Technology Networks

The Scientific Observer

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Leveling the Field in Ancient DNA Research

A Journey Into Predatory Science

Babies, Parenthood and the Brain

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Leveling the Field in Ancient DNA Research

Molly Campbell

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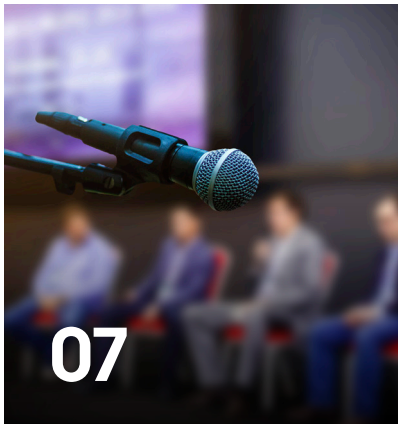

EDITORS' NOTE

The start of the year may see you making plans for the months ahead, including which conferences and events you would like to attend. However, not all conferences deliver what they promised, as Ruairi J Mackenzie reported in his investigation of predatory conferences. Find out more about these events and how to spot them in *A Journey Into Predatory Science.*

In this issue, the newsroom highlights research investigating why women are at higher risk for Alzheimer's disease than men and covers the approval of lecanemab, a new drug that targets the underlying mechanisms of the disease. Focus is also given to a study that used ancient DNA (aDNA) to reveal clues about Scandinavia's genetic history over the last 2,000 years.

The study of aDNA and what it can tell us about our past is a rapidly growing area, with the 2022 Nobel Prize for Medicine or Physiology awarded for Neanderthal and Denisovan DNA discoveries. In this month's feature article, Molly Campbell explores this fascinating area of research and how inclusion and representation are critical considerations for those working in the field. Insights from Professor María del Carmen Ávila Arcos, leader of the International Laboratory for Human Genome Research in Mexico, describe how aDNA is helping to understand Mexico's colonial history and the genetic legacy of the transatlantic slave trade in Mexico, as well as efforts to promote sustainable aDNA research.

Switching from studying our past to looking to the future generation, Sarah Whelan explores research investigating parent-child interactions and how they can influence brain development. In *Babies, Parenthood and the Brain: What Do We Know?* we learn about how a baby's language development can be affected by its mother's mood and how a father's post-baby stress could be linked to a child's behavior later in life.

We hope you enjoy this issue of *The Scientific Observer*. Subscribe to make sure you never miss an issue.

Have an idea for a story?

If you would like to contribute to *The Scientific Observer,* please feel free to email our friendly editorial team.

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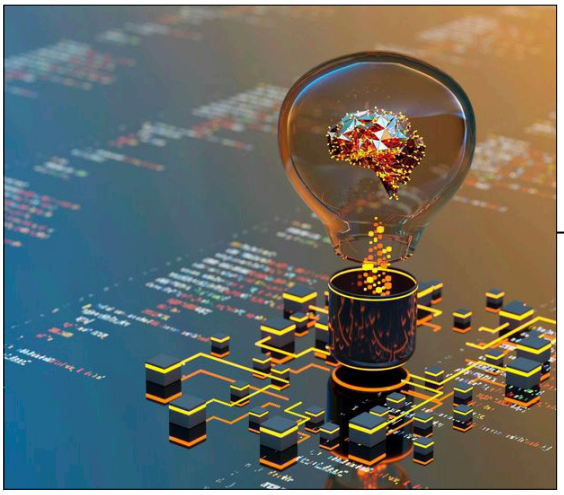
From the Newsroom



SCIENCE IS BECOMING "LESS DISRUPTIVE"

MOLLY CAMPBELL

Despite "unprecedented expansion of scientific and technological knowledge", the rate of innovation in science is slowing down, according to a new study by researchers at the University of Minnesota.

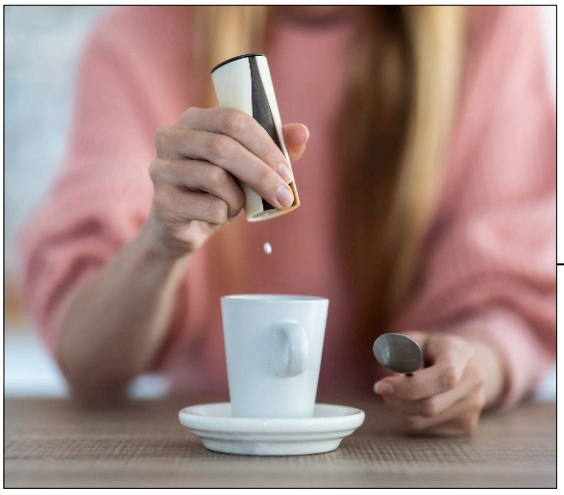
JOURNAL: *Open Heart.*

UV RADIATION CONTRIBUTED TO MASS EXTINCTION EVENT

MOLLY CAMPBELL

A new study of sunscreen-like chemicals detected in fossilized plants suggests ultraviolet (UV) radiation contributed to mass extinction events.

JOURNAL: *Science Advances.*



CAN TOO MUCH SWEETENER AFFECT YOUR GRANDCHILDREN'S ANXIETY?

RUAIRI J MACKENZIE

A new study suggests that aspartame, the common sweetener, produces anxiety-like behavior in mice, an effect that was passed on to multiple subsequent generations.

JOURNAL: *PNAS.*

NEW ALZHEIMER'S DRUG LECANEMAB GRANTED ACCELERATED APPROVAL

RUAIRI J MACKENZIE

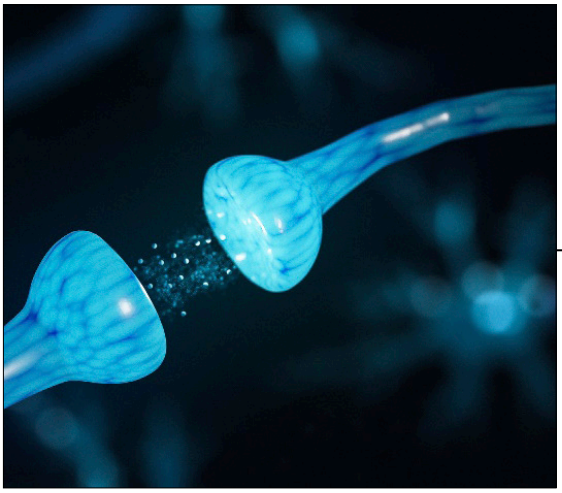
The US Food and Drug Administration (FDA) has given a new Alzheimer's drug the green light. The compound, lecanemab (Leqembi) is a monoclonal antibody, part of a new class of treatments that target the underlying mechanism of disease. It was approved using the FDA's accelerated approval pathway.

ANCIENT DNA REVEALS CLUES FOR SCANDINAVIA'S GENETIC HISTORY

SARAH WHELAN

Researchers have studied ancient and modern Scandinavian genomes to understand the region's ancestry and gene flow over the past 2,000 years, including during the Viking age.

JOURNAL: *Cell.*



PROTEIN MODIFICATIONS MAY EXPLAIN WHY MORE WOMEN GET ALZHEIMER'S DISEASE

SARAH WHELAN

A new study has discovered that a modified immune system protein is more common in women with Alzheimer's disease than men, providing a molecular clue as to why women are at a higher risk of the disease.

JOURNAL: *Science Advances.*

Lars Einarsson.

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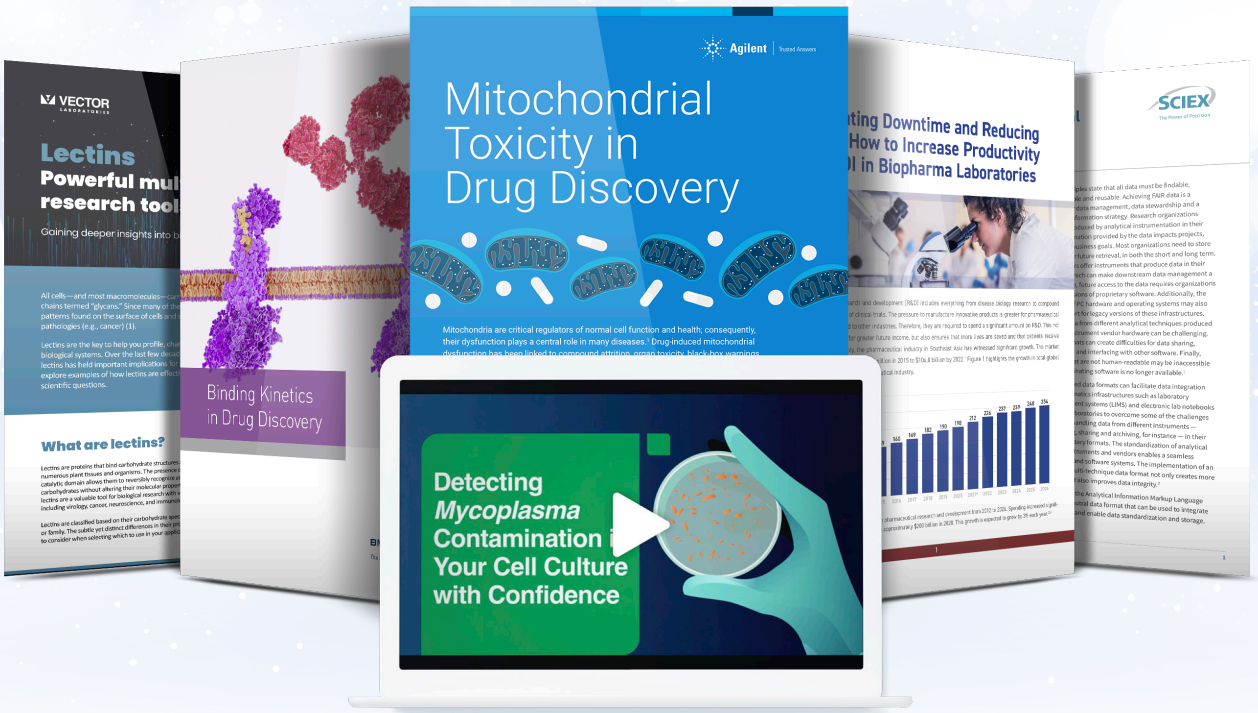

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A Journey Into Predatory Science

RUAIRI J MACKENZIE

Since this investigation was published over three years ago, predatory conferences have continued to proliferate. The move to online conferences during the COVID-19 pandemic has made the business of organizing these events even easier. As Technology Networks begins a new project studying the spread of predatory events that will be released later in 2023, we wanted to republish this investigation and repeat our call for readers to share their stories of predatory science.

An academic conference can be the highlight of an early-career researcher's calendar. It presents a chance to share knowledge with like-minded scientists and hear experts discuss the pressing topics in their field. Usually conferences are tightly regulated operations, and fierce competition between attendees to get their abstracts accepted into the agenda is common. But that's not always the case.

There is a growing underbelly of conferences that might walk and talk like the real thing but have none of the editorial standards expected by academics and have developed a reputation for advertising with fake agendas and high prices. These are "predatory conferences", named after the more well-known sister industry of "predatory publishing", where typically open-access model publications accept submissions without a proper peer review process, but with a steep publication price.

Our chance investigation started after a message from a stranger took me inside a predatory conference and has uncovered how predatory science has ensnared scientists at every level and made a small fortune for the conference organizers.

The message that kicked things off came from Zsuzsa Farkas, a Hungarian-born neuroscience student, who studies at BPP University in the UK. She had been looking forward to Conference Series LLC's 4th International Congress on Addictive Behavior and Dual Diagnosis. Speaking to *Technology Networks*, she expressed how she had been "really excited" to book her place at the conference, which was set to take place on September 5, 2019. Promising workshops, oral plenaries, keynote lectures and a student poster competition, the conference seemed to tick every box.

It was when Farkas first submitted her registration fee of £225 ($275)

that things started to feel wrong. Her payment was initially declined, so she gave Conference Series a call. A man called "Sam" picked up, who told her that the payment hadn't gone through, but an inquiry with her bank suggested the money had been taken out of her account. Eventually Farkas received a typo-filled email saying the company had received the money. By this point she had looked up Conference Series online, and realized that its parent company, Hyderabad, India-based OMICS International, was renowned as a predatory publisher. For Farkas, who, as of July 2019, has been unable to retrieve her payment, this was more significant than feeling tricked: "I am not working at the moment and study 4-6 hours a day, 5-6 days a week. I feel very disappointed and taken advantage of. I am a student, who has a limited amount of money, so I cannot just throw away £225 for nothing."

FINDING FAKE SCIENCE

Sadly for Farkas, if she had waited just a few more weeks to book her place, she might have seen the announcement that the US Federal Trade Commission had been awarded $50 million in a lawsuit against OMICS. The court proceedings revealed how OMICS had been engaging in several unethical publishing practices. These included making up its own version of the widely accepted Impact Factor journal rating system when Thomson Reuters excluded OMICS journals and tricking reputable scientists into being editors on their journals.

But what struck me about Farkas's story is that, without any clear link on the Conference Series website connecting them to OMICS, it would be easy to think they were offering a typical conference package. The company claims to arrange thousands of conferences a year, on virtually every topic you could imagine – aquaculture, glycobiology, recycling, high energy physics, midwifery. Could an operation of this size really be predatory? What would one of these events actually look like from the inside?

Perhaps somewhat serendipitously, I saw that, just a short drive from my home, Conference Series was hosting the "23rd International Conference on Neurology & Neurophysiology" alongside the "24th International Conference on Neurosurgery & Neuroscience" at a hotel in Scotland's capital, Edinburgh. I couldn't exactly pass up the opportunity to get some answers, so I set out to find what really happens at a predatory conference.

Edinburgh skyline, seen from Calton Hill, Scotland.

iStock, evenfh

A REAL EVENT?

Edinburgh is no stranger to conferences. The city's ancient skyline is quite the draw for eventgoers, and there are a host of venues scattered across the UNESCO heritage sites in the city's Old and New Towns. The conference I was to attend was being hosted at the Leonardo Hotel Murrayfield, quite far from the city center, in the quiet suburban area of Clermiston. When I arrived at the Leonardo, I wasn't really sure what to expect. Would the conference even go ahead? Farkas clearly felt that she had paid £225 for an event that wasn't even real, so I quickly went to the front desk to check the event was actually happening. The concierge assured me that, yes, the conference was taking place.

Reassured that I hadn't had a wasted journey, I needed to address the small matter of how I was going to get into the conference, given that I hadn't been able to get a press pass through the Conference Series website.

I went through to the conference lobby. Sure enough, there was a registration area, although it appeared to have been hit by a mortar. Nametags and registration documents were scattered around a desk in disorganized piles, with just one young staff member manning the booth. I asked her if I would be able to get into the conference as press. I didn't have any identification beyond my business card, but she waved me through, to a room with about 50 attendees.

Farkas may have been worried about having paid money for a non-existent event, but this was very much a real conference, with a full speaker schedule, including a keynote. Quite a renowned keynote, as it happened, as Professor Koji Abe, of Okayama University in Japan, stood up. Abe is an influential figure in amyotrophic lateral sclerosis (ALS) research, having helped popularize the use of edavarone, one of the few promising drugs with therapeutic potential in the field. He was listed in the program as giving not just one but two lectures. Perhaps Farkas's skepticism had been misplaced. After Abe had finished his plenary, however, things started to get a little *weird*.

THE CASE OF THE MISSING PLENARY

Abe was given an official Conference Series certificate, took a quick photo, and then speedily left the room, muttering something about needing to catch a flight. Some confused glances were exchanged in the audience at this, as there were just two hours until Abe's next talk was scheduled.

It was to be somewhat less than two hours, in fact, as the next plenary speaker, Tofael Hossain Bhuiyan, a clinician at Rangpur Medical College Hospital in Bangladesh, didn't come up to speak when his name was called by the session chair. He was nowhere to be found. The explanation for this was quite literally that he had "gone missing." It was at this point that I realized this wasn't going to be your typical conference.

The morning's talks proceeded at pace, with speakers touching on a dizzying array of topics. Variety in a conference schedule isn't unusual, but there was almost no organization or theme to the talks. Neurology case studies were followed by in-depth presentations on basic neuroscience. Clearly, the "23rd International Conference on Neurology & Neurophysiology" and "24th International Conference on Neurosurgery & Neuroscience" had been simply smashed together to create a loosely connected talk series that was baffling to attendees. I spoke to one fellow conference-goer, Francesca Morelli, a clinician who was then studying at Erasmus Medical Center in the Netherlands. "When I looked at the agenda for the first time, I noticed the program was heterogeneous, there were so many different topics," said Morelli. "I really didn't get what the educational value of the whole conference could have been." But by the time she saw the formal agenda, Morelli, eager to present at an international conference, had her poster accepted into the agenda. For a fee, of course.

This sense of the surreal was heightened by the organizers' seeming disregard for the agenda. With an entire keynote speaker missing, we reached the intended lunchbreak at about 10am. Rather than have a break for discussion, the conference just plowed on, meaning we were given a talk scheduled for 3.50 pm at around midday. Of the nine talks after Abe's that I stayed for, four were cancelled due to missing speakers, including Abe's second presentation. He had, indeed, needed to catch that flight.

As the mishmash of presentations broke for lunch, I used the opportunity to quiz the session chair, Ludmila Zylinska, who was from the University of Lodz in Poland. She explained to me that she had originally been booked as a speaker, before being asked to become the session moderator at the last minute. She didn't know who many of the speakers in her session were. She told me that around a third of the two-day event's speaker lineup had not arrived. Zylinska wasn't affiliated with Conference Series, and the only representative from the company, it seemed, was the administrator who had let me in at the door.

A DISORGANIZED COMMITTEE

No clearer on how the event took shape or who was running it, I tracked down a researcher I recognized from the conference website, a member of the conference organizing committee. This was Felix-Martin Werner, a researcher at Euro Akademie Pößneck in Germany. Unlike Zylinska, Werner readily admitted having worked with both Conference Series and OMICS in the past. Werner said that, despite being on the organizing committee, he had had nothing to do with picking the speaker lineup, this was pre-decided by Conference Series.

What about the other committee members? One was a professor at the Karolinska Institute in Sweden, whom I managed to reach in a phone call I made in the lunch break. He informed me that he was unable to attend the conference, as he was sick. Another member of the committee emailed me saying he was getting married in Brazil. The fourth member was unreachable. I had a quick chat with some conference attendees sitting in the hotel lobby. They had traveled from the Philippines to attend, spending thousands of pounds on flights in the process. They seemed to have enjoyed the morning's talks but said they were disappointed that some speakers had not turned up. Morelli echoed this sentiment, and raised concerns about the conference's organization, "The general discussion after the lectures was poor. At other conferences I have attended, the chair can lead the discussion, or ask critical questions about the lectures, and that is what I have missed."

I decided I had seen enough, but as I prepared to leave, I caught up with Werner again to ask how he had gotten involved with OMICS. He spoke with surprising frankness about how he had been offered the editorship of one of their journals, the *Journal of Cytology & Histology*. He told me that in his position as editor, he had reviewed more than 30 papers, but due to OMICS's struggle to get reliable reviewers, had had to review a number of papers he had limited understanding of. The journal has a publication fee of €1100 per paper. Werner brightly told me that he received a reduced rate for publishing in his own journal. My surprise at this state of affairs must have told on my face, as he sought to explain that other, eminent scientists were involved with the journal and that, despite its problems, it had some stature. He mentioned that his co-editor was George Perry, a professor at the University of Texas at San Antonio. Perry is also the editor of the *Journal of Alzheimer's Disease*, one of the most respected publications in the field. Why was a respected neuroscientist registered as the editor of a predatory journal? I realized that the links between predatory conferences and predatory publishing might be stronger than I had first thought, and resolved to find out how OMICS had managed to convince so many researchers with their events and journals.

A NEW WAY FOR ACADEMIC JOURNALS?

"I wanted to make a difference in the way they ran the journal. I'm an experienced editor and I wanted to make an impact on the publication's quality," Perry tells me, after I get hold of him a couple of weeks after the conference. He explains that OMICS reached out to him some years back, asking if he would be able to take up an editorial position. Perry saw OMICS' open-access model as a different way for researchers to approach publishing: "I was really intrigued by the open-access

A scientific conference.

iStock, Cimmerian

model because I thought it was going to change the way journals function. Now, I'm not so sure."

Perry tells me he repeatedly raised his concerns about OMICS' editorial process, even threatening to resign his editorship if changes weren't made. At first, that worked, and practices were altered, sometimes overnight, says Perry, especially when he talked directly to OMICS founder and CEO, Srinababu Gedela (Gedela did not respond to requests for comment for this article). Over time, however, OMICS employees stopped responding. "They're not terribly capable people," Perry tells me. Eventually, he had had enough. "I can tell you it's extremely difficult to resign from them. I tried to resign a number of times." Perry tells me he has never met Werner, and that he has completely lost faith in what he initially thought were OMICS' good intentions: "I don't feel that they have a commitment to moving forward. I did feel that years ago. That's why I stayed with them. I felt that very strongly because I really was intending to change the picture of that publication. I thought that the information flow in science was going to change."

THE 48-HOUR PEER REVIEW PROCESS

I reach back out to Morelli, now back at home in Italy. I'm keen to hear how the second day of the conference went. Suffice to say, not much better. "When I was showing my poster, the colleagues who were supposed to judge them did not look so keen to ask critical questions. The whole thing didn't appear very professional," she says.

After the conference, Morelli found that the email address she had used to register was being spammed with messages asking for article submissions to OMICS journals, promising that her submissions would be reviewed in just two days. "That's an impossible timeframe to get proper peer review," says Morelli. "This opportunity can be appealing for young researchers, who need to publish. There is some real pressure behind it".

THE PREDATOR'S TRAP

Predatory science, be it in the form of journals or conferences, sounds easy to avoid on the surface; a less-than-honest operation that can be simply outsmarted. However, after talking with the conference attendees and Perry, I was left with the realization that predatory organizations are smarter than they may first appear. Their habit of preying on early-career researchers works because they are pushed into attending and showing off their work at conferences by the present-or-perish system. This is only complicated when predatory conference companies advertise talks that aren't there, or poster competitions that merely go through the motions.

Morelli says that it's not straightforward to judge the quality of a conference before attending it, but she won't ever attend another Conference Series meeting.

Perry's situation shows that even respected, veteran scientists can be exploited by predatory outfits, who squeeze them for every drop of money or credibility they can. Morelli believes that more needs to be done to get the word out about predatory science to researchers at every level, be it senior scientists, early-career researchers, or even students like Farkas. "I think it's a fraud, actually. I strongly believe that the scientific community should discourage students, doctors and researchers in general from attending these conferences. We need a blacklist of conferences that we can't trust. I hope people will open their eyes and be more aware of the problem."

Have you attended a predatory conference and have a story to share? If so, we would like to hear from you at editors@technologynetworks.com

Leveling the Field in Ancient DNA Research

MOLLY CAMPBELL

Some stories of history are written in ink, and others are written in nucleotide bases. Ancient DNA (aDNA) analysis – the study of DNA from archaeological or paleontological specimens – is perhaps the closest scientists will ever come to a time machine – a window into the past. In this feature article, we explore how inclusion and representation are critical considerations when we look through that window.

THE REALIZATION OF A "GLORIOUS DREAM"

In 1984, Dr. Russell Higuchi – then a postdoctoral researcher in the laboratory of the late Professor Allan Wilson at the University of California, Berkeley – led a study often cited as building the foundations of aDNA research. It was, at least, the first academic account of the field's development. The researchers extracted mitochondrial DNA (mtDNA) from dried muscle samples belonging to a 140-year-old quagga from the Natural History Museum in Mainz, Germany. The evolutionary history of the quagga – extinct as of 1883 – carried physical traits resembling both zebras and horses; to which was it more closely related? Higuchi and his team's successful sequencing of the two short mtDNA sequences confirmed that, indeed, the quagga was more closely related to zebras than to horses. Specifically, it shared a common ancestor with a mountain zebra (known as the Equus zebra) several million years ago.

In an accompanying commentary to Higuchi's paper, British geneticist Sir Alec Jeffreys expressed that "any hopes that molecular biology and paleontology can be fused into a grand evolutionary synthesis by studying fossil DNA, still look like nothing more than a glorious dream." Given the ever-expanding volume of aDNA studies published in the literature today, and the field's recent win of the 2022 Nobel Prize for Medicine or Physiology, you might interpret Jeffrey's reservations as... pessimistic? However, he spoke to the tremendous challenges associated with extracting and studying aDNA – including DNA degradation and exogenous DNA contamination. It would take the introduction of the polymerase chain reaction (PCR) in the 1980s, and the profound impact of next-generation sequencing

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technologies (NGS) in the decades that followed to create the flourishing research field we see today.

It seems Jeffreys' "glorious dream" has been realized. But what has it taught us?

LEARNINGS FROM THE PAST

Almost four decades have passed since Higuchi and colleagues' quagga paper. During that time, the breadth and scope of aDNA studies has expanded exponentially. DNA from archaeological samples has helped to reconstruct the evolutionary history of the human species; the first draft Neanderthal genome was sequenced by Professor Svante Pääbo – dubbed the "Dark Lord" of aDNA by some – and colleagues in 2010. Since then, new branches of the human family tree have been identified, such as the Denisovans. Knowledge of our partial ancestor's DNA code has even helped to understand why some people might be more at risk of suffering certain diseases, like COVID-19, than others.

aDNA, recovered from the teeth of individuals laid to rest in graves inscribed with "pestilence", shed light on the origins of the Black Death. A bubonic plague outbreak that claimed 50–60% of West Eurasia's population in just seven years, the Black Death's "launch point" is now believed to lie somewhere in the wider Tian Shan area, an impressive mountain system that straddles the border between China and Kyrgyzstan. Successful sequencing of the woolly mammoth (*Mammuthus primigenius*) genome has even made the prospect of "reviving" the extinct species a plausible reality, with a little help from genetic engineering.

Looking to the past might well offer scientists clues on how to handle the inevitable challenges our planet is yet to face, such as the impact of global warming. In late 2022, a study published in *Nature* outlined the discovery and analysis of aDNA obtained from clay and quartz samples collected from a geologic land point known as the København Formation in northern Greenland. The work uncovered a two-million-year-old ecosystem, one that weathered extreme temperatures. Such a climate would have required adaptation from organisms inhabiting the environment to survive. "It is possible that genetic engineering could [be used to] mimic the strategy developed by plants and trees two million years ago to survive in a climate characterized by rising temperatures and prevent the extinction of some species, plants and trees," Professor Kurt Kjær, a geology expert based at the University of Copenhagen, and co-author of the study said. "This is one of the reasons this scientific advance is so significant because it could reveal how to attempt to counteract the devastating impact of global warming."

Year upon year, records of the oldest DNA recovered and sequenced are shattered. Comprehensive reviews of the field, such as Orlando et al.'s *Ancient DNA Analysis,* offer further reading of work that lies beyond the scope of this article. However, as the study of aDNA continues to evolve, there are wider societal issues being probed, with arguments for greater inclusion, equality and respect for Indigenous communities and their oral histories growing louder. Professor María del Carmen Ávila Arcos, who leads the International Laboratory for Human Genome Research (LIIGH) in Querétaro, Mexico, is one of the researchers championing for sustainable practices.

CHALLENGING UNDERREPRESENTATION IN THE GLOBAL CATALOGS OF GENETIC VARIATION

After her initial interest in aDNA was piqued by the early Neanderthal DNA papers, Ávila Arcos observed how a large proportion of genetics research focused on European or European-descent populations. Sadly, this issue is not confined to the perimeters of the aDNA field. Appeals for increased diversity in genomics research – often used to inform disease risk, progression and treatment in modern medicine – have increased over recent decades. Progress in acting on such calls, however, has been criticized.

"While the majority of ancient DNA research is focused on big-picture, curiosity-driven or 'blue skies' questions, there is a growing appreciation that ancient DNA can be used for more applied aspects of science,"

– Dr. Nicholas Rawlence, director of the Palaeogenetics Laboratory at the University of Otago, wrote in a 2021 editorial published in *Frontiers in Ecology and Evolution*.

Ávila Arcos' chose to direct her time and efforts to counterbalance the unevenness in the field. At LIIGH, her research group explores the genetic history of understudied populations – particularly Indigenous and Afromexican peoples – combining DNA from ancient and modern-day populations. The study of aDNA in this context carries great significance for understanding Mexico's colonial history, and for providing present-day populations with knowledge of their genetic background, she explains.

During the 16th century, the Spaniard Hernán Cortés landed on the shore of

Veracruz on the Gulf of Mexico, accompanied by "conquistadores" (meaning "conqueror" in Spanish). Cortés journeyed onward to the Aztec capital of Tenochtitlán (now Mexico City), eventually colonizing the region and claiming the Aztec empire for Spain, naming it "Nueva España" – "New Spain". Hundreds of years of human suffering would follow. The impact on the Indigenous population was devastating. Not only did European colonization inflict extreme massacre through violence and displacement of the Natives, but it also introduced deadly epidemics. It is suggested that the susceptibility of Native populations to "old world" diseases may have even contributed to the European conquest being possible.

Up to 90% of Native populations were lost in some regions, Ávila Arcos explains: "This drastic reduction in the size of the Native populations decreased the amount of genetic diversity in the Indigenous population, and what we observe today in the present-day population is only a fraction of what existed over 500 years ago."

"To have an accurate notion of the amount of genetic diversity that existed prior to colonization, and how this has changed through time – resulting in the genetics of present-day Indigenous populations (and admixed Mexicans too) – we can leverage the power of aDNA."

FURTHER NEGATIVE CONSEQUENCES OF COLONIZATION – DISEASE

Ávila Arcos is also harnessing aDNA analysis to understand the genetic legacy of the transatlantic slave trade in Mexico. During the Colonial period, millions of individuals from the West Coast of Africa were enslaved and forced to work as laborers in the Americas. "The contribution of enslaved Africans to the construction of our nation has been neglected for centuries, which has resulted in an erasure of past and present Afrodescendants in Mexico," Ávila Arcos says. "Today, several social movements are demanding a recognition of the contribution of Afrodescendants to our history and to our present."

The steps at the National Palace in Mexico City, Mexico. Painted on the wall is a mural by the artist Diego Rivera, one of several painted between 1929 and 1951.

iStock, Joel Carillet

The ongoing research – called "The Afro-Mexico Genomics Project" – started nine years ago, and has received support from Stanford University (where Ávila Arcos completed her postdoctoral research) and The National Autonomous University of Mexico (UNAM). "It started from an authentic interest in learning more about the genetic contribution of African genes to our genetic pool, and also from the frustrating realization of the systematic and institutional efforts to erase Afrodescendants from the idealized narrative of Mexico being the product of solely Indigenous and European admixture," Ávila Arcos explains.

In collaboration with Afrodescendant communities from the Pacific coast of Mexico (regions called Costa Chica and Veracruz), the project team is sequencing DNA extracted from the saliva of over 300 participants and genotyping them. "In parallel we started a project to genetically characterize aDNA from samples of individuals very likely of African ancestry, dated to the early colonial period in Mexico," she explains. Though the work has not yet been published, Ávila Arcos says their current data shows, for the first time, the extent of genetic variation shared between modern African populations present in Afrodescendants from Costa Chica and Veracruz. "We observed higher values in Costa Chica than in Veracruz and have been able to suggest likely places of origin in Africa for this African genetic component," she explains.

Understanding *which* viruses may have contributed to the large-scale death

Returning genetic ancestry results to participants of the Afromexico Genomics Project.

"One important motivation behind our work is the underrepresentation of Mexicans, particularly Indigenous and Afromexicans, in the global catalogs of genetic variation, which dispossesses them from the knowledge of their genetic history and potential beneficial findings,"

– Ávila Arcos.

of Native populations is another important application of aDNA for Ávila Arcos. Her team extracted and enriched viral DNA from skeletal remains found in mass graves located in present-day Mexico City, dating back to the 16th century. The application of aDNA analysis in this context is referred to as paleovirology, and it helped the team shed some light on pathogen biology and transmission during this period. "A remarkable finding obtained from aDNA was that some African-born individuals – who were likely taken to New Spain under force as part of the transatlantic slave trade – carried some viruses: hepatitis B and human parvovirus B19, that were also of likely African origin," Ávila Arcos explains. "This implied that some of the pathogens that were circulating during colonial times had an African origin, highlighting additional negative consequences that the European colonization carried for Indigenous and African populations."

Paleovirology can also offer evidence on ancient social interactions, as a 2020 study of the "red complex" – a collection of three oral bacteria: *Tannerella forsythia*, *Porphyromonas gingivalis* and *Treponema denticola* – revealed. Known to contribute to periodontal disease, *T. forsythia* was detected in dentin and dental calculus samples obtained from skeletal remains spanning the Pre-Hispanic and Colonial period in Mexico. Analyzing the *T. forsythia* genomes, Ávila-Arcos and colleagues noted the presence of specific genes in the Pre-Hispanic individuals that were absent in Colonial individuals – and vice versa. "This study highlights the potential for studying ancient *T. forsythia* genomes to unveil past social interactions through analysis of disease transmission," they write.

TOWARDS SUSTAINABLE aDNA RESEARCH

Ávila Arcos hopes the impact of her work "brings perspective to our rich and diverse past and present, and the need to level the field for historically oppressed populations." She emphasizes, "I also hope it reveals the fabulous potential that aDNA carries to study the many aspects of our biological past. Mexico, as a megadiverse country, has a very interesting natural history – and aDNA can help us study it with a temporal lens."

Leveling the field is not a simple endeavor, however. A consideration for her lab – and the work of any scientist pursuing aDNA analysis – is the cautious handling of ancient material. aDNA analysis requires the destruction of irreplaceable ancient human samples, a responsibility that Ávila Arcos does not carry lightly: "In Mexico, archaeological remains are considered national patrimony. Their destructive analysis should be well justified and

aDNA, A "CELEBRITY" SCIENCE

For a variety of reasons, aDNA studies carry significant appeal for the mainstream media. This includes the popularity of films such as *Jurassic Park* and *Jurassic World*. In her book *Ancient DNA: The Making of a Celebrity Science*, Dr. Elizabeth Jones, historian of science and postdoctoral researcher at the North Carolina State University, suggests that the field should be considered a "celebrity science" which "evolves within a shared conceptual space of professional, press and public expectations that contribute to the shaping of the science."

Pavel Galeana.

carried out responsibly and ethically," she says. The ability to sequence sedimentary aDNA (sedaDNA) may provide a solution in the future. "We are just starting to realize that soil is a magnificent DNA reservoir of whole ancient ecosystems, and it shows a lot of promise for the study of ancient humans, too. I think in the future there will be a lot more focus on sedaDNA for the study of our population history." Ávila Arcos adds, "The best part is that we wouldn't rely solely on destructive analysis of precious human samples to do so!"

Ávila Arcos' work also carries heavy ethical implications – she deals with incredibly sensitive topics and delving into history can no doubt affect present-day populations. "We need to be extremely careful about how we present and discuss our results. We try to always be very careful not to perpetuate damaging narratives or discrimination," she says. Alongside colleagues, Ávila Arcos published a perspective article in *Frontiers in Genomics,* which outlines recommendations for sustainable aDNA research in the Global South. This is a term often used to describe lower-income countries, including those that have been historically oppressed by colonialism.

The team state that the appeal of aDNA studies in the media, combined with trends for this work to be published in "high impact" journals, is driving the collection of ancestral human remains with limited or no engagement with local researchers and appropriate communities.

Dr. Gabriel Renaud, associate professor at the Technical University of Denmark (DTU) – whose research interests center around aDNA sequencing and population genomics – offers his thoughts on the challenges in this space: "The discussion about having 10 or so large ancient DNA labs, mostly found in wealthy countries, that use material from less wealthy countries and publish articles in prestigious journals to tell the history of cultures – that they are often only *vaguely* familiar with – is a movie that we have seen over and over. It reeks of 19th-century 'archeology'," he says.

"We need to strike the right balance between giving back to less wealthy countries – especially to the local scientists that provide the expertise – the need to be careful about telling the story of marginalized populations that have suffered from either genocide or colonization, and first-world scientists who want to do the right thing," Renaud adds.

Much of the discussion and debate surrounding ethical practices in aDNA stem from Indigenous populations claiming respectful treatment of their ancestors' remains and respect of their oral histories, Ávila Arcos says: "Many studies (some stemming from the big labs Renaud mentions) publish papers without proper consultation with Native communities, and do not include them in the discussion, or even check if their findings are somehow in conflict with their oral narratives." Given the violent colonial history of abuse, exploitation and marginalization, minimizing Indigenous voices is a further perpetuation of historical damage, she adds.

How do we strike the balance proposed by Renaud? A "global" approach to aDNA research in the Global South is put forward by Ávila Arcos and colleagues in their *Frontiers* perspective: "This would entail applying global premises of sustainability and justice and maintaining awareness of the historical harms caused by scientific colonialism, extractivism and other forms of exploitation of Global South nations by Global North researchers," they write. "I think my Indigenous colleagues have done a great job at highlighting these issues," Ávila Arcos states. However, their fight for sustainable practices is far from over.

THE CHALLENGE IS PART OF THE RESEARCH, *NOT* A DISTRACTION

Earlier this month, a commentary was published in *Human Genetics and Genomics (HGG) Advances* by Kowal et al. The article is a response to guidelines shared in *Nature* on "the ethics of DNA research

▼ *Dr. Ávila Arcos explains the genetic ancestry results to a participant from Veracruz.*

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on human remains" by Alpaslan-Roodenberg et al. in 2021. According to the *Nature* paper, the guidelines are the culmination of a widespread agreement that globally applicable ethical guidelines are needed for aDNA research, but that recent recommendations are not generalizable worldwide.

Alpaslan-Roodenberg et al.'s proposal is as follows (paraphrased as per the commentary piece in HGG):

1. Follow research regulations
2. Prepare a research plan before study
3. Minimize destructive analyses to "human remains" for future study
4. Make genomic data openly available to the scientific community
5. Consult with relevant stakeholders, which they define as "including but not limited to local communities, archaeologists, anthropologists, geneticists or curators"

However, Kowal et al. argue that "these guidelines do not sufficiently consider the interests of community stakeholders, including descendant communities and communities with potential – but yet unestablished – ties to ancestors." The *HGG* commentary highlights three concerns: the separation of "scientific" and "community" concerns, the commitment to open data which "ignores the principles of Indigenous Data Sovereignty" and the potential risks of not consulting communities that do have established – or potential – ties to ancestors.

"Indigenous consultation for aDNA research is still not a standard in many Global South countries. For this reason, we highlight the need to open spaces for Indigenous scientists and stakeholders to debate these pressing issues," Ávila Arcos says.

Such open spaces include the SING (Summer Internship for INdigenous peoples in Genomics) consortium workshops that have been conducted in the U.S., Canada, Australia and Aotearoa (New Zealand). SING is "working with leaders to change the narrative of Indigenous genomics", and Ávila Arcos is proud that the most recent consortium took place in Oaxaca, Mexico: "One of the debates was ethical aDNA research in the context of Mexico. I was pleased to hear from the Indigenous and Afrodescendant students that took part in the workshop. They are the people that really need to be leading these discussions. I hope to incorporate some of the learnings that stemmed from these discussions in my future studies," she says.

Kowal et al. emphasize that aDNA researchers must not focus on the bare minimum research practice that is legally necessary. Rather, aDNA scientists must lead efforts to ensure communities from across the globe are identified and "engaged in research that affects them". They acknowledge this task will not be without its challenges – nevertheless, "the key difference between our approach and that of Alpaslan-Roodenberg et al is that we see these challenges as part of the research, rather than a distraction from the scientific endeavor," they write.

"I envision a future in which collaborations between resourceful aDNA labs and local research groups are more horizontal and mutually beneficial," Ávila Arcos concludes.

▼ *Participants of the Afromexico Genomics Project receiving their genetic ancestry results.*

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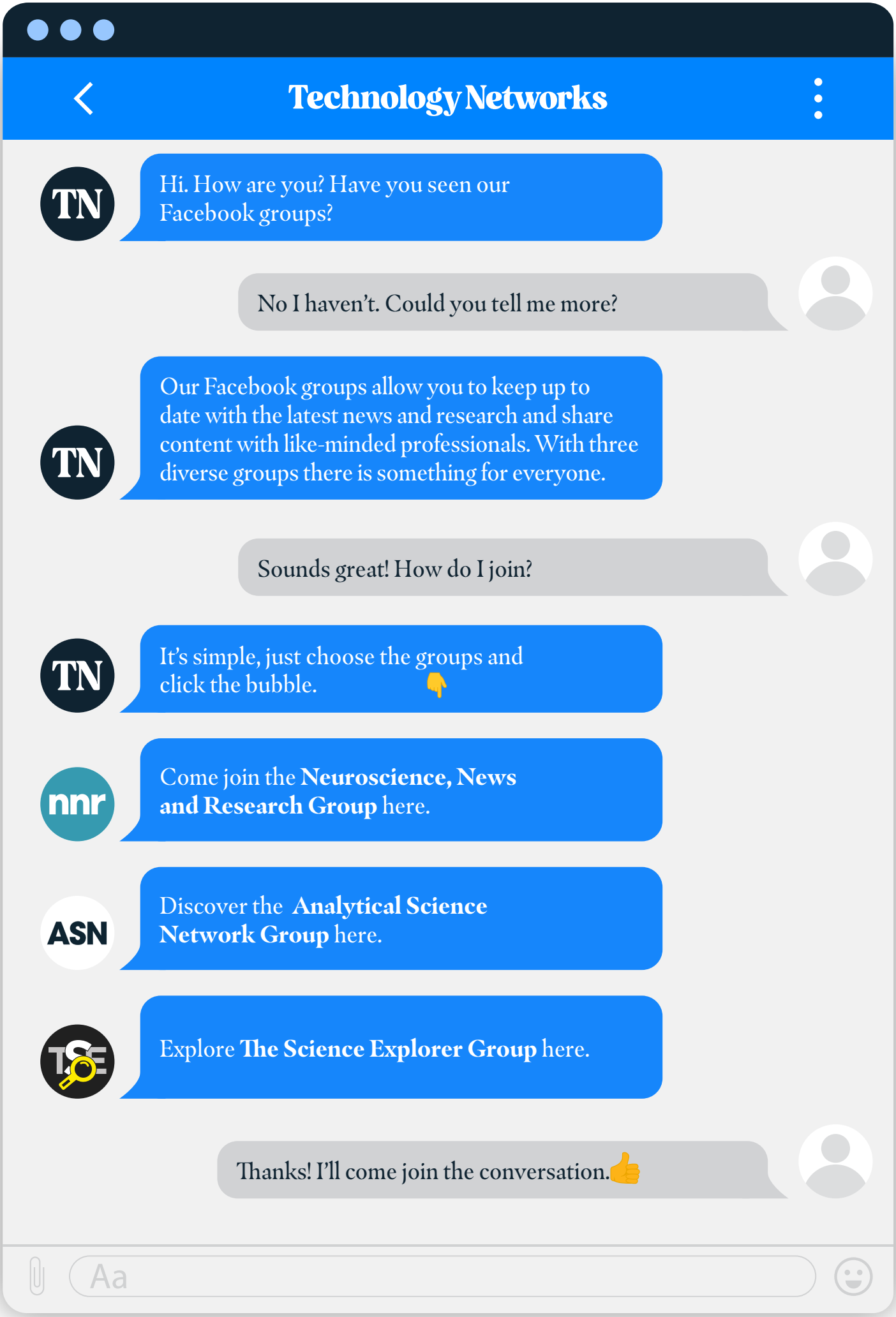
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Aa

Babies, Parenthood and the Brain: What Do We Know?

SARAH WHELAN

Early in life, interactions between babies and their parents or caregivers help to cultivate the infant's growing brain. The brain's basic architecture is mostly present at age two, and selective "pruning" of the neural connections formed during this period continues to adulthood. As a result, these structures are formed through interaction with their early life environment.

Not only can a child's brain be influenced by their parents, but there is also neurological evidence that parents' brains can be rewired to nurture and protect their newborns. Changes in the maternal brain are well studied, and hormones such as oxytocin, prolactin and estradiol all influence maternal behavior in rats and other mammals. However, although changes to paternal brains do occur, these are less well understood.

So, what have we learned about parent–child interactions and brain development from recent research?

WHY BABY TALK SOUNDS SIMILAR AROUND THE WORLD

"Baby talk" – scientifically known as "infant-directed speech" – can help infants to learn their native language. The simple sentences, slow melodic speech and elongated vowel sounds characteristic of infant-directed speech help babies capture a language's intonation and structure. In fact, directing baby talk from other languages toward adults can even help people to pick out new words in unfamiliar languages.

By analyzing infant-directed speech across 21 different societies, a new study led by Harvard researchers suggests that consistencies across cultures show that baby talk may have evolved in response to intense functional pressure. 1,615 recordings of baby- and adult-directed speech and song were collected, covering 18 different languages from 12 language families. They developed a machine learning algorithm, which they found could differentiate adult- or infant-directed speech patterns in the recordings from

acoustic features such as rhythm and pitch. This shows that baby talk shares many common features across different languages, particularly regarding pitch.

HOW MOM'S MOOD MAY AFFECT HER BABY'S LANGUAGE DEVELOPMENT

With the importance and ubiquity of infant-directed speech well established, another study has explored how postpartum depression (PPD) can impact a child's early speech development. PPD can be defined as major depression after childbirth, and it reportedly affects around 10% to 15% of new mothers in Western countries.

To understand the link between PPD and children's language development, Dr. Gesa Schaadt and colleagues at the Max Planck Institute for Human Cognitive and Brain Sciences investigated how the mood of 46 mothers affected their baby's ability to distinguish different speech sounds. Electroencephalography (EEG) data from six-month-old infants, whose mothers indicated a more negative mood two months after birth, revealed that these children had a less mature speech processing ability called the "mismatch response".

The infants were less able to distinguish different sounds from each other, a complication associated with the development of speech disorders later in life. The researchers stress the importance of infant-directed speech for language development, concluding that mothers reporting a more depressive mood may use more monotonous, less infant-directed speech.

DAD'S POST-BABY STRESS LINKED TO KIDS' BEHAVIOR LATER IN LIFE

Bringing a new baby home can be a challenging time for parents. Now more than ever, paternal mental health is being highlighted in the periods both before and after birth, as rates of new fathers seeking help with their mood remain low and the relationship between paternal stress and child outcomes is under-researched.

"To ensure the proper development of young children, appropriate support is also needed for mothers who suffer from mild upsets that often do not yet require treatment," Schaadt says.

A recent study from King's College London has suggested that there is a strong link between paternal stress levels – but not maternal stress – and the development of emotional and behavioral difficulties in their child at age two.

The researchers, led by clinical psychologist Dr. Fiona Challacombe, used data from the Finnish CHILD-SLEEP cohort. They gathered questionnaire responses on stress, anxiety and depression from 901 fathers and 939 mothers throughout pregnancy and the postnatal period. 7% of fathers experienced high stress in the perinatal period (the time just before and after birth), rising to 10% at two years postpartum. The strongest link was between paternal stress at three months postpartum, and emotional/behavioral problems when the child reached two years of age. This was the case even after accounting for maternal stress, anxiety and depression.

Dr. Challacombe continued by saying, "Future research needs to focus on understanding the mechanisms by which this effect may be acting – whether it is paternal behaviors or the impact on maternal behaviors. This will help design the right interventions for fathers. The rise in paternal stress at two years indicates that this does not dissipate over time – returning to work, chronic sleep difficulties and behavioral difficulties becoming more apparent may all contribute."

A NEW STUDY PROVES THE EXISTENCE OF "DAD BRAIN"

Many changes occur in the brains of new mothers, including changes in the volume of gray matter linked to social cognition and theory of mind (the ability to infer others' thoughts and feelings). New evidence now also points to changes in the brains of new fathers leading to the development of so-called "dad brain". Researchers from the University of Southern California, led by Darby Saxbe, professor of psychology, explored how these neuroanatomic changes occur, highlighting parenthood as an important period for plasticity in the adult brain.

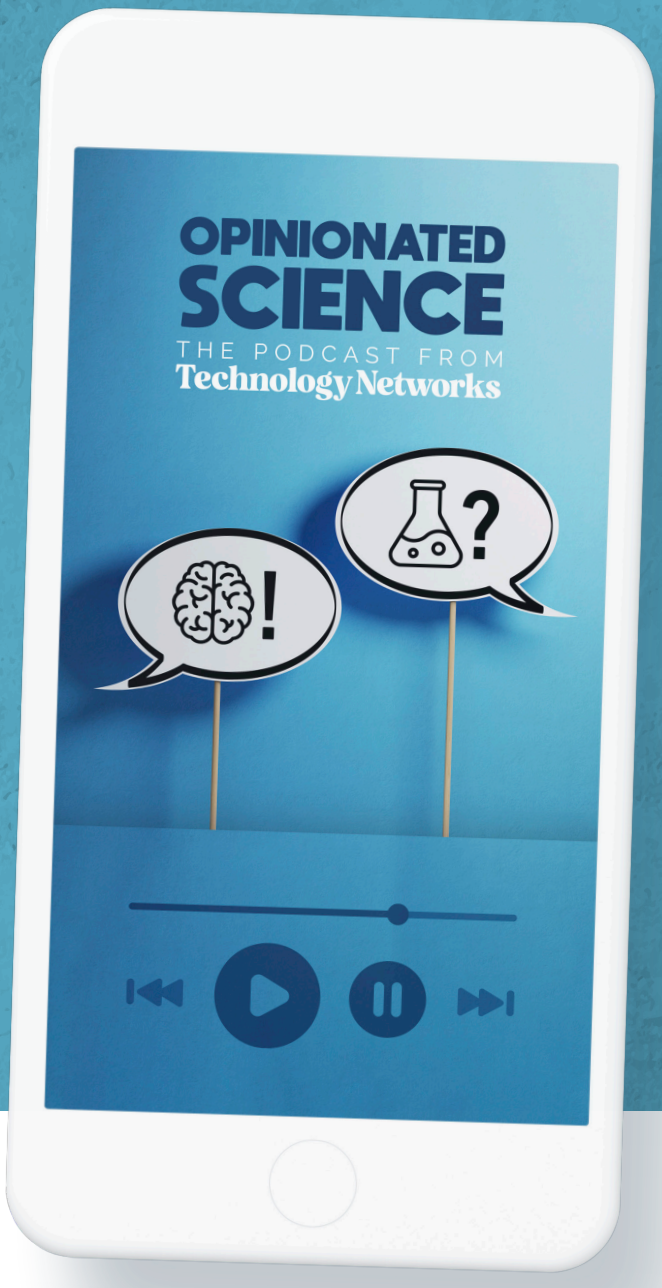
Saxbe and colleagues studied structural neuroimaging data from a total of 40 expectant fathers (20 in the US and 20 in Spain) before and after the birth of their first child as well as 17 childless men (all in the Spanish group).

Across both study locations, significant changes were detected in the brain's cortex. This is the outermost layer that is involved in attention, planning and executive functioning. Comparison of the pre- and post-baby scans showed structural changes in portions of the cortex with roles in processing visual information and in the "default mode network" thought to be involved in empathy. None of these changes were observed in the childless men.

"It's too soon to speculate with such a small sample but it might suggest that more, higher-order cognitive processing is involved in fatherhood specifically," Saxbe said, "whereas mothers are also showing change at the more basic mammalian level. In any case, the fact that we have found changes in the cortex both for fathers and mothers suggests that there is some remodeling of the social brain taking place."

SHAPING NEURAL DEVELOPMENT

These studies highlight the importance of the interactions between parents and infants, which can help to shape the neural and cognitive development of both babies and parents. Future studies may support caregivers to give their infants the best start in life and help us to understand the changes that parenthood brings to the adult brain.



The Future of Vaccines

Opinionated Science welcomes Dr. Armand Balboni for a remarkable behind-the-scenes look into the world of vaccines.

Lucy and Armand discuss everything from how vaccines are developed, to future strategies for global vaccination – including a push toward needle-free vaccinations.

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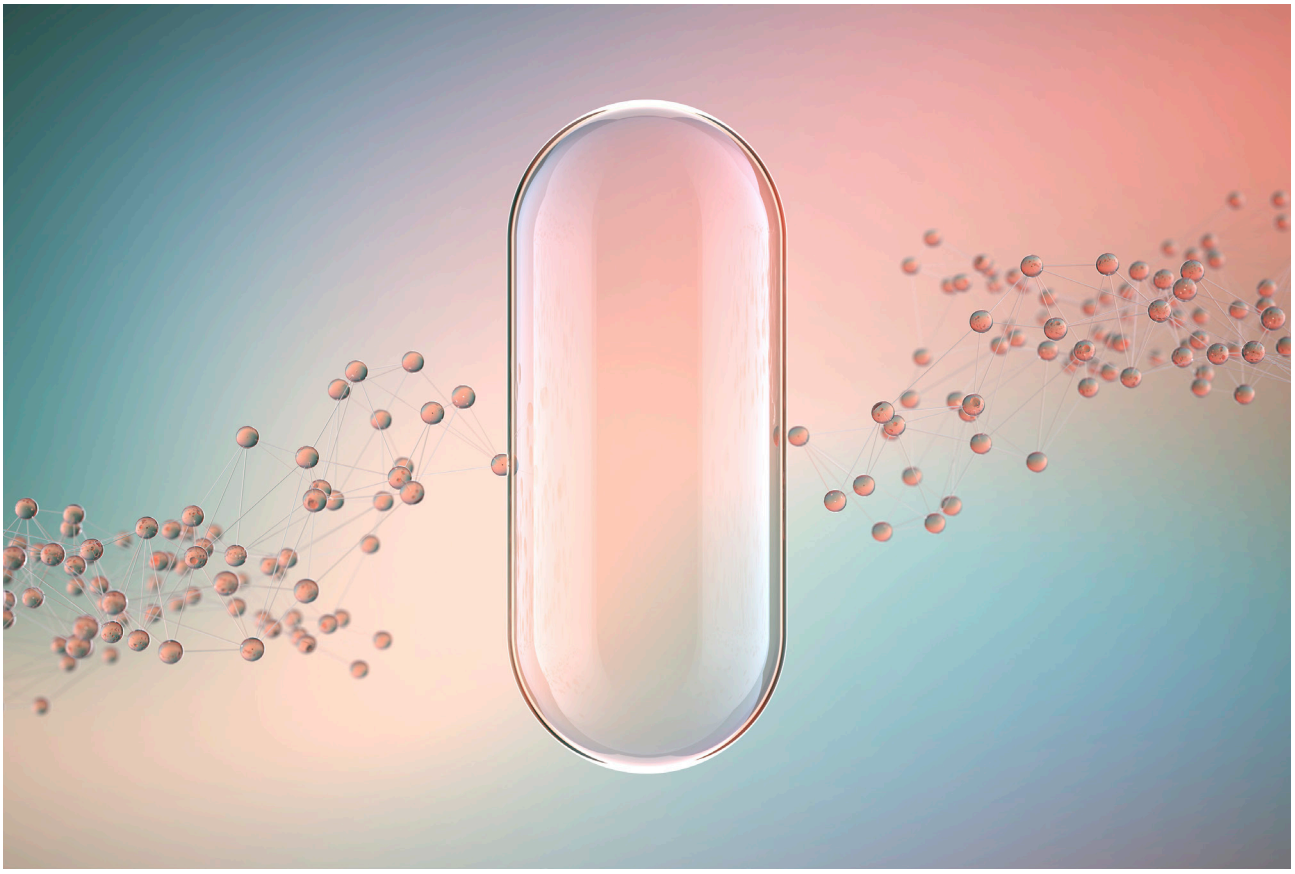

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Improving Drug–Receptor Interactions To Make Medicines Work Better

LAURA ELIZABETH LANSDOWNE

Technology Networks had the pleasure of speaking with Laura Heitman, professor of molecular pharmacology within the Division of Drug Discovery and Safety at the Leiden Academic Centre for Drug Research (LACDR), Leiden University, to learn more about her research focused on drug–target kinetics. Heitman discusses why it is important to determine the length of time a drug stays bound to its target, explains how you can assess a drug's target-binding kinetics and touches on how kinetic computational studies are helping to advance the field.

Laura Lansdowne (LL): Could you tell us about your work focused on understanding and improving drug–receptor interactions?

LAURA HEITMAN (LH): In general terms the research in my group focuses on the theme "**novel receptor concepts to target membrane proteins**" with the ultimate aim to make medicines work better. I have selected membrane-bound proteins, such as G protein-coupled receptors (GPCRs), as many drugs act via these and they play a pivotal role in disease. Of note, the concepts that I work on are in principle "disease-agnostic" and can be applied to many targets and disease areas.

At the start of my tenure back in January of 2009, one of such concepts, i.e., "drug-target residence time" or "drug–target binding kinetics" had not received much attention, if any at all. Since then, it is slowly being realized that the time a drug remains bound to its target may be of greater importance than affinity, in terms of its effect in the patient. More papers are being published that describe the importance of optimizing a drug's binding kinetics. However, few still report on this novel parameter as a *prospective* tool, i.e., designing compounds to have optimal kinetics, rather than "stumbling upon" a compound with an interesting kinetic profile. In the last years, my group has developed several robust and accessible **kinetic assays** and started to publish such data.

Specifically, we were able to show for the first time that the binding kinetics of a drug on its target can be tuned by a medicinal chemistry approach, next to their affinity. This might have great clinical value, as retrospective analysis proves that some marketed drugs have clinical efficacy due to a long target residence time. For example, using one of our in-house designed and synthesized long residence time (RT) CCR2 antagonists, we have shown that high receptor occupancy in an atherosclerosis mouse model was key for high efficacy. Notably, this high (or extended) receptor occupancy results in so called insurmountable antagonism, i.e., antagonists that cannot be disrupted/counteracted by high local concentrations of the endogenous receptor agonist that is often causal to the disease state. As a logical extension to "long" target residence time, my group is currently also working on covalent ligands. As these molecules stay bound to their target infinitely (limited by the protein's life cycle), antagonists will be insurmountable.

LL: How are the binding kinetics of a drug to its target characterized?

LH: This can be done quantitatively and qualitatively depending on the method used. We tend to use radioligand binding assays to qualitatively assess a drug's target-binding kinetics. This can either be done directly by radio- or fluorescently labeling the drug of interest, or indirectly by using a so-called competition association assay where one reference labeled ligand is used that then competes with an unlabeled ligand of interest. In both cases, data analysis by non-linear regression models will provide you with the kinetic rate (k_{off} and k_{on}) values.

"More papers are being published that describe the importance of optimizing a drug's binding kinetics. However, few still report on this novel parameter as a prospective tool," says Heitman.

With regard to quantitative analysis, one can consider using washout assays where wash-resistance of binding or a certain functional effect can be observed. Moreover, in functional assays one can also assess an antagonist's level of "insurmountability", which is basically a phenomenon that occurs when an antagonist occupies the target for an extended amount of time, resulting in a dampening of the maximum agonist response in that functional system.

LL: Is there one experimental technique that you feel has been most impactful?

LH: The introduction of the "surface plasmon resonance" technology has really helped to generate kinetic parameters in early drug discovery. Although some developments are being made, this technique is still not readily available or easily amenable to membrane-bound proteins.

LL: Why are the kinetics of association and dissociation of a target–ligand complex so important?

LH: Despite the efforts (and successes) in finding high-affinity and selective candidate drugs, attrition rates in clinical trials are disappointingly high. Novel concepts such as drug–target binding kinetics are seen as increasingly important for *in vivo* efficacy and safety. This is most likely true because dynamic flow and metabolism in the human body often prevent drug molecules from reaching equilibrium conditions that are otherwise readily attained in the test tube (i.e., equilibrium parameters are still the standard in early drug discovery). Moreover, in a disease-state often different conditions arise at the target site, i.e., increased levels of endogenous agonist, as mentioned above. The compounds' kinetic behavior (association velocity to the target and to metabolic enzymes, dissociation from the target, etc.) might in fact be the guiding principle to obtain a desired and durable effect *in vivo*. Hence, it is important to get a better understanding of the drug–target interaction that is needed and to optimize this at a molecular level *in vitro*. Thus, providing the prospect of better chances for kinetically-optimized candidate drugs in later phases of the drug development process.

LL: How are advances in computational models influencing our ability to explore binding kinetics?

LH: This is not my area of expertise, but I would say that slowly more progress is being made in the field of kinetic computational studies. There are two computational techniques that can aid in understanding and optimizing drug–target binding kinetics – molecular dynamics (MD) and machine learning (ML). For both, ligand–protein structures are needed, accompanied by computing power (MD) and kinetic data (ML). Depending on the type of protein (i.e., membrane-bound or cytosolic) structural data is limited, and kinetic data is currently also still scarce due to its underappreciation. Once the limitations are lifted, these techniques can be used to visualize molecular mode of target interaction, dissociation and maybe even association (MD), and aid in binding kinetics prediction for hit–lead optimization (ML).

Laura Heitman was speaking to Laura Elizabeth Lansdowne, Managing Editor for Technology Networks.

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