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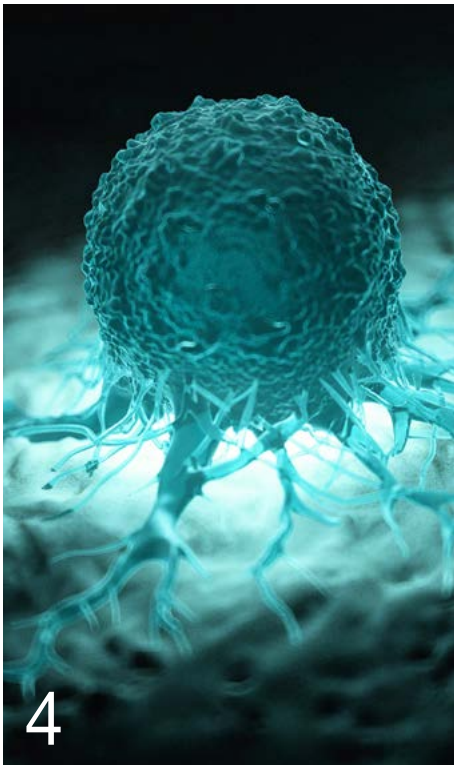
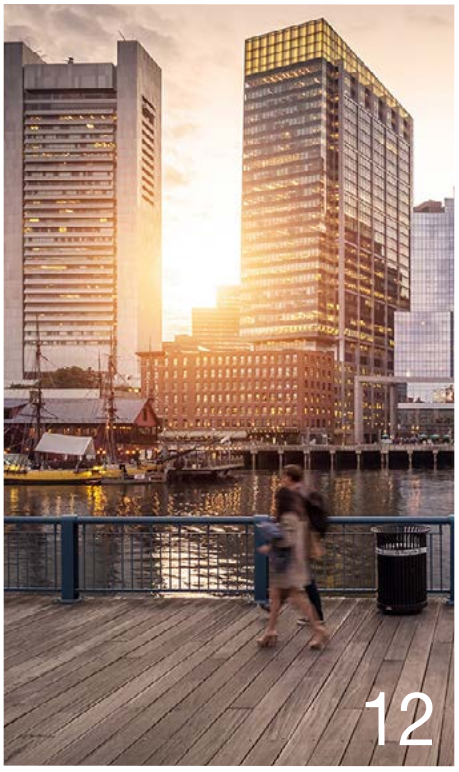
CONTENTS

16
COVER STORY
Tapping into Wastewater Testing to Predict Virus Surges



4
"Tumor Avatars" Could Help Identify Effective Cancer Treatments



12
Old Offices Become New Laboratories

28
Buildings Made of Timber Are Reaching New Heights

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SUPPLIER ARTICLES

8
Tips for Inventory Planning

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AirClean Systems Ductless Chemical Workstations 20
Applied Biosystems qPCR Systems and Assays 6
Applied Biosystems Starter Kits 27
Avantor J.T.Baker BAKERBOND PROchievA Resins 7
Biotek Instruments Microplate Washers & Dispensers 30
BUCHI Products for Organic Synthesis 21
Decon Labs CiDehol 70 25
Fisher Scientific Edge Program 14
Fisher Scientific Safety 23
Fisherbrand Real-Time Electrophoresis Systems 32
Fisherbrand Sonic Dismembrators 24
Heidolph Hei-TORQUE Overhead Stirrers 24
KNF Neuberger LABOPORT Vacuum Pumps 20
Medicom SafeMask Procedure Earloop Face Masks 31
Metro Plastic Storage Shelving with Microban 26
Millipore EZ-Fit Filtration Units & Manifolds 22
Nasco Whirl-Pak Sterilized Sample Collection & Processing Bags ... 26
TCI Chemicals for Organic Synthesis 15
Thermo Scientific Chromatography Vials 22
Thermo Scientific NanoDrop One Spectrophotometers 10
Thermo Scientific Organic Synthesis Compounds 11

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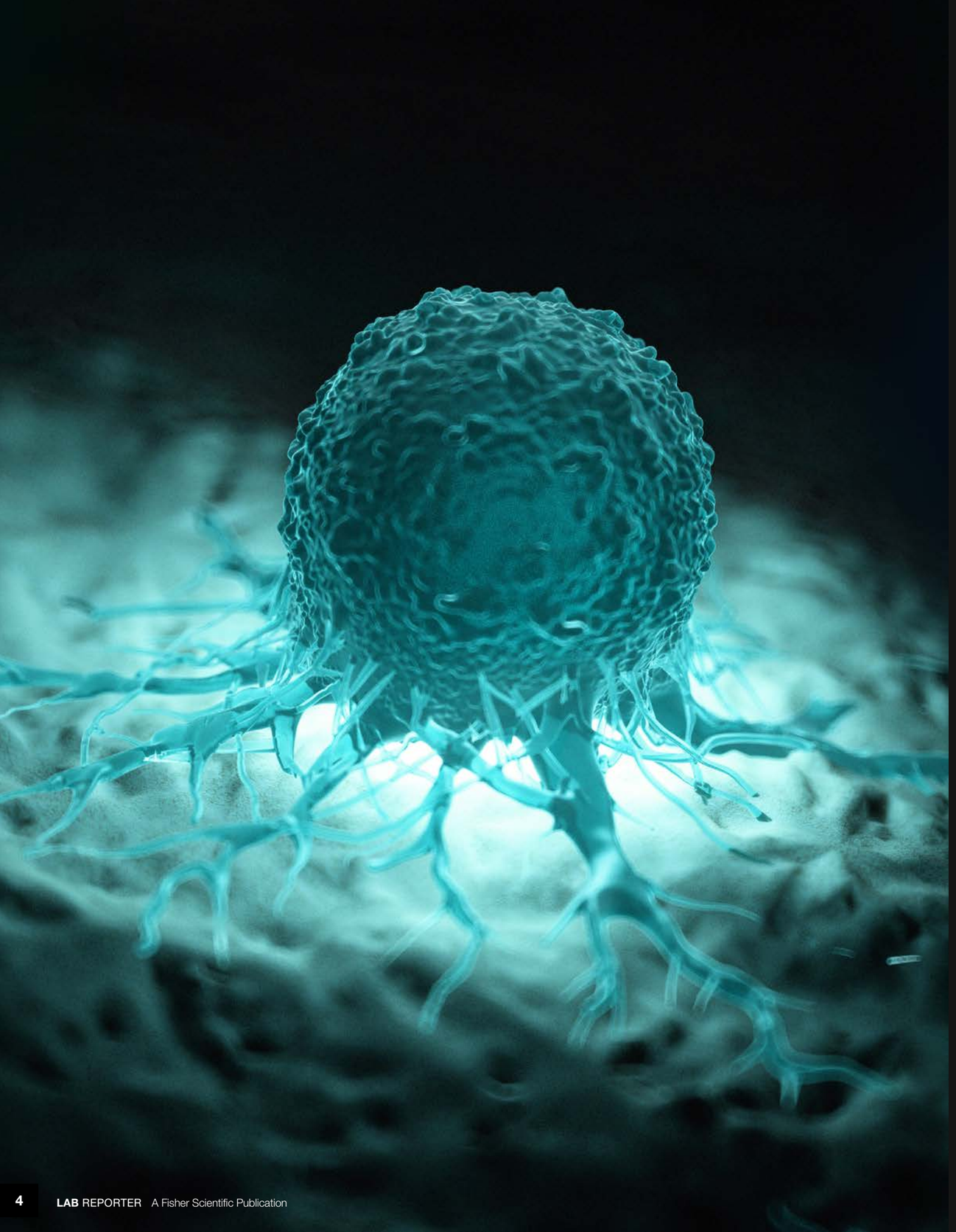

“Tumor Avatars” Could Help Identify Effective Cancer Treatments

By Mike Howie

Finding an effective cancer treatment isn’t always easy. While immunotherapy is popular and can be highly effective, it doesn’t work for every patient. To care for their patients, doctors must first find the right treatment, a process that can be tiring and discouraging for someone with such a serious illness. But that process might soon be easier.

Researchers from the Netherlands Cancer Institute (NKI) have devised a method of identifying effective cancer treatments in the lab with a tumor sample, leaving patients out of what can be a rigorous process.

> “We’ve solved a major problem many scientists had been facing,” Thommen said.

The method, described by Daniela Thommen, a cancer researcher at NKI, is simple in concept: “We first cut patient tumor samples into small pieces and then treat these ‘tumor avatars’ outside the patient’s body with different therapies to see which one works.”

The idea behind the process is so simple that it may sound obvious, but there was reason to question the accuracy of the approach. It’s possible that tumors could react differently once removed from the body, meaning that successful treatment in the lab wouldn’t necessarily translate to successful treatment in the patient. But the team’s results were encouraging.

“We’ve solved a major problem many scientists had been facing,” Thommen said, “preserving a tumor’s original composition and structure outside of the patient in the lab.”

The study focused on a type of immunotherapy called a PD-1 blockade. As with other immunotherapies, a PD-1 blockade uses T-cells to find and destroy cancer cells. However, some cancer cells are able to inactivate T-cells and evade destruction. To prevent this, a PD-1 blockade uses inhibitors to stop cancer cells from inactivating T-cells. This type of therapy has proven effective against some forms of melanoma, kidney cancer, lung cancer, and some other cancers. After linking lab and clinical results of 38 patients, the researchers found that the response of tumor avatars successfully predicted how the patient would respond to therapy.

“These results confirm that we have now a very powerful model system in place which we can use to develop new diagnostics, and in this way personalize immunotherapy,” Thommen said. The team also found some unknown predictors of whether a tumor will respond to or resist immunotherapy, including three subgroups of tumors that do not respond, and discovered that responsive tumors had been infiltrated by specific immune cells and formed tertiary lymphoid structures. These markers can now be tested to verify how well they can predict a therapy’s effectiveness.

> “We first cut patient tumor samples into small pieces and then treat these ‘tumor avatars’ outside the patient’s body.”

More work must be done before this method of identifying a cancer treatment can be widely used, but for now the results — published July 8, 2021, in *Nature Medicine* — are promising.

Mike Howie is a Thermo Fisher Scientific staff writer.

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Tips for Inventory Planning

The year 2020 was an unprecedented time. The world's true heroes shone through. First responders, hospital workers, and pharmaceutical and laboratory workers all did more than their part. Not only did they contend with a global pandemic, but they fully understood the implications. Personally stressed, their support systems were also strained. Businesses and supply chains were extremely challenged.

The availability of personal protective equipment (PPE) became a real issue at the beginning of the pandemic. With the outbreak of COVID-19, demand for PPE peaked at 20 to 40 times normal consumption levels. Governments and other organizations with robust and active acquisition programs found themselves at an advantage.

With vaccines available and the worst of the pandemic likely behind us, we can begin to assess how to improve inventory planning systems so we may be better prepared for the next emergency.

Best Practices for Creating Your Plan

1. **Inventoried products should always be within their stated shelf life.**

The central concept of life cycle management lies at the core of a robust stocking program. Organizations are well served by maximizing usable stock by tracking expiration dates and replenishing outdated products with new items as needed.

2. **Limiting product options simplifies things.**

A larger number of different products makes the task of monitoring product use and shelf life more complex. Simplify inventory management by choosing PPE designed to fit a broad range of employees.

3. **Track product use to align stock levels with minimum readiness levels.**

Knowing the day-to-day PPE consumption levels and the possible duration of an emergency event can help you determine the optimal quantities of products available for frontline workers.

4. **Include PPE products that match your needs.**

Disposable N95 particulate respirators, including 3M Aura Particulate Respirator 9205+, N95, and the 3M Particulate Respirator 8511, N95, can help reduce exposure to viruses transmitted through inhalation. However, reusable respirators like 3M's 6500 QL series of half-facepiece reusable respirators or powered air-purifying (PAPR) respirators like the 3M Versaflo TR-300+ assemblies may be more economical and practical in certain situations.

5. **Stock respiratory PPE in sizes that will fit most users.**

Filtering facepieces, elastomeric respirators, and other tight-fitting respiratory protection products must seal snugly to the wearer's face to ensure that inhaled air travels through the respirator's filter. Since facial features, face shapes, and head size vary, employees may experience different risks of exposure with a respirator. Fit testing is essential for all tight-fitting respirators to help ensure a good respirator-to-face seal in order for the respirator to function as intended.

6. **Get help from experienced distributors or manufacturers with staggered procurement options, emergency use authorization, product life cycle management strategies, and other product management issues.**

The COVID-19 PPE stockpile management program demonstrated the need for a stock management program based on a resilient supply chain. Flexible supply chains may be able to respond to short-term spikes in demand while maintaining longer-term procurement needs.

7. **Source products from suppliers with global footprints, adequate raw material sources, and production capabilities that can help mitigate export restrictions in specific countries.**

You may be well served by working with manufacturers that have a global footprint and production capabilities. Producers with broad production footprints can provide products from their many manufacturing sites located in different geographies.

8. **Work with suppliers that can meet variations in demand.**

COVID-19 tested supply chains and the public health system. Building capacity, metering consumption, maximizing access to supplies by fast-tracking regulatory approvals, and other flexible procurement methods can help to address spikes in demand.

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9. Source products from companies familiar with emergency preparedness.

Many pandemic plans lacked the logistics and supply chain components for successful implementation, which also exacerbated the scarcity of critical products. Suppliers with emergency and infectious disease outbreak experience may be able to mobilize resources more rapidly and use their institutional memory to work more effectively.

10. Partner with suppliers rather than just purchasing products.

Relationships between organizations and suppliers can range from basic procurement to sharing of global best practices. If the concept of stockpiling is new to you, knowledge sharing in your decision-making process can help you create the most value for your organization.

11. Demand-planning tools can help with scenario planning and analytics.

Most emergency plans include roles and responsibilities for disasters and national outbreaks. These plans help leadership have a clear command and control structure and act decisively in a crisis. However, make sure to also include a logistics and supply chain appendix to describe the resources required to accomplish the mission. It also helps to work with organizations that can assist in these critical areas.

This list of 11 best practices for maintaining product stockpiling is a starting point. Contact 3M or other experienced professionals for assistance in developing your individual plan.

We are eager to work with governmental and other organizations to support robust, resilient, and sustainable stockpile programs to protect the health and lives of healthcare and other essential frontline workers who keep our society functioning.

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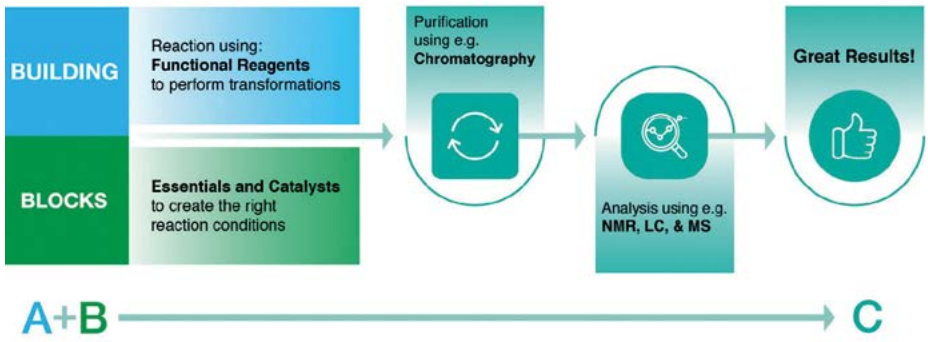

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Old Offices Become New Laboratories

Construction Considerations

By Kylie Wolfe

After a year plus of remote work, office buildings aren't in high demand — at least not in the traditional sense. What began as a necessary health and safety measure for thousands of companies became a permanent fixture, one that's resulted in plenty of vacant spaces. At the same time, the scientific community stepped in to help address pandemic-related concerns and the need for life sciences laboratories sharply increased.

Although many employers have transitioned to a work-from-home model, or at least a hybrid one, most scientists need an in-person option. This, alongside a greater demand for science-based work, is convincing building owners to convert empty structures into flexible lab spaces.

Supply and Demand

Per Statista, 16.4 percent of downtown office buildings were vacant in early 2021. That's up from 13 percent the year prior. Rent prices for conventional office spaces have gone up 15 to 30 percent, depending on the location, since 2016. But, for lab spaces, prices have risen more than 60 percent in major cities during the same period.

As of April 2021, there were 1.9 million workers in the biotechnology and life sciences industries, a record high according to the United States Commercial Real Estate Services. Paired with increased funding and empty office spaces nationwide, this gives landlords reason to change their focus and laboratories reason to expand, each meeting a new need.

Offices vs. Labs

It takes years to build from the ground up, but adapting already-existing spaces can take only 18 months. Though this helps labs get started sooner, they have unique needs that leave building owners with a long list of renovations.

Offices have basic amenities in place: restrooms, elevators, lobbies. But lab spaces require much more, even things that aren't always visible. In addition to equipment and instruments, labs need a greater floor-to-floor height to house ductwork, wiring, and gas lines above a drop ceiling. This helps maintain a sterile environment at the benches below. The floors should also withstand 125 to 150 pounds per square foot, accommodating heavy freezers and fume hoods. Of course, reinforcing and reworking a building's structure is no small task.

According to SGA, an architectural firm, some labs must limit floor vibrations to 2,000 micro inches per second (MIPS) or less. Office spaces have a higher limit, usually 4,000 MIPS. Laboratories have special ventilation requirements, too, and need proper storage rooms for hazardous substances. Research settings tend to use more electricity and water, with each one routed throughout the lab for easier access. Instead of the 12 to 14 watts per square foot that offices require, labs allot 25 to 29 watts per square foot, a statistic from Building Design & Construction. Other essentials, like service elevators, emergency generators, and gas connections, only add to the construction list.

A Flexible Future

Like everyone, building owners have had to adapt to evolving circumstances. In their case, converting existing spaces into new labs has been one of the best ways to pivot. Cities like Boston, San Francisco, and San Diego are witnessing this most, but Seattle, Philadelphia, New York, and Chicago are not far behind.

As the biotechnology boom continues, there's an opportunity for companies to establish labs closer to large research universities. While landlords hope to attract tenants, scientists hope to attract talent to their new-and-improved buildings.

This content was inspired, in part, by "'A Wild 15 Months': Pandemic Spurs Conversion of Offices to Labs," The New York Times, July 27, 2021; "Biotech, Life Science Building Owners Look to a Post-COVID Future," Lab Manager, July 27, 2021; and "How to Reposition A Building For Life Science Tenants," SGA, Accessed August 2021.

Kylie Wolfe is a Thermo Fisher Scientific staff writer.

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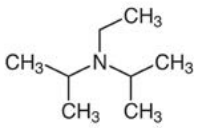

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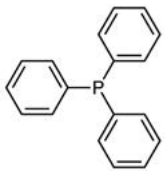

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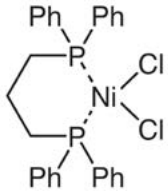

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Tapping into Wastewater Testing to Predict Virus Surges

By Christina P. Hooton

A pathogen can move silently through a community before making its presence known. Contagious people may experience delayed symptoms or be asymptomatic, unknowingly infecting others. Suddenly, many people are sick with the same illness. Heading off a virus before it becomes a problem at a city or state level requires knowing people are sick before they do. Achieving this kind of prescience seems somewhat unlikely, but wastewater, an abundant and accessible resource, has recently become a popular place to look for warning signs.

Researchers and communities all over the world have been trying to understand the effectiveness of wastewater-based epidemiology in predicting surges in COVID-19 cases. Because someone infected with the virus starts shedding it in their stool before experiencing symptoms, wastewater testing may help us anticipate an increase in cases earlier than clinical test results.[1] And, like clinical testing, detection is possible in both symptomatic and asymptomatic patients.

The technique is not new. In 2013, a wild polio epidemic was detected using environmental surveillance of sewage in Israel.[2] This type of monitoring at a national level is beginning to take shape in the United States in response to the pandemic. The Centers for Disease Control and Prevention (CDC) and the U.S. Department of Health and Human Services created the National Wastewater Surveillance System (NWSS) to better understand the extent of SARS-CoV-2 infections in communities. Eventually, state, tribal, local, and territorial health departments will be able to submit their wastewater testing data through a portal, and the data will be summarized and interpreted to help inform public health actions. Additionally, the CDC is allocating $33 million for public health laboratories to start conducting wastewater testing.

Testing the Power of Wastewater

Two University of Minnesota Medical School researchers have been studying the effectiveness of wastewater testing in predicting COVID-19 case increases across their state. Assistant professors Glenn Simmons Jr., PhD, and Richard Melvin, PhD, collected and analyzed samples from wastewater treatment plants in 19 Minnesota cities from May 2020 through August 2020. The team initially began testing on-campus residence hall sewage to predict and prevent COVID-19 outbreaks among students and eventually set their sights on something with broader impacts. They specifically sought to understand what would happen in a large region with diverse populations over a long period of time. A preprint version of their study is available on medRxiv and is currently undergoing peer review.

They were able to detect the presence of SARS-CoV-2 RNA in the wastewater of cities with populations ranging from 500 to over 1 million people 15 to 17 days before new clinical cases were confirmed. Since they scaled up from sampling 19 cities once per week to sampling 44 cities twice per week, this window has narrowed to between 10 and 14 days.[3]

“Looking at the wastewater, you see what’s going to happen in the future with clinical cases. And that has happened consistently since wastewater testing has been going on in our lab,” said Dr. Simmons.

This type of information is especially valuable in areas where access to testing varies. Dr. Simmons said he first approached this project from an equity perspective. “In Duluth, we have different pockets of folks that have different circumstances. Drive-thru testing is very convenient, but what about for people who don’t have cars?” he posed. Some cases could go undetected.

Creating a Steady Flow of Data

Initiating a research project like the one in Minnesota required participation and buy-in from multiple wastewater treatment plants in different locations. Additionally, they needed sufficient lab staff to process the samples, a resource that was in short supply during that period of the pandemic. They recruited recent graduates to work in their lab and solicited participation from wastewater treatment plants through the Minnesota Environmental Science and Economic Review Board website.

Once the framework was in place, composite samples were collected by plant personnel on a weekly, and eventually biweekly, basis, and shipped to the lab overnight on wet ice. Upon receipt, lab personnel sterilized the sample tubes and pasteurized the samples in preparation for RNA extraction. The extracted RNA samples were then tested for SARS-CoV-2.

Extracting Meaningful Information

Collecting wastewater from a variety of cities meant there would be a significant number of variables affecting the concentration of pathogens. These include the presence of industry and variations in the size and flow rate of each wastewater facility.

continued from page 17

Tapping into Wastewater Testing to Predict Virus Surges

To account for the variations at each facility, the researchers used Pepper Mild Mottle Virus as a standard. This pepper virus is the most abundant RNA virus in human feces and remains stable in a variety of environmental conditions.[4] They measured the impact of system variations on pepper virus concentration levels and ranked each facility accordingly.

Additionally, the team needed to normalize the raw data to turn it into digestible information suitable for public consumption. They created Melvin's Index, a simplified value for tracking virus levels compared to the pepper virus.

Moving Forward with Wastewater Testing

While wastewater testing is proving to be an effective tool in tracking the rise and fall of virus cases, there is still information it can't provide. Dr. Simmons mentioned the limitations in approximating how many people are infected based on wastewater alone. The number of variables makes it a complex guessing game.

Clinical testing is still the most accurate way to count virus cases. However, if a significant enough increase in the virus is seen in wastewater before clinical cases start to rise, resources can be allocated to the affected areas.

This happened recently in Davis, California. Health officials and researchers saw a potential rise in cases thanks to wastewater surveillance, and local officials sent out alerts and encouraged people in the affected neighborhoods to get tested. Paired with patient sampling, they were able to determine that the Delta variant was in the mix.[5]

Variants are another piece of the puzzle Dr. Simmons and his team would like to integrate into their studies through the end of the year. And there is potential for future viruses. Influenza, for example, was successfully detected in wastewater during the 2009 H1N1 pandemic, according to a Netherlands study. "One of our desires is that this system stays in place, and we just change out what we're looking at. Or we create a panel of different targets that we're looking at whether it's some other emergent tropical disease, like Nipah virus or chikungunya, or SARS," said Dr. Simmons.

He points out that by providing surveillance data about new and emerging viruses in small doses as it becomes available to us through techniques like wastewater testing, we're creating an ongoing conversation with people and helping them to better understand the science without overwhelming them. This type of dialogue and transparency will continue to be a crucial part of dealing with public health crises now and in the future.

Christina P. Hooton is a Thermo Fisher Scientific staff writer.

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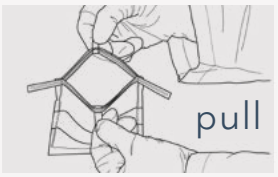

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Buildings Made of Timber Are Reaching New Heights

By Gina Wynn

Around the world, innovative builders are constructing with sustainability in mind by choosing wood as their main building material. And they are taking their structures to new heights.

Still the most popular building material in the U.S. for homes, standard lumber was replaced by steel as the go-to material for taller buildings in the mid-19th century. A light, durable metal, steel made it possible for buildings to stretch more than 40 or 50 stories into the clouds. Steel also didn't go up in flames as easily as wood. Most big cities have experienced "great fires" throughout history that destroyed entire city blocks and have since put strict fire codes in place.

New and Improved Wood

For the type of mass timber that has been catching the attention of environmentally minded developers in recent years, susceptibility to fire has not been a problem. Known as cross-laminated timber (CLT), it is made up of several layers of lumber boards bonded with adhesives and pressed to form single, solid rectangular panels. It is typically cut to the desired dimensions before being sent to construction sites where it is fastened to other pre-cut pieces like IKEA furniture. Europeans have found success with the material and have been building with it for nearly 30 years.

As for fire resistance, studies have shown that the technology is on par with other building materials. Tests of five-ply CLT panel walls resulted in the material lasting 3 hours and 6 minutes after being subjected to temperatures exceeding 1,800 degrees Fahrenheit, according to Think Wood. That far exceeds the two-hour rating required by building codes.

A Sustainable Alternative

CLT is also a more sustainable building material. It can be made from sawmill scraps or newly harvested lumber of any age and size and still be as strong as steel. In addition, the pieces required for building can be prefabricated in factories instead of being prepared at the building site. This makes construction go faster and reduces truck traffic and the need for road closures.

Also, the process for creating CLT requires much less energy than steel production (which involves melting rocks) and results in fewer carbon dioxide emissions. Steel manufacturing accounts for around seven percent of the world's carbon dioxide emissions, according to Global Efficiency Intelligence.

Compared to building with concrete, the most widely used building material in the world, CLT usage results in an immediate 50 percent reduction in emissions according to Anna Ervast Oberg. A project manager with the Swedish firm Folkhem, she was interviewed by *The New York Times* about her company's new CLT development, Cederhusen. She added that over the lifetime of a typical concrete building, roughly 70 percent of carbon emissions would result from the two-year construction period.

Another big benefit to CLT is that it sequesters the carbon that was absorbed before the trees were harvested for lumber. That carbon will remain trapped in the CLT in the walls of buildings for the foreseeable future — and will not be released back into the Earth's atmosphere.

The Wooden Building Boom

Developers worldwide are taking note of these environmental benefits. In Austria — a pioneer in the timber revolution — they used CLT to construct the 24-story HoHo Vienna high-rise that extends nearly 276 feet above northeast Vienna. It houses a hotel, restaurant, wellness center, and offices.

With forests as its main natural resource, Austria has regulations in place that protect valuable forested areas. They help forest managers ensure that after logging each year, over 141 million cubic feet of trees remain in the forest, continually increasing timber stocks. This means that over 35 cubic feet of wood grows back every second and the timber used for the entire HoHo Vienna project will have grown back in only one hour and 17 minutes, according to Housing Evolutions by Housing Europe.

International Competition

Across the pond, another wooden skyscraper is scheduled for completion in 2022 in Milwaukee. The high-end apartment complex will reach 25 stories and stand 284 feet, overtaking the Mjøstårnet (280 feet) in Norway as the tallest timber tower. Developers of the Milwaukee project claim it will offset the equivalent of carbon dioxide produced by 2,500 cars or enough energy to power 1,200 homes per year.

As of June 2021, 1,169 multi-family, commercial, or institutional mass timber projects had been completed or were being designed in all 50 of the United States.

Other non-U.S. locations already reaping the environmental benefits of mass timber buildings include Finland and British Columbia, and designs have been proposed for the Netherlands and London. In collaboration with University of Cambridge researchers, architects and engineers hope to construct an 80-story, one-million-square-foot skyscraper that would stand 984 feet tall at the Barbican. If completed, it would become the world's 18th tallest building, surpassing Four World Trade Center in New York City.

It's no wonder the construction industry has become enamored with CLT. Among other advantages, CLT adds less carbon dioxide to the atmosphere, enables faster construction, causes less disruption to cities, and cuts labor costs. The stronger, dense material also makes buildings lighter, which means they can continue climbing higher. Whether the world's lumber supply can keep up with demand remains to be seen. If it can, only the sky is the limit to wooden skyscraper innovation.

This content was inspired, in part, by "4 Things to Know About Mass Timber," Think Wood; "Milwaukee Is On Track To House World's Tallest Timber Skyscraper," NPR, December 7, 2020; "Will the skyscrapers of the future be made out of wood?" National Geographic, January 13, 2020; and "Wooden Buildings Reach for the Sky," The New York Times.

Gina Wynn is a Thermo Fisher Scientific staff writer.

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