life IN THE lab

LIFE SCIENCES SOLUTIONS, INFORMATION, AND SCIENTAINMENT

ISSUE 26 | MAY 2019

Scientific Trailblazers

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ThermoFisher SCIENTIFIC

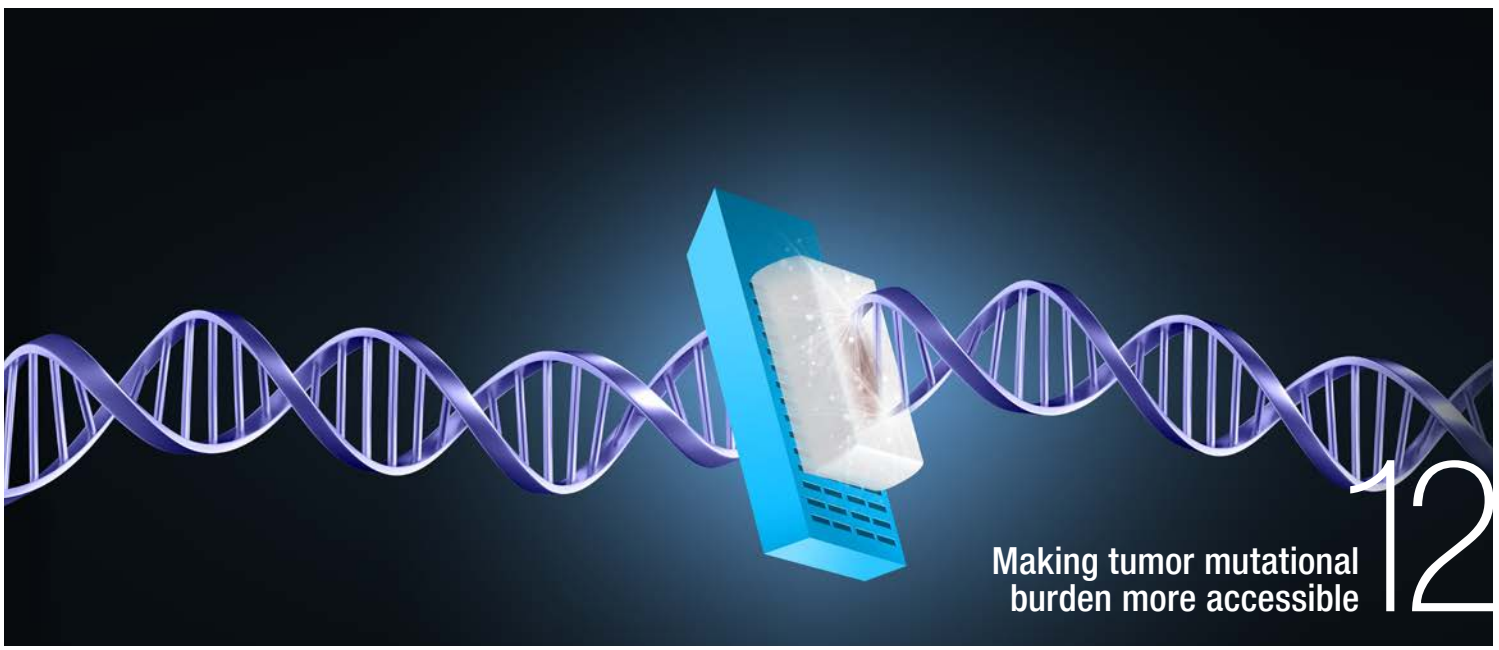
IN THIS **ISSUE**

BLAZING NEW PATHS TOWARD DISCOVERY

Many of us are familiar with famous scientists like Pasteur, Einstein, Crick, and Franklin, but life sciences are ever-evolving. This issue highlights the accomplishments of new scientific pioneers as well as advances in technology. Stories like these continue to inspire us to break limits and propel scientific discovery.

CELEBRATING #SCIENTIFICTRAILBLAZERS

Bernard Katz. Alexander Hoffman. Barbara McClintock. Alan Turing. These are just some of your favorites. Use the hashtag #ScientificTrailblazers to celebrate someone you consider to be a trailblazer in science.



ROAD TO SUCCESS WITH CRISPR-Cas9

"A failed experiment will at some point be followed by a breakthrough"
– Olivier Humbert, PhD

When asked what drives him to keep seeking answers to the challenges he faces in the lab, cancer researcher Olivier Humbert cites the "refreshing and inspiring vision and quest for life" of his two children. No wonder it filled him with pride last year when his daughter gave him a Father's Day card that read, "I want to be a scientist because they do cool things."

In fact, Humbert and his colleagues are doing some of the coolest, most cutting-edge research in science today. They are working to improve the efficacy and safety of CRISPR-Cas9 gene editing in blood stem cells. Derived from the components of a simple bacterial immune system, the revolutionary CRISPR-Cas9 system enables highly targeted gene editing of a wide variety of cell types.

While CRISPR-Cas9 gene editing already shows remarkable promise, it is still a new technology that requires perseverance. Humbert views such challenges as part of the inevitable trial and error of scientific research. "A failed experiment will at some point be followed by a breakthrough," he says. "You have to keep reminding yourself that discoveries are built upon failures; be patient and work methodologically when designing your experiments."

His other solution to dealing with frustrations is sometimes simply to take a break, to take a step back and think about what could have gone wrong—and in his case, a break might turn into a bicycle ride. "When time permits, a long ride helps me reboot and clear my mind," he explains. A bike ride may at first seem too removed from lab experimentation to function as a source of scientific problem-solving, but consider Dr. Humbert's initial childhood interest in science: "Growing up, I spent a lot of time outside surrounded by nature," he says. "That really triggered my curiosity about how living things work and how they're put together—so that's what brought me to the field of science in the first place."

The sense of wonder Humbert discovered as a child exploring the natural world resonates with the sense of renewal he experiences now on epic bike journeys. It informs his dedication to solving important challenges in the lab; and it clearly has helped instill a love of science in his own children. If Humbert's pioneering work with CRISPR-Cas9 technology leads to more effective ways to treat cancer, who knows? Perhaps his children will someday follow in his tracks and be part of a generation of scientists that makes cancer a thing of the past.

Read Olivier Humbert's full story and meet more innovators at **thermofisher.com/keepseeking**

MEET THE INNOVATORS

Connecting rare kids with rare bears
Christina Waters

Meet the flow guy
Steve McClellan

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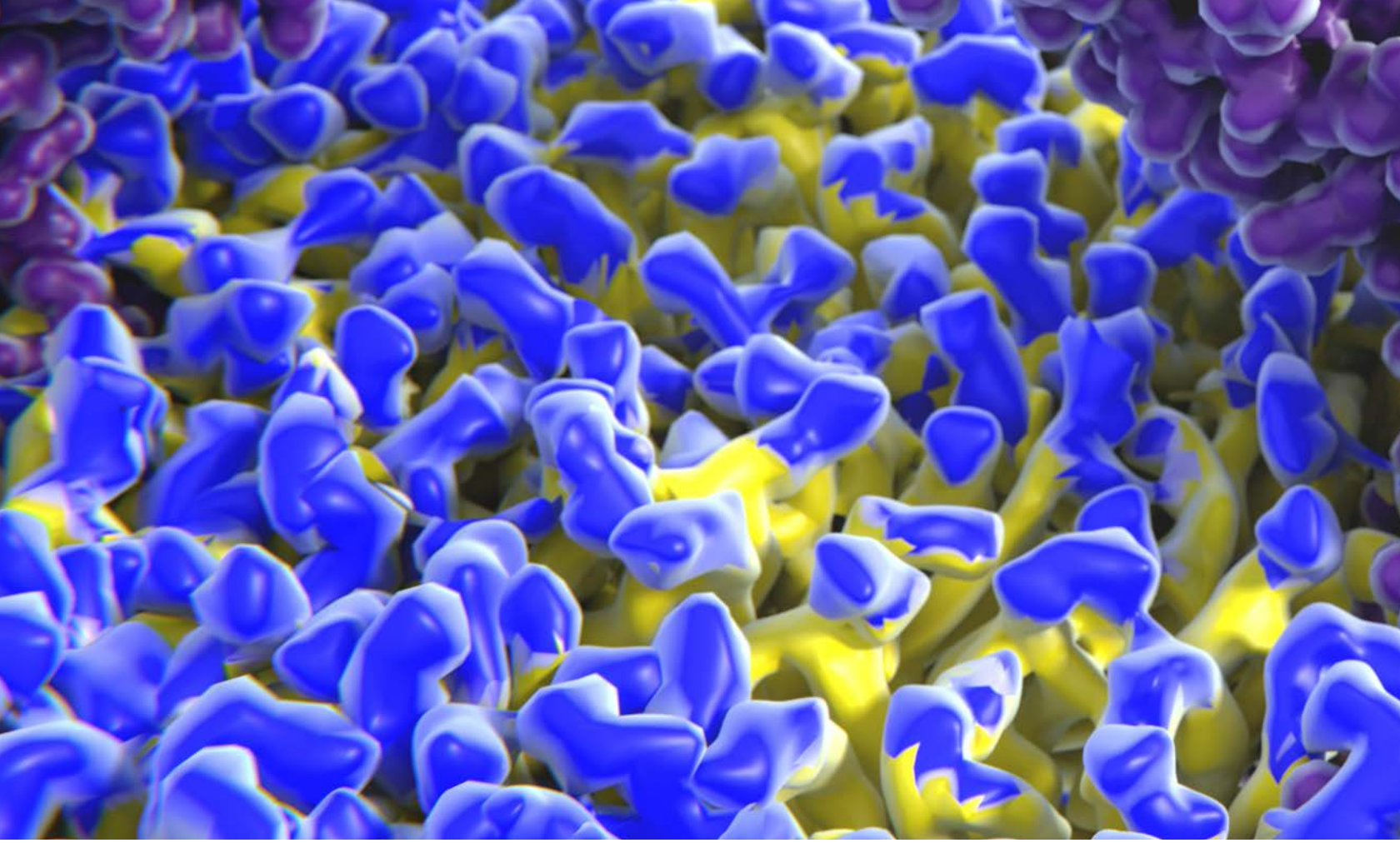
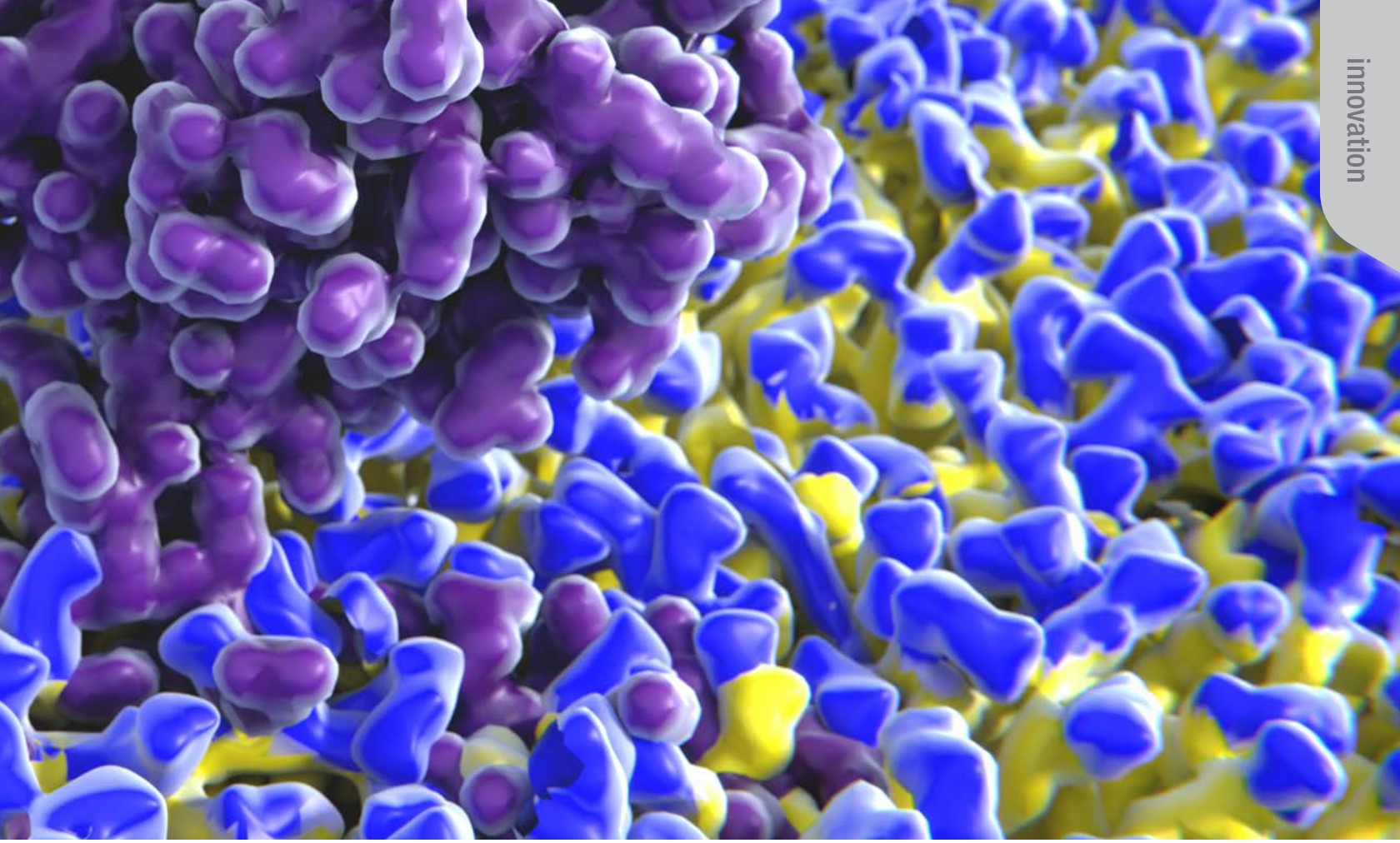


USING FLOW CYTOMETRY TO CREATE BIOLOGICS

Amy Twite, PhD
Director of Chemistry
Valitor, Inc.

Biologics are one of the fastest-growing drug categories in the United States. This diverse class of drugs includes biomolecules, antibodies, and peptides. While small compounds are limited in targets, biologics have the capacity to treat many previously untreatable conditions. We interviewed Amy Twite, PhD, director of chemistry for Valitor, Inc., about how she is working to improve the availability of biologics to treat diseases such as wet macular degeneration and cancer.



What is the mission of Valitor?
Valitor is working on a biologic platform for sustained activity and residency for prolonged therapeutic activity after administration. By immobilizing biologics on our biopolymer platform, we can greatly increase the therapeutic half-life from hours to days in many tissues and solid tumors.

Can you describe the platform's use in the immuno-oncology space?
Directing therapies like CAR T cells or activated cytotoxic T cells to solid tumors can be challenging. Inhibitory checkpoints, along with certain cytokines and tumor-residing cells, can dampen or shorten the duration of these treatments' cytotoxic effects. We are using our platform to regulate cytokines and immune cells for enhanced tumor targeting and clearance.

Describe the use of flow cytometry in your experiments.
One use of flow cytometry is to analyze the subsets of cells affected by biopolymer-bound therapeutics. We use it to measure the number of activated immune cells and the changes in those cells' phenotype distribution over time when exposed to our drug. We can also use it to assess the *in vitro* residence time of our platform vs. unmodified antibodies. Phenotyping panels and flow reagents like Invitrogen™ CellTrace™ dyes help us understand which populations are expanding over time. We can also label our biopolymer-bound therapeutics to assess how they interact with the targeted cells, and their interaction time *in vitro*.

Describe why the Invitrogen™ Attune™ NxT Flow Cytometer is helpful for your work.
We were lucky to discover the Attune NxT Flow Cytometer when we were looking to replace an older instrument. It's a great flow cytometer that provides ease of use for non-immunologists, while rapidly providing data of superb quality.

Do you have any tips for designing a panel for T cells?
Cells in a tumor microenvironment are dynamic. Cells can be found more on a spectrum of phenotypic marker expression dependent on the tissue and disease. It's very helpful to take advantage of the services Thermo Fisher Scientific offers, like panel design to get a jump forward on complex panel development.

What is one factor that helps your flow experiments succeed?
The support we receive is outstanding. Technical support from Thermo Fisher expert reps helps me to proceed with critical experiments. It's easy to shoot texts or emails to them to ameliorate panic moments when issues arise during valuable experiments.

Learn more about flow cytometry at **thermofisher.com/flow**

MULTIPLE TECHNOLOGIES FOR GENE EXPRESSION

Our customers explain why this is an important aspect of their research

There are many gene expression solutions, and each technology provides value at a different stage of research. A typical workflow might consist of a transcriptome-wide analysis, such as biomarker discovery mediated via gene expression microarrays, or RNA sequencing. Another workflow, such as validation, focuses on smaller sets of genes or more samples, such as verification of results with real-time PCR. Thermo Fisher Scientific is the only provider of all three of these gene expression technologies, enabling your success with the ability to transition from one method to another at various stages of your research without a loss of biomarkers.

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applied biosystems

Concordance of transcriptome sequencing, microarrays, and qPCR using Ion AmpliSeq Transcriptome kits, Clariom D Assays, and TaqMan Assays

This technical note shows the high concordance of data between transcriptome sequencing, gene expression microarrays, and real-time PCR. Data from a set of 70 differentially expressed genes across Applied Biosystems™ TaqMan® Gene Expression Assays, Applied Biosystems™ Clariom™ D Assays, and the Ion AmpliSeq™ Transcriptome Human Gene Expression Kit had a high statistical correlation. Thus, results across these technologies are comparable. You can switch between technologies, have confidence in the data, and not have to worry about repeating your experiments.

Download it today at **thermofisher.com/geneexpression**

HERE'S WHAT CUSTOMERS HAVE TO SAY ABOUT USING MULTIPLE TECHNOLOGIES

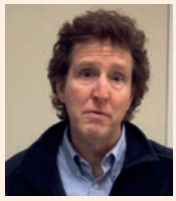
Type II diabetes research:

"One of the advantages to working with Thermo Fisher is the extensive portfolio of products that they offer… There's an ability to choose the technology that best suits the particular kind of follow-up study." **– Dr. Iain Gallagher, Health Sciences and Sport, University of Stirling**

Tumor biology research:

"We use different technologies at different stages of the project. So, in the discovery phase, we want to have as much information as we possibly can. But as we progress through the project, we're interested in developing a test that is clinically useful. So that puts a different focus on which technology you use at that time." **– Dr. Darren Roberts, Department of Translational Radiobiology, University of Manchester**

Stroke research:



"It's been a great opportunity working with Thermo Fisher, from the beginning to the end of the development of our products. I think the support is unparalleled, which really goes beyond the products. I think what's really kept us on track and put us on the pathway to be very successful in what we do is the combination of outstanding sales support, service, understanding of the products, and the ability to meet our needs as we build for the future." **– Jeff June, CEO and Founder, Ischemia Care**

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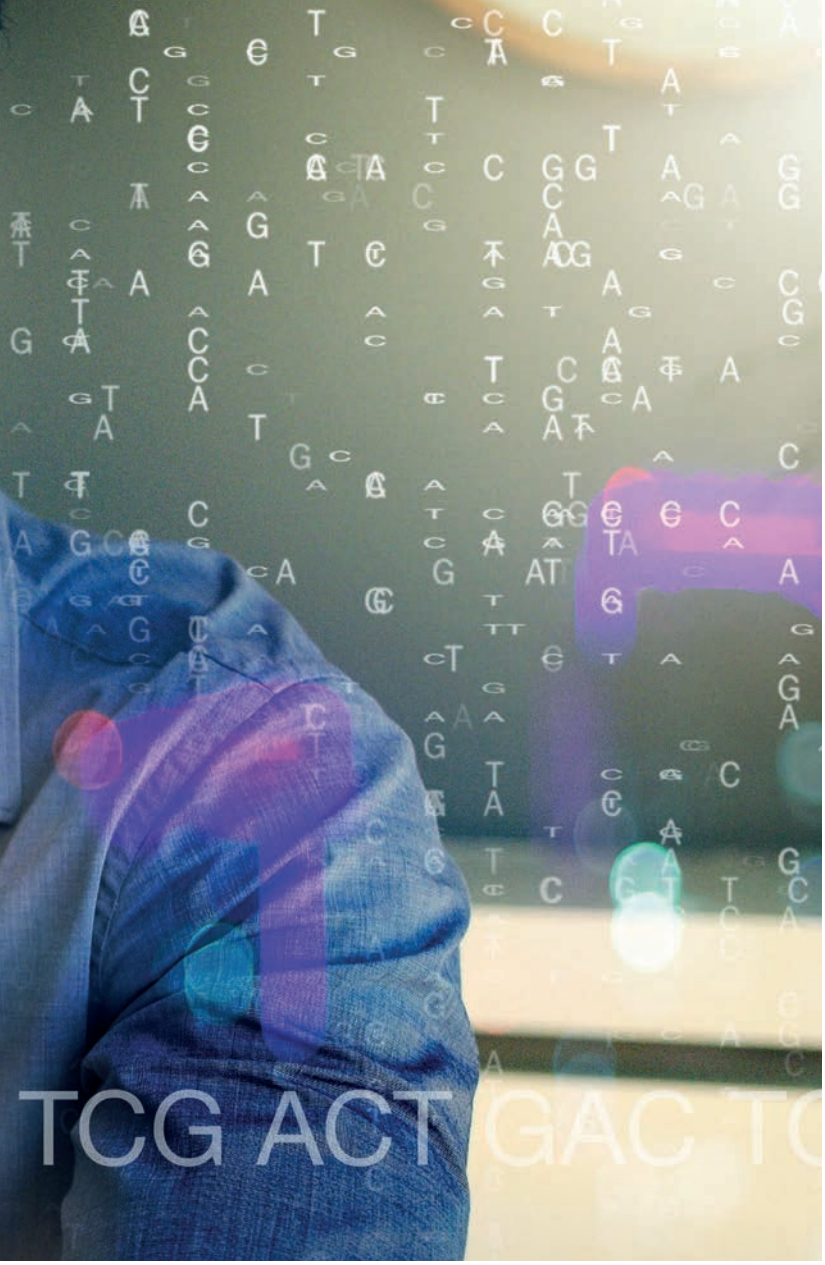

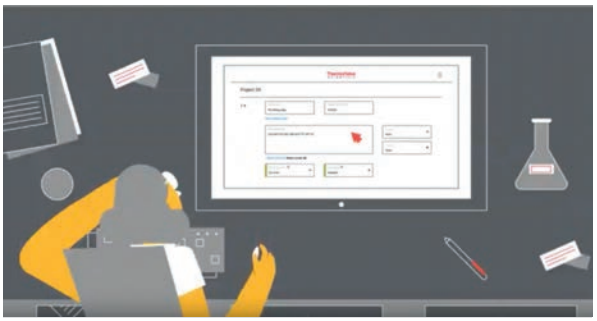

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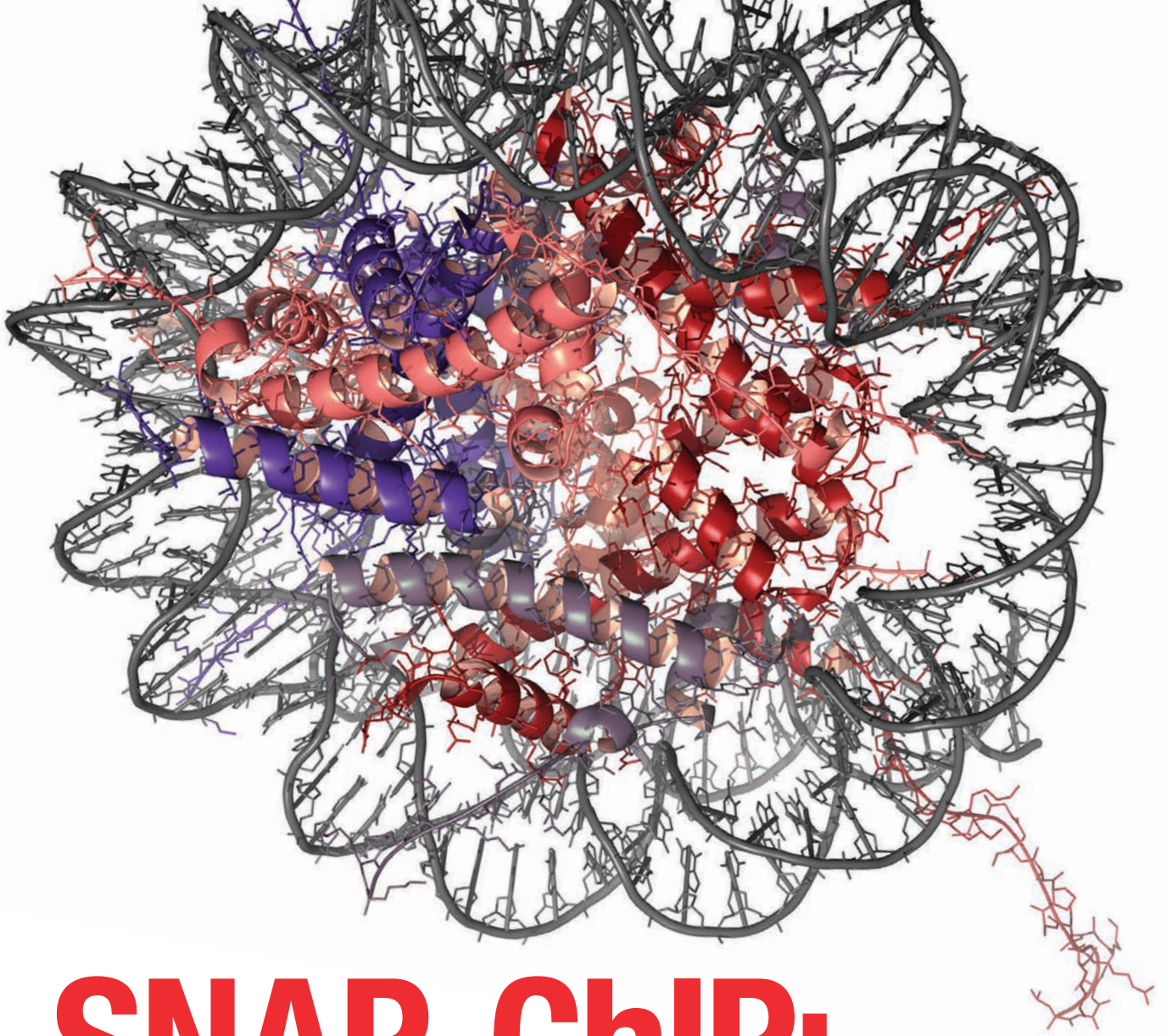

SNAP-ChIP:

A BIG LEAP FORWARD FOR EPIGENETICS RESEARCH

Eliza Small, PhD
R&D Scientist
Protein and Cell Analysis
Thermo Fisher Scientific

WHAT MAKES THIS NEW TECHNIQUE INNOVATIVE AND POWERFUL?

Eliza Small, PhD, is a scientist working on the Invitrogen™ antibodies portfolio for epigenetics research. She's leading a collaboration with EpiCypher on a new way to identify highly specific histone antibodies for chromatin immunoprecipitation (ChIP). EpiCypher has a technology called SNAP-ChIP (with "SNAP" meaning "sample normalization and antibody profiling") that is being used to rigorously validate our histone antibodies. We sat down with her to understand what makes this new technique unique, innovative, and powerful.

Tell us about SNAP-ChIP technology and why it's different.
SNAP-ChIP is a technology developed by Alex Ruthenburg's lab at the University of Chicago to normalize ChIP experiments and originally was called ICe-ChIP. It works by using recombinant nucleosomes containing a variety of histone modifications and each nucleosome has a unique barcode associated with the DNA wrapped around it. The panel of recombinant nucleosomes is used as a spike-in to a cell lysate followed by the researcher's favorite ChIP workflow. After pulldown and DNA elution, qPCR is used to quantitate the pulldown efficiency of the recombinant nucleosomes, which can be used to compare ChIP experiments by using this spike-in as an internal normalization. SNAP-ChIP is also a powerful method for determining how specific your antibody is, as you can learn how much of your antibody is pulling down the modification you are interested in compared to a panel of other histone modifications.

What makes this different from other validation testing methods?
A common method for validating histone modification antibodies is peptide arrays. This method is great for a screen of many modifications and to understand if neighboring modifications influence antibody recognition. Arrays, however, are asking the antibody to recognize a spotted peptide, and a ChIP experiment is asking an antibody to recognize a modification in the context of chromatin. There have been hints in the literature for some time that peptide arrays might not be the best method of determining antibody specificity; and recent published work (Shah, RN et al, 2018), along with our own analysis of our portfolio, has shown there is no correlation between the specificity of peptide arrays and SNAP-ChIP.

Why is this important?
Specificity is crucial to your experiment. In ChIP you are identifying where a modification resides on the genome as well as where it does not. With this information, researchers are gaining an understanding of the role of different modifications in gene expression. If your antibody is pulling down the modification you are interested in in addition to other modifications, the data can be very misleading as you will be misidentifying histone occupancy.

How will the introduction of SNAP-ChIP change epigenetics research?
SNAP-ChIP brings a new accuracy to ChIP experiments to ensure an antibody is pulling down what we think it should be. That's what has interested us in the antibody group at Thermo Fisher Scientific, and why we began working with EpiCypher to test our antibodies. SNAP-ChIP also provides an internal normalization control, which gives researchers much greater confidence in making comparisons between ChIP experiments.

Specificity is crucial to your experiment. In ChIP you are identifying where a modification resides on the genome as well as where it does not.

Does this mean peptide arrays shouldn't be used anymore?
Peptide arrays should absolutely be employed, just not for determining ChIP specificity. The lack of correlation between ChIP specificity and peptide array has revealed that specificity for antibodies is application-dependent, at least in the case of histone modifications.

If a scientist was thinking of doing their first ChIP experiment, what advice would you give to help achieve successful results?
ChIP is a complicated experiment with many steps. Optimization of each step, including choosing antibody, is essential for success. I highly recommend using SNAP-ChIP in your workflow when using histone antibodies. No matter what target you are interested in studying, look at the data provided for an antibody to understand specificity. You want to see regions of the genome enriched where you expect your target, and regions depleted where you do not expect your target. Additional specificity that you might want is a knockdown, knockout, or ChIP-western, where you perform a western blot after the pulldown step. These are all methods that help give confidence that your antibody is specific to the intended target.

Learn more about ChIP at
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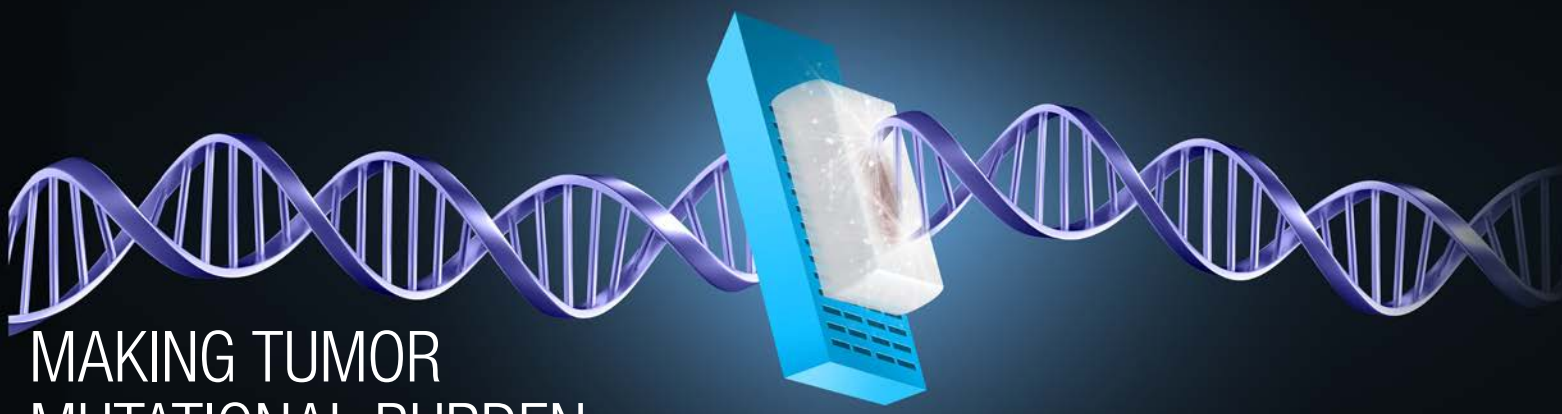

MAKING TUMOR MUTATIONAL BURDEN MORE ACCESSIBLE

When ideas and innovations evolve into standards and practice

Tumor mutational burden (TMB) is an emerging biomarker that measures the total number of somatic mutations found within the tumor genome. Evidence suggests that it could also be a predictive biomarker. There are multiple groups around the globe addressing TMB challenges, but two in particular are focused on standardization, in an attempt to take the science to the next level.

Creating a common language: Friends of Cancer Research

Different labs may report different measurements, making it difficult to use TMB as a biomarker. Currently, there are no universal standards for TMB calculation and reporting. Friends of Cancer Research has organized stakeholders across all health sectors to review the current methods of TMB calculation and reporting in order to create a consensus on how best to standardize and validate them.

"In this competitive environment, we were pleasantly surprised that everyone saw the need, and that at the end of the day this is going to help support everyone's objectives and goals. So, we are very fortunate to have a very collaborative atmosphere," said Dr. Mark Stewart, vice president of science policy for Friends of Cancer Research.

Making the most of poor-quality samples: MolecularMD

Poor-quality formalin-fixed, paraffin-embedded (FFPE) DNA samples can generate false-positive SNV calls and can falsely elevate TMB scores. MolecularMD has two practical solutions that use either increased filtering (10%) in the TML2.0 workflow in Ion Reporter™ software, or a duplicate-analysis workflow (whole-exome sequencing + targeted for correlation). Both reduce the false-positive variant calls and help enable higher accuracy in the TMB determination of FFPE samples.

"The simplicity of the Ion AmpliSeq™ workflow and the streamlined analysis allow the potential to deliver results quickly," said Dr. Jin Li of MolecularMD.

AN EMERGING IMMUNO-ONCOLOGY BIOMARKER

The Ion Torrent™ Oncomine™ Tumor Mutation Load Assay is a robust, targeted next-generation sequencing (NGS) assay designed for tumor profiling by annotation of cancer driver variants. It offers accurate quantification of TMB from limited FFPE samples. Our streamlined, built-in analysis solution allows you to confidently detect cancer driver variants and assess TMB in ~2.5 days for your research studies.

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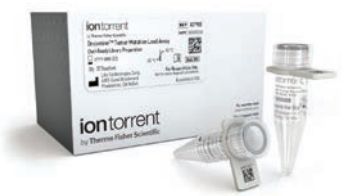

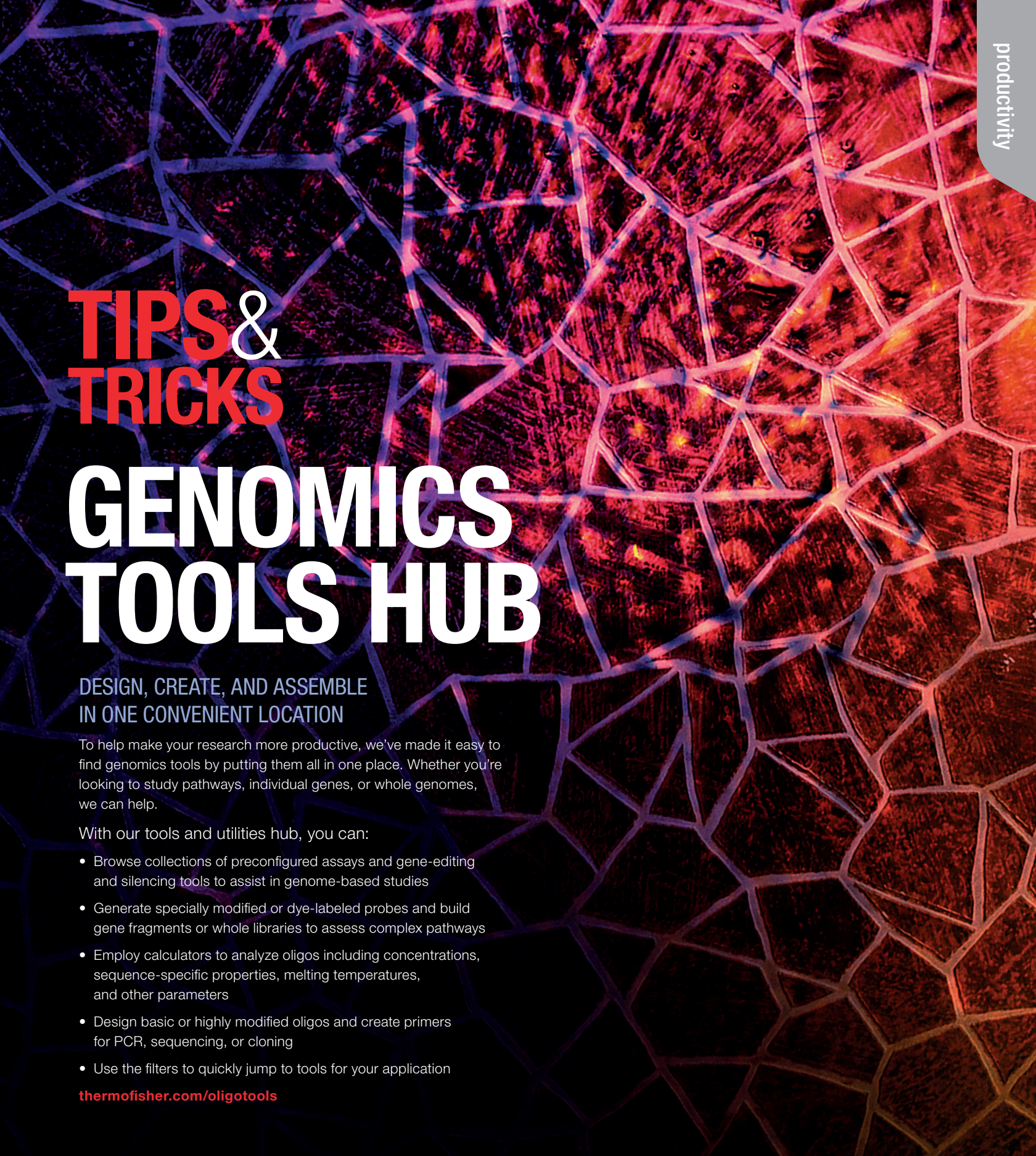

TIPS & TRICKS

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- Design basic or highly modified oligos and create primers for PCR, sequencing, or cloning
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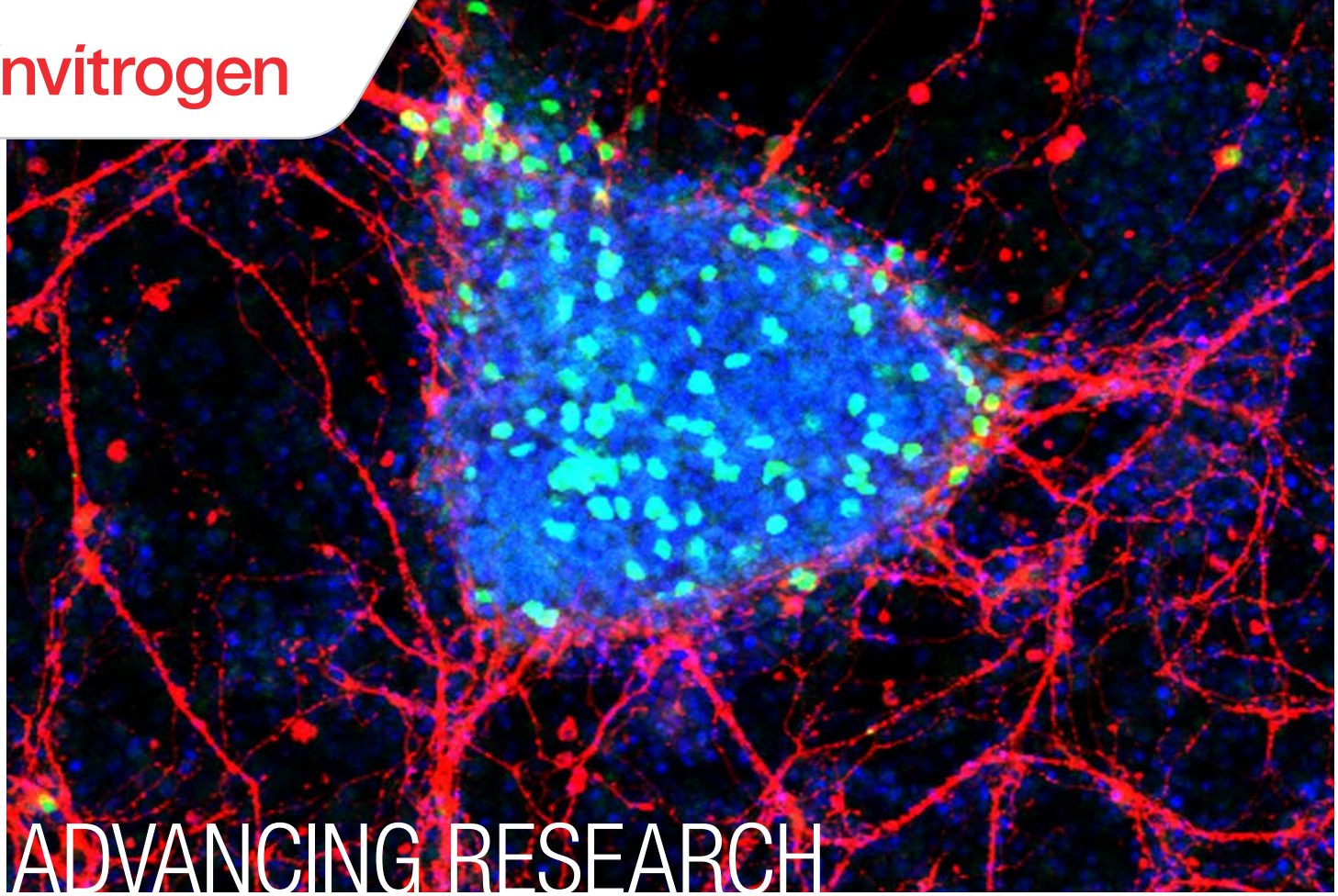

ADVANCING RESEARCH

BLOCK BY BLOCK

Dr. Sandeep Gupta
Sandeep received his PhD in 2015 from the Indian Institute of Technology, Kanpur (India). His research in the Butler lab at UCLA is focused on understanding how bone morphogenic protein (BMP) signaling performs diverse functions such as patterning and regulating neuronal growth in the dorsal spinal cord.

Molecular biology building blocks help progress neuroregenerative spinal cord therapy

Building blocks are defined as the basic units from which something is built up. Since a finished product is only as good as the foundation upon which it is laid, the building blocks must be of the highest quality in order for the final goal to be accomplished. This is also true in molecular biology. Molecular biology building blocks are the everyday reagents that are used as part of an experiment. Without high-quality reagents, the final result of the experiment is compromised.

Take, for example, the work of Samantha Butler's laboratory at the University of California Los Angeles: their primary focus is on repairing spinal cord injuries through neuroregenerative treatments using stem cells. Dr. Sandeep Gupta, a researcher in Butler's laboratory, works to understand the basic mechanisms behind how the spinal cord is formed during embryo development, and how that can apply to therapies for spinal cord injury.

What defines a spinal cord injury?

Any sort of damage to the spinal cord that can impair its function is considered a spinal cord injury. This impairment can be temporary or permanent, although most often it is a permanent situation. Spinal cord injuries are estimated to affect over a million

people in the United States alone. More than 2,000 permanent spinal cord injuries occur each year, the majority of which are seen in military personnel. These conditions have a significant impact on our society, for both the medical personnel treating the injuries (at a cost of $40 billion annually) as well as for the caretakers of those individuals. Not only do patients lose movement, but they also lose sensation, which causes a disconnect from their environment and a reduction in their quality of life.

What is the goal and mission of your research?

We currently don't have any means to reverse spinal injuries. Available methods mainly utilize the neuroprotective properties of certain chemicals and proteins that facilitate blood flow to the injured area and limit further damage. However, a proposed option is neuroregenerative, where the focus is on the regeneration of the lost neurons. This goal is typically accomplished through exercise or through the application of specialized cells: neural stem cells that can actually build the lost neurons inside the body. My research focus is to investigate how this can be achieved.

Why is neuroregenerative research important beyond the current motor neuron recovery?

Significant progress has been made generating the *in vitro*–derived motor neurons required to restore coordinated movement. While these motor neurons are important, they do not address the problem of sensation. Your body needs constant feedback to guide the motor system to function. For example, if you cannot sense pain, you cannot guide your motor neurons to avoid the source of the pain. Movement cannot function without sensory information, which is why we are focused on understanding the molecular mechanism of sensory interneuron differentiation to define ways to convert induced pluripotent cells (iPSCs) into sensory neurons.

What molecular biology building blocks are you using in your research, and what do you consider the most important?

We have a multitiered approach to our research. To identify what new genes are involved in the differentiation of stem cells into spinal cord neurons, our initial discovery strategy uses RNA-Seq. Once those genes have been identified, we then use RT-qPCR to confirm that they are not due to experimental error. We consider RT-qPCR to be one of the most important tools that we use every day. This technique helps to confirm that differentiation is proceeding correctly by detecting markers at certain timepoints during the process. Assaying these markers through RT-qPCR is an easy, high-throughput, and robust method.

Your body needs constant feedback to guide the motor system to function. For example, if you cannot sense pain, you cannot guide your motor neurons to avoid the source of the pain.

It is also the first line of investigation used to check if differentiation has improved with the inhibition or activation of certain signaling pathways. It is very important to use RT-qPCR in my research to help successful monitoring of the differentiation process.

What features of RT-qPCR reagents are important to you?

We run 6–12 samples at a time every day. Therefore, speed is of high importance to reduce processing time. We also need a high-fidelity system that will consistently produce cDNA copies of any long RNA templates. This was a problem, until we began using Invitrogen™ SuperScript™ IV Reverse Transcriptase. The SuperScript IV reagent is very fast and efficient. We're able to produce a much higher cDNA yield in 20 minutes, vs. 50 minutes per reaction previously. With SuperScript IV reagent, we're consistently producing results using long RNA templates, which was difficult before.

Why are you interested in an induced pluripotent stem cell (iPSC) system, and what do you see as the future of cell therapy using this approach?

iPSCs are remarkable tools, since you generate the cells directly from the patient. In doing so, there is no risk for rejection of the cells when transplanted and the patient can receive the maximum benefit of the treatment. Before we can use this approach, however, we still have a long way to go with the research. We don't know how these neurons are born in the spinal cord. The neurons in the spinal cord are connected in a very precise way. We still do not understand how they connect and how they find their partner for a correct function. To restore spinal cord injuries, we have to figure out how to make these spinal cord neurons in a dish and test if they can make a desired connection when putting them back in the injured spine. They can also be an excellent platform to screen potential drugs that might be effective for growing the axons for a particular neuron.

As you can see from Dr. Gupta's research, knowledge of how neurons are first developed is crucial to creating these cells in a clinically relevant setting that can then be used for neuroregenerative spinal cord stem cell treatment. It is the foundation for this therapy; and to ensure that the proper building blocks are being laid, Dr. Gupta trusts the initial investigation of his research to high-quality molecular biology reagents for his experiments.

To learn more about Dr. Gupta and the work that Dr. Butler's laboratory is accomplishing, go to **https://butlerlab.neurobio.ucla.edu/research**

To learn more about SuperScript IV Reverse Transcriptase, go to **thermofisher.com/ssiv**

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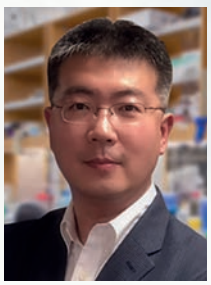
CUSTOMER SPOTLIGHT: USING THE EXPICHO SYSTEM FOR HIV VACCINE DEVELOPMENT



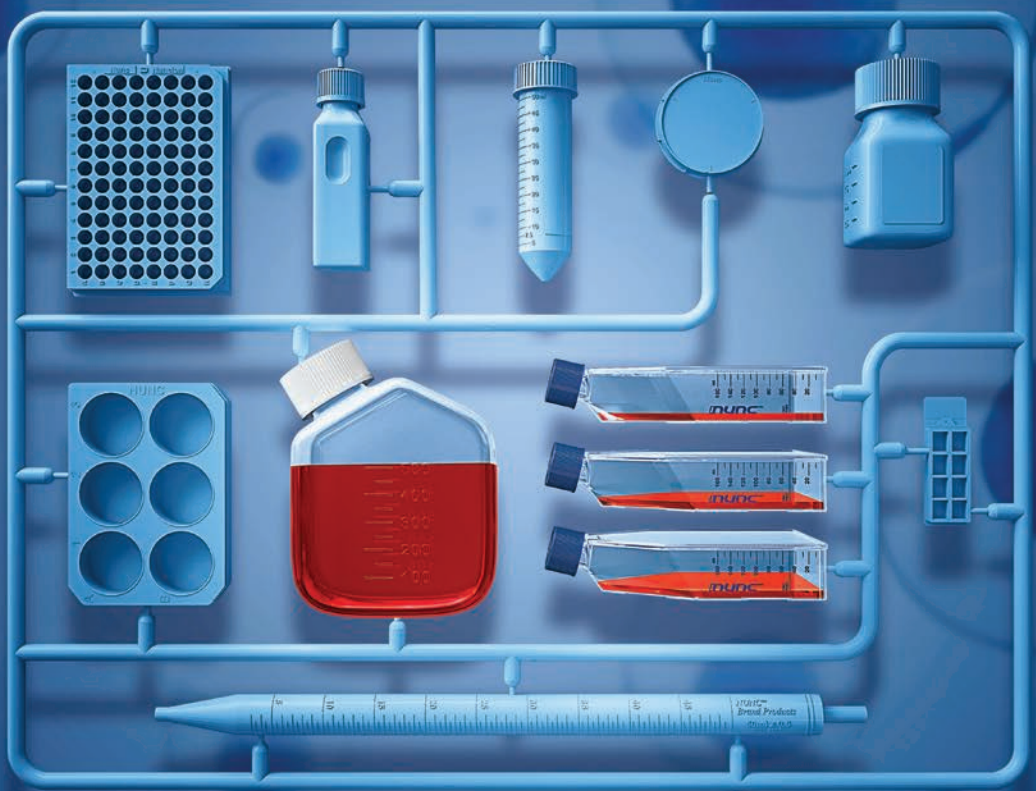
Dr. Jiang Zhu, associate professor at the Scripps Research Institute in La Jolla, California, recently published a paper in *Science Advances*. This paper documents high titer, purity, stability, and effectiveness at raising Tier 2 broadly neutralizing antibody responses with HIV nanoparticle vaccines expressed in the ExpiCHO Expression System—showcasing the system's value as a production platform. Due to Dr. Zhu's hard work, this could become an important and historic next step in the development of a truly effective HIV vaccine.

"Together, ExpiCHO [products] provide a robust expression system for producing both native-like trimers and gp140 nanoparticles, with important implications for manufacturing." – Dr. Jiang Zhu

thermofisher.com/expicho

gibco

BETTER TOGETHER



Gibco™ media and Thermo Scientific™ Nunc™ cell culture plastics with Nunclon™ Delta surface are a proven combination for consistent cell growth.

Want to learn more? Look up your cell line using the Nunclon Delta surface data tool and see for yourself how cells thrive in Nunc cell culture dishes.

thermofisher.com/bettertogether

LET'S SOCIALIZE

Scientists all over the world are sharing their labs' cell culture projects on social media.

Show us your cell culture journey by tagging #gibcocellculture and #nunccellculture

GIBCO CELL CULTURE HEROES

Cell Culture Heroes is a global webinar series that spotlights PhD and postdoc researchers with the primary focus of telling the story of their research.

Meet one of the Gibco™ Cell Culture Heroes: Devanjali Dutta is a postdoctoral researcher in Professor Hans Clevers' group at the Hubrecht Institute in the Netherlands. She is currently using human tissue–derived 3D organoid cultures to study host–microbiome interactions, infectious diseases, and cancer. She received her PhD in 2015 from the University of Heidelberg in Germany, where she studied at the lab of Professor Bruce Edgar. Her doctoral research involved the development of methods to isolate and profile rare cell types and tumor cells from the fruit fly midgut, and the generation of transcriptome profiles of the cells of the adult *Drosophila* intestinal epithelium.

Why did you choose cancer research?
As a kid I lost my grandfather to cancer. That was my first introduction to the deadly disease. Since then I have always wanted to contribute to this field, in understanding the root cause of cancer and finding new drugs to tackle it. While cancer research has made tremendous progress, I feel there are many more unexplored avenues in personalized cancer therapies that still need to be improved. It is therefore my endeavor to contribute my bit by using organoid technology to fight cancer.

I have always wanted to contribute to this field, in understanding the root cause of cancer and finding new drugs to tackle it.

What motivates you to succeed in your field?
I'm encouraged by the fact that what we do is going to help millions of people who suffer from the disease. It's a huge responsibility, as well as a motivation to do my best.

Describe yourself with three words:
Adventurous, curious, problem-solver.

What is your favorite day of your life thus far?
The day I got my PhD. My parents were there, and it was the best moment ever.

Is outreach/STEM important to you? Why?
Yes, it's very important for me. I believe every individual has the same basic rights to education and should be given an equal opportunity regardless of class, color, nationality, or gender.

Favorite phrase?
Let's do it!

Why did you become a scientist?
Being from a family of scientists, it was only natural for me to be in science because since childhood I have always marveled at the living world around us. Furthermore, meeting and being trained under some of the best scientists of our generation inspired me to follow their footsteps to discover the unknown and add my little bit to society.

Why did you want to be a Gibco Cell Culture Hero?
I wanted to be a part of a growing community of #scicomm advocates who were promoting education and driving tomorrow's breakthroughs.

Apply to be a Cell Culture Hero now to share your science with the world.

thermofisher.com/cellcultureheroes

THE AR-ENABLED LAB

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New Smart Remote Support platform uses augmented reality (AR) to help reduce instrument downtime from days to minutes, compared to on-site repair

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Virtually transport one of our specialists into your lab in as little as 20 seconds

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Connect with specialists using any Internet-enabled mobile device

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Show our support team exactly what you are seeing

On-screen annotations
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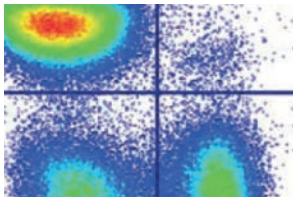
We offer full system support, troubleshooting the instrument and its onboard computer. Using IT-friendly remote support access, our engineers can navigate your desktop to better understand and address your computer- or software-related questions

Science can't wait on instrument downtime. Start your AR journey with Smart Remote Support by visiting **thermofisher.com/smartremote**

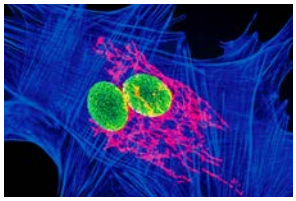
Five steps to a science–life balance

These 5-step workflows can help you get out of the lab by 5:00, so you can do the things you love. **thermofisher.com/keepseeking**

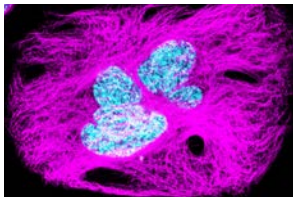
Discover all of our 5-step workflows



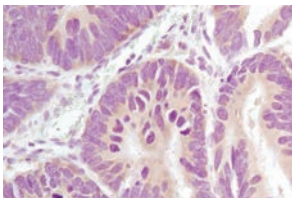
Design intracellular flow cytometry experiments



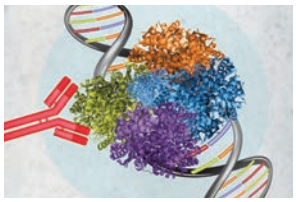
Publication-quality fixed-cell images



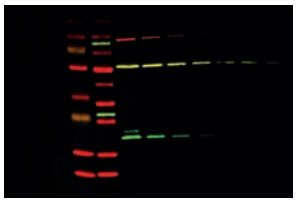
Capture beautiful live-cell images



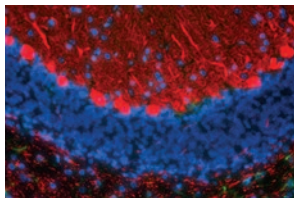
High-quality IHC images



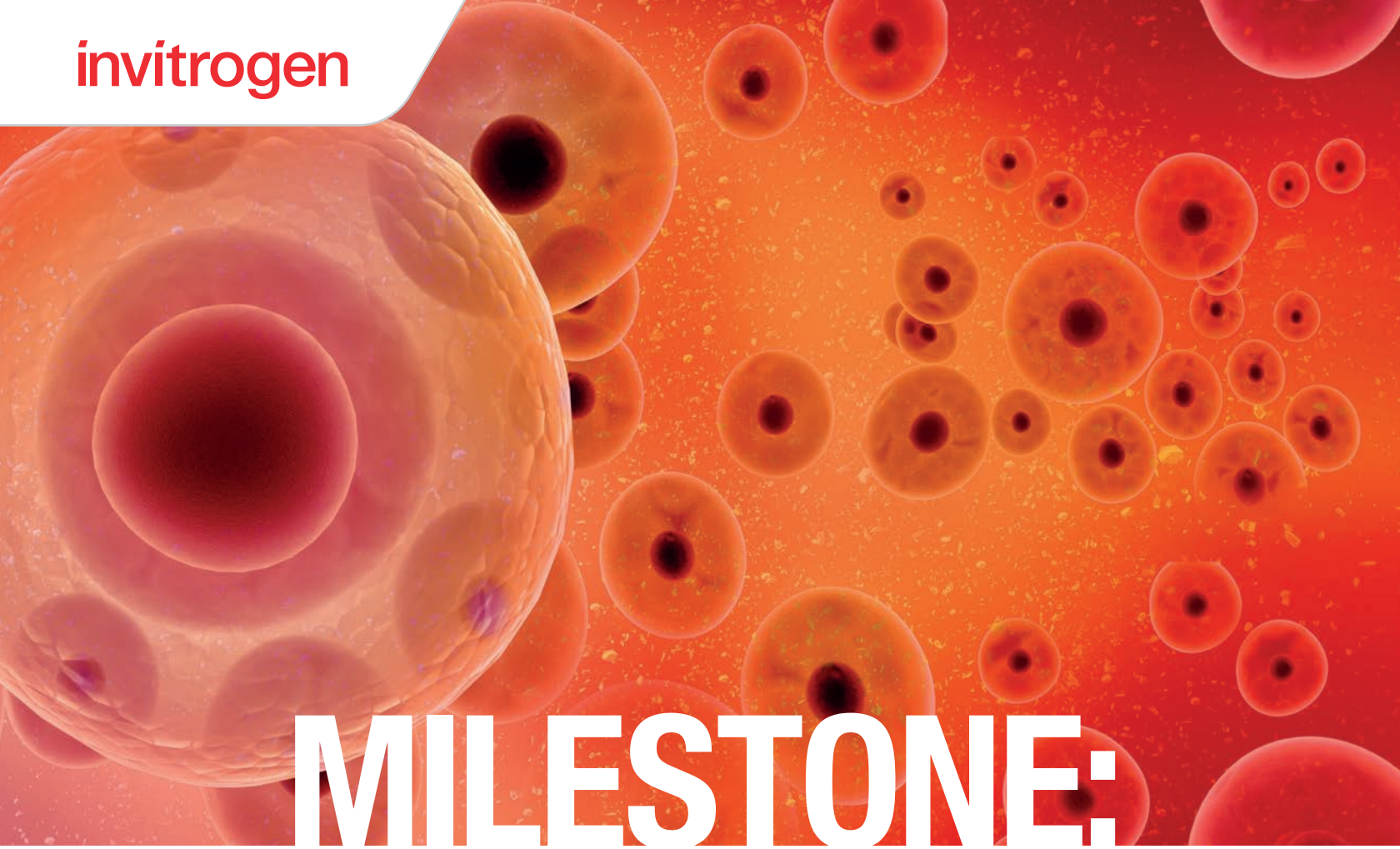
Successful ChIP experiments



Easily get optimal fluorescent multiplexed western blots



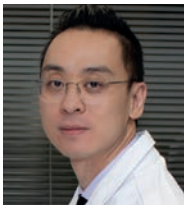
Improve your success modeling Parkinson's disease using human iPSCs in 5 steps



MILESTONE:

ANOTHER RESEARCHER INCREASES CELL COUNTING EFFICIENCY

And the 10,000th Countess cell counter goes to…
Dr. Brian Wong at Washington University



Brian Wong, PhD
Assistant Professor,
Department of Surgery,
Washington University
School of Medicine,
St. Louis, Missouri

In 2008 the Invitrogen™ Countess™ Automated Cell Counter was launched and became almost instantly famous for saving people from the tedious task of manual cell counting. Ten years later, the updated Invitrogen™ Countess™ II Automated Cell Counter was shipped to the 10,000th customer, Dr. Brian Wong at the Washington University School of Medicine. In this interview, he tells us how the game-changing Countess II Automated Cell Counter increases efficiency in his lab.

What is the scope of your research?
We are seeking to understand the role of lymphatic vessels in transplant rejection in multiple solid organ transplant settings (e.g., heart, lung, kidney), and to determine whether targeting cellular metabolism can be an effective therapeutic option to improve organ transplant survival.

How were you counting cells prior to purchasing the Countess II Automated Cell Counter?
Using a Neubauer hemocytometer. I had previously used a Countess device in other labs.

How do you anticipate the Countess II device will help in your research?
I anticipate that it will help to optimize our workflow in counting cells from *in vitro* culture and *in vivo* isolation, reducing the amount of time required while maintaining accuracy of cell counting.

An important part of my passion is the mentorship of others to pursue science.

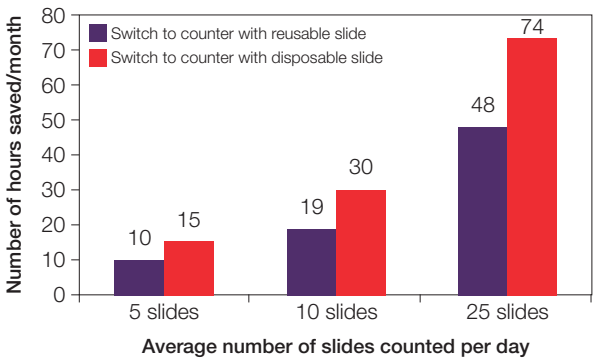
What challenges do you face in your research?
With an unlimited number of possible questions to ask, I am challenged with deciding whether seeking the answers to a particular question are worth pursuing and how much effort to devote to it. A reality of science is how to effectively manage resources, finances, and time to produce high-quality work. I am constantly looking for ways to increase efficiency; that is why I chose the Countess II device.

What drives your passion for science?
The notion that every day, the work we do in the laboratory can contribute to the discovery of things that no one else knows. These discoveries can change how we understand biological mechanisms in cells, as well as how these systems may be aberrantly dysregulated in disease. An important part of my passion is the mentorship of others to pursue science, and working with the scientific community to collaborate in answering important research questions.

TIME SAVINGS = COST SAVINGS

Did you know that the additional time it takes to manually count cells compared to automated cell counting is often overlooked as an added cost? An individual counting five slides per day can save ~15 hours per month by switching to an automated counter, freeing up resources to focus on other lab projects.

thermofisher.com/countess

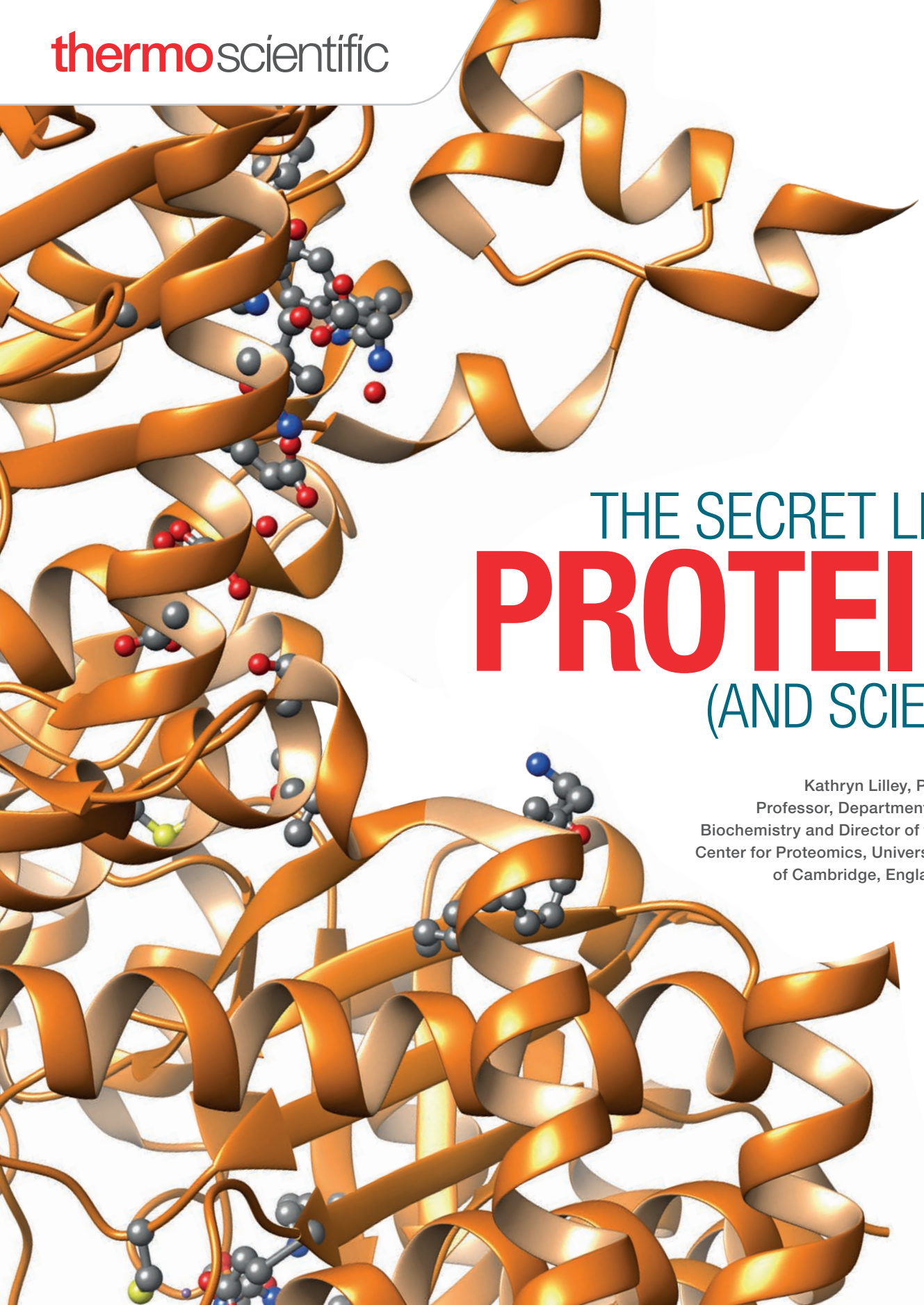


REDUCE BOTH ENVIRONMENTAL IMPACT AND COST

Many labs continue to perform tedious manual cell counting in order to avoid costs associated with automating the task, including disposable slides and tips. The Countess II FL instrument was designed to work with a reusable glass slide instead, which helps significantly reduce the long-term consumable costs and environmental impact.

Pictured at left is the waste generated by one box of 50 disposable slides for cell counting. If a lab uses five slides per day, they would generate 24 times this amount of waste per year. Since the Countess II FL instrument is compatible with either disposable or reusable slides, you can decide which works best for your lab.

thermoscientific



THE SECRET LIVES OF PROTEINS (AND SCIENTISTS)

Kathryn Lilley, PhD
Professor, Department of Biochemistry and Director of the Center for Proteomics, University of Cambridge, England

In some ways, the journey of Kathryn Lilley resembles that of the proteins she studies: The path isn't always straight, and there's always more than one job to do.

"Some proteins, we know pretty much everything there is to know about them," says Dr. Lilley, professor in the Department of Biochemistry and director of the Center for Proteomics at Jesus College at the University of Cambridge, England. "But others have a hidden side that could be a significant portion of their function."

Her primary area of focus is spatial proteomics: specifically, why and how proteins get to the correct place in the cell to allow them to function.

"If there was one thing I'd like other scientists to learn from what we are doing, it's that you can't assume you know everything most proteins do and how they do it," she emphasizes. "In fact, a lot of proteins are moonlighting and multitasking—they have a completely different job in another part of the cell."

Dr. Lilley knows a thing or two about moonlighting. From a very young age, she had a beautiful voice and sang competitively. Growing up, her family assumed she would pursue music as a career. She still sings now and again in local concerts (her favorite opera is Carmen), but Lilley now spends far more time in the lab than on stage.

"I first chose science as a musical escape," she reveals. "I had always paid way more attention in biology than my other subjects in school, but really I was going through a hard time with my voice, and the sciences were a safe haven for me to leave competitions for a time and avoid taking music academically in further education."

That experience as a performer ultimately enhanced her ability to both teach and share the results of her research with other scientists. "I'm used to being in front of a crowd, so giving talks and communicating about my work comes easily," she says. "I try to incorporate my theatrical training and I become very animated when I discuss my research."

Interest in proteins began at university, after she conducted an experiment measuring enzyme kinetics using alcohol dehydrogenase. "I suddenly understood what proteins were all about," Lilley recalls. "They were these machines of the cells that do all the work."

After moving to Cambridge, Lilley worked on a project mapping proteins to the Golgi apparatus in plant cells. The techniques she and her colleagues developed gave proteins an address in the cell. But as she learned more about where different proteins live, she began to ask a different question: How did the proteins get there?

"I began to wonder how the cell knows to portion out copies of the same protein to different places," she says. "Those questions led me to think more about the sites where the proteins are synthesized and what really controls this process."

Her findings could help inform therapeutic targets for neurodegenerative disorders and various forms of cancer and other diseases. The implications can be profound. For example, if a protein has other functions in a different part of the cell, and a new drug knocks out that function, it may have an unintentional effect.

And as Dr. Lilley well knows, unintentional effects can lead to profound changes. That's precisely how a remarkable amateur opera singer became a trailblazing scientist.

Read more on Dr. Lilley's latest work:

Combining LOPIT with differential ultracentrifugation for high-resolution spatial proteomics. Geladaki A, Kočevar Britovšek N, Breckels LM, Smith TS, Vennard OL, Mulvey CM, Crook OM, Gatto L, Lilley KS. *Nat Commun.* 2019 Jan 18;10(1):331. doi: 10.1038/s41467-018-08191-w.

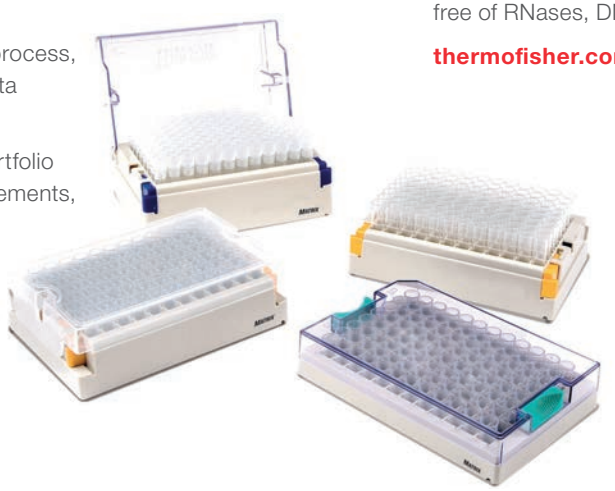
ESSENTIALS
FOR DIRECT-TO-CONSUMER TESTING

As direct-to-consumer (DTC) genetic testing broadens, the need for reliable and agile lab essentials grows

The digital age and the expectation of unfettered access to information is leading to enormous innovations in healthcare, including the rise of DTC testing solutions. What was once used to tell people about their heritage is now informing them of genetic predispositions to a variety of medical conditions, including cancer and Alzheimer's disease.

As consumers embrace the ability to learn if they are at risk for specific illnesses, the global healthcare community has more genomic samples to study than ever before. To ensure these samples are safeguarded, the FDA has shared detailed documentation of the methods researchers can use to collect, process, transport, and store genomic data safely and without bias.

To further evolve our labware portfolio and align with modern lab requirements, Thermo Fisher Scientific monitors both the scientific advancements, and recommendations and regulations.



ABGENE POLYPROPYLENE MICROPLATES AND DEEPWELL PLATES

Thermo Scientific™ Abgene™ plates allow for easy handling of dilutions, aliquots, and samples and facilitate quality-assured storage of analytes for either intermediate or long-term use. To help ensure the highest molecular-grade quality, all plates are manufactured in a cleanroom facility using virgin polypropylene resin. They are certified free of RNases, DNases, and human DNA.

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MATRIX 2D BARCODED OPEN-TOP STORAGE TUBES

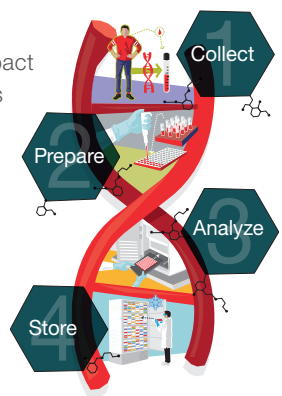
Thermo Scientific™ Matrix™ tubes are among the leading solutions for the reliable storage of genomic samples. Complete with laser etching for a permanent, high-contrast 2D barcode, these tubes offer maximum traceability for a variety of sample types.

thermofisher.com/storagetubes

GENOMICS WORKFLOW

Genomics data has had a transformative impact on the life sciences and healthcare industries and it will continue to advance. The integrity of the samples being collected now may help determine diagnoses and treatments well into the future. We're committed to help ensure that samples are protected at every stage of the workflow, helping scientists to reach that next breakthrough.

thermofisher.com/genomicsworkflow



CRYOGENIC SOLUTIONS

Our sample storage portfolio also offers a variety of cryogenic solutions, including Thermo Scientific™ Nalgene™ General Long-Term Storage Cryogenic Tubes and Thermo Scientific™ Nunc™ Biobanking and Cell Culture Cryogenic Tubes, which are both ideally suited for storing high-value genomic samples at all cold room temperatures, including vapor- phase liquid nitrogen.

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SCIENTAINMENT

DID YOU KNOW?

CHEMOTHERAPY'S ROOTS IN NATURE

The plant kingdom has been a source of clinical anticancer agents for decades. In fact, the National Cancer Institute (NCI) has screened approximately 35,000 plant species to date for potential anticancer activities.[1] Naturally derived compounds attack cancer cells during various phases of division.[2] Did you know that some of today's well-known chemotherapies started as plant-based discoveries?

1. **Taxanes**—derived from the bark of the Pacific Yew tree, *Taxus brevifolia*, paclitaxel (Taxol) and docetaxel (Taxotere) are antimicrotubule agents for the treatment of breast, ovarian, pancreatic, and non-small cell lung cancer.[3]
2. **Vinca alkaloids**—obtained from the Madagascar periwinkle plant, *Catharanthus roseus*, vinblastine (VBL), vinorelbine (VRL) vincristine, and vindesine (VDS) are the four major alkaloids in clinical use. These are also microtubule disrupters, and they've been used to fight breast, bone, and blood cancers.[4]
3. **Camptothecin**—extracted from the bark of the Chinese "Happy Tree," *Camptotheca acuminata*, this topoisomerase inhibitor has been used in antitumor activity.[5]
4. **Podophyllotoxins**—first produced from a near-extinct Indian mayapple plant, *Podophyllum emodi*, these compounds and derivatives such as etoposide (Etopophos) are another class of topoisomerase inhibitors used to treat small-cell lung, blood, and testicular cancers.[6]
5. **Anthracyclines**—from the soil fungus *Streptomyces*, antibiotics such as doxorubicin (rubex) is an intercalating DNA agent with antitumor properties used in the treatment of breast and ovarian carcinomas.[7]

References:

1. *Curr Drug Metab* (2008) 9:581–591.
2. *Int J Pharm Sci Res* (2015) 6:4103–4112.
3. https://www.cancer.gov/research/progress/discovery/taxol
4. *Int J Prev Med* (2013) 4:1231–1235.
5. *Bioorg Med Chem Lett* (2017) 27:701–707.
6. *ScienceDaily* American Society for Horticultural Science (2009) September 8.
7. *J Cancer Ther* (2015) 6:849–858.

BEYOND THE LAB
ADVOCATING FOR SCIENCE

Catharine Young, PhD
Senior Director of Science Policy
Biden Cancer Initiative

Good old-fashioned perseverance and basic research have been the genesis of impactful scientific work. However, scientists blaze trails outside of the lab, too; and their stories unveil aspirations powered by the same pioneering spirit that drives discoveries at the bench.

Catharine Young, PhD, is the senior director of science policy for the Biden Cancer Initiative, championing scientists and their impactful work in cancer research. She reveals that she has always been drawn to science. Having grown up in South Africa, Catharine has cultivated a passion for travel and adopts a macro view of science and the part it plays around the world. She says that having a broader impact on a global scale has always been an inherent component of the work she does, and it's what ultimately drew her to the field of science policy.

Catharine was a keynote speaker at the Immuno-Oncology Summit in Boston last fall, where we were able to catch up with her and learn more about the inspiring path she chose.

How do you think the impact from a career in science policy has been different from, say, working in a lab?
I think this raises a key question about how we as a community measure scientific impact. The contribution of a scientist working at the bench has incredible impact when it comes to discoveries that can be used for biomedical innovation and new medical therapies. However, on the flip side the impact of science

As a scientist, I believe it is our responsibility to be engaged with the broader research system.

policy lies in providing the fundamental infrastructure for scientists to be successful—from protecting federal scientific funding to cementing the importance of the inclusion of science in government decision-making at both a national and international level.

What is one thing the world needs to understand about scientists, and how can a scientist do their part in advocating for science?
Scientists are really burdened by the research culture and the restrictive system they find themselves in. The constant pressure to publish, to navigate the tenure process, to be continually successful when it comes to securing funding creates a very challenging environment. As a scientist, I believe it is our responsibility to be engaged with the broader research system. This could include providing your voice and support for certain legislative action, or it could mean taking steps to reach out to the community and share your science in an effective and easy-to-understand way.

Thermo Fisher Scientific joined the Cancer Moonshot℠ Initiative in 2016. The Biden Cancer Initiative builds on that work. Both programs are bent on accelerating science—do you have one of your own?
Supper with a Scientist—an effort to break down the barriers with scientists and the public and to have a dedicated and focused conversation about science, in an informal and enjoyable setting. Some of the feedback we have received has confirmed that this is an experience people are yearning for, particularly as we find ourselves constantly bombarded with misinformation. One guest noted it was "one of the most eye-opening and most-needed evenings in [their] recent history."

Read the full interview and learn more about Catharine Young at **thermofisher.com/lifeinthelab**

ARE YOU LOOKING FOR GRANT OPPORTUNITIES? APPLY TO OUR CANCER RESEARCH FOUNDATION.

Thermo Fisher Scientific recognizes that every factor in the fight against cancer is crucial. That's why we enable cancer researchers to achieve their goals by providing best-in-class educational resources, support, and tools that help accelerate outcomes in cancer research from discovery to validation.

To further support this effort, we have launched our Cancer Research Foundation, enabling groundbreaking cancer researchers like you to gain access to some of our most innovative instruments, devices, and other products. Every three months, we will offer two valuable product bundles that you can apply for by submitting short grant proposals.*

Find out more at **thermofisher.com/cancerresearchfoundation**

* Restrictions, terms, and conditions apply. Grant program will be updated every three months. See complete rules at **thermofisher.com/cancerresearchfoundation**.

TEN BREATHTAKING TRAILS

Life at the bench can have its challenges. If you're searching for a way to decompress, connect with nature. Fresh air can reduce stress and even energize you. Here are ten amazing long-distance trails from around the world to inspire you to find balance in your life outside the lab.

LIFE OUTSIDE THE LAB

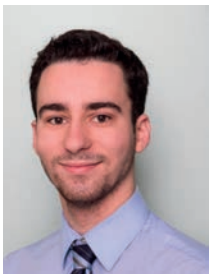
- Te Araroa—New Zealand (1,900 mi/3,000 km)
- Tour du Mont Blanc—Switzerland, Italy, and France (110 mi/170 km)
- Everest Base Camp Trek—Nepal (78 mi/130 km, round trip)
- Overland Track—Australia (40 mi/65 km)
- Long Range Traverse—Canada (22 mi/36 km)
- Appalachian Trail—United States (2,200 mi/3,500 km)
- Inca Trail to Machu Picchu—Peru (26 mi/43 km)
- Otter Trail—South Africa (25 mi/41 km)
- Torres del Paine W Trek—Chile (50 mi/80 km)
- Grand Canyon Rim to Rim—United States (24 mi/38 km)

Can't get away for a multi-day hike? Try doing a segment of one of the longer trails listed above, or just go to a local spot for the day. A Stanford University study found that walking or hiking in a natural area (as opposed to an urban setting) for as little as 90 minutes resulted in reduced neural activity in a part of the brain linked to depression, as well as increased feelings of well-being.[1] So lace up those hiking boots and hit the trail next weekend—you'll be glad you did.

1. Atchley RA, Strayer DL, Atchley P (2012) Creativity in the Wild: Improving Creative Reasoning through Immersion in Natural Settings. *PLOS ONE* 7(12): e51474.

BEHIND THE LAB COAT

First-generation college graduate studies treatments for Alzheimer's disease



Joshua Leitão, ScM
Research Assistant and Lab Manager,
Brown University,
Providence, Rhode Island

What's your favorite memory you have of your work?
When my research supervisor documented the work my lab members had conducted and submitted it to a scientific journal; it was accepted!

Which scientific discovery inspires you?
The discovery of the double helix structure of DNA inspires me when I'm performing molecular biology experiments.

Why did you choose to pursue science?
I knew very early on that I wanted to pursue science: specifically, biotechnology. I was fascinated with how scientists could manipulate microbes to produce lifesaving drugs and vaccines. I truly wanted to be a part of the biotechnological revolution. In high school, I enrolled in a biotech academy, which required me to do a science project and present my results at the school's science fair. As a junior, I developed a small project that investigated nicotine levels in various tobacco plant species. I earned an award, and that's when it clicked in my head, "I can do science." At Roger Williams University I graduated *summa cum laude* with a double major in biology and chemistry, a minor in public health, and a certificate in biotechnology. As a first-generation college student coming from a less-fortunate background, I'd never even thought about furthering my education after college. Obtaining a bachelor's degree was considered the highest achievement, academically speaking, in my family. But instead of transitioning to a career in the industry, I entered a master's program in molecular microbiology and immunology (MMI) at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. I found myself drawn to a lab that investigated the host immune evasion mechanisms by the parasite *Trypanosoma brucei*, which is the causative agent of human African trypanosomiasis (HAT). My master's degree provided a platform for my interest in vaccines, as I was interested in investigating how microbes can bypass the host immune system. I currently work at Brown University in Providence, Rhode Island as a research assistant and laboratory manager in the Department of Molecular Biology, Cell Biology, and Biochemistry (MCB). I am leading projects investigating the regulation of autophagy via genetic and pharmacological approaches in *Caenorhabditis elegans*, with implications of treating Alzheimer's disease. Overall, as a scientist, my goal is to utilize the skills and knowledge I have gained to develop lifesaving therapeutics to impact human health.

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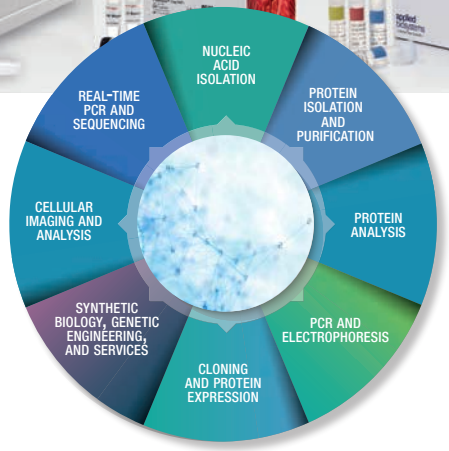

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