DEERFIELD®

JUNE 2020

NEWSLETTER – VOL. XVI

CONTENTS

MESSAGE FROM DEERFIELD MANAGING PARTNER, JAMES E. FLYNN:

During these extraordinary times, we'd like to take a moment to acknowledge the unprecedented dual crisis upon our nation.

Over the course of the last few months, images of unimaginable human loss in the midst of a pandemic and its continued devastating impact, have been replaced by those of acts of racism, intolerance, and hopelessness.

Importantly, these disturbing events have brought added focus to how Black people and other minority groups are treated, even in the hands of those whose job it is to protect. While these issues have gained greater attention in recent weeks, partly because of the outrage expressed by people of every demographic, each day there are uncountable acts of this nature that go unnoticed.

Also striking, the impact of Covid-19 has not been evenly distributed and disproportionately affects people of color. Here in Upstate New York, over 17% of the deaths from Covid-19 have been among Black people, despite the fact they represent less than 10% of the population.

These data serve to illustrate the deep biases that remain embedded in society that relate to access to care. The imbalance in the composition of leadership and boards of healthcare companies demonstrates clearly that this bias is just as strong when considering access to opportunity.

We must capture this moment of raised awareness and heightened energy to effect real change. We must do better. Not only because we have to, but because we want to.

At Deerfield, we are strong advocates for diversity of backgrounds and ideas, and we are deeply committed to maintaining an inclusive work environment for people of all races, ethnicities, genders, religions, and sexual orientations.

We believe that providing a platform for the voices of a diverse set of stakeholders introduces new, and better ideas. And in the case of healthcare, it could spark more inclusive and creative solutions to the industry's complex set of challenges.

We must address society's social inequities, including those in patient care. We must partner with our local communities in the fight against racism and other injustices. We must acknowledge the pain, grief, and fear that many families are feeling now, and we must listen to those families. Only then can we begin the path toward sustained structural change and healing.

Through our Deerfield Fellows program, we have proactively engaged a diverse group of students from the City University of New York (CUNY) to create opportunities to learn about careers in healthcare finance and entrepreneurship. We now count many of these talented individuals as our colleagues.

Our hearts go out to everyone during this difficult period. The times ahead will be tough, as our nation continues to face many public health, economic, and social challenges. Despite these challenges, we must find a way to use this time of despair as an opportunity to come together and create solutions.

Through the Deerfield Foundation, we've made investments that address the social determinants of health in communities of color, both here in the U.S., as well as in Africa and Asia. In addition, we have created Break into the Boardroom and Women in Science programs to drive change in gender diversity in the boardroom and entrepreneurship. However, we, too, must do more, and will.

We'd also like to use this opportunity to recognize the devoted, selfless individuals who have been on the frontlines of the Covid-19 pandemic. You are our heroes, and we thank you for your hard work and dedication.

In addition, we want to commend our partners across the healthcare industry who have worked tirelessly to care for patients, conducted urgent research for a cure or a vaccine, ramped up testing, and accelerated production of essential ventilators, masks and other critical supplies to keep our nation's healthcare workers safe as they put their own lives on the line.

We remain committed to our Foundation partners, especially those hit hardest by the public health crisis. To date, our Foundation has pledged approximately one million dollars toward emergency funding to organizations that were in need of urgent resources in order to provide continued care to their communities. Should any of our Foundation partners continue to experience Covid-19 disruptions and need our help, our support will continue with additional contributions.

Among specific services and supplies that our Foundation has helped support:

- Little Sisters of the Assumption – Increased availability of food pantry items for New York City families.
- Coalition for the Homeless – Supported efforts focused on providing nutritious meals, clothing, and hygiene resources to homeless New Yorkers.
- God's Love We Deliver – Home-delivered nutritious, medically tailored meals for men, women and children living with HIV/AIDS, cancer and other serious illnesses.
- Queens Community House – Donated funds specifically to its Home Delivered Meals program, which serves both seniors and families in need within the Queens, New York community.
- Children's Health Fund – Increased access to and availability of personal protective equipment (PPE), including masks, gowns, and other essential gear.
- Health Equity International – Expanded access and supply of PPE, including masks, gloves, gowns and other essential equipment. In addition, financial support was provided to build new temporary units for isolation, care and treatment, as well as to enable required surge staffing.

- Covenant House – Covered the increased costs of food, staffing, cleaning supplies, medical supplies and costs associated with retrofitting quarantine rooms.
- Lwala Community Alliance – Helped procure PPE for its facilities, Lwala healthcare workers, and wider PPE need for frontline health workers across Migori County. Funding will also be used toward measures to reduce crowding, designate isolation areas, and increase infection control, as well as to deploy mental health counselors for Lwala frontline health workers.
- The Family Center – Supported through direct payments to families in dire financial need during the Covid-19 pandemic based on a criterion determined by The Family Center.
- The Cabrini Immigrant Services of NYC – Funding provided for pantry items to provide meals. Also, supplied hygiene resources to the community.
- Mexican Coalition – Funding provided families with money to pay for food and their cell phone bills.
- Meals provided to multiple healthcare workers at Mount Sinai, Memorial Sloan Kettering, NYP/Columbia, NYCH+H, and Richmond University Medical Center hospitals in New York City, as well as at Mount Sinai South Nassau in Oceanside, New York.
- Social Security Works Education Fund – High quality facial masks donated to essential workers in low income areas.
- Foundation Source EAP – Emergency assistance provided in the form of grants to families in urgent financial need.
- CorVent Medical – Funding provided toward commercialization of first disposable, critical care ventilator that can be rapidly manufactured at low cost for the purposes of pandemic response to meet each patient's respiratory needs.
- Gates Philanthropy Partners – COVID-Zero initiative, in partnership with the Gates Foundation, to fund the development of vaccines, treatments, and tests to support countries with fragile healthcare systems to prevent, detect, and respond to the pandemic.
- Dana Farber Cancer Institute – Funding provided for PPE for frontline healthcare workers, Covid-19 research, and services for oncology patients who were unable to have direct patient care due to the health crisis.

INFOCUS

Covid-19… Testing a Nation, Both Literally & Figuratively

By Leslie Henshaw

There is widespread agreement that more Covid-19 testing is critical to re-opening economies around the world, minimizing Covid 19-related mortality and morbidity and furthering our understanding of how to combat this virus. That said, there is widespread confusion and frequent disagreement around how to test, when to test, what to test and how results should be interpreted. There is a dizzying array of things to consider and even many policymakers continue to misunderstand the data their testing strategies have been generating and the conclusions they should be drawing.

While testing advances and new insights are emerging daily, likely rendering certain of my statistics and conclusions obsolete by the time this reaches your desk, I'd like to tackle a general overview of the testing landscape and share some views and opinions about the role of testing.

Current Testing Landscape

At its core, diagnostic testing plans need to ensure that people with symptoms can be tested and receive results within timeframes that are useful for clinical care, contact tracing and informing public policy decisions. According to the Covid-19 Tracking Project[1], from March 1st through June 30th, the United States completed fewer than 33 million Covid-19 tests, with recent daily volumes still falling well short of the 2-10 million tests per day that epidemiologists estimate are necessary to safely reopen the U.S. economy. Bridging this gap will require new public-private partnerships, rapid advances in testing technology, a ramp-up in reagent supply, and the repurposing of existing lab technicians and equipment to Covid-19 testing.

Types of Tests

Tests to support treatment decisions and a contact tracing / isolation strategy must detect the presence of the virus itself and deliver rapid results with a high degree of accuracy. Currently, methods for detecting active infection include:

- Clinical diagnosis – based on symptoms and radiologic scans
- Nucleic acid tests – detection of viral RNA based on PCR, NGS and CRISPR techniques
- Antigen tests – detection of viral proteins through ELISA or lateral flow assays

Each of these approaches has distinct advantages and disadvantages with regard to specificity, sensitivity, scalability, ease of test administration/collection, ability to quantify viral load, turnaround time and cost. I suspect our national solution will rely on a mix of all of these testing approaches, with specific test selection being situationally dependent. For instance, weekly testing of Amazon workers in a low prevalence state is likely to optimize for different features than testing surgical teams operating on immunocompromised oncology patients.

In contrast, tests to inform epidemiological studies and identify potential immunity status are based on detecting evidence of a past infection. These serology tests work by screening for antibodies against the virus present in a person's blood. These tests currently have wider error bars than viral tests and, until there is more conclusive evidence that certain antibody levels do confer immunity, are not directly actionable. As such, they are not currently being viewed as a reliable back-to-work testing strategy.

Until recently, even state governments were confused about the distinctions between these tests and were erroneously

[1] https://covidtracking.com/why-it-matters

combining them in the reporting metrics around testing volume and prevalence rates.

Testing's Value Proposition

Testing plays many important roles, ranging from guiding the clinical management of patients, to facilitating contact tracing, to providing students and employees the peace of mind to return to work and school.

From a clinical perspective, definitive confirmation of viral presence, particularly in vulnerable populations, enables more rigorous monitoring and, hopefully over time, the utilization of drugs and treatment protocols capable of improving outcomes when introduced early in the course of infection.

In the case of contact tracing and segmentation, widespread testing is foundational to effectiveness. Because live coronavirus has been shown to shed at high concentrations from the nasal cavity before symptom development, broader population testing is critical to lowering the significant proportion of infections that currently result from contact with pre- or asymptomatic carriers.

Lastly, and while tied somewhat less directly to managing disease, regular testing of specific populations will also play a critical role in our nation's Covid-19 response. Targeted testing can likewise uncover pre- and asymptomatic individuals so that they and those they have interacted with can be quarantined, but perhaps more importantly, it can promote the confidence necessary for individuals to re-engage in former activity.

Numerous surveys suggest that as much as half the population is anxious about returning to work or school, and, even if partially symbolic, the application of routine workforce and student body testing will bolster confidence in organizations' commitment to safety thus helping to reduce fear, which will be critical to economic recovery.

Conclusion

At the highest level, testing is important and the country needs to quickly build more capacity. While testing capacity remains a scarce resource, we need to be intentional about what capacity is deployed where and how innovation and investment are incentivized to drive additional access.

Current laboratory resources, whether in academia or commercial labs, were not well-organized to pivot quickly to Covid-19 testing, to aggregate customer demand through convenient supply chain management or to deliver results to an expanded group of stakeholders rapidly and in an easily aggregable manner.

Testing has historically been anchored around the physician as gatekeeper, for both ordering and communication of results. Many of the key use cases discussed here will be organized outside the physician office and thus will require new methods of capturing samples and reporting results.

The imperative for speed will drive demand for more rapid and at-home testing, and the concurrent need for serving up results in immediately actionable ways will drive the need for more integrated, end-to-end solutions.

Leslie Henshaw is a Partner on the Healthcare Services group at Deerfield.

RESEARCH BITES

Deerfielders Weigh in on a Safe Return to Work Policy Amid Covid-19 Crisis

Antibody testing provides a data-driven path to getting people back into the economy

The availability of point-of-care antibody testing—also known as serological testing—may provide a feasible roadmap for getting people back to work safely following the Covid-19 crisis, according to an editorial published in the peer-reviewed journal Contemporary Clinical Trials Communications[2].

"You can't stop the economy forever," asserted New York Governor Cuomo in a March news conference, according to STAT[3]. "So we have to start to think about, does everyone stay out of work? Should young people go back to work sooner? Can we test for those who had the virus, resolved, and are now immune and can they start to go back to work?"

Regardless of whether they already have immunity to the virus, millions of Americans may try to return to work, potentially undoing all the benefits of the shutdown, suggests the editorial.

Antibody testing, the authors argue, could clarify a person's status quickly in real-time and reveal whether they have been exposed to Covid-19. Accordingly, a person who mounts an IgG positive response (suggesting the presence of immunoglobulin G antibodies) would most likely now be immune to the virus and an IgM positive result would point to the process of developing immunity in someone who more recently became infected.

"Unlike the PCR tests (a measure of virus material), the immediate results and unconstrained supply of antibody tests could fundamentally change the way we manage this epidemic," says Robert Jackson, MD, a co-author of the paper. "And from an economic perspective, it could lead to a tractable path for people to return to work. Collecting the data and tracking individuals longitudinally, in order to confirm the hypothesis, will be necessary."

And barring any HIPAA concerns, the authors propose that persons with positive antibody tests during periods of social distancing could get a bracelet, which indicates that they are immune-protected and can return to work. Those without a bracelet would still be asked to practice social-distancing and not yet resume their normal activities. But this approach could potentially get at least some portion of the economy back running again, suggests the authors.

According to the authors, the antibody tests are cheap, easy to administer, and could be made available at every hospital.

"Broad testing is in society's best interest," says Alex Karnal, a co-author of the editorial. "Until we make serological tests available in a robust way, it's as if we are flying a plane without navigation."

Authors of the editorial, titled, "Let's Get Americans Back to Work Again," are: Alex Karnal, Partner and Managing Director; Robert Jackson, MD, Partner and Chief Science Officer; and Joe Pearlberg, MD, PhD, Vice President of Scientific Affairs, all at Deerfield; and Amitabh Chandra, PhD, McCance Family Professor at Harvard Business School and Weiner Professor at the Harvard Kennedy School.

[2] https://www.sciencedirect.com/science/article/pii/S2451865420300430

[3] https://www.statnews.com/2020/03/25/coronavirus-experts-craft-strategies-to-relax-lockdowns/?utm_source=STAT+Newsletters&utm_campaign=7d40a83803-Daily_Recap&utm_medium=email&utm_term=0_8cab1d7961-7d40a83803-151550053

Alex Karnal Appointed to Covid-19 Advisory Group

Deerfield Partner and Managing Director selected by Connecticut Governor Ned Lamont to provide counsel on the State's reopening plan following global pandemic

Deerfield Partner and Managing Director, Alex Karnal, was recently appointed by Connecticut Governor Ned Lamont to the Reopen Connecticut Advisory Group to provide counsel on the reopening of the State's economy and education system.

Like other states in the Tri-state area, Connecticut had been very active in March and April in trying to manage the Covid-19 health crisis. Karnal had been engaging with Governor Lamont at the outset of the local outbreak and providing insights on the best roadmap for safely reopening the economy.

"It is critical that any reopening plan asks difficult public health questions that inform rational decision-making for the public good," said Karnal. "I was honored by this invitation to join Governor Lamont and his team in the most urgent initiative of our time and am up for the challenge."

Could a Common OTC Antacid Be the Answer to Covid-19?

Early results of retrospective study shows association between Pepcid use and improved clinical outcomes

A review of 1,620 medical records of hospitalized Covid-19 patients suggests that those who took Pepcid (famotidine), a common heartburn medication, were more than twice as likely to survive the virus, compared to patients who didn't receive the drug, according to the journal Gastroenterology[4].

The retrospective study[5] compared 84 hospitalized Covid-19 patients who received famotidine with 1,536 Covid-19 patients in the same hospital who did not. The researchers found that 10 percent of patients who received famotidine were placed on a ventilator or died, compared to 22 percent of patients who didn't receive famotidine.

Pepcid, which has been on the market for nearly 40 years, is a histamine-2 blocker that works by decreasing the amount of acid the stomach produces.

Michael Callahan, MD, an infectious disease doctor affiliated with Massachusetts General Hospital, was the first in the U.S. to call attention to the drug, according to Science Magazine[6]. Callahan, along with colleagues in China, began to note that many of the survivors in China tended to be poor and asked why.

In reviewing 6,212 Covid-19 patient records, Callahan and his colleagues in China noticed that many of these survivors had also been suffering from chronic heartburn and were taking Pepcid, rather than the pricier omeprazole (Prilosec),

[4] https://www.gastrojournal.org/article/S0016-5085(20)34706-5/pdf
[5] https://www.cuimc.columbia.edu/news/heartburn-drug-may-have-potential-against-covid-19
[6] https://www.sciencemag.org/news/2020/04/new-york-clinical-trial-quietly-tests-heartburn-remedy-against-coronavirus

considered the medicine of choice both in the U.S. and among wealthier Chinese.

Then in New York, Timothy Wang, MD, Chief, Division of Digestive and Liver Diseases at Columbia University Irving Medical Center, shared his results of the review of the 1,620 records and added Callahan and Northwell Health researchers as co-authors, according to *Science*.

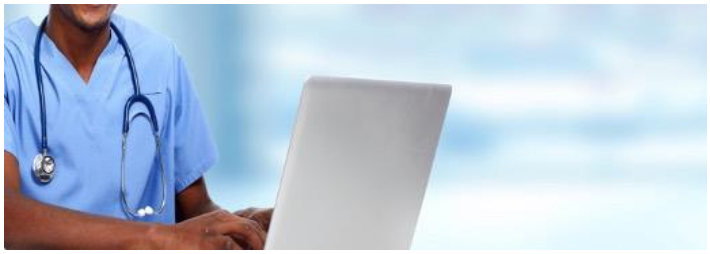
But before drawing conclusions, the researchers emphasized the importance of waiting for the results of the randomized clinical trial that is underway, which is viewed as the real test. Doctors cautioned the public, including on CNN, against starting Pepcid and stressed that more research is needed.

"While these preliminary results are intriguing, it's important to keep in mind that this study merely found an association and may only be a coincidence," says Deerfield Partner Zheng Su, PhD. "Only a rigorously designed randomized clinical trial could confirm efficacy against Covid-19."

Callahan told Science that the Pepcid lead underscored the importance of science diplomacy in the face of an infectious disease that knows no borders. When it comes to experience with Covid-19, he says, "No amount of smart people at the [National Institutes of Health] or Harvard or Stanford can outclass an average doctor in Wuhan."

Online Physician Survey Research:

A report on the current state in academia



Online physician surveys could be improved by way of more robust reporting of sample coverage and non-response bias implications, according to a study by researchers at the University Illinois at Chicago and the Deerfield Institute.

The paper, "Method and Transparency of Online Physician Surveys: An Overview," published in the journal, Survey Methods: Insights from the Field[7].

"This study highlights how researchers are currently reporting consistent measures of sample source, sample response rates, and the use of ethical research protocols," says Dan Glass, PhD, Managing Director, Global Market Research for the Deerfield Institute.

Over the past twenty years, published academic survey research targeting physicians has moved to an online environment, though there is little information currently available regarding the practice of online survey research with healthcare professionals, according to the researchers.

To address this concern, the investigators assessed the methodologies disclosed in a sample of 200 published papers that report findings from web-based surveys of physicians.

Fifteen methodological aspects of web surveys were coded from each paper, and a transparency index based on aggregation of these various indicators was constructed to evaluate overall survey quality. Some indicators, such as the source and type of samples, along with information regarding ethical aspects of protocols, were commonly referenced, the researchers reported.

In contrast, however, the use of incentives, and discussion of potential coverage and processing errors were reported less frequently.

[7] https://surveyinsights.org/?p=12496

The investigators hypothesize that these reporting patterns may be more of a product of journal requirements. As web surveys are destined to serve as an important modality for data collection from physicians and other healthcare professionals for the foreseeable future, say the study authors, it is important to encourage—if not require—researchers to regularly disclose a broader range of quality indicators when disclosing their research findings.

"Understanding how consistent these studies report standard measures of survey error is critical to evaluating the quality of the research. Allowing readers to judge critically these additional measures of survey quality and sample representativeness is important and provides for a broader and more informed view," says Dr. Glass.

Huntington's New Drug Targets Identified

A new genetic screen in mice uncovers protective genes against the disease

Neuroscientists affiliated with the Picower Institute for Learning and Memory at MIT, Broad Institute of MIT and Harvard, and University of Texas MD Anderson Cancer, have discovered a family of genes involved with the development of Huntington's disease.

Results of the study were published in the January 20, 2020 issue of Neuron[8] MIT/Picower Institute postdoc Mary Wertz is the lead author of the paper.

Using a new screening technique in mice not previously possible in the mammalian CNS, the researchers revealed genes that are protective against the toxic effects of a mutation that causes the disease.

One potential drug target, known as the Nme gene family, emerged from these efforts. According to the researchers, this gene family may normally help cells to break down the mutated build-up before it forms the clumps seen in the brains of Huntington's patients. Nme had previously been linked to cancer metastasis, but not Huntington's disease.

All of the approximately 22,000 protein-coding genes in the mouse brain were investigated by way of the new screening tool, which could also potentially inform on other neurodegenerative diseases, including Alzheimer's and Parkinson's.

"This is a nice example of using 'functional genomics' to identify 'genetic modifiers' that may be predictive of therapeutic interventions," said Matt Nelson, PhD, Vice President of Genetics and Genomics at Deerfield. "Identifying genetic modifiers, either via human genetic experiments of nature or functional genomics studies like this one, is an increasingly interesting idea."

Adapted from MIT press release[9]

[8] https://www.cell.com/neuron/fulltext/S0896-6273(20)30004-0

[9] http://news.mit.edu/2020/new-drug-targets-huntingtons-gene-0130

Artificial Intelligence STAT!

Machine learning joins the OR, radiology suite, and doctor's office

Two separate studies in Nature reported on recent developments in artificial intelligence that suggest it could help improve cancer diagnoses and better guide treatment.

Brain Tumor Diagnosis

In a paper published in the January 6, 2020 issue of Nature Medicine[10], investigators evaluated a streamlined, faster approach for accurately diagnosing brain tumors in real-time through the combined use of advanced optical imaging and machine learning during surgery.

The research showed a reduction to two and a half minutes in the time it takes to analyze tissue biopsies from a patient's tumor while they are still on the operating table.

Typically, the traditional method is labor intensive, taking 20 minutes or longer, as it requires sending the tissue to the pathology lab for freezing and staining prior to studying under the microscope.

In comparison, the new technique uses lasers to create images and a computer to interpret them, all in the operating room. Outcomes for both approaches were similar, with the AI-based diagnoses having an accuracy rate of 94.6 percent, compared to 93.9 percent with the pathology lab interpretation. Using the same technology following the biopsy, the surgeons are able to detect and remove the tumor.

Daniel A. Orringer, MD, a neurosurgeon at N.Y.U. Langone Health, is the senior author of the paper.

For more details on the study, see also NYU Health Langone's press release[11].

Breast Cancer Screening

In the January 1 issue of Nature[12], researchers from the U.S. and Britain evaluated a new AI system for breast cancer screening. The study, which was paid for by Google, found that the AI tool does a better job at reading mammograms—essentially outperforming human readers.

To assess outcomes in the clinical setting, the investigators curated large datasets from the U.K. and U.S., showing an absolute reduction of 5.7 percent and 1.2 percent (in the U.S. and U.K., respectively) in false positives, and 9.4 percent and 2.7 percent in false negatives.

According to a report[13] published at healthaffairs.org by researchers affiliated with Harvard, Boston Children's Hospital, and Macquarie University in Sydney, Australia: "If we assume a false-positive rate of 11 percent and overdiagnosis rates of 22 percent and 86 percent for invasive breast cancer and DCIS (abnormal cells inside a milk duct), respectively, the national cost of false-positive mammography results and breast cancer overdiagnoses among women ages 40–59 is about $4 billion each year."

The researchers told the New York Times[14] that the AI tool did, in some instances, miss a cancer that radiologists found, suggesting a need for a new area of inquiry and study. Still, the researchers reported in the paper that this new AI system paves the way for clinical trials to improve the accuracy and efficiency of breast cancer screening.

According to the New York Times[15], Google has already created algorithms to help detect lung cancers on CT scans, diagnose eye disease in diabetics and identify cancer on microscope slides.

[10] https://www.nature.com/articles/s41591-019-0715-9
[11] https://nyulangone.org/news/new-laser-based-imaging-system-artificial-intelligence-algorithm-used-conjunction-accurately-identify-brain-tumors
[12] https://www.nature.com/articles/s41586-019-1799-6
[13] https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.1087
[14] https://www.nytimes.com/2020/01/01/health/breast-cancer-mammogram-artificial-intelligence.html
[15] https://www.nytimes.com/2019/05/20/health/cancer-artificial-intelligence-ct-scans.html?searchResultPosition=1

Identifying Patients at High Risk for AFib or Death

And in other AI developments, two studies presented at the 2019 American Heart Association (AHA) Scientific Sessions[16] in Philadelphia found that AI could identify patients at high risk for arrhythmia or death, even when doctors don't.

An electrocardiogram, also known as an EKG or ECG, is a test used to measure the electrical activity of the heart.

The researchers hypothesized that a "deep" learning model could predict atrial fibrillation (AFib), or irregular heartbeat. The most common type of heart arrhythmia, Afib could significantly increase a person's risk of developing a severe stroke.

Using more than 2 million EKG results pulled from three decades of medical records from a Pennsylvania and a New Jersey health system, the investigators created the neural networks, characterized as "advanced, multi-layered computational structures", to predict the future events.

Among the top 1 percent of high-risk patients, one-third were diagnosed with AFib within a year, as the model forecasted.

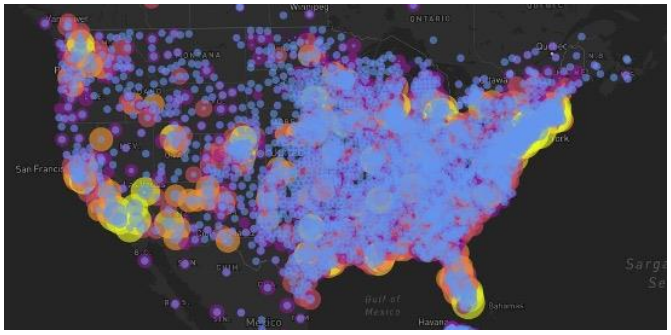
As for AI allegedly doing a better job at predicting which patients were most likely to die within one year of any cause, the researchers reported that the neural network was able to identify risk patterns in EKGs that were undetectable and initially read as normal by three separate cardiologists.

The researchers are currently investigating whether the predictions can be used to improve health outcomes.

Brandon Fornwalt, MD, PhD, the senior author on both studies, is an associate professor and chair of the Department of Imaging Science and Innovation at Geisinger in Danville, Pennsylvania.

Finally, in more recent AI News...

Online warning system created by epidemiologists at Boston Children's Hospital was among first to sound the alarms about the pandemic



HealthMap screenshot showing the spread of Covid-19 in the U.S.
Using AI and data mining, HealthMap spots disease outbreaks and issues location-specific alerts.

It was a Boston Children's Hospital website in late 2019 that may have been the first to capture worrisome reports of a new kind of pneumonia in Wuhan, China.

Cofounded by John Brownstein, chief innovation officer at Boston Children's Hospital and a professor of medicine at Harvard Medical School, HealthMap[17] uses artificial intelligence to search social media and other information streams for indications of disease outbreaks.

According to Science Magazine[18], the one-line email bulletin that HealthMap surfaced on December 30, 2019 characterized the urgency as a three out of five, with seven people already in critical condition.

Dr. Brownstein told Fortune Magazine[19], "I thought, if you could tap into that [the data-filled internet], you could build a whole new view of global health."

Fortune reported that the platform is also a success, in part, due to the nine day-to-day implementers: "Google.org Fellows" who are on-site at Boston Children's Hospital.

Not surprisingly, the Google employee Fellows working at the hospital are experts in data mining, database development, data visualization, user interfaces and mapping, among other related specialties.

[16] https://newsroom.heart.org/news/artificial-intelligence-examining-ecgs-predicts-irregular-heartbeat-death-risk
[17] https://www.healthmap.org/en/
[18] https://www.sciencemag.org/news/2020/05/artificial-intelligence-systems-aim-sniff-out-signs-covid-19-outbreaks
[19] https://fortune.com/2020/05/18/coronavirus-tracking-google-healthmap-partnership-covid-19/

IP CORNER

Infringement Under the Doctrine of Equivalents: Lessons from *Ajinomoto Co. v. ITC*

By Mark Shtilerman, PhD, JD

The boundaries of a patent grant are defined by the words of the patent claims. Patent claims are presented in numbered paragraphs at the end of each patent. Literal patent infringement occurs when an accused product falls within these words. Infringement under the doctrine of equivalents (DOE) occurs when the product does not literally infringe, but for all intents and purposes does the same thing. The criteria to determine infringement under the DOE are known as the function-way-result framework, and states that the differences are small and "the accused product performs substantially the same function in substantially the same way with substantially the same result as each claim limitation of the patented product.[20]" The DOE thus allows the courts to prevent a copyist from making small changes to the product to place it just outside of the words of the patent claims.

It was recognized since the early days of biotechnology that the DOE may be particularly applicable to patents claiming specific nucleic acid or protein sequences. Many different nucleic acid sequences encode the same protein due to the degeneracy of the genetic code. Proteins also can tolerate multiple amino acid substitutions without significant changes to their function. In August of 2019, the Federal Circuit, the court that hears all appeals of patent cases, addressed infringement under the DOE for a sequence claim in the case of *Ajinomoto Co. v. ITC*[21]. This was the first case where an accused product was found to infringe on a nucleic acid sequence claim under the DOE.

The patent at issue involved an improved method for increasing L-tryptophan production in bacteria[22]. The method introduced multiple copies of the nucleic acid encoding for the YddG protein, so the bacteria produced more of this desired protein[23]. The patent claimed the nucleic acid sequence of the gene and the amino acid sequence of the target protein. Ajinomoto had originally tried to claim the YddG protein sequence, but the patent office rejected this initial claim because at the upper limit of the claimed sequence variability, the claim would cover an unrelated known protein. Rather than disclaiming this specific sequence, Ajinomoto chose a different strategy and claimed the native *E. coli* protein encoded by a nucleic acid that is highly similar to the native nucleic acid sequence. Arguably, the patent applicant disclaimed more than it had to. The patent was subsequently granted.

One of the accused products imported by CJ Cheiljedang was manufactured using YddG protein encoded by a codon-randomized nucleic acid sequence. Due to the degeneracy of the genetic code, CJ Cheiljedang used a nucleic acid sequence that produced a protein nearly identical to the native *E. coli* protein, while different from the native nucleic acid sequence.

The accused product utilized a codon-randomized nucleic acid sequence and did not literally infringe on the patent claims. Its nucleic acid sequence was not highly similar to the native one. The majority of the Federal Circuit, however, found that this product infringed under the DOE. The YddG protein in the accused product performed the same function (export of L-tryptophan) to achieve the same result (accumulation of L-tryptophan in culture medium). The majority concluded that the function was performed in the same way because the protein sequence was 85-95 percent identical. The dissenting judge believed that the theory of prosecution history estoppel (PHE) should have precluded the finding of infringement under the

[20] *Warner-Jenkinson Company, Inc. v. Hilton Davis Chemical Co.*, 520 U.S. 17 (1997).
[21] *Ajinomoto Co. v. Int'l Trade Comm'n*, 932 F.3d 1342 (Fed. Cir. 2019).
[22] U.S. Patent No. 7,666,655.
[23] YddG protein is an aromatic amino acid transporter that causes the bacteria to excrete L-tryptophan into the culture medium.

DOE. PHE applies when a patent application filed with broad claims is rejected by the patent office, and the claims are narrowed in response. The portion of the claim that is removed from patent coverage is considered dedicated to the public and cannot be reclaimed.

Ajinomoto Co. v. ITC was the first time the appellate court addressed the infringement of a sequence claim under the DOE. There are lessons to be learned from this case by both patent applicants and patent attorneys. First, while the DOE remains a viable doctrine to support broader patent coverage, applicants should be very careful when filing initial claims. Second, patent applicants and patent attorneys need to take extra consideration when narrowing patent claims in response to the patent office's arguments.

While the full implications of *Ajinomoto Co. v. ITC* will take some time to manifest, the decision is a positive outcome for the biotechnology industry.

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We are committed to connecting our featured candidates with company boards that could benefit from their expertise. Please reach out to Leslie Henshaw at lhenshaw@deerfield.com to inquire about meeting Ms. Chris Bellon or having us search our database for other candidates with a specific set of skills currently being sought for an identified board opportunity.

INTRODUCING…CHRIS BELLON

Photo credit: Beam Therapeutics

Current Position: SVP, Chief Legal Officer for Beam Therapeutics, a publicly traded biotechnology company developing precision genetic medicines through the use of base editing.

Previous Roles: Prior to joining Beam, Chris served as the General Counsel and Corporate Secretary for Forma Therapeutics; the SVP of Legal Affairs for Relay Therapeutics; and VP of Legal Affairs and Corporate Secretary of Blueprint Medicines. Before joining Blueprint, she served in legal leadership roles at Hydra Biosciences and Infinity Pharmaceuticals. Earlier in her career, she practiced law in the Boston office of Fish & Richardson P.C.

Education: Columbia Law School (JD), Massachusetts Institute of Technology (PhD, Organic Chemistry), Yale University (BS, Chemistry)

Key Expertise/Skill Sets: Chris enjoys bringing diverse groups within companies together; trained first as a scientist, then as a lawyer, she has expertise in integrating input from different functional areas of the company to structure and execute complex biotech/pharma collaborations. She is known for her ability to craft strong and sustainable intellectual property strategies in complicated patent landscapes. She thrives on building companies and leading them through the private-to-public transition and has guided three companies through initial public offerings or reverse mergers.

Professional Interests: Chris is passionate about mentoring people from different disciplines. Sought out by colleagues both within and outside her company, she enjoys helping people build and manage their careers. She also believes in building communities; fortunate to work in Cambridge, Massachusetts, she assembles intercompany networks to foster a sense of "one big Cambridge biotech."

Personal Interests: Chris and her husband are the proud parents of two daughters, one a rising junior in college, and one hoping to start classes on campus (instead of online) this fall. Chris is an active – in many senses of the word – fundraiser for the Boston Museum of Science (MoS), summiting Mount Washington four times and running the Boston Marathon three times to raise funds for the MoS, where she also serves on the Board of Trustees.

CAPTURED OUR INTEREST

By Christine Livoti

Coronavirus clinical trial disruption quantified

A German researcher has taken on the task of measuring the extent of upheaval in the conduct of clinical trials during the coronavirus pandemic. After examining the more than 2,000 trial records from clinicaltrials.gov that had been suspended, terminated or withdrawn since mid-January, it was determined that at least 1,000 studies had been halted by the coronavirus.

Endpoints News
https://endpts.com/more-than-1000-clinical-trials-were-stopped-by-the-pandemic-including-dozens-in-phiii/

Mount Sinai unveils post-Covid-19 care center plans

Mount Sinai Health System, one of the major medical centers at the pandemic's epicenter in New York, has announced plans for a Center for Post Covid Care to help patients recovering from the virus and follow their recovery longer term. The center will provide multispecialty care while monitoring for any long-term complications. Patients will have the option to enroll in a Covid-19 registry.

Fierce Healthcare
https://www.fiercehealthcare.com/hospitals-health-systems/mount-sinai-launches-post-covid-care-center-for-ongoing-treatments

Researchers tabulate excess deaths during Covid-19

A team of researchers from the Health Care Cost Institute (HCCI) examined morbidity data from obituaries and found excess death to be as much as 16 percent greater than average, compared to previous years. Their analysis came to a similar conclusion as a Centers for Disease Control review looking at death certificates.

HCCI
https://healthcostinstitute.org/annual-reports/daily-deaths-during-coronavirus-pandemic-by-state

Relaxed regulatory requirements for digital tools

The FDA has relaxed some regulatory requirements during Covid-19, including the need to file premarket notification for certain digital tools. Akili, the maker of a video game for children with ADHD, had been awaiting a regulatory approval pre-Covid-19, but has since rolled out its platform under the relaxed rules. The game, called Endeavor, is meant to improve attention and inhibitory control.

STAT News
https://www.statnews.com/2020/04/22/akili-launches-endeavor-adhd-game

HHS Portal Goes Live for Uninsured Covid-19 patients

The U.S. Department of Health and Human Services (HHS) unveiled a new research portal to aid providers billing for Covid-19 related services to uninsured patients. As of now, those services will generally be reimbursed at Medicare rates, however it is unknown when those funds may run out. Funding for the uninsured has initially been provided under provisions of the CARES Act.

HHS
https://www.hhs.gov/about/news/2020/04/27/hhs-launches-covid19-uninsured-program-portal.html

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