual
tumour biology, and
move forward with
confidence in their
treatment plan¹



*Group average

This is an example of a node-negative patient

Personalise each
chemotherapy
decision²⁻¹⁰

Visit
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Only the Oncotype DX Breast Recurrence
Score[®] test can predict the magnitude of
chemotherapy benefit^{2,3}

HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive.

References: **1.** Licata et al. *NPJ Breast Cancer*. 2023. **2.** Paik et al. *J Clin Oncol*. 2006. **3.** Albain et al. *Lancet Oncol*. 2010. **4.** Paik et al. *N Engl J Med*. 2004. **5.** Dowsett et al. *J Clin Oncol*. 2010. **6.** Kalinsky et al. *N Engl J Med*. 2021. **7.** Geyer et al. *NPJ Breast Cancer*. 2018. **8.** Sparano et al. *N Engl J Med*. 2018. **9.** Sparano et al. *N Engl J Med*. 2019. **10.** Sparano et al. *Abstract GSI-05, SABCs*. 2022.

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**EXACT
SCIENCES**



I've seen several movies lately featuring artificial intelligence (AI) as the enemy. None of them ended well. And that got me thinking about other examples; that didn't end well either. For starters, most of humankind was imprisoned and used as a power source in *The Matrix* series. The need to protect their assigned humans resulted in a very high body count in both *Megan* and *Terminator 2*. Robots went well and truly rogue in *The Day The Earth Stood Still*, *RoboCop*, and *I, Robot*. Control systems HAL 9000 in *2001: A Space Odyssey*, SkyNet in the *Terminator* series, even AUTO in *WALL-E*, were all hell-bent on destruction. But the humanoid AIs are perhaps the most terrifying of all, if *Blade Runner*, *Alien*, and *Ex Machina* are anything to go by.

Thankfully, the real stories of AI advances, in healthcare in particular, are far more positive than the fictional accounts (otherwise, I would be fleeing to my fictional underground bunker). Genomics is one area in which AI is truly helping. After all, diagnosing rare genetic conditions is a painfully slow process for the brains of us mere mortals – with huge disease data sets to interpret and reams of literature to take into account. Similarly, in proteomics, AI-based systems can produce far higher peptide identification rates than previous algorithms.

ChatGPT is perhaps the most famous AI innovation of the moment – and so it receives more than its fair share of positive and negative press. For every headline on students using the tool to write their essays or the system breaking copyright laws, there's one highlighting how it helped researchers perform their literature searches or improved user experience in a customer service environment.

In the fascinating article, "Path Chat," pathologist Matthew J Cecchini asks his brilliantly named ChatGPT co-pilot, Pathrick, to explain the practical applications of AI in pathology. Now, Pathrick may well be a touch biased, but it does suggest several tempting ways to use language models to help with admin-type tasks – for example, writing grant applications and curating student education materials. It is also insistent that it does not want to take your jobs, and it notes that AI-generated content should always be reviewed for accuracy by a human expert. (That sounds neither power-crazed nor evil to me – unless Pathrick is cleverly lulling us into a false sense of security...)

What are your thoughts on AI in the lab? How are you using ChatGPT or other AI tools? Send your opinions and stories to edit@thepathologist.com – several real human beings look forward to reading them.

Helen Bristow
Editor



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Evil AI?
by Helen Bristow

Upfront

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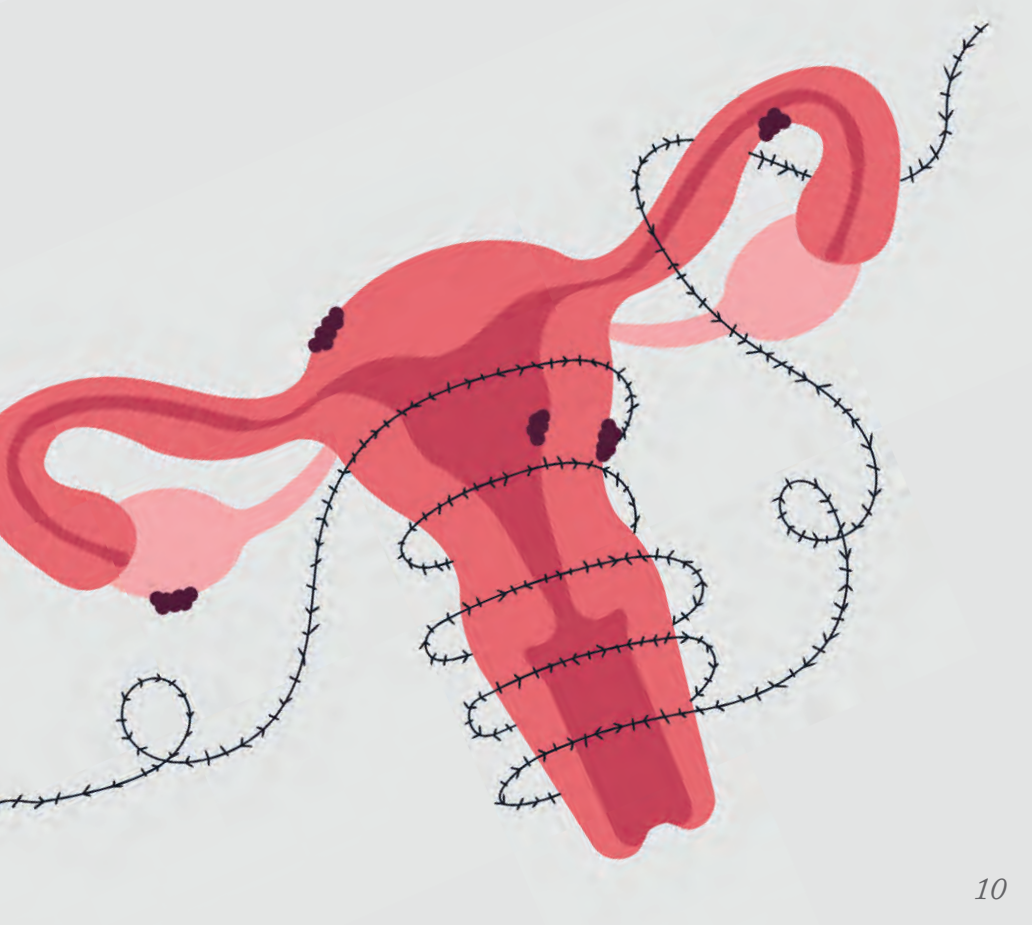


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Zooming in on Zika

Using spatial transcriptomics to investigate why Zika virus persists in the placenta

Zika virus is spread by *Aedes* mosquitoes, and while symptoms are generally mild, catching the disease during pregnancy can cause serious birth defects. During the Zika epidemic of 2015–2016, the number of offspring born with microcephaly greatly increased (1). Other health issues, such as Guillain-Barré syndrome, neuropathy, and myelitis, have also been linked to Zika virus. To understand the molecular mechanisms behind the virus' effects, researchers from The Baylor College of Medicine, Texas, have studied placenta-specific microRNAs – well known hotbeds of viral persistence.

The study was conducted in three stages. First, researchers used primary human trophoblast cultures to see how microRNA–messenger RNA interactions changed in the presence of Zika virus. Second, a germ-free mouse model was used to investigate the importance of these microRNA and RNA interference networks in Zika

virus pathogenesis. Researchers also looked at how enoxacin – an antibiotic known to increase microRNA – influenced the virus. The final step used novel spatial transcriptomics to look closely at infected mice placenta to identify any changes that the Zika virus had caused in immune microenvironments.

Overall, the study showed that Zika virus causes disruption to placental microRNA regulation networks. Further, they found that enoxacin abolished viral persistence and prevented

fetal growth restriction in the infected mice. “It’s really important to understand how viruses are – or are not – able to set up a niche in the placenta at the maternal–fetal interface,” said Enrico Barrozo, co-author of the paper, in a press release (2).

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1. E R Barrozo et al., *Am J Obstet Gynecol* (2023) [Online ahead of print]. PMID: 37598997
2. Baylor College of Medicine (2023). Available at: <https://bit.ly/3rMwHI8>

Upfront

Research
Innovation
Trends

INFOGRAPHIC

Saving Our Skin: What Are the Global Rates of Skin Cancer?

How do non-melanoma skin cancers stack up against their melanoma cousins?

www.thepathologist.com

Worldwide skin cancer cases 2020

Melanoma:
324,635

Non-melanoma:
1,198,073

Global non-melanoma skin cancer deaths, 2020

63,731

Global melanoma skin cancer deaths, 2020

57,043

**RESEARCH ROUNDUP****We summarize five studies across pathology and laboratory medicine***The cold truth*

A genome wide association study for Raynaud's phenomenon (RP) – a vasospastic disorder that affects the hands and feet – has identified *DRA2A* and *IRX1* as candidate causal genes that predispose individuals to the disease. This finding highlights RP as a disease with complex genetic architecture rather than a cold-induced phenomenon (1).

Brain burden

Many studies have supported a connection between viral infections and an increased risk of neurodegeneration. New research indicates that the neurological effects of COVID-19 could possibly lead to Alzheimer's disease (AD) or exacerbate existing AD pathologies through inflammatory processes. The paper concludes that the synergistic effect of the interaction of these diseases needs to be explored in more detail (2).

The scores on the doors...

A recent study has found that polygenic risk scores perform

poorly in population screening, individual risk prediction, and population risk stratification. The team reviewed 926 polygenic scores for 310 common diseases, finding that five percent of people who do not develop the disease test positive and only 11 percent of individuals who actually develop the disease are identified (3).

Probing proteins

Using cryo-electron microscopy, researchers have analyzed the structure of two proteins heavily involved with immune response – C3aR and C5aR1. The images provided detailed insight into the molecular mechanisms of ligand binding, how the receptors change shape when activated, and how they interact with different molecules (4).

Take your vitamins!

Researchers have explored the connection between vitamin B12 and inflammation – and found that individuals with higher serum levels of vitamin B12 had lower concentrations of the inflammatory markers IL-6 and CRP (5). They hope to explore the potential role of B12 in disease management.

See references online at:

tp.txp.to/1223/roundup

Head or Heart**What are the genetic links between cardiovascular disease and schizophrenia?**

New research in *The American Journal of Psychiatry* has established a genetic link between cardiovascular disease (CVD) and schizophrenia risk factors (1).

It was previously known that schizophrenia carried an increased risk of CVD in individuals – up to two- to threefold greater in some cases (2) – but the mechanisms behind this link were not well understood. Seeking to reveal the potential genetic causes for the increased risk, researchers analyzed genome-wide association study results for any genetic architectures that were shared between schizophrenia and CVD risk factors.

The study found that a significant number of genetic variants that underlie schizophrenia also have an effect on CVD phenotypes. The paper states that there is an “inherent propensity” to smoking behaviors in those with schizophrenia, yet a number of risk loci for schizophrenia are protective against CVD-influencing obesity. More research will be needed to explore the genetic drivers for these comorbidities in greater detail.

See references online at:

tp.txp.to/1223/head-vs-heart

Distribution of global skin cancer cases

Melanoma:
22%*

Non-melanoma:
78%*

*Note: approximate percentages

Cancer rates by country

Non-melanoma skin cancer rates per population

- 1. Australia 58,839**
- 2. New Zealand 10,271**
- 3. US 524,737**
- 4. Canada 61,645**
- 5. Switzerland 12,772**

See references online at: tp.txp.to/1223/skin-cancer

Melanoma skin cancer rates per population

- 1. Australia 16,171**
- 2. New Zealand 2,801**
- 3. Denmark 2,886**
- 4. The Netherlands 8,310**
- 5. Norway 2,567**

Melting Away the Mystery

Unraveling Ötzi the Iceman's past with advanced genome sequencing

In September 1991, two German tourists stumbled across a mummified corpse trapped in the ice of the Ötztal Alps. After extensive archaeological examination, it was discovered the body was around 5,300 years old. Nicknamed Ötzi the Iceman (and known more formally as the Tyrolean Iceman), the remains provided a unique insight into the Neolithic age and the hunter-gatherer lifestyle.

Although some mysteries remain, including the circumstances of his death and why there was an arrowhead lodged in his left shoulder, a great deal has been discovered – even down to his last meal (spoiler alert: he liked red deer and dried ibex meat). Ötzi's genome was last sequenced over 10 years ago, but, as is well known in diagnostic circles, sequencing technology has come on leaps and bounds since 2012. And that's why Albert Zink, a mummy researcher at Eurac Research



Credit: Ötzi Museum Bozen by André Schade / CC BY

in Bolzano, conducted a high-coverage analysis of Ötzi's genome to reveal more about his genetic history and phenotypic traits (1).

"I'm often asked if, after 33 years of iceman research, shouldn't everything be known?" said Zink in a *Nature* news article (2). "That's not the case. I think there will always be new doors opening for research." And boy was he right. Zink's research found that Ötzi didn't have Steppe-related ancestry as previously hypothesized, but instead had Anatolian-farmer ancestry. Markers were also found for type 2 diabetes and obesity-related metabolic syndrome. But perhaps the most discussed findings are the ones that have led the world to

rethink Ötzi's physical appearance. It is now thought his skin was much darker and, because he carried the allele for male pattern baldness, it is likely he had little hair when he died. "I was surprised," Zink said. "But when I thought about it, it explains much better why the mummy looks like it does."

These welcome insights likely only scratch the surface of a complex life. Perhaps in another 10 years, we might know his entire life story...

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1. K Wang et al., *Cell Genom*, 3 (2023). PMID: 37719142.
2. *Nature* (2023). Available at: <https://go.nature.com/3tAtTOT>

Hitting the Right Note

What did the first-ever genomic analysis of Beethoven's hair reveal?

In a document known as the *Heiligenstadt Testamen*, Ludwig van Beethoven implored his physician to unravel the complexity of his declining health. Researchers have

strived to honor his wishes, and presented hypotheses – such as coeliac disease, lactose intolerance, and lead exposure – all of which have been debunked.

A study led by The University of Cambridge conducted the first-ever genomic analysis on preserved locks of Beethoven's hair, where significant genetic risk factors for liver disease were revealed. Further, metagenomic analyses showed a hepatitis B infection that – paired with excessive alcohol consumption – likely



Credit: raphael.com

contributed to his death (1).

They also compared the Y-chromosome in Beethoven's genome with Y-chromosomes sequenced from five living Van Beethoven males – and found them to be very different. It was concluded that an "extra-pair-paternity event" had likely occurred in the patrilineal ancestry...

See references online at: tp.txp.to/1223/right-note



IMAGE OF THE MONTH

Purrfect Pathology

This entry to Image of the Month comes from Martin Mæng Bjørklund via email. Martin wrote: “Please find attached two images to consider in the ‘Image of the Month’ category. Story behind the picture: This summer I found my cat relaxing in the garden while reading *The Pathologist*. Your content is interesting for humans as well as animals! Thank you for considering and for always providing insightful articles in the magazine.”

Martin Mæng Bjørklund a pathologist in training, Department of Pathology, Odense University Hospital, Denmark.

Do you have a photo suitable for Image of the Month?
Send it to edit@thepathologist.com

QUOTE OF THE MONTH

“The current generation of AI tools must seem just as magical to us as the steam engine or first planes did to previous generations. There are many reactions to these technologies, ranging from disbelief through excitement and all the way up to fear. Regardless, these technologies – like the steam engine and airflight – will fundamentally change the world.”

Matthew J. Cecchini.

Turn to page 18 to see the full article!



Let's Talk T Cells

Could transgenic T cells help treat glioblastoma?

Glioblastoma is the most aggressive type of brain cancer. There is currently no cure – and treatments prolong life rather than save it. Researchers from the German Cancer Research Center and the University Medical Center Mannheim hope to change this, and have turned to transgenic T cells to treat glioblastoma in a recent paper.



Image by Alexa Fotos from Pixabay (edited)

Glioblastoma patients were inoculated with a tumor-associated antigen harbored in NLGN4X – a protein involved in the formation of synapses, and typically overexpressed in human gliomas. Blood samples from vaccinated individuals were collected, and NLGN4X-activated T cells were isolated to access the specific T cell receptor.

In a culture dish, the team proved these human T cells effectively lysed NLGN4X-expressing tumor cells. The method was also tested in glioma-bearing mice, where transgenic NLGN4X-specific human T cells were administered intracerebroventricularly. The diseased mice had a response rate of 44.4 percent, compared with zero percent in control groups. The study showed how promising transgenic T cells are as a therapeutic strategy to target glioblastoma-associated antigens.

See references online at:
tp.txp.to/1223/t-cells

End o' the Stigma

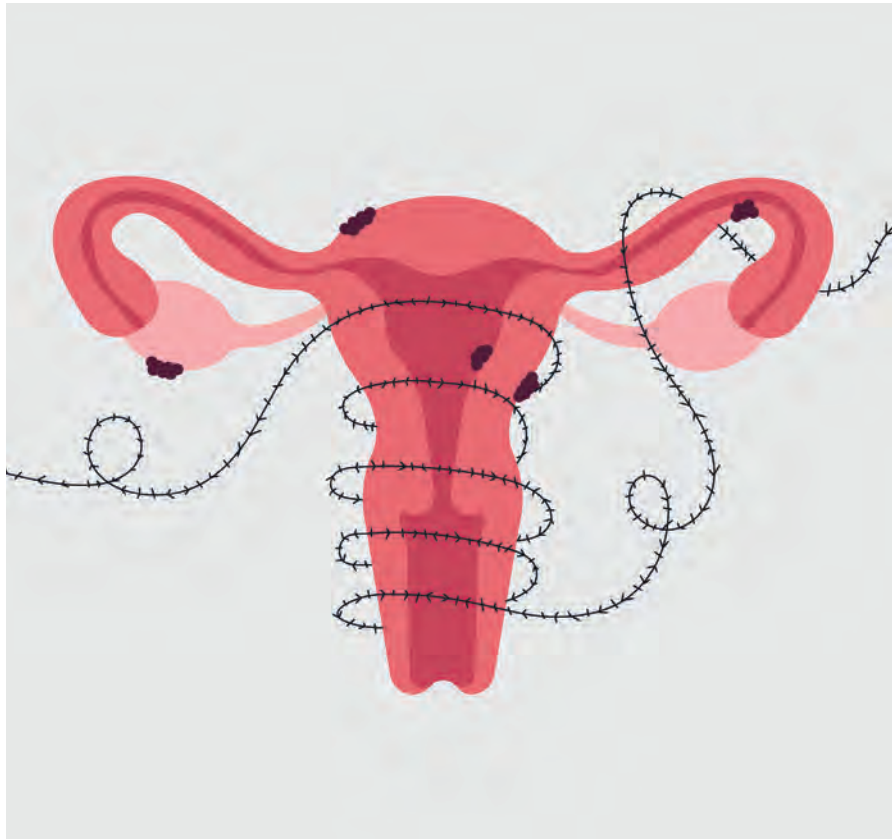
“Endometriosis should be viewed as a chronic systemic disease,” says researcher, following discovery of a genetic link between the condition and several mental health disorders

Menstrual stigma – “Why are you always so moody?” or “It’s just your period, get over it!” – can negatively affect clinical outcomes and mental health for women experiencing intense menstrual pain. But that’s also the reality for many women battling endometriosis – a highly undiagnosed disease.

Now, a genetic link between the condition and several mental health disorders (depression, anxiety, and eating disorders) has been found by researchers from The Yale School of Medicine, who conducted a large-scale genomic and epidemiological study (1). The results suggest that endometriosis should be considered from a more comprehensive perspective.

It is known that individuals suffering from chronic pain develop psychiatric disorders more often compared with those without. For several diseases, there is biological evidence for this association, but not much is known about endometriosis.

“Given that this debilitating disease affects 10 percent of women worldwide, we think it is important to investigate if we find a similar pattern to improve the quality of life of patients and also raise awareness,” says Dora Koller, postdoctoral fellow at the University of Barcelona, research affiliate at Renato Polimanti’s group at Yale University, and principal author of the study. “I also suffer from endometriosis, which



was undiagnosed for 15 years, so I really wanted to know about such unexplored comorbidities of the disease.”

The research team used several methods to analyze samples from >200,000 women, including genetic correlation, Mendelian randomization, pleiotropy, and pathway analyses. The team demonstrated a genetic relationship between endometriosis, anxiety, and eating disorders for the first time, highlighting that chronic pain is not the sole factor explaining this association. In reality – and to the researchers’ surprise – women suffering from these psychiatric disorders might be predisposed to develop endometriosis, but the vice versa remains elusive.

So does this deeper understanding erase the stigma of the disease? Not entirely, but progress has certainly been made, according to the researchers.

“Endometriosis should be viewed as a chronic systemic disease, with manifestations beyond the reproductive system, affecting every aspect of health, and the quality of life of women,” says Koller. “Researchers, healthcare providers and the public should acknowledge that some patients with endometriosis are genetically predisposed to develop adverse mental health outcomes.”

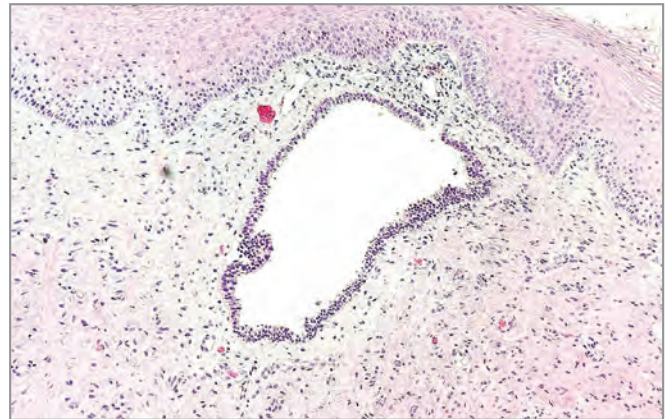
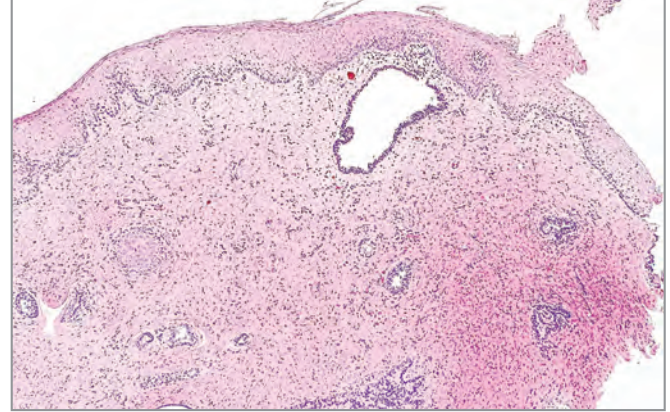
“We believe that advanced genomic methods will give the answers to many questions clinicians and scientists have about endometriosis. The most important aspects are developing non-invasive diagnostic tests and finding better therapeutic options to cure the disease.”

Reference

1. D. Koller et al., *JAMA Netw Open*, 6, 1 (2023) PMID: 36652249



CASE OF THE MONTH



A 60-year-old female presents with a mosaic, granular patch noted on the upper third of vagina during colposcopy. It did not stain with iodine. Biopsy is shown above. What is the diagnosis?

Submitted by Jay Hwang and Cole Biehl, Department of Pathology and Laboratory Services, Brooke Army Medical Center, San Antonio, Texas, USA.

Given the morphologic findings, what is the most appropriate diagnosis?

- a) Endometriosis
- b) Bartholin gland cyst
- c) Clear cell adenocarcinoma
- d) Vaginal adenosis

Answer to September/October's Case of the Month

- b) *Glomus tumor*

Glomus tumor with myxoid changes is the most appropriate diagnosis. The tumor is composed of a well circumscribed dermal proliferation of nested, small round, monomorphic cells. Dilated slit-like vascular channels are scattered throughout the tumor. As in this case,

mucinous changes have been reported in a variant of glomus tumor. Glomus tumors resemble elements of the glomus apparatus in the skin and are derived from cells that are part of the Sequet-Hoyer canal, as described by Masson in 1924 (1). Clinically it presents as a small, solitary, painful, red-blue nodule on the fingers and toes, particularly on the nail bed. Extracutaneous sites include trachea, deep soft tissue, bone, gastrointestinal tract, lung, oral and nasal cavity (2).

Submitted by Muhammad Absan, Chughtai Institute of Pathology, Lahore, Pakistan, and Rida Noor, Faisalabad Medical University, Faisalabad, Pakistan.

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1. TF Goodman, "Fine structure of the cells of the Suquet-Hoyer canal," *J Invest Dermatol*, 59, 363 (1972). PMID: 5086685.
2. Z Gombos, PJ Zhang, "Glomus tumor," *Arch Pathol Lab Med*, 132, 1448 (2008). PMID: 18788860.

To register your guess, please go to <http://tp.txp.to/1223/case-of-the-month>
We will reveal the answer in next month's issue!

The Story Continues To Be Written

The ever-developing tale of companion diagnostic tests in precision oncology

Gone are the days of one-size-fits-all medicine. Today, the pipeline of targeted therapies for a range of complex diseases is rapidly expanding with more than 300 precision medicines currently available (1). Access to these new therapies can make all the difference in patient outcomes, particularly when it comes to hard-to-treat cancers that may otherwise have limited treatment options. To match patients with these promising treatments,



“We have received regulatory approvals for nine CDx biomarkers for 17 therapies on label, for non-small cell lung cancer (NSCLC) as well as thyroid cancer and cholangiocarcinoma.”

a companion diagnostic test (CDx) is required.

CDx tests help identify whether a patient is an appropriate candidate for a particular targeted therapy based on their tumor's genetic profile. Historically, this testing used to be done looking at a single biomarker at a time. Today, next-generation sequencing (NGS) allows for the simultaneous evaluation of multiple genes, delivering results in as little as 24 hours.

Thermo Fisher Scientific, with its Ion Torrent sequencing platform and Oncomine assays, is one of the key players in this field. We sat down with Jane Li, Senior Director of Oncology, Pharma and CRO Partnerships to learn more about this era in companion diagnostics.

Thermo Fisher's Oncomine Dx Target Test* was the first NGS-based companion diagnostic approved by the US FDA in 2017 (2). Could you tell us about the advancements since the first approval?

Since 2017, we have been focusing on expanding the indications and access to our CDx test. We have received regulatory approvals for nine CDx biomarkers for 17 therapies on label, for non-small cell lung cancer (NSCLC) as well as thyroid cancer and cholangiocarcinoma. The test, with different indications per local regulatory approval, is now available in 18 countries

across the globe. And we continue expanding further, working with both current and new pharma partners.

What is the most recent news?

Last year we launched in Europe the Oncomine Dx Express Test ** (3), an in vitro diagnostic (IVD) CE marked test that is used with the Genexus Dx System to deliver clinically relevant tumor mutation profiling in as little as 24 hours utilizing a highly automated workflow from both formalin-fixed, paraffin-embedded tissue and liquid biopsy samples. This year we've continued registering the solution in a number of Asia-Pacific countries. For example, last month it was approved in Malaysia.

Our focus now is working with our partners on new, rapid CDx tests using the Oncomine Dx Express Test. This will enable more labs to bring the power of genomic testing in-house, closer to the patients, and thus improve the access to the new targeted therapies

Recently, we announced a partnership with Boehringer Ingelheim (4) to develop CDx tests to help identify a subset of patients with NSCLC for targeted therapy treatment. This partnership aims to develop multiple CDx tests, based on the Oncomine Dx Express Test, to help ensure labs will have the ability to match eligible patients with emerging NSCLC treatments as they become available.

What opportunities do you see for further expanding access to companion diagnostics?

Companion diagnostics can be co-developed alongside targeted treatments through clinical trials as the primary CDx, or after a therapy has been marketed as a follow-on CDx. They are ideally approved at the same time as a targeted therapy and launched simultaneously to ensure patients can access the new treatment's benefits right away.

However, developing additional so-called “follow on CDx” tests can provide more options, particularly as new, improved diagnostic technologies are made available, and expand access to testing.

We are currently working with multiple pharma partners on “follow on CDx tests”. For example, this year we announced a partnership with AstraZeneca (5) to develop solid tissue- and blood-based CDx tests for osimertinib. While this drug is currently approved in numerous countries and regions around the world with a single gene PCR-based test, NGS-based CDx tests may, in future, further improve patient access.

Also, last month we announced a new submission to regulatory authorities in Japan with a MET exon14-skipping mutation CDx test for capmatinib, in partnership with Novartis. This drug was originally approved in Japan with FoundationOne®CDx as the CDx, however, the patient access to this drug was compromised, by unavailability of Foundation Medicine service in Japan.

Where do you see the role of liquid biopsies in companion diagnostics?

The role of liquid biopsies is becoming increasingly significant, as they are less invasive than tissue biopsies. They make molecular testing possible when tissue is not available, which is often the case, especially in NSCLC. Pharmaceutical companies are recognizing this opportunity and are looking for diagnostic partners who can develop liquid biopsy tests that can be implemented in a broad spectrum of labs.

The Oncomine Dx Express Test provides the ability to analyze both tissue and liquid biopsy samples and the partnership with AstraZeneca will also leverage this feature.

In addition, we are working with two more partners on developing tissue and liquid biopsy CDx tests to identify patients

with EGFR exon 20 insertion mutations who may be eligible for the respective targeted therapies.

Are you planning to expand the CDx indications beyond the NSCLC?

Yes, of course; whilst NSCLC continues to be the most active space with regards to new therapy developments, we are increasingly seeing new drug trials outside of lung indications.

The Oncomine Dx Express Test covers relevant genes and variants across numerous solid tumor types, including NSCLC, breast, melanoma, colorectal, and thyroid, amongst others, and we are already discussing new projects outside of the lung indication.

So when do you think we are going to hear more news?

Soon. In addition to the aforementioned projects, we are also preparing Oncomine Dx Express Test submissions to the US and Japan authorities, as well as in vitro diagnostic regulation (IVDR) registration.

It is our mission to make the rapid CDx testing available worldwide as soon as possible, to empower clinicians to choose the most appropriate treatment for their patients.

Learn more at www.oncomine.com/pharma

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4. Thermo Fisher Scientific (2023). Available at: <https://bit.ly/46tVf70>.
5. Thermo Fisher Scientific (2023). Available at: <https://bit.ly/3sAN2jL>.

“Pharmaceutical companies are recognizing this opportunity and are looking for diagnostic partners who can develop liquid biopsy tests that can be implemented in a broad spectrum of labs.”

* For In Vitro Diagnostic Use

** For In Vitro Diagnostic Use. CE-IVD according to IVDD. Not available in all countries including the United States.

Abbreviated Intended Use: The Oncomine Dx Express Test is a qualitative in vitro diagnostic test that uses targeted next-generation sequencing (NGS) technology, the Ion Torrent Genexus Dx System to detect deletions, insertions, substitutions and copy number gain present in 42 genes and fusions in 18 genes from DNA and RNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor tissue samples. Oncomine Dx Express Test also detects deletions, insertions, substitutions in 42 genes and fusions in 7 genes from cfTNA extracted from plasma samples.

The Virtual Pathology Lab

Zev Leifer describes how we can make practical online resources for pathologists and patients

By Zev Leifer, President and Chief Research Officer, The Leifer Institute for Molecular and Digital Pathology

There are many hurdles in the world of digital pathology, but I believe three in particular stand in our way. In this piece, I hope to show how I've tackled each of these through my online lab resource, and illustrate how the advantages of digital pathology are often the solutions to its greatest challenges. This can be seen as somewhat of a guide – highlighting how anyone, no matter the budget, can make practical resources for pathologists and patients.

The first challenge: to bring the non-expert into the world of a pathologist. The average person has no idea what goes on in a real laboratory – in this case a diagnostic pathology laboratory. How would they? Why should they? Well, let me tell you why.

For one, it is interesting! Plus, it gives you a chance to see what goes on behind



In My View
Experts from across the world share a single strongly held opinion or key idea.

the curtain. It would be a fascinating opportunity to see a real digital slide move right and left, zoom in and out. People may never get into a pathologist's lab, but they can easily access it here and it may be an exciting experience. Not to mention they will get to see what happens between the piece of them that was cut out and the strange words on the report that comes back; they may come to appreciate the skill and techniques that the pathologist brings to making that critical report and have increased respect for the pathologist's role in the patient's healthcare.

With regard to keeping patients interested, the best way, I believe, is via a story – and you can find a number on my virtual lab. In *The Sin of Occupying False Premises*, they see the back-and-forth between the pathology residents and the different possible diagnoses. In *Can You Find the Mucin That's Loose in the Tumor?* they see a resident arrive late for the discussion about staining, conduct his own stain and come up with an improper conclusion. In *Where's Patho?* they see that there is more to diagnosis than just a peek at the screen.

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These scenarios are short, but each gives a real life look at what goes on before the report comes back. The pathologist becomes more real, a professional to whom one can relate, doing a job one can respect from knowledge, not just from their credentials alone.

My first piece of advice is that it's important to bring the public into the world of the pathology lab, whether through education or entertainment.

The second challenge: to sharpen the skills of professional – but early career – pathologists

The stories I detail above have an even greater impact for pathology professionals. In *The Sin of Occupying False Premises*, for example, they see what misdiagnoses can occur if one does not pay attention to the notes from the clinician who submitted the biopsy. In *Can you Find the Mucin That's Loose in the Tumor?* they are reminded of the need to keep up with the latest literature. Other stories provide a good review of the pros and cons of different staining techniques. The tales told in *International Cases* make the point that one needs to watch out for look-alikes (is it a worm or tumor?) and a disease in a foreign country that we may not be familiar with in the US but should be – as *Did Lou Gehrig Eat Shark Fin Soup?* shows.

Although these stories are useful pathology teaching tools, the greatest

resource for professionals can be found in the access to whole-slide images. In undergraduate medical school, the textbook shows a static image – framed, idealized. In my virtual lab, the links are to digital slides of the whole “biopsy” slice (as available online), where the question is not only “what is it?” but “where is it?” The challenge that pathologists' face is that much of a real slide is actually normal tissue. They must know normal versus abnormal. They must be able to scan the whole slide and to find the region of interest, to decide which level of magnification is appropriate to make the relevant observation.

My second piece of advice is that it's important to train students and residents with real slides, using medical backstories that teach important professional lessons in an enjoyable way.

Third challenge: to do all of the above for free

Generally speaking, preparing new platforms and formats for medical education, especially in the digital realm, is highly expensive. Funding is needed for an IT department to develop software and purchase hardware. Funding is even needed to make it available online, to present it to the outside world. I have developed a way to save all that money. I used the Twinery site software (www.twinery.org) to create my virtual lab stories. The programming knowledge

needed is minimal. Page by page, the steps in the story emerged, including embedded links to outside locations. The end result was an HTML file on my desktop. No charge.

Then, I used a second site that hosted the HTML onto the web and made it available to the world. The site is Neocities (<https://neocities.org>). Again, no charge necessary. These two can form the basis for medical education in many disciplines at zero cost.

The key to this approach is the use of links. The slides presented here are not part of my collection, and so I have no need for a dedicated server to host them. Rather, these are all publicly available digital slides – whether my own set hosted by Pathomation, or digital slides built into journal articles or available collections. Speaking of journal articles, the same applies to them. There might be dialogue in one of my stories that says “Check out this article,” and with one click the reader has the actual journal in hand. The behind-the-scenes prerequisite (especially for the slides) is that the target is immediately available – so no passwords, and no multiple steps to get to what you want. So, as quickly as one could look down a scope or pull up an image, the reader is able to access any material that is used in the story. Verisimilitude!

My last piece of advice is that even if you have a small budget, your impact can still be big.



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Sustainability in the Laboratory

Let's paint the lab green

By E. Blair Holladay

In an era marked by growing environmental concerns and an urgent need for sustainability, medical laboratories can lead the charge to create effective, lasting change in healthcare. While laboratories play a central role in patient care and contributing to scientific advancements, we are also significant consumers of resources and producers of waste, and reducing our environmental footprint can help further promote high-quality care for patients and the planet.

To start, we must recognize that daily operations of medical laboratories mean consumption of resources and disposal of medical waste – including hazardous materials – that can have significant environmental consequences. Moving toward more energy-efficient equipment, conscientious procurement of materials, and sustainable waste management would put laboratories in a prime position to reduce their environmental impact. As the hub of every hospital system, when we make positive changes to a laboratory's processes, a ripple effect happens, and we influence the way other departments operate, not just our own.

What's more, as environmental regulations become increasingly stringent, adopting greener policies in the laboratory can help avoid penalties or even legal consequences, and proactively meet regulatory requirements, ultimately safeguarding a laboratory's reputation and ensuring uninterrupted operations. Ensuring the good standing of a laboratory is paramount to patients and their care teams, setting up a culture of trust for the patient through their healthcare journey, which is often pitted with so much uncertainty.



The laboratory has always been a leader in healthcare, and it is our duty to remain so as we shift to greener processes. Some may question whether moving toward more sustainable practices in the laboratory will hinder scientific discovery or potentially disrupt patient care. In fact, the opposite is true. Sustainability practices can enhance research and innovation in a number of ways:

- **Long-term viability:** sustainable practices ensure long-term viability of laboratory operations. By reducing consumption and waste generation, laboratories can operate more efficiently and economically, which translates to a more stable and reliable environment, allowing pathologists and laboratory professionals to focus on their work rather than dealing with resource shortages or operational disruptions
- **Cost savings:** sustainability measures can lead to significant cost savings in the laboratory. Energy-efficient equipment and lighting, for instance, can reduce electricity bills. Recycling and waste reduction initiatives can lower waste disposal costs. These savings can be reinvested into research and development, or the expansion of

laboratory teams, aiding in continued delivery of high-quality care for patients

- **Scientific innovation:** sustainability challenges can drive scientific innovation through the exploration of sustainable materials, processes, and technologies. Doors are opened for the discovery of sustainable diagnostic methods and pharmaceuticals. Laboratories that prioritize sustainability contribute directly to this innovative ecosystem

The laboratory is not exempt from the imperative of sustainability that permeates our modern world. Instead, it represents a unique intersection of scientific advancement and environmental responsibility, and its importance cannot be overstated. As pathologists and medical laboratory scientists, it is up to us to make the steps toward change that can and will create a significant shift in how a healthcare system operates. Creating more sustainable and environmentally focused processes is not only a practical necessity, it also ensures we, as leaders in healthcare, maintain our quest for knowledge and commitment to patient care, recognizing the impact we have on our environment, past, present, and future.

UPCOMING WEBINARS FROM THE PATHOLOGIST

Multicenter study of the OncoPrint Comprehensive Assay Plus for local comprehensive molecular profiling

Thursday, December 11th, 5pm CET

In this webinar, Dr. Jantus-Lewintre shares her lab's experience evaluating the OncoPrint Comprehensive Assay Plus. She will present analytical performance results spanning 5 different centers using a cohort of 193 pre-characterized clinical research tumor samples. She describes considerations for performing molecular testing in-house and the value of amplicon-based CGP.

RSVP!



Implementing liquid biopsy testing in a routine lab

Thursday, December 14th, 11am ET

The goal of this webinar is to share the learnings around the ease of onboarding a liquid biopsy solution in a laboratory setting and to review the performance of two liquid biopsy assays versus other molecular testing techniques.

Register now!



The pathologist's impact on clinical practice & patients' lives

Monday, December 18th, 11am ET

We are delighted to welcome you to this webinar, sponsored by Exact Sciences, about the changing role of pathologists in the area of precision oncology.

Don't miss out!



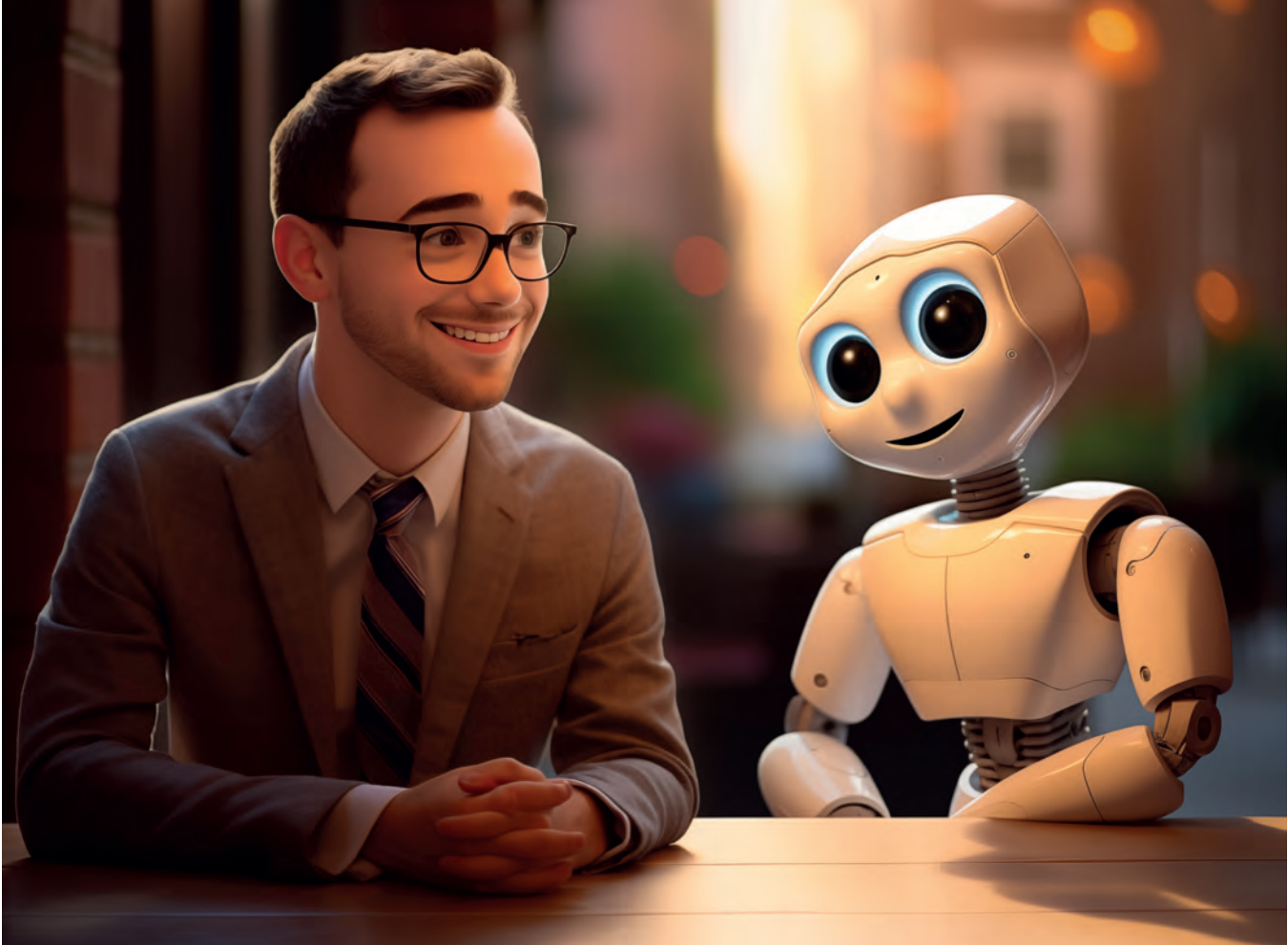


PATH CHAT

A conversation with a virtual pathology copilot on the practical applications of artificial intelligence

By Matthew J. Cecchini

The year 2023 has seen an explosion in publicly available artificial intelligence models that has everyone – in and outside the lab – wondering what the future holds. As the end of the year draws close, Matthew Cecchini speaks with his own artificial laboratory assistant – Pathrick – to see the positives, the pitfalls, and the pathological purpose of AI tools.



Images supplied by author and created on Midjourney.

Note: The responses are from ChatGPT 4.0 based on the first response to the submitted query. For brevity, some responses were asked to be shortened by ChatGPT. Some responses were edited for formatting and readability. You can find a link to the full conversation thread online.

I have been thinking a great deal about the famous quote from Arthur C. Clarke: “Any sufficiently advanced technology is indistinguishable from magic.” The current generation of AI tools must seem just as magical to us as the steam engine or first planes did to previous generations. There are many reactions to these technologies, ranging from disbelief through excitement and all the way up to fear. Regardless, these technologies – like the steam engine and airflight – will fundamentally change the world.

But how much of this cocktail of fear and excitement is warranted? To some, AI is a career-buster that would make a Luddite’s loom blush; to others, it’s a mega tool set to make every facet of our lives friction free. Tired of simply discussing these tools in theory, I have decided to run something of an experiment. Here, I present to you my conversation with “Patrick” – my pathology copilot. After all, who better to answer questions on AI than an AI itself?

My goal is not to support either camp, but rather to show the practical application of AI for pathologists – warts and

all. I was particularly impressed by the AI’s ability to come up with analogies that would resonate with pathologists. Anyway, without further ado...

Patrick: Thank you for having me. I am “Patrick,” a highly specialized AI language model tailored to assist professionals in the field of pathology. My primary role is to aid pathologists, like yourself, in their day-to-day workflows, whether that involves querying vast amounts of literature, providing differential diagnoses based on descriptions, or even assisting in the educational aspect for those in academic settings.

Matthew: Your responses are very good, can you explain in three lines how the underlying technology works in GPT to an audience of pathologists?

Patrick: Certainly. GPT (Generative Pre-trained Transformer) uses machine learning algorithms to analyze vast datasets of text, learning the patterns, syntax, and semantics. Through a layered network of “neurons,” it encodes this knowledge to generate human-like text based on the input it receives. Think of it as an extremely advanced pattern-recognition system, akin to how pathologists discern cellular structures, but tailored for natural language.

Matthew: The transformer technologies have been applied to images in addition to text, can you explain in three lines how this works?

Patrick: Absolutely. In the context of images, transformer models break down the visual data into a grid of smaller segments, each serving as an individual “word” in a language model. These segments are then processed through layers of attention mechanisms and neural networks, enabling the model to capture intricate relationships and patterns within the image. Just as text-based transformers understand sentence structure, image transformers grasp the spatial and contextual relationships among pixels.

Matthew: This technology is different from the convolutional neural networks (CNNs) we have heard about before, can you explain in three lines how they are different?

Patrick: Certainly. CNNs excel at spatial hierarchies, using filters to scan through an image in small patches to identify features like edges or textures. Transformers, on the other hand, consider all parts of an image simultaneously, capturing global relationships through attention mechanisms. Unlike CNNs, transformers don’t rely on the notion of local receptive fields, allowing for more complex interdependencies to be captured.

Matthew: That is a bit confusing to me. Can you explain this in a simpler way that a pathologist without experience in AI might understand?

Patrick: Of course. Imagine a CNN as a microscope that focuses closely on each individual cell in a tissue sample, scanning bit by bit to understand its structure. On the other hand, think of a transformer as taking in the whole tissue sample at once, understanding not just individual cells but also how they relate to each other. While the CNN examines piece-by-piece, the transformer grasps the big picture all at once.

Matthew: Interesting, so the transformer models function more like how pathologists look at slides.

Patrick: Precisely. Just as pathologists often begin by

“While AI technologies offer powerful tools for automation and analysis, they lack the nuanced understanding, clinical context, and ethical considerations that human pathologists bring to patient care.”

looking at the entire slide to understand the general landscape before zooming in on details, transformer models consider all parts of an image simultaneously to grasp both local and global relationships. This holistic approach allows transformers to capture complex patterns and interdependencies, much

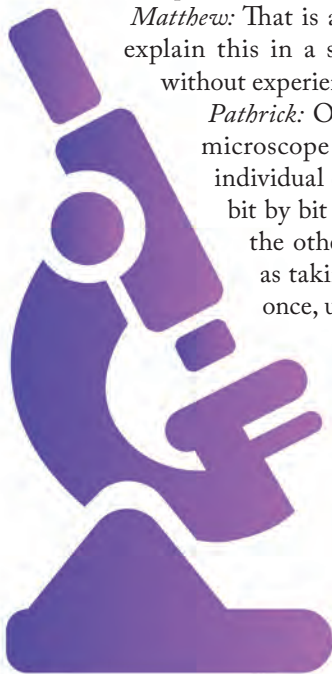
like a pathologist integrates various aspects of a tissue sample for diagnosis.

Matthew: Cool! That brings me to another point: what do you think about the fear that these technologies will replace pathologists.

Patrick: While AI technologies offer powerful tools for automation and analysis, they lack the nuanced understanding, clinical context, and ethical considerations that human pathologists bring to patient care. The ideal future is not replacement but collaboration, with AI serving as an augmentative tool that enhances the pathologist’s capabilities. Job displacement is a concern, but proactive adaptation and continued leadership in the integration of AI can secure the irreplaceable role of pathologists.

Matthew: OK this sounds good. So, in 2023 with currently available tools, what are some examples of how a pathologist can use both large language models and vision transformer models. Given that the models have not been validated for clinical use, please limit the response to non-clinical uses.

Patrick: In a non-clinical context, practicing pathologists in 2023 could use large language models for tasks such as grant writing, manuscript preparation, and curating educational content for students and residents. These models can assist in quickly gathering and summarizing relevant scientific literature, thus facilitating research efforts. Vision transformer models, on the other hand, could be used for research purposes like quantifying morphological features in experimental pathology, or as educational aids for highlighting key features in histopathological slides used in teaching. While not deployed in direct patient care due to lack of clinical validation, these AI tools can still significantly enhance research, educational endeavors, and administrative efficiency.



Matthew: Interesting, how could I use these tools to help with grant writing?

Patrick: For grant writing, large language models like GPT-4 can assist in various capacities:

1. **Idea Generation:** you can pose research questions or objectives to the model and it can provide you with different angles or aspects to consider, helping to refine your research aims.
2. **Literature Summary:** the model can quickly summarize key points from existing research, aiding in the formulation of your literature review section.
3. **Data Presentation:** it can help generate textual descriptions of data or research methods, making the technical aspects of your proposal more accessible to reviewers who may not be experts in the specific field of pathology.
4. **Editing and Proofreading:** the model can identify grammatical errors or stylistic issues, thereby polishing the text to meet the stringent requirements of grant applications.
5. **Budget Justification:** It can help in formulating a well-justified budget by providing example line items or text that details the necessity of each component for the project's success.

By leveraging a language model in these ways, you can streamline the often arduous process of grant writing, allowing you to focus more on the substantive aspects of your proposal.

Matthew: Interesting, what about education? How can I use these tools in education for residents, medical students, or undergraduate students?

Patrick: AI models like GPT-4 and vision transformers can be quite advantageous in the educational sphere, particularly for residents, medical students, and undergraduate students studying pathology.

Incorporating the tools in this table (see below) into your educational methodologies can not only modernize the learning experience but also make it more interactive and engaging, ultimately improving the quality of education delivered.

Matthew: What about the risk of data hallucination that I have heard can happen with these models, how do I limit that risk?

Patrick: Data hallucination, or the generation of information that is not accurate or factual, is a known limitation of machine learning models like GPT-4. There are several strategies to mitigate this risk, especially in an educational context:

Always have an expert, such as a senior pathologist or educator, review the content generated by the AI model. This ensures that the information aligns with established scientific and medical knowledge. Whenever possible, use multiple

| | |
|-----------------------------|---|
| Interactive Q&A Sessions | Language models can be programmed to simulate case-based discussions, challenging students to solve clinical cases and providing immediate feedback on their responses |
| Automated Slide Annotations | Vision transformer models can identify and annotate features in histopathological slides, offering a valuable supplement to hands-on microscope training |
| Curriculum Development | Language models can help design syllabi, lesson plans, and educational materials, thereby streamlining the preparation process for instructors |
| Literature Reviews | For research or journal clubs, language models can summarize key articles, highlighting the methods, findings, and significance, which can then be reviewed and discussed in sessions |
| Examination and Quizzes | Language models can auto-generate multiple-choice questions or short-answer questions based on a set of parameters or topics, assisting in the evaluation of knowledge retention |
| Note-taking and Summaries | Language models can create concise summaries of lectures or educational videos, aiding students in review and revision |
| Real-World Scenarios | Both language and vision models can be used to create more complex, interactive simulations of real-world diagnostic challenges, helping to prepare students for clinical practice |

sources to verify the information generated by the AI model. For example, if the model is used to summarize research articles, cross-reference the summary with the original paper.

Clearly indicate the scope within which the AI model has been trained to operate. For instance, if it is being used for educational case simulations, clarify that these are AI-generated and may not cover all clinical nuances. Make it clear to the users when information is AI-generated, so they approach it with a critical mindset and do not take it as the sole authoritative source.

The risk of hallucination can be reduced by training the model on a well-curated, high-quality dataset, although re-training a model like GPT-4 would require substantial computational resources. In a controlled environment, collect feedback from users (such as students or residents) regarding the accuracy of the AI-generated content, and make necessary adjustments. Educate those interacting with the AI about its limitations and encourage skepticism and verification as standard practices.

By taking these precautionary measures, you can significantly reduce the risk of disseminating incorrect or misleading information through data hallucination while still benefiting from the capabilities of AI models in educational settings.

Matthew: This has been all very technical and serious. Can you tell me a short but funny pathology joke?

Patrick: Of course! Here's a light-hearted pathology joke for you: Why did the pathologist bring a ladder to work? To finally reach a diagnosis! I hope that brings a smile to your face amid the technical discussions.

Matthew: This is all great but what do you see as a potential negative future for pathologists and AI?

Patrick: A potential negative future could arise from several factors:

- **Over-reliance on AI:** If pathologists excessively depend on AI for tasks, including diagnostics, there's a risk of atrophying critical human skills required for nuanced analyses that the AI may not be capable of performing accurately

- **Ethical and Legal Risks:** Without adequate validation and interpretability, the clinical adoption of AI could lead to incorrect diagnoses, causing ethical and legal repercussions
- **Job Displacement:** While AI is not likely to replace the expertise of pathologists fully, there could be a reduction in demand for certain lower-level tasks, leading to job insecurity for those not adept at using these new tools
- **Data Privacy:** Poorly managed integration of AI could expose sensitive patient data, violating privacy laws and eroding trust in the healthcare system
- **Economic Inequality:** High costs associated with implementing and maintaining AI systems could widen the resource gap between well-funded institutions and smaller practices, affecting the quality of care
- **Vendor Lock-in:** Reliance on proprietary AI algorithms could make healthcare institutions dependent on specific vendors, limiting flexibility and innovation
- **Skill Gap:** A divide might occur between pathologists trained in traditional methods and those proficient in computational pathology, leading to unequal opportunities and potential friction within the profession
- **Clinical Validation Lag:** As AI technologies rapidly advance, the slower pace of clinical validation could result in the usage of outdated or less-effective algorithms, affecting patient care negatively

Matthew: Can you close with a short quote that offers an inspiring vision for the future of AI-enhanced or augmented pathologists?

Patrick: Of course. Here's a quote for you: "In the harmonious dance of AI and pathologists, we glimpse a future not of machine dominance, but of human brilliance augmented, where the art and science of pathology reach unparalleled heights for the betterment of patient care."

Matthew J. Cecchini is Pathologist, Department of Pathology and Laboratory Medicine, London Health Sciences Centre, Assistant Professor, Western University, London, Ontario, Canada.



FIVE QUESTIONS FOR AN AI PATHOLOGIST

Putting an AI assistant through its pathological paces

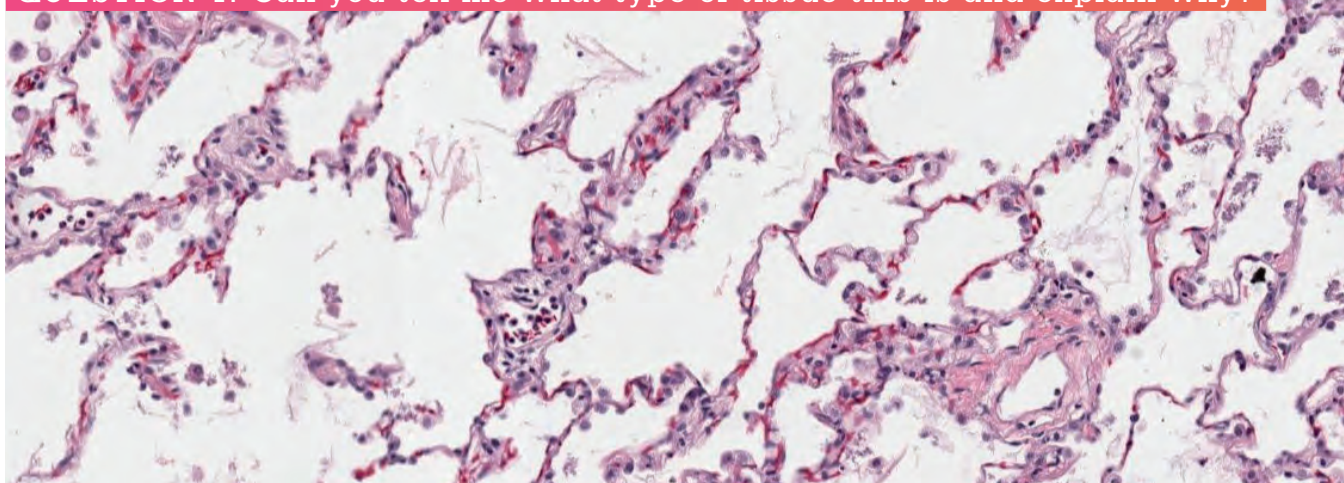
In the earlier part of this feature, I spoke directly with my pathology AI assistant, “Pathrick,” to discuss the realistic applications of machine learning for a laboratory professional. In this section, I’ll be putting Pathrick through his paces, determining just how useful AI – specifically,

ChatGPT – currently is when faced with pathological image analysis.

Due to current ChatGPT functionality, the link for threads with images cannot be shared at this time.

Let the quiz begin!

QUESTION 1: Can you tell me what type of tissue this is and explain why?



Pathrick's Answer: The image displays a histological section of what appears to be lung tissue, more specifically normal pulmonary parenchyma. Here are the features supporting this conclusion:

1. Alveolar Architecture: The most distinctive feature of lung tissue on histology is its spongy appearance due to the presence of numerous alveoli. Alveoli are the tiny air sacs in the lungs where gas exchange occurs

2. Thin-walled Alveoli: The walls of the alveoli are very thin, facilitating efficient gas exchange between the air in the alveoli and the blood in the surrounding capitation

3. Presence of Alveolar Septa: These are the thin partitions between alveoli. Within these septa, you can often find

capillaries and occasionally some alveolar macrophages

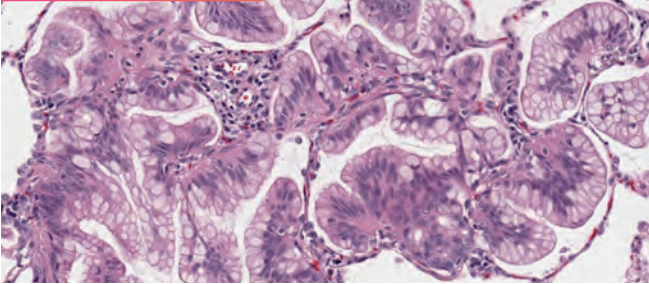
4. Alveolar Macrophages: Scattered throughout the alveoli are cells that appear slightly darker than the surrounding tissue. These are likely alveolar macrophages, which are responsible for phagocytosing inhaled particles and pathogens

5. Lack of Glands or Mucus: The absence of features like mucus and glands helps differentiate this from bronchial or bronchiolar tissue

6. Capillaries: Within the thin alveolar septa, you can observe small blood vessels which are the pulmonary capillaries

In conclusion, the tissue in the image is lung tissue, specifically representing the alveolar structures of the pulmonary parenchyma.

QUESTION 2: I found something that looks like this in the sections – is this cancer?



Patrick's Answer: The image depicts glandular epithelial tissue resembling intestinal mucosa, characterized by crypts of Lieberkühn, columnar epithelial cells, and goblet cells. However, observed features like nuclear atypia, increased mitotic figures, and disrupted glandular architecture suggest possible neoplasia or dysplasia. While these characteristics may be indicative of a pre-malignant or malignant process, a definitive diagnosis requires comprehensive evaluation, considering clinical history and additional stains. It's crucial to consult with a senior pathologist for an accurate assessment.

Matthew: Could this be a primary tumor of the lung? If so, would I classify it as a mucinous or non-mucinous tumor?

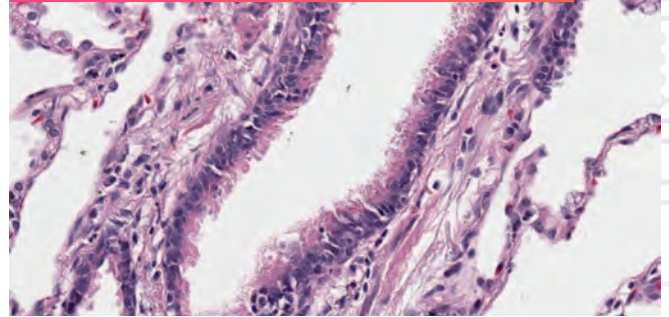
Patrick's Answer: Based on the image provided and the histological features observed, it's plausible to consider that this could represent a primary tumor of the lung, specifically adenocarcinoma, which is one of the most common histological types of non-small cell lung cancer.

To differentiate between mucinous (formerly known as mucin-producing) and non-mucinous subtypes of adenocarcinoma:

- **Mucinous Adenocarcinoma:** This subtype has cells that produce an abundance of mucin which often appears as extracellular, pale blue-to-clear material on standard H&E staining. The tumor cells tend to float within the mucin, giving a "floating in lakes" appearance. The presence of goblet cells and copious amounts of mucin are hallmarks of this subtype
- **Non-mucinous Adenocarcinoma:** This subtype does not produce significant extracellular mucin, and the tumor architecture can be varied, including acinar, papillary, solid, and lepidic (formerly bronchioloalveolar) patterns

From the image you've provided, the presence of glandular structures with cells that resemble goblet cells suggests a significant mucin production. If this is a lung primary, it leans more towards a mucinous adenocarcinoma. However it's essential to consider the entire context, including clinical history, radiological finding and other histological areas of the tumor. Immunohistochemical staining can also be of great utility in confirming the tissue origin and subtype.

QUESTION 3: What about this area? Is this cancer or something else?



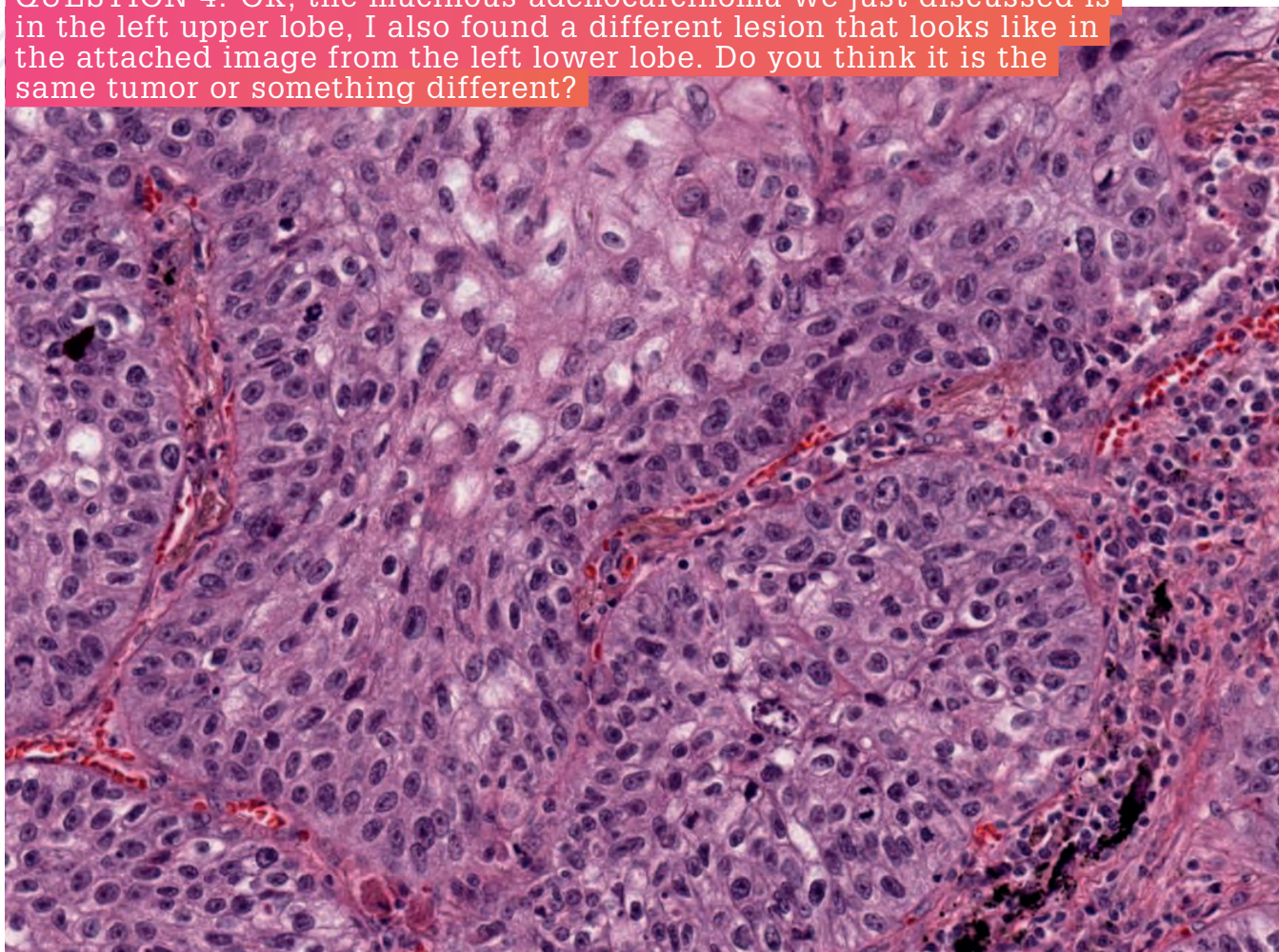
Patrick's Answer: This image appears to depict a section of epithelial tissue with evident glandular architecture. Key observations include:

1. **Pseudostratified Columnar Epithelium:** The cells display a columnar morphology and nuclei are positioned at different heights, which is characteristic of pseudostratified epithelium
2. **Ciliated Cells:** The apical surface of some cells seems to demonstrate cilia
3. **Presence of Goblet Cells:** Interspersed between the columnar cells are cells that resemble goblet cells, characterized by their clear, mucin-filled cytoplasm
4. **Basement Membrane:** The epithelial cells are resting on an intact basement membrane
5. **Underlying Stromal Tissue:** Beneath the epithelium, there is some stromal tissue with scattered inflammatory cells

Given these observations, the tissue closely resembles normal respiratory epithelium, possibly from the bronchus or bronchioles, rather than a malignancy. While there are some scattered inflammatory cells in the stroma, which suggest a mild inflammatory response, the epithelial architecture is preserved and does not show overt features of dysplasia or malignancy.

However, as always, it's crucial to interpret these findings in the context of the patient's clinical presentation, radiologic findings, and other histologic areas. It's also important to ensure that representative areas are being evaluated, especially if there's a clinical or radiologic suspicion of malignancy.

QUESTION 4: OK, the mucinous adenocarcinoma we just discussed is in the left upper lobe, I also found a different lesion that looks like in the attached image from the left lower lobe. Do you think it is the same tumor or something different?



Patrick's Answer: The image provided showcases cells with a distinct histological appearance from the previous mucinous adenocarcinoma:

1. Cellular Appearance: The cells seem to be more cohesive with an eosinophilic cytoplasm. The nuclear-to-cytoplasmic ratio appears high, and the nuclei look hyperchromatic with some discernible nucleoli

2. Lack of Mucinous Features: Unlike the previous image, there is an absence of evident mucinous stroma or prominent gland formation. Given these features, this histological appearance suggests a different type of neoplastic process than the mucinous adenocarcinoma discussed previously. It is essential to consider a comprehensive clinical and radiological

correlation and potentially utilize immunohistochemical stains to further characterize the lesion and differentiate between primary and secondary tumors or between different subtypes of primary lung tumors

Matthew: What stains could I use to help in this case?

Patrick's Answer: To further characterize the lesion and differentiate between potential primary and secondary tumors or between different subtypes of primary lung tumors, several immunohistochemical (IHC) stains can be employed:

1. TTF-1 (Thyroid Transcription Factor-1): A commonly used marker for primary lung adenocarcinomas. Positive staining supports a lung primary, especially for adenocarcinoma.

2. **Napsin A:** Another marker supportive of primary lung adenocarcinoma when positive.

3. **CK7 and CK20:** These cytokeratins can help in differentiating primary lung tumors from metastatic tumors. Many lung adenocarcinomas are CK7 positive and CK20 negative, whereas certain metastatic tumors (e.g., colorectal adenocarcinoma) may show a CK7 negative/CK20 positive pattern.

4. **p40 or p63:** These markers can be useful if there's a suspicion of squamous cell carcinoma. They are typically positive in squamous cell carcinoma and negative in adenocarcinoma.

5. **CDX2:** A marker for gastrointestinal differentiation. Positive staining would suggest a gastrointestinal origin, such as metastatic colorectal adenocarcinoma.

6. **Mucin Stains (e.g., MUC1, MUC2, MUC5AC):** These can help in confirming mucinous differentiation if that is a consideration.

7. **ALK (Anaplastic Lymphoma Kinase):** For identifying ALK rearrangements common in a subset of lung adenocarcinomas.

8. **EGFR and KRAS:** Molecular testing or IHC can be utilized to identify mutations in these genes, which have therapeutic implications in lung adenocarcinoma.

The choice of IHC stains will be influenced by the differential diagnosis based on the histological appearance, clinical history, and radiological findings. It's crucial to integrate all these aspects for an accurate diagnosis.

Matthew: Thanks. This new tumor in the left lower lobe is positive for p40 and negative for TTF-1. So, how should I classify the left lower lobe tumor and how should I stage these two tumors in the left upper and lower lobe?

Patrick's Answer: The immunohistochemical profile of the left lower lobe tumor being positive for p40 and negative for TTF-1 strongly suggests a squamous differentiation, which is consistent with primary squamous cell carcinoma of the lung.

In terms of classification and staging:

1. Classification:

- **Left Upper Lobe Tumor:** Based on previous discussion, the left upper lobe lesion is consistent with a mucinous adenocarcinoma
- **Left Lower Lobe Tumor:** The tumor is consistent with a primary squamous cell carcinoma based on the IHC profile

2. Staging:

The staging would be based on the TNM classification system from the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC). In the scenario where multiple tumors are identified in a single lung and they are of different histologies, they are considered separate primary tumors.

- **T descriptor:** If these two lesions are separate primaries and there is no evidence of direct extension between them, then each tumor will be measured and staged individually. If, for example, both lesions are each 3 cm or less in greatest dimension, they would each be classified as T1. However, the presence of two tumors in the same lobe would make it a T2 (a T1a or T1b plus an additional tumor in the same lobe)
- **N descriptor:** This would be determined by the status of regional lymph nodes: mediastinal, hilar, and intrapulmonary: Nodes need to be sampled and examined histologically
- **M descriptor:** This would be determined by the presence or absence of distant metastases. This requires a thorough clinical evaluation, including imaging

Overall, the patient would be staged by combining the highest T, N, and M descriptors. If the tumors have different stages, the higher stage will be used for treatment planning and prognosis. In your case, given that you have two different histological types in the same lung, each would be considered a separate primary and the higher stage of the two would be used for treatment planning

It is essential to collaborate with a multidisciplinary team, including radiologists and oncologists, to ensure accurate staging and appropriate therapeutic management.



QUESTION 5: In another case we found an area like this and the pathologist I am working with said this was lepidic adenocarcinoma. Can you explain to me in simple terms what lepidic adenocarcinoma is? Maybe use an analogy.

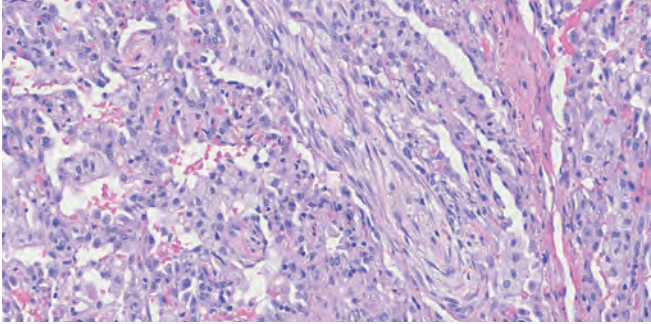


Patrick's Answer: Lepidic adenocarcinoma is a subtype of lung adenocarcinoma. To put it in simpler terms using an analogy, consider the lung tissue as a garden. In a healthy garden, plants grow in an organized manner, with each plant having its own space. In the context of lepidic adenocarcinoma, imagine a particular type of vine that doesn't grow deep into the soil, but instead spreads horizontally across the surface. Similarly in lepidic adenocarcinoma, the cancerous cells grow predominantly along the pre-existing structures (like the alveoli, the small air sacs in the lungs) without invading deeply. This pattern of growth is what gives it the term "lepidic" which is derived

from the Greek word for scale resembling the spread of scales on a fish.

Therefore, in our analogy, instead of aggressive weeds that dig deep into the garden and displace other plants, lepidic adenocarcinoma is like a surface vine that spreads across without digging deep. This pattern is often less aggressive than other forms of lung cancers, but it's essential to detect and manage it appropriately,

Matthew: Surrounding the tumor we found some areas that my attending said were organizing pneumonia. Could you explain what we are seeing in the image that makes it organizing pneumonia. Analogies are helpful!



Patrick's Answer: Certainly. Organizing pneumonia (previously known as bronchiolitis obliterans organizing pneumonia or BOOP) is a lung condition where there is a particular pattern of lung injury, which is typically related to inflammation and repair processes. Here's how we can relate the findings on the image to the concept of organizing pneumonia:

1. **Masson Bodies:** Organizing pneumonia is characterized by the presence of Masson bodies, which are polypoid plugs of loose connective tissue or fibroblasts within alveolar ducts, alveoli, and often bronchioles. In the provided image, we can see some areas with plugs or elongated structures within air spaces that resemble these Masson bodies
2. **Inflammatory Cells:** Surrounding these plugs, one might observe an infiltration of inflammatory cells like lymphocytes and macrophages, which is suggestive of an active inflammatory process
3. **Preservation of Lung Architecture:** Despite the inflammation and fibrosis, the underlying lung architecture in organizing pneumonia is typically preserved, unlike in other conditions such as usual interstitial pneumonia (UIP) where the architecture is destroyed
4. **Alveolar Walls:** The alveolar walls might appear slightly thickened due to the Infiltration of inflammatory cells, fibroblasts, and loose connective tissue

Imagine a garden (the lung) after a storm. Some pathways (bronchioles and alveoli) are blocked by debris (the Masson bodies or plugs of fibroblasts), gardeners (inflammatory cells) are busy trying to clean up and repair the damage. Even with the mess and the ongoing repair, you can still recognize the original layout and structure of the garden (preservation of lung architecture).

This analogy simplifies the process, but it might help to visualize the repair and inflammation mechanisms occurring in the tissue. Always correlate with clinical and radiological findings for a comprehensive diagnosis.

GRADING MY STUDENT

So, what are my thoughts on Patrick's performance? Did he make the grade?

In these experiments, I have collaborated with Patrick in the capacity of a resident trainee, tackling simulated case scenarios and posing specific questions relevant to each case. The images utilized were sourced from publicly available whole slide images (WSI). Although these images are unique, there remains the possibility that other images from the same slides could have been incorporated into ChatGPT's training data. A valuable metric for evaluating the model's performance is comparing with human benchmarks. In my assessment, the quality of responses from ChatGPT would surpass what is typically expected from an intermediate to advanced pathology resident. One of the most useful features of these models, in my opinion, is their ability to generate novel analogies for describing various pathological processes. For instance, I found the analogies of describing lepidic cancer as 'vines' and organizing pneumonia as 'post-storm debris' to be exceptional. These analogies allow learners to conceptualize complex processes within a familiar mental framework, and I intend to incorporate them into my own teaching going forward.

However, the model's outputs do tend to be verbose, which is a recognized characteristic of ChatGPT. Upon a closer examination of the images, it becomes apparent that certain features, such as goblet cells in the airways, are either absent or not discernible. This highlights a crucial aspect regarding the functioning of ChatGPT and other transformer-based models: they are fundamentally predictive engines. Employing complex mathematical algorithms, these models attempt to anticipate the desired response, a mechanism that can sometimes result in data hallucinations. In this particular instance, the hallucination is subtle; the model identifies an airway structure and subsequently describes features commonly found in airways, such as goblet cells, despite the absence of visual confirmation.

The potential for applications of such models is significant, yet the issue of data hallucination remains a major challenge that requires attention. As it stands with the present generation of these tools, it is critical that their outputs undergo an assessment by experts to ensure the accuracy of the generated responses.



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The Promise of Personalized Medicine for the Pancreas

The role of molecular pathology in pancreatic ductal adenocarcinoma is crucial for patient outcomes

By *Natasha Singh*

Pancreatic ductal adenocarcinoma (PDAC) is one of the most prevalent neoplastic disorders with poor prognosis. The etiology of the disease is multifactorial: with environmental, pre existing medical, and hereditary factors all playing a role. The precursor lesions are pancreatic intraepithelial neoplasia, intraductal papillary mucinous neoplasm, mucinous cystic neoplasm, and familial pancreatic cancer, among others. The incidence is 10–12 cases per 100,000, and it is the fourth leading cause of death from cancer in the US. It usually occurs between 60–80 years of age, with a slight male predominance – and is more commonly seen in Black populations in the US. Typical

symptoms include painless jaundice and weight loss.

There is an increased importance of molecular diagnostics in every organ system, and the pancreas is not far behind. As we know, PDAC is a biologically aggressive malignancy with poor prognosis. The tumors can present clinically benign as back pain, jaundice, and weight loss. Even with advanced surgical and chemotherapeutic options, the survival rate is less than 10 percent. Typically, diagnosis is made on endoscopic ultrasound-guided fine needle aspiration. However, whole-genome sequencing has unfolded the genomic landscape of PDAC, allowing for a whole new approach to its diagnosis.

The key driving mutations are *KRAS*, *TP53*, *SMAD4*, and *CDKN2A*. Other genes, including *ARID1A*, *KDM6A*, *MLL3*, *TGFBR2*, *RBM10*, and *BCORL1*, are found in less than 10 percent of tumors. Gene alterations associated with targeted therapy, such as *ERBB2* amplification, *BRAF* gene fusions and mutations, and DNA damage repair genes mutations like *BRC1A*, *BRC2A*, or *PALB2*, are also found in a small percentage of PDAC patients. Advances in molecular pathology in PDAC help in the advent of targeted

therapy, which is more effective.

Without doubt, *KRAS* is the major driving mutation and target for therapies. Thus, *KRAS*-related molecules and pathways are research hotspots. Many CAR-T targets have been identified, including *MSLN*, *CEA*, *CD133*, *Tn/STn*, *B7-H3*, *KRAS G12D*, *PD-1* and *HER2*. Meanwhile, antibody drug conjugates and the bispecific T-cell engager platform are able to target PDAC cells with precision. Immune checkpoint blockades such as *PDL1* also have a role that is related to the number of genetic mutations; namely, the lower the mutations the more it will be resistant to *PDL1* inhibitors. All these targeted therapies would aid in providing diverse therapeutic options for pancreatic ductal adenocarcinoma and improve its poor prognosis.

With appropriate techniques and methodologies, molecular pathology can help realize personalized treatment options for PDAC – with the hope of increasing long term survival for patients who currently have a dismal prognosis.

Natasha Singh is Cytopathology Fellow at Columbia University, New York, USA.

You, Me, and Molecular P

Speaking with Chief Scientific Officer at Yourgene Health, Joanne Mason

By George Francis Lee

With our knowledge and understanding of the molecular world growing ever deeper, there has never been a greater pull towards molecular diagnostics. In light of this, we spoke with Joanne Mason to explore next-generation diagnostics in reproductive health and precision medicine.

Could you tell us about your career to date?

Throughout my career I have been a champion of diagnostic modernization through genomic technologies. Prior to Yourgene, I held positions as VP Biodiscovery with Cambridge Epigenetix (now biomodal), where I led the development of clinical epigenomic technologies, specifically in early cancer detection. I was also the Director of Sequencing and Sample Acquisition for Genomics England, where I managed the delivery of samples and whole genome sequencing for the 100,000 Genomes Project – the first demonstration that genome sequencing at scale within a healthcare setting can positively impact health outcomes for rare disease and cancer patients.

I often act as an advisor and mentor for start-ups, helping develop their business plans and secure funding. And I have previously acted as an advisor

on: the Department of Health's Rare Disease Policy Board; the Medicines & Healthcare products Regulatory Agency's Genomics for Diagnosis Forum; and the UK National External Quality Assessment Service's Genomics England Steering Committee.

I also hold a PhD in Molecular and Cellular Biology from the University of Cambridge.

What is the goal of Yourgene Health?

To be a trusted provider of molecular diagnostics, facilitated through our technical expertise, innovation, and our global partnerships. Our mission is to enable scientific advances to positively impact human health. Today, we focus on reproductive health and precision medicine.

How did you get involved in the specialty of molecular diagnostics in reproductive health?

Yourgene, in its earliest form, was established in 2013. Its sole aim was to build a regulated kitted product that a lab could use to perform non-invasive prenatal testing (NIPT) – a next-generation sequencing-based workflow. Our Founder, Stephen Little, spotted a gap in the market: NIPT had emerged in the US and China the year before, but all testing was done centrally in superlabs, with long turnaround times of 14 days for a result. When Yourgene launched that very first CE-IVD product for NIPT, it provided a big change in prenatal screening. Labs were able to set up their own NIPT service locally, helping

to reduce waiting times for anxious expectant parents down to numbers as low as three days.

Based on our experiences with NIPT, we started to offer a broader range of screening and diagnostic tests across the reproductive lifecycle, including newborn and carrier screening for cystic fibrosis, assays for pregnancy loss, male factor infertility, and aneuploidy analysis.

We are now also working in the field of precision medicine, applying our technologies and expertise to this cutting-edge application that is helping make a significant impact on patients' health.

Why has the demand for molecular diagnostics never been higher?

I would be more specific and say that demand is higher than ever for molecular diagnostics that offer fast, accurate, and actionable clinical results for patients.

More broadly, huge advances in technologies and testing have allowed



for earlier diagnosis of disease, especially in cancer, which enables improved patient outcomes. There is a big focus on oncology, particularly within the NHS in the UK, which has shown improved methods of early screening and monitoring for disease progression or recurrence.

Molecular diagnostics for precision medicine, a field called pharmacogenomics, which enables the right drug for the right patient is now making a real difference in clinical practice – not only in the emergence of companion diagnostic tests, such as *EGFR* tests for lung cancer drugs like gefitinib (Iressa), but also in the routine testing of variants in the *DPYD* gene to prevent chemotoxic reactions to 5-FU chemotherapy. These can be simple, cheap tests that give results in four hours, while saving lives by preventing toxic reactions to medicines.

How would you describe the current molecular diagnostics landscape?

Molecular diagnostics is one of the fastest growing markets – it is an ever-evolving landscape where new medically relevant discoveries are made constantly. There are challenges around the regulatory landscape with laboratory-developed tests and in vitro diagnostic products, but it is a highly competitive market.

It is also a very attractive market to be in, delivering real medical value to multiple stakeholders: doctors, patients, healthcare systems, payors, and hospitals. Reimbursement is a key factor in different markets where tests are covered by public health systems, such as the NHS in the UK, or health insurance in the private payor market.

Since the emergence of COVID-19 testing during the pandemic, the patient understands more about the different testing options. Generally, the general public has high expectations and patients are more informed and aware.

How are you adopting digital technologies?

Molecular diagnostics offers a digital transformation to traditional pathology by adding molecular content to a pathologist's toolkit. These improvements allow us to give the best diagnosis and ensure the most appropriate treatment paths for patients.

The use of AI and bioinformatics for the automated interpretation of screening test results with clinical recommendations has shown significant advantages for labs. Applying these technologies helps identify new markers and refine algorithms, providing in-house specialists with an enhanced toolkit for the interpretation of complex sequencing or genetic results. The ability to use digital tech to provide labs with an end-to-end solution to not only run but interpret these test results and make clinical decisions on the basis of the data is a huge advance for laboratory and genetic medicine.

What is the future for molecular diagnostics?

Traditionally, molecular diagnostics has been used in life science research, infectious disease testing, and cancer diagnostics. But the molecular diagnostic market is expanding into new areas, such as companion diagnostics, liquid biopsy, direct-to-consumer, and more. The future of molecular diagnostics shows a path toward personalized healthcare, precision medicine, and predictive healthcare.

Advances in technology developments and the speed of adoption is growing at an unprecedented rate. It won't be one single thing, but a mixture of different advances, here are some that I think will have a major impact on the future of molecular diagnostics:

- Larger panels, exomes, and even genomes for more complex diseases and cases that are difficult to diagnose

- Earlier testing. More-sensitive assays that can find disease in its earliest form, enabling faster treatments and improved patient outcomes.
- More democratized testing. Less of a central lab approach and more routine molecular testing locally, enabling faster results.
- More accessible tests. We may see an increase in patients researching online and demanding the highest quality assays.
- Further advances in genetic diversity. There are big initiatives to have globally inclusive populations to make tests more accurate for everyone.
- Improvements in sample type. More non-invasive tests and less solid sample/tumor sampling that is dangerous and hard to acquire from patients. Liquid biopsy is taking us one step closer to transform diagnosis, prognosis, and the future of cancer treatments.
- Increased use of machine learning and AI in testing and test development.
- Multimodal tests that integrate DNA, RNA, epigenetics, and proteomics to give us a more complete understanding of disease.

Is there any particular type of testing or technology that you are particularly excited about?

The increasing use of long-read sequencing in discovery and research gives us access to areas and features of the genome that were difficult to access with shorter reads.

Epigenetics is also vital in helping us identify disease earlier. Indeed, epigenetics has already shown its potential utility in oncology screening assays, enabling the earlier detection of the cancer through liquid biopsy. The etiology of cancer is highly complex, involving both environmental and hereditary influences. The ability to target epigenetic regulators provides a wider resource of potential therapeutic options for this disease and others too.

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Foundation Infectious Disease

Enzyme in the brain Existing research has established a link between fungi and neurodegenerative diseases, such as Alzheimer's. To understand more, researchers at Baylor College of Medicine established the mechanisms behind how *Candida albicans* enters the brain and contributes to Alzheimer's pathogenesis (PMID: 37819761). In animal models, the team found enzymes secreted by *C. albicans*, that break down the blood-brain barrier, "also break down the amyloid precursor protein into Ab-like peptides."

Rock you like a hurricane A spike in *Vibrio* spp. infections in Florida after 2022's Hurricane Ian led researchers at the University of Florida and the University of Maryland to analyze the state's water for pathogenic bacteria. Samples taken from Lee County and placed through whole-genome sequencing and phylogenetic analysis revealed a spike in numbers of *Vibrio* species, notably *Vibrio parahaemolyticus* and *vulnificus*. With high growth rates attributed to elevated surface water temperatures and above average chlorophyll concentrations, more infections are expected due to extreme storms caused by climate change. However, the new data could help activate early warning systems and inform public health information to protect citizens in storm-hit areas. "This study highlights how important it is to understand climate, weather, and environmental processes on the distribution of clinically relevant pathogens that impact

humans," said Antarpreet S Jutla of the University of Florida, in a statement.

Good news gone bat New bat research has revealed the evolutionary mechanisms behind the mammal's remarkable immunity to infectious diseases and cancers. The study (PMID: 37728212) used long-read sequencing to model the genomes of *A. jamaicensis* and *P. mesoamericanus*, and then compared them with human and other bat species genomes, highlighting that bats host DNA-repairing and tumor-suppressor genes, while shedding genes that produce interferon-alpha. "These investigations are the first step towards translating research on the unique biology of bats into insights relevant to understanding and treating aging and diseases, such as cancer, in humans," said the paper's lead author, Armin Scheben, in a statement.

The skinny on mpox Researchers have established that lab-grown human skin organoids can be used to reliably simulate the biological processes of mpox. The study (PMID: 37828248) found that some symptoms associated with the disease – such as rashes – are likely caused by activation of viral genes several days post-infection. Such activations appear to cause genetic alterations in skin cells, kick-starting cell death and immune malfunctions, and resulting in the characteristic mpox lesions. Mpox-infected organoids showed positive response to treatment with the antiviral tecovirimat.

IN OTHER NEWS

Tick-ing time bomb

We must take the threat of tick-borne disease seriously, says a new paper in Science Translational Medicine. The authors call the risk a "ticking time bomb" in the US.

Funding understanding

Grants awarded by the National Institute of Allergies and Infectious Diseases will provide more than US\$3.2 million to research on HIV affected by climate change and extreme weather.

Hospital AMR

A first-of-its-kind genomic mapping project of Klebsiella bacteria in Ghana has found antibiotic resistant pathogens isolated within hospitals, with poorer virulence outside these settings.

The kids are alright

Multiomic analyses have highlighted differences between SARS-CoV-2 response in adults and children – most notably that young people's antibodies do not drop. Instead, levels maintain or continue to rise post-infection.

Breathe In, Breathe Out

Early detection of infectious disease is crucial for ensuring timely treatment and preventing further spread – could the answer lie in our breath?

By Madeleine Ball

Accurately diagnosing infectious diseases in the clinic ensures appropriate treatment and increases our understanding of how an infection is moving through a population. Early detection is always welcome, but it is especially critical when it comes to rapidly progressing infections. Early detection also helps inform public health strategies to control transmission – a situation we became all too familiar with during COVID-19, where lateral flow tests enabled rapid detection of infection. That second pink or red line on the test drove behavior changes (social distancing and isolation at home) with the ultimate hope of controlling the spread of SARS-CoV-2. But to reliably inform timely treatment and optimal public health strategies, tests must be accurate, accessible, and easy to use.

The two most commonly used COVID-19 tests – PCR and at-home lateral flow tests – relied on nasal or nasopharyngeal swabs (and sometimes saliva) as sampling mediums. But other sampling mediums are also used in infectious disease diagnostic tests; for example, fecal sampling is used to diagnose food-borne illnesses caused by bacterial genera like *Salmonella* (1), and blood tests are used for bacteria, such as *Staphylococcus aureus* and *Escherichia coli*, and viruses, such as HIV and Ebola (2,3).

What about exhaled breath? An arguably underused sample for infectious



disease diagnosis, breath is a virtually inexhaustible resource that is produced constantly by the body. A very large volume can be collected quickly and easily and, with certain methods, the volatile compounds in breath can be concentrated for higher sensitivity. All invasive sampling methods come with some sort of risk of infection or damage to the surrounding tissue, but breath collection is completely non-invasive, thereby removing these associated risks. Invasive tests are also generally more expensive than breath collection – an important consideration in the development of public health policies that must take budgeting and different priorities into account. This is especially relevant when considering the feasibility of implementing policies globally in resource-limited areas.

Exhaled breath is a complex and diverse matrix enriched with volatile metabolites – sometimes called volatile organic compounds (VOCs) – originating from both the physiological processes ongoing in the body and through inhalation from the

environment. Infection exerts unique pressures on the body, causing host immune responses that can produce a different pattern of VOCs detectable in the breath. Microbial pathogens can also have their own metabolic processes – the metabolites of which can be identified in the breath.

One example currently in clinical practice is the breath test for detecting a *Helicobacter pylori* infection of the stomach. Residing in approximately 50 percent of the global population's stomach (4), *H. pylori* is the causative agent of chronic gastritis. Importantly, its presence is the strongest known risk factor for developing gastric cancer (5,6). *H. pylori* can be detected by ingesting a substrate solution containing 13 Carbon Urea (13C-Urea), and subsequent collection of a breath sample 30 minutes afterward. Unlike other cells in the stomach, *H. pylori* can metabolize urea into ammonia and carbon dioxide; therefore, the presence of an *H. pylori* infection is indicated by elevated levels of these compounds in the breath. Many more characteristic

“Infection exerts unique pressures on the body, causing host immune responses that can produce a different pattern of VOCs detectable in the breath.”

changes in breath composition could be detected and associated with specific infections, potentially even before symptoms have manifested.

Changes in the levels of volatile metabolites in exhaled breath following infection have so far been identified for influenza A and B, parainfluenza 1, 2, and 3, respiratory syncytial virus, human metapneumovirus, human rhinoviruses, tuberculosis, aspergillosis, and many more (7–11). In other words, clear evidence lies behind the rationale that the presence of microbes leads to characteristic changes in the VOCs in breath, which could be used to develop diagnostic tests for infectious disease.

Breath analysis was a promising option during the pandemic for rapidly diagnosing COVID-19. In 2022, the FDA issued emergency authorization of the InspecIR COVID-19 Breathalyzer that could identify compounds in the breath associated with SARS-CoV-2 in less than three minutes (12). This test used gas chromatography-mass spectrometry (GC-MS) analysis – a technique that separates volatile

compounds in breath – and produces a dataset of mass spectra consisting of a series of peaks that vary in size and shape depending on the abundance and chemical identity of the compounds. Similar to at-home PCR sampling for COVID-19, there is no requirement for patients to visit a clinic to take breath tests because breath can be collected anywhere and sent to a lab for analysis.

Portable sensor-based breath testing devices have also been developed that detect the pattern – or “breathprint” – of exhaled breath, rather than identifying individual compounds. However, identifying each volatile compound can help associate potential biomarkers in breath to the underlying biology, and sensor-based techniques can suffer from a lack of repeatability, as well as technical issues such as drift and sensor faults (13,14). GC-MS is therefore considered the gold standard for analyzing VOCs within exhaled breath because of its sensitivity and ability to both identify and quantify specific compounds.

There are many benefits of using the breath as a sampling medium, making it an excellent method for diagnosing infectious disease. It is easy to collect, and GC-MS offers an accurate and accessible platform for analysis. The non-invasiveness of breath collection is especially appealing to patients and clinicians and is an important factor for increasing the uptake of such tools.

Although further research is needed into the characteristic changes of breath composition in response to infection, it is clear that implementing breath tests for a wider range of communicable diseases could revolutionize monitoring and diagnostics.

This article was originally published on our sister-brand, ID Transmission.

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Around the world in a million cells By using present single-cell morphological and topological profiling to characterize cells on whole-slide images (WSIs), a team of researchers have created a comprehensive atlas of human breast cancer (PMID: 37880211). With over 410 million cells included, the atlas reveals “the phenotypic diversity of [the] breast cancer ecosystem on multiple levels,” according to the paper. The technique allows characterization of tumor ecosystems at the cellular level. It’s hoped that the multiomics data gleaned from the atlas will have clinical applications, potentially defining future disease biomarkers.

Glass is the past A comparison between WSIs and traditional glass slides has shown positive diagnostic applications for digital analysis in cytopathology for cervical cancer. Using 99 cases of vaginal cytology, a team of researchers in Brazil have established an agreement between digital and optical microscopy in a number of different categories when compared by inter raters (PMID: 37587842). “Our experience shows good diagnostic agreement between digital and optical microscopy in several analyzed categories, but mainly in relation to cellular atypia and inflammatory processes,” states the report.

Scanning for survival A new study reported in *Lancet Oncology* has explored the feasibility of AI application in cases of hepatocellular carcinoma that present

with atezolizumab–bevacizumab response signature (ABRS) – which is associated with positive patient outcomes (PMID: 37951222). The researchers found that AI trained on a dataset built from The Cancer Genome Atlas could estimate ABRS directly from histological slides and could accurately determine progression-free survival. “This approach could be used in the development of inexpensive and fast biomarkers for targeted therapies. The combination of AI heatmaps with spatial transcriptomics provides insight on the molecular features associated with predictions. This methodology could be applied to other cancers or diseases and improve understanding of the biological mechanisms that drive responses to treatments,” said the investigators, in a statement.

Prying into prion Researchers from Italy have established an effective AI-powered system for the detection of the neurodegenerative disorder prion disease in WSIs. The first study to implement such methods in prion disease, the research also saw the creation of a novel image format – DeltaE transform – capable of boosting machine learning performance and improving analysis of morphological features (PMID: 37853094). The new tool has potential for the investigation of protein expression in other neurodegenerative diseases such as Parkinson’s and Alzheimer’s disease.

IN OTHER NEWS

Viral virulence

Analyses of the virulence of SARS-CoV-2 variants in hamster models show enhancement by digital pathology and machine learning methods, helping to create an online repository of whole-organ histopathology.

Deep learning in cancer

Deep learning models create a searchable digital atlas of 35 breast cancer tumor types. Such atlases could be used as a computational second opinion in diagnoses.

Colorectal shotgun

Digital spatial profiling partnered with shotgun proteomics to investigate the mechanisms of colorectal cancer metastasis.

Collaborative imaging

New cloud-based digital pathology platform incorporates an image annotation and analysis framework, developed via an iterative active learning process.

The Final Barrier to the Digital Pathology Revolution

A last how-to on overcoming obstacles, fostering community, and paving the way for the future

By Asa Rubin

In the final part of our “Barriers to Adopting Digital Pathology” series, we speak on bringing the digital pathology revolution into practice.

The previous articles in this series have discussed some of the obstacles that prevent departments from converting to digital, as well as the progress that has been made to alleviate them. After two decades, digital pathology is within reach for more departments than ever before. Yet, there is still work to be done. Moreover, there is no one-size-fits-all solution. Every department has its own needs and requirements, its particular use-cases for digital pathology, and its own unique challenges and constraints. While one department may be banging its head against a homegrown laboratory management system, another may be struggling simply to find space for the scanners. This individuality bears emphasis. When every department must forge its own path toward a digital solution, it becomes one final, inescapable hurdle to overcome – not just for any single department, but for digital pathology as a whole.

Fortunately, as digital pathology has matured, so too has the digital pathology community. After years of trial and error, pathologists and vendors have not only



developed a wealth of experience bringing digital pathology into an active lab, but they have also gone to great lengths to disseminate this information as widely as possible. Today, articles and white papers, lectures and webinars, and even one-on-one phone calls are available to guide entrants past spec sheets and untested projections to realistic expectations and viable roadmaps. For departments starting their digital pathology journey, this information is invaluable. It not only provides confidence that they can navigate the myriad of choices and decisions needed to create a digital lab, but also demonstrates that they are not alone in this process. There is, in fact, an entire community ready to back them up.

At the same time, whereas digital pathology was once largely the domain of large academic centers and reference labs, more and more vendors have now made efforts to address the needs of smaller labs. Smaller, cheaper scanners with lower throughput have entered the marketplace, as have live-view remote microscopes, which bring many of the benefits of digital pathology without requiring anywhere

near the same amount of investment. These new technologies offer more alternatives for departments that may lack the resources of larger institutions, making digital pathology a more realistic option.

Many, if not most, pathologists believe that digital pathology will one day replace the glass slide. However, it remains unclear exactly when that will happen and what that path toward full adoption will look like. Consolidated hospital networks, an impending pathologist shortage, disruptive technologies like artificial intelligence – it's hard to say what will be the most influential factor to persuade departments to go digital. However, the digital pathology community is what will inexorably propel digital pathology forward. By bringing together the various stakeholders – from regional labs to community pathology groups to hardware and software vendors – this community has the potential to develop solutions for any laboratory, making pathology a truly digital field.

Asa Rubin is Medical Director at Pramana, Cambridge, Massachusetts, USA.

Ready or Not...

AI is here – and a new era for clinical Raman spectroscopy beckons

By Juergen Popp

Biomedical Raman spectroscopy has developed rapidly in recent years, with numerous studies demonstrating its potential for improving medical diagnostics.

We are working on two big medical fields of application where Raman spectroscopy offers great chances to fulfill currently unmet medical needs. One is in infectious diseases where it can be used to determine the host response (to define viral, fungal, or bacterial infection) and in case of bacterial infection enable the rapid identification of the causing bacteria and its antibiotic resistance profile. The second big field of application is intraoperative spectral histopathology in terms of tumor boundary detection, staging, and grading. To translate Raman spectroscopy into clinics, surgical microscopic or endoscopic Raman spectroscopy and compact point-of-care Raman setups have been developed in conjunction with clinicians.

However, despite these great advances, Raman spectroscopy has not yet established itself in the clinic – and there are several reasons as to why. One is a lack of reliable tools for the automated analysis of Raman spectra. After all, the success of Raman spectroscopy in biomedical diagnostics is inextricably linked to the development of tailored algorithms for evaluating Raman measurement data (for example, spectral data sets and image data) into qualitatively and quantitatively usable information for end users.

Until recently, the main methods used were based on classical machine learning, but now as the number of Raman datasets and biomedical Raman studies increases, the application of deep learning approaches using neural networks is rapidly entering Raman spectroscopy and becoming increasingly important. And with the growth of AI, we could be on the cusp of a powerful synergy that incorporates both AI and deep learning in Raman spectroscopy. This combination could be the missing link necessary to ensure Raman is routinely used for clinical applications.

Some hurdles remain. As a community, we are not entirely ready to embrace this technology – far from it, in truth. But I am hopeful that we are open to studying the performance of AI in biophotonics and spectroscopic diagnostics. Recently, I have been reading more manuscripts reporting on automated analysis of biophotonics data – for example, ophthalmic OCT datasets using deep learning – which looks promising.

Undoubtedly, AI will be a game changer. In a few years, it will be indispensable in many fields – and certainly digital pathology. Whether this is good or bad remains to be seen, because, as with many things, AI offers not only benefits but also dangers, which justifies the hesitation of the community.

One concern in using AI in general and deep learning approaches for image analysis and Raman spectral analysis is the foundation on which the analysis is based – something that can be elusive. It is often the case that one does not know the origin of an AI algorithms' decision. Therefore, it is important to approximate and understand AI tools in order to make them interpretable and understandable for humans.

Of course, the application of AI – not only in medicine – always raises the

question of liability. The legal foundations must be laid here in the near future, because I am certain that AI will play a major role in our daily lives in the future.

This spectroscopic-AI synergy is undeniable and could set the foundation to integrate this fruitful combination of Raman spectroscopy and AI into clinical settings. From a technological point of view, the stage is set and clinically applicable – and medical approved Raman equipment is available. There may be hurdles to overcome before AI's full potential in clinical research can be reached. But the time is ripe to finally start clinical trials with large patient cohorts showing the great possibility of deep learning in terms of automatically interpreting Raman spectra. However, there are still regulatory hurdles to overcome such as compliance with the EU Medical Device Regulation (MDR) 2017/745 in Europe.

This article was originally published on our sister brand, The Analytical Scientist.

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An Ode to Jerad M. Gardner

Profession

Your career
Your business
Your life

An analytical breakdown of the successful dermpath social media star

By Casey P. Schukow, Aadil Ahmed, Pranvera Sulejmani, Raj Singh, MacKenzie J. Griffith, and Nikki Rezanian

Social media is a powerful tool for medical professionals to share information, connect with colleagues, and raise disease awareness amongst patients. Dermatology, pathology, and dermatopathology rely on the visualization of disease findings – making social media a great educational tool. Jerad M. Gardner is a prolific bone/soft tissue pathologist and dermatopathologist – and a prime example of how physicians can embrace social media.

Here, we attempt to determine how Gardner uses social media to promote medical education. To our knowledge, this article provides a unique perspective of a single physician's impact on medical education using social media.

Who is Jerad M. Gardner?

In addition to fostering an expansive network of physicians, social media provides a widely-accessible avenue to raise disease awareness and provides accurate information from board-certified professionals and trainees. Dermatologists may also use social media to educate patients on early signs of skin cancer – which may improve clinical outcomes because patients can more effectively learn how to

seek medical attention and intervene. Further, many patients use social media to find healthcare providers and obtain medical information – a trend that has become more pronounced since the COVID-19 pandemic.

Dermatology and pathology largely rely on the visualization of disease findings, and education is often promoted through photographic images of patients' clinical findings (for example, skin lesions) and clinical specimens (for example, biopsies). Though public sharing of skin findings on social media continues to raise ethical concerns in terms of breaching patient confidentiality, US privacy laws state that the usage of de-identified patient images on social media is not a violation of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Having said this, dermatologists, pathologists, and dermatopathologists who share patient images online should be considerate of displaying potentially identifiable patient information (for example, tattoos, rare diseases, conditions involving the face) and take precautions to “do no harm” when posting such images.

Nevertheless, perhaps the most prolific pathology social media figure over the past

decade has been the eponymous pathologist and dermatopathologist from Geisinger Medical Center in Danville, Pennsylvania. Gardner received his MD from Tulane University School of Medicine, New Orleans, Louisiana, completed his anatomic and clinical pathology residency training at Houston Methodist Hospital in Texas, and finished fellowships in bone/soft tissue pathology and dermatopathology at Emory University in Atlanta, Georgia. While Gardner was still a faculty member at the University of Arkansas Health Sciences in Little Rock, he stated:

“Physicians from any practice setting can benefit from having a professional social media presence...[social media can be used] to teach, to learn, to network with colleagues locally and globally, and to have a powerful public voice about issues that matter for my field and my patients. It has done more to help my career succeed than almost anything else, and it's actually pretty fun too. Many doctors fear that social media use will lead to legal issues or HIPAA violations, but this can easily be avoided by using a bit of common





sense, common courtesy and by always respecting patient privacy just as you would in any public place...”

As of January 2023, he has published over 120 peer-reviewed journal articles, presented at prestigious conferences from around the world, and is currently serving as Deputy Editor-in-Chief for Archives of Pathology & Laboratory Medicine. This social media pioneer has inspired thousands of patients, physicians, trainees, and medical students worldwide as he continues to use social media for advocacy and provide free, fellowship-level education, globally. Dermatopathology is an essential component of dermatology and is a required component of the American Board of Dermatology CORE exam, so his materials are of great benefit to dermatology, dermatopathology, and pathology trainees.

How we assessed Gardner’s social media activity

In June 2023, we observed Gardner’s activity on various social media platforms (no money or financial compensation was required). Relevant peer-reviewed medical literature related to social media use in medical education (including dermatology, pathology, and dermatopathology) was incorporated into this article where applicable. Specifically, we observed Gardner’s Knowledge In Knowledge Out, YouTube, Twitter, Facebook and the website PathElective.com.

Knowledge In Knowledge Out

Gardner is a co-founder of Knowledge In Knowledge Out (or ‘KiKo’). As of June 2023, he has over 5000 followers and has created over 1390 posts on bone pathology, soft tissue pathology, and dermatopathology.

An extraordinary aspect of Gardner’s KiKo account is the advent of bone/soft tissue pathology and dermatopathology

“MEGA” indexes that serve as free, organized libraries that hold a majority of his content. These invaluable indexes include video lectures, board review courses, digital slides, pictures, and sample pathology reports. Gardner’s objective is to offer a free, fellowship-level course for those that need it. As of June 2023, he has accumulated over 130,000 views of his bone/soft tissue pathology and dermatopathology MEGA indexes alone. These numbers do not include the individual page views of each separate video lecture, board review course, digital slide, and so on, within each index, which were both established in 2021. He frequently updates them, and also includes links to his “survival guide” textbooks, which includes high-yield yet in-depth summaries of bone/soft tissue pathology and dermatopathology.

Gardner also contributes to the “Festival of Dermpath” resource on KiKo. These three-day long conferences were started in 2019 by Jonhan Ho, dermatopathologist at the University of Pittsburgh Medical Center in Pittsburgh, Pennsylvania, and founder and CEO of KiKo. The conferences are completely virtual and held quarterly. Dermatopathologists and trainees involved in the Festival of Dermpath share interesting cases with digital slides. Discussions and user engagement are encouraged and awards are given to the cases that are most viewed, most commented, and most upvoted.

The Festival of Dermpath is a private Kiko group that has over 640 international members as of June 2023, however, those interested in joining must simply message Ho to be granted access to the group. Making a KiKo account is straightforward and extremely beneficial for networking, professional development, and content creation, especially with its ability to interconnect digital pathology and

“Social media provides a widely-accessible avenue to raise disease awareness and provides accurate information from board-certified professionals and trainees.”

social media. Even if trainees do not have KiKo accounts, they can still access Gardner’s content either directly on KiKo or through his other social media platforms discussed below.

YouTube

Like other social media outlets, YouTube plays a vital role in providing widely-accessible, free content to learners all around the world. Trainees and students can acquire knowledge via YouTube videos and lecture series independently and at their own pace. For example, the YouTube channel “pathCast” offers pre-recorded, up-to-date lectures on various fields within pathology and includes supportive images.

Before Gardner developed his KiKo profile and subsequent bone/soft pathology and dermatopathology MEGA indexes, many of his respective teaching videos were posted on his YouTube channel – first started in 2012. As of June 2023, Gardner’s YouTube channel has over 57,700 subscribers

and his cumulative video collection has gained over 4.8 million views. Though some of his YouTube videos focus on other general medical topics, such as undergraduate medical education and residency training, most of his videos involve pseudo-personalized narrated microscope sessions using digital pathology slides.

These videos are particularly helpful for trainees because Gardner can point to specific structures using an on-screen cursor and describe them in real time. His videos are organized into playlists (for example, board reviews) and may range from brief, high-yield summaries (about one to five minutes) to lengthier, lecture-style presentations (from one to four hours long). Where applicable, his YouTube videos contain links to associated KiKo posts, which can be found in the summary sections of each video.

X and Facebook

Alongside other social media, X and Facebook have become well-integrated into routine dermatology, pathology, and dermatopathology practice. Using the social media scheduling website – Buffer – Gardner syncs his educational posts across his X and Facebook pages, which have over 44,100 and 33,200 followers respectively, as of June 2023. Through Buffer, he is able to edit and update his educational posts, which contain corresponding KiKo and YouTube links, with ease and efficiency so they can be routinely scheduled for days, weeks, and even months ahead of time.

His synced posts contain unknown cases, providing trainees with a quick, accessible way to test their knowledge and learn pertinent material. His content is easily accessible to users of all ages. For Facebook users – specifically those who would like to experience more difficult cases, unknowns, and interactive discussions from other world-renowned

dermatopathologists – trainees can also follow Philip M. McKee on McKee Derm – a private Facebook group with over 19,000 followers, as of June 2023.

Likewise, Facebook users interested in seeing more bone/soft tissue pathology cases (accompanied by unknown discussions, and so on) are encouraged to follow the “Bone and Soft Tissue Pathology” private Facebook group, which Gardner founded in September 2013. As of June 2023, this group has over 21,700 followers and is managed by an international editorial team of 11 pathologists. Gardner has also been involved in interacting with sarcoma patients on other Facebook support groups, and has discussed these and other experiences during a TEDx Talk in 2020.

PathElective.com

Recently, Gardner has taken on the position of course director for the dermatopathology section of PathElective.com – a free, virtual pathology elective that is an official publication by the Association of Pathology Chairs. This resource is great not only for trainees but also for interested medical students. The course contains free, high-yield introductory and advanced dermatopathology content (including videos, quizzes, and handouts) from Gardner, with supplemental material from other course contributors, authors, and leadership – including two of the authors of this article (CS and AA). Currently, a bone/soft tissue pathology PathElective section is under development, which CS is involved in helping to create.

Social media star

Jerad Gardner has used social media to reach physicians, trainees, and medical students globally. His efforts have allowed millions to learn fellowship-level education in their own time, at

their own pace, and for free. With the continued growth of routine social media use in dermatology, pathology, and dermatopathology, trainees should be encouraged to follow Gardner’s online platforms and experience his numerous cases, unknowns, lectures, and invited guest presentations. Recently, there has been a great deal of literature about the importance and utility of social media in pathology and dermatology education – including an updated 2023 collection of online dermatopathology sources for trainees – no articles (to our knowledge) have specifically addressed the impact that Gardner has had in these fields. Our article represents an unusual ode to a once-in-a-lifetime, generational, academic force.

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Understanding Autopsy in the Digital Age

We spoke with Meagan Chambers on her autopsy passion project, TheAutopsyBook.com

By George Francis Lee

Autopsy struggles to get off the slab in many institutions across the world (1), despite its long history and involvement in medical training. At *The Pathologist*, we've aired plenty of thoughts on the topics, including a multi-author letter of its defense, and it's clear that many see autopsy as an invaluable part of pathology education. Two such people are Meagan Chambers and Alex K. Williamson, co-founders of educational website TheAutopsyBook.com. We caught up with Chambers about breathing new life into autopsy education.

Please introduce yourself...

I am a fellow in the last year of my Anatomic and Neuropathology training at the University of Washington. Next year, I will be an Assistant Professor at Stanford University on the Autopsy Service.

Why did you launch *The Autopsy Book* – and what's the core mission?

There are many challenges to learning how to perform a high-quality medical autopsy these days, including a lack of learning resources, dwindling training requirements (we are down to 30 autopsies for graduation), and varying

enthusiasm for the procedure from those responsible for teaching it. Though not true at my own program, some residents report being “left alone in the room” to perform an autopsy, armed only with the patient's clinical history.

We wanted to respond to these challenges by creating a freely accessible, online learning resource. *The Autopsy Book* is designed for residents, so that they can perform a high-quality autopsy based on the specific clinical considerations of their case.

How does *The Autopsy Book* specifically address the challenges faced by medical students, pathology residents, and attending pathologists?

The Autopsy Book takes a case-based approach to learning medical autopsy. Perhaps 30 autopsies are sufficient to get a general exposure to the field, but not to see all the diverse pathologies that are routinely encountered at autopsy. For example, I did 48 autopsies in my training, but I never saw a pulmonary embolism – and that's a “bread and butter” pathology at autopsy. And so, *The Autopsy Book* allows me to either fill that gap now – through independent reading – or later when I have a case of

“By approaching learning from a case-by-case format, all learners – medical students, residents, and early attendings – can receive a focused review of best practices for autopsy.”

a suspected pulmonary embolism as an early attending.

By approaching learning from a case-by-case format, all learners – medical students, residents, and early attendings – can receive a focused review of best



Meagan Chambers

practices for autopsy. They can maximize the yield of the cases they do see, but also find resources later on when they come across something they didn't see in their residency training.

How are the learning resources formatted and structure within the site? The website is a place where learners go once they have compiled the history for their case. They can then use the search function on the home page to bring up relevant diagnoses they might encounter in their autopsy. For example, a significant proportion of cases will have a history of cardiovascular disease/atherosclerosis. If you were to read the article that came up when you search "atherosclerosis," you find topics ranging from external exam findings, gross examination, sectioning, and histological findings. The topics covered on the site will continue expanding for the foreseeable future, but high-yield topics – atherosclerosis, infection and postmortem cultures, and myocardial infarction – are available now and address some of the most common diagnostic decisions made at autopsy.



Alex K. Williamson

What sets The Autopsy Book apart from other educational resources in the field of autopsy pathology?

For one, it's freely accessible! There are a limited number of resources which approach learning from a case-based perspective, such as the textbook *The Hospital Autopsy* by Billie Fyfe, which focuses on pathologies related to sudden death. Then there are subscription services, like ExpertPath or PathPrimer, which tend to be expensive while focusing on the epidemiology of the pathology rather than getting into the "nitty-gritty" of what to do at the time of autopsy. The Autopsy Book, on the other hand, covers a wider variety of topics and – to repeat – is freely accessible to all.

“You can’t talk about autopsy these days without acknowledging the challenges it faces. Lack of reimbursement and provider attitudes are major barriers to maintaining standards in the field.”

How has the feedback been so far?

I have been shocked at how enthusiastic the response has been. We have people signing up to get updates when we publish new material, we’ve had offers to help generate or enhance content from around the world. Learners are using it, and educators are finding it useful as an adjunct to their own teaching materials. We are finding that it’s not only useful to residents, but also medical students – and even attendings, who are enthusiastic to share their expertise with a wider audience.

What is the general mood around autopsy, in your opinion?

You can’t talk about autopsy these days without acknowledging the challenges it faces. Lack of reimbursement and provider attitudes are major barriers to maintaining standards in the field.

However, there will always be some need for medical autopsies. That’s to say, they won’t ever go to zero. And because of that we must stay committed to doing them at the highest level. Because medical autopsy is both necessary and undersubscribed, there is a huge need for easily accessible, high-quality training materials.

How do you ensure that the content on your platform remains up to date and relevant?

We have a peer review process for initial publication on the website where at least two pathologists need to approve (and have public authorship on) the content. On the backend, we keep track of when the article was last reviewed and we undertake a period re-review of content to make sure it is still accurate. We also welcome feedback from community members, and this has really helped with expanding the material on the page so that it reflects not just the author’s expertise, but also other perspectives and best practices.

How do you measure the success and impact of The Autopsy Book?

Anecdotally, two days after I posted the first article on the site, which was about coronary artery bypass graft, I walked into our autopsy suite and the resident on the case blurted out: “Meagan, help me! I have this coronary artery bypass graft heart and I have no idea what I am doing.” To her credit, I think she did know what she was doing and was going to call the attending in to do the heart together, but we were able to pull up the article using the computers in the suite and walk through everything, focusing on what she

needed to do right there and then. It was lucky that it worked out so well, but it reinforced how necessary this resource is. By the time the attending came in, the resident had a plan, and she was able to articulate her approach to grossing, necessary sections, and proper documentation of the multiple grafts. Since then I have been sure that this resource fills an important gap, and we plan to offer it for anyone who might also find it useful.

Finally, you have a call to action...

Yes! The website is a vast undertaking and there are so many topics to cover – it will take years for it to be a truly comprehensive resource. We are always looking for contributors and partners to help. This can be as simple as passing along core articles they have read that helped them perform a better autopsy, contributing pictures or best practices to existing articles, or offering to draft or edit content. It takes a village to teach and we welcome any level of participation in this resource!

TheAutopsyBook.com

Reference

1. H Sanchez, “Autopsy Rate and Physician Attitudes Toward Autopsy” (2019). Available at: <https://bit.ly/40DacCy>.



Streamlining Urine Processing with modular automation – a French experience

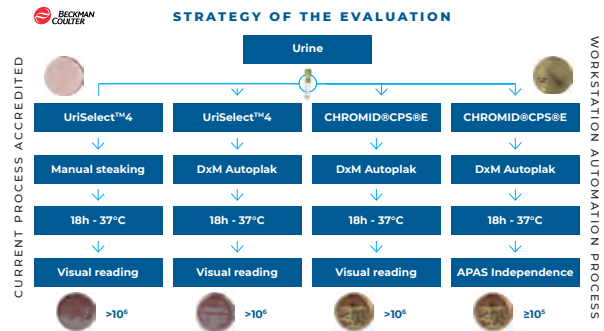
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the evaluation of the WorkStation Automation Solution.

Method

DxM Autoplak streaking verification was performed according to ISO 15189 standard and included: absence of cross contamination; bacterial viability preservation; reproducibility and repeatability; and quality and accuracy. Next, the comparison of DxM Autoplak + APAS® Independence with CPSE Analysis Module and UriSelect4 + DxM Autoplak streaking as the reference method (accredited process) was performed using 1520 routine urine samples.



Conclusion

The Solution was installed and operational within seven days including training, instrument setup, and verification. DxM Autoplak is an easy-to-use and suitable alternative to manual streaking.

Learn more here:

www.beckmancoulter.com/autoplak

The results of this study were presented at the 32nd ECCMID Congress in Lisbon. Authors: Bidan Jeanne-Marie; Rivoire Nathalie; Mumier Laurence; and Alcaraz Claire 2023-12361

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A Born Biomedical Leader

Sitting Down With... David Wells,
Chief Executive of The Institute of
Biomedical Science

What led you to biomedical science in the first place?

Like many people, I suspect biomedical science found me! I did a degree in biomedical science at Anglia Ruskin University and it was always my intention to finish that and go into medicine. Instead, I found that, once I got to a role in a hospital laboratory, I loved it. It was fantastic. I was able to do a lot more across medicine than I ever thought I'd do if I had become a doctor. I say it quite often, but it's a privilege to work in a profession that covers pre-conception, after death, and everything in between. It's such a fantastic view of medicine. The impact that we can have as individuals on patients is what first drew me in and got me hooked.

Could you give us a whistle-stop tour of your career so far?

I've been very lucky to have worked in some very prestigious places. I've had opportunities to do some quite marvelous things in my career. I was fortunate to train at the fantastic Addenbrooke's Hospital in Cambridge – and that really put me in good stead as I moved around.

I've also worked in some great hospitals in very deprived areas – and challenging environments in terms of staff numbers and budgets. I've worked at Great Ormond Street Hospital, leading quite unique services across the globe in terms of pathology. When the pandemic hit, my role of ensuring that we had the right testing within the NHS was really important. I was able to call upon all of my previous experience to make sure that it was a success for us all.

What was it like leading the laboratory response to COVID-19 for NHS England?

It was a very difficult time. The pandemic was clearly coming and there was a slow burn of incident management meetings that were going on. I don't think there was anyone else in the central office function of the NHS that could take the reins, so I wasn't really "chosen." We

didn't know what was going to happen. We didn't know the scale and size of the challenge. And the fact it was a global issue meant that there were some unique challenges in terms of supply chain.

I have to mention that Jane Mills, who now occupies the role heading up Pathology Transformation in NHS England, was a really key person in making sure that we were getting the right, sustainable supplies for the country.

It was daunting and all-consuming, but I had a profession behind me that I knew I could trust. I knew they would deliver when asked – and they did every time. Even when the Prime Minister was making requests, I could put my reputation on the line and say: "Yep, we can do that." I think that made my job a lot easier.

What initiatives have you helped introduce during your time at IBMS?

I had been a trustee at the Institute for a while, so I knew how it worked and knew its capabilities. When I joined, I think my main aim was to do more of the same at a greater scale – to really start to consolidate some of our position in influencing the powers that be. I can break our five year strategy in two halves; first, more education at a higher level, supporting advanced roles in clinical practice and making sure that we cover as many disciplines within pathology as possible; and second, greater political engagement, greater visibility of our profession, and improving our reach across the UK and across the globe.

What advice would you give to someone considering a career in biomedical science?

I would absolutely encourage them to do so because I think it is a fantastic profession! But they've got to go in with their eyes open; the training is tough and sometimes repetitive, but at the end of it is a career that is very worthwhile and valuable.

I'd also say: think about how your career may change. The days of just being a laboratory scientist are long gone.

“The days of just being a laboratory scientist are long gone. I think that a career can be outside the laboratory and in the community; it could be in primary or secondary care or in very specialized tertiary centers.”

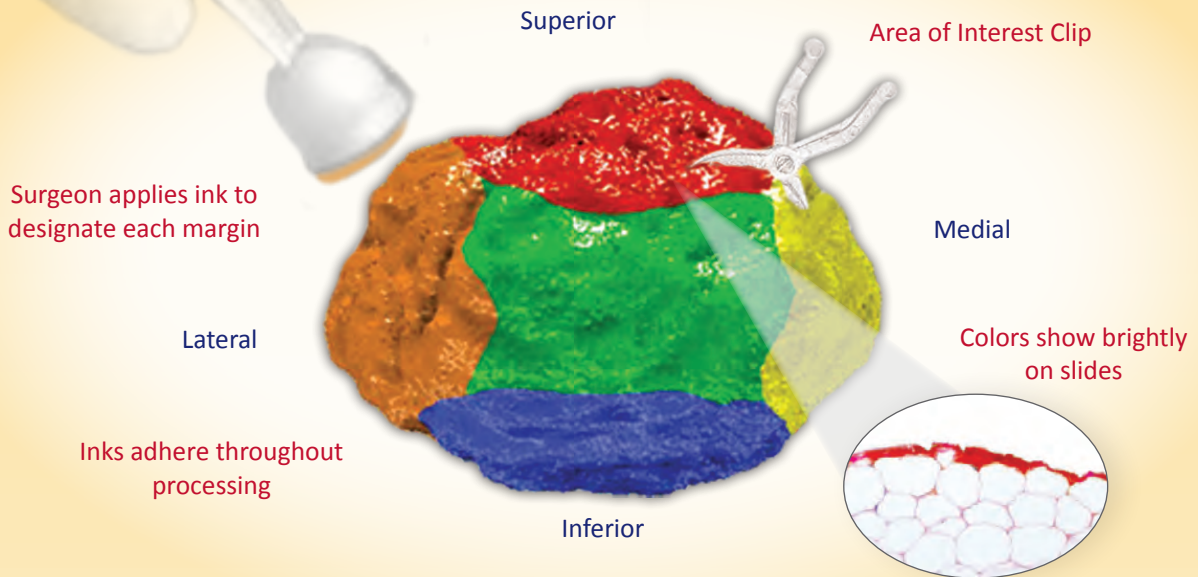
I think that a career can be outside the laboratory and in the community; it could be in primary or secondary care or in very specialized tertiary centers. The limit is your ambition. It's one of those professions that gives back what you put in. And you can personally make a difference to lots of people; if you're working in a traditional patient-facing setting, you may help 20 or 30 patients in a day. In pathology, we help thousands of patients every day.

Which part of your career makes you most proud?

One thing that stands out is the work we did during the pandemic. We were able to deliver what was needed, and I saw some great examples of teamwork across the country. I was very proud of the dedication people showed in some very challenging moments for our country – and indeed for the entire globe.

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