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FALL 2022

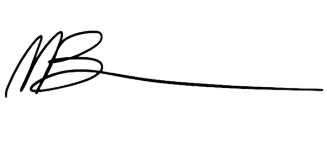
Dear Readers,

I want to start off by extending my gratitude to the rest of the E-Board, and our teams of writers, editors, and artists. Our publication has grown significantly since I first joined in the fall of 2020, which was only made possible by the hard work of our dedicated members and our shared passion for writing about healthcare in an engaging and artful way.

During my three semesters as VP of Editing, one of my roles was to approve topics selected by writers, and I consistently encouraged writers to research the most recent developments in the topics that interested them. I believe that we are the best advocates for our own health and the health of our communities when we stay informed about the newest discoveries—whether they are exciting, innovative, concerning, or even scary—because it is in our best interest to know what lies beyond the horizon in the world of healthcare. I hope that as you read the Fall 2022 issue of *The Cornell Healthcare Review*, both in print and online, you learn something new and find nuanced perspectives on the health issues and trends of tomorrow.

Lastly, I want to acknowledge *Priya Mukhi*, a dear friend who is also graduating and departing the E-Board this semester. Priya inspired me to join CHR, and her work as Co-President last year facilitated the tremendous expansion of our publication. I am continually inspired by her love for medicine, public health, and health equity, which has surely left a positive impact on CHR, and makes me hopeful and excited to see how this publication evolves in the future.

Happy reading!
Mark Bodik on behalf of the Cornell Healthcare Review E-Board



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Artificial Turf and its Unknown Health Consequences

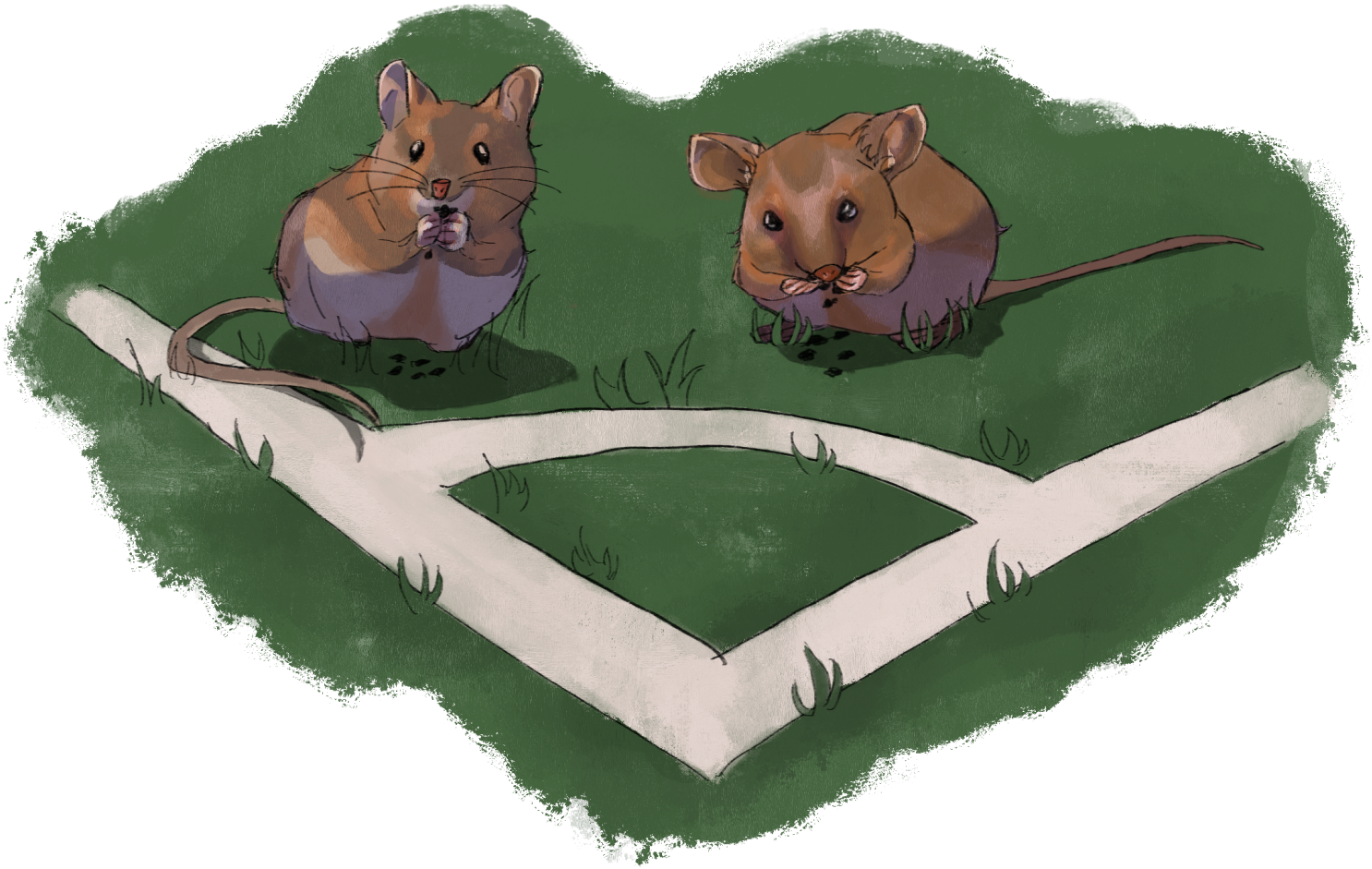
by Juliana Josinsky, Biological Sciences '25

Many cities, high schools, universities, and professional sports teams believe they have made suitable investments in switching from natural grass to artificial turf fields. Artificial turf fields are on the rise because they are more cost-effective in the long term than natural fields, and synthetic fields do not need to be watered or fertilized [1]. However, are the financial savings from these investments worth the possible price of athletes' health? Artificial turf fields are composed of painted synthetic fibers resembling grass and pellets made from tires to resemble soil [1]. These tire pellets typically contain carcinogens, mutagens, and endocrine disruptors [2].

The health effects of these pellets are still largely unknown to scientists. Despite this, the anecdotal evidence about athletes who have played on synthetic fields and developed health conditions years later is enough to scare many parents and coaches. For example, Amy Griffin, an assistant coach for the women's soccer team at the University of Washington, created a list of all her current and former players who were diagnosed with cancer [1]. In 2014, there were 53 players on her list, and more than 60% of the players were goalkeepers [1]. If the tire crumbs contribute to the occurrences of cancer, it would make sense that more goalkeepers would develop cancer due to their increased exposure to the pellets. Goalkeepers constantly dive towards the ground to protect the goal which makes ingesting, inhaling and absorbing the pellets through open cuts more likely [1].

Due to Griffin's list, the Washington State Department of Health conducted a study, but it determined that soccer players were not at an increased risk for cancer due to playing on synthetic fields with tire crumbs [1]. However, the study only measured whether the rate of cancer diagnoses in soccer players in the area was higher than the expected cancer rates for a standard population [1]. Therefore, the conclusion of the Washington State Department of Health does not undermine the possibility that exposure to tire pellets may increase one's risk of developing cancer.

There is also conflicting scientific evidence about whether the chemicals in the pellets and blades of artificial fields, such as polycyclic aromatic hydrocarbons (PAHs) and phthalates, are absorbed by humans at high enough levels to pose a significant health risk [2]. The National Toxicology Program conducted a study where they exposed mice to rubber crumbs in various ways. The mice fed the crumbs had statistically significantly lower



Artwork by Joyce Wang '25

ovary and thymus weights and different hematology values than the control group [2]. The mice with rubber crumbs in their beds had statistically significantly higher liver weights [2]. Despite these findings, they concluded that these results were not biologically relevant and that the leaching of chemicals from the rubber pellets was low [2]. This study suggests that chemicals in rubber pellets do not contribute to adverse health outcomes.

Other studies have found opposing results. For example, one study conducted in Japan examined the risk of cancer amongst children who played on a playground with a natural soil surface and children who played on rubber surface playgrounds [3]. Scientists calculated the absolute risk of developing cancer by adding the risk of ingesting, inhaling, and contacting PAHs through the skin for rubber playgrounds and soil playgrounds [3]. From this, results were confirmed through the Monte Carlo simulation (MCS), a statistical program which allows researchers to input variables and determine how the variable changes the outcome. Through the MCS tool, researchers found the risk of cancer was about 10 times higher for children exposed to rubber surface playgrounds vs. soil playgrounds [3].

There are other adverse effects of playing on synthetic fields that are empirically supported by data. Synthetic fields tend to retain more heat than grass fields which increases the chances of skin burns. According to Penn State University's Center for Sports Surface Research, synthetic fields can reach temperatures between 140° F and 170° F when the weather is hot and sunny, whereas grass fields rarely reach above 100°F due to evaporative cooling and transpiration [4]. Human skin burns within two seconds of contact at temperatures above 120°F [4]. In addition, studies have found higher injury rates among athletes on synthetic fields. A systematic review published in the American Journal of Sports Medicine evaluated the results of 53 studies between 1972 and 2020 which examined the risk of overall and lower extremity injuries on both old-generation and new-generation artificial turf [5]. This review found that among both types of turf, there was a higher rate of foot and ankle injuries on artificial turf than on natural grass [5].

Future studies are necessary to further clarify how detrimental artificial turf with tire crumbs may be to human health. However, the potential risks of synthetic fields outweigh their benefits, especially as universities and professional sports teams continue to invest in their athletic teams. Since the research is still ongoing, all organizations should protect athletes' short-term and long-term health by utilizing natural grass fields.

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More Than a Man's Best Friend

by Ngoc Truong, Biological Sciences '24

Few things can elicit admiration-filled "aws" and make our voices soar five octaves higher quite like pets can. Our fluffy (or bald) companions, including man's best friend and our cat masters, undoubtedly reduce stress and help release "happy" hormones. But, how else do they affect our bodies? Studies have proven the advantages to our health that are associated with interacting with animals for those of all ages, socially, mentally, and molecularly. Most notably, pets can play vital roles in improving mental health and physical health, child development, and the well-being of older persons.

As college students, most of us are well-versed in the language of stress and burnout. The general consensus on the importance of mental health on holistic health is growing by the day, and pets are a major source of healthy hormones for the mind. A 2012 study showed that animals reduce anxiety, depression, and loneliness, as well as high blood pressure [1]. Serotonin, prolactin, and oxytocin, a trio known as the happy hormones, are elevated because of human-pet interaction. Pet therapy is a great reflection of this phenomenon; animals "provide a non-judgmental form of interaction that can motivate and encourage people… Veterans with PTSD have also found therapy pets helpful" [2]. Pets can be a source of unconditional love, but many times, people cannot afford them, have no time to care for them, or feel undeserving. Rest assured, however, pets will always be a source of happiness, whether in passing or not.

Meeting social, emotional, and educational needs are imperative standards for healthy child development. Along with several contributing factors such as adequate sleep, exercise, and a healthy diet, most children receive their social and emotional needs from family and friends [3]. Children in households with a pet, however, can derive some of these necessities from their animals as well. Studies have shown that "children's relationships with familiar animals, especially pets, are unique and different from their relationships with others in their social world," and "exposure to pets should facilitate the establishment and maintenance of relationships with peers" [4]. In a separate study, researchers found that teenagers who cared for a fish were "more disciplined about checking their own blood glucose levels" than those who didn't care for a fish [5], suggesting ownership in any form helps to foster valuable qualities for one's entire life. Moreover, owning pets can also facilitate frequent exercise such as walking, playing, and running, which in turn can improve all areas of life and support developmental well-being.

People age, but the need for social interaction and affection doesn't change. For the elderly, "aging is generally associated with an increase in dependency, multimorbidity, and social isolation," and many times, human socialization is less than what it is in their earlier years (Patto, 2020). Pet ownership, although not a replacement for human interaction, may promote healthy upkeep, such as physical activity, crucial for

Artwork by Nabiha Zaman '23

the physical well-being of people and especially for the elderly. Ruzić et al. [6] "evaluated elderly patients during the first year after myocardial infarction: the group that performed a regular dog walking three times daily had better cardiac performance after 1 year than the group of non-dog owners [7]. Moreover, pet ownership provides a sense of companionship, which may be more important for those dealing with the common tragedies including grief and loneliness. At old age, physical diminishes are bound to occur, such as the stiffening of the blood vessels (as implied before), weakening of bones, and diminished eyesight and hearing [8]. Having a pet (or even better, a guide animal) can directly improve these declines.

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A Body of Plastic

by Gavin Zhou, Biological Sciences '25

Perhaps the single most ubiquitous material in the world right now is plastic, and more specifically, microplastics. Microplastics, pieces of plastic smaller than 5 millimeters in length, can be found practically anywhere in the world. They have been found in the oceans, in the soil, and in the air. They have been found in places untouched by human civilization—from polar ice masses to the depths of the Mariana Trench [1]. These microplastics, being so widespread and hard to avoid, may have health consequences that are not well-known or studied.

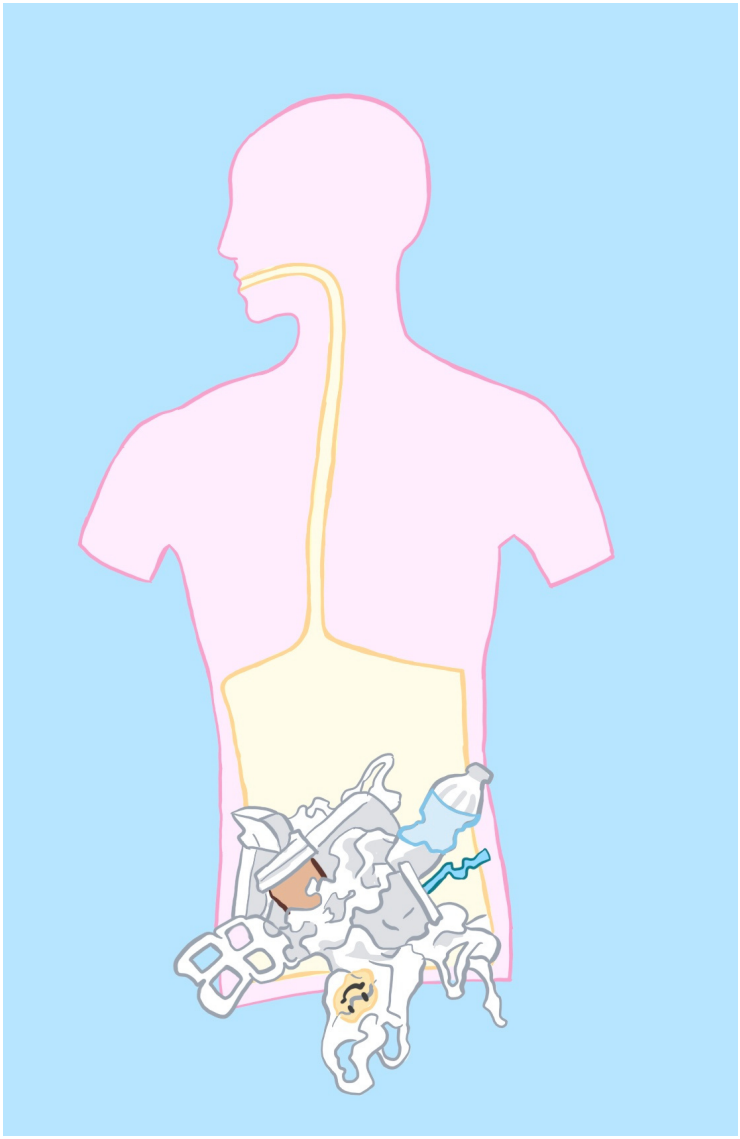
Since 1907, when the first plastic was manufactured, the plastics industry has only continued to grow [2]. According to Verla et al., 0.35 million metric tons of plastic were manufactured in 1950, and in 2017, 348 million metric tons were manufactured [2]. These production numbers only increase as the demand for plastic continues. Being a resistant material relative to its weight and cost to manufacture, plastic is now everywhere in the daily lives of people worldwide.

Macroplastics, pieces of plastic larger than 5 millimeters in length, are often noted as a key environmental pollutant. They are known to harm animals, disrupt ecosystems, and accumulate in large patches in coastal areas and the ocean [3]. Environmental processes can fragment these macroplastics into smaller pieces called microplastics. In addition to being produced from the degradation of macroplastics, microplastics are also often intentionally produced for use in cosmetics and wastewater treatment [2]. As aforementioned, microplastics are incredibly widespread to the point where they are the most plentiful solid waste in the world [1].

Given how widespread microplastics are, their ingestion is difficult to prevent. Microplastics have been found in various types of food and beverages such as bottled water, fruits, and vegetables [1]. The dangers of ingesting microplastics are not particularly well-studied, but research supports the idea that microplastics negatively affect humans in three ways: chemically, physically, and biologically.

Since microplastics have a high surface area relative to their volume, they are very good at absorbing toxic chemicals including heavy metals such as arsenic, cadmium, chromium, copper, and manganese [2]. Other chemicals that can be absorbed by microplastics include pesticides and other persistent organic pollutants. According to Campanale et al., such chemicals are known to be toxic, mutagenic, or carcinogenic, effects that are very detrimental to human health [4].

Physically, microplastics can cause damage as well. If inhaled, microplastics cannot be cleared from the respiratory system, causing inflammation or respiratory lesions. Similar issues can arise in the gut following the ingestion of microplastics [2]. In addition to the toxic chemicals that they can carry, microplastics can also carry organisms like bacteria, leading to harmful infections [5]. An increase in these microorganisms can create antibiotic-resistant bacteria on microplastics, which like other chemicals, can be absorbed into microplastics. Furthermore, the combination of bacteria and antibiotics can lead to dangerous enhanced superbugs [1]. The number of ways microplastics can negatively affect human health is concerning.



Artwork by Fiona Reilly '26

Research on microplastics is a fairly recent venture, meaning there is still much that is not known about the direct effects of microplastics on human health. Much more study is needed to understand the issues microplastics can cause and to identify ways to remedy these issues. Some scientists recommend reducing waste at the source, treating waste in a way that does not release microplastics, and using plastic that can be readily biodegraded.

Further research is needed to identify more specific and effective solutions, but it is known that microplastics are found in what we eat, what we drink, and what we breathe, and that the properties of microplastics make them more prone to carry toxic chemicals and microorganisms. Something so prevalent, yet with effects so unknown, certainly requires more investigation.

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The Consequences of Consanguineous Marriages on a Population

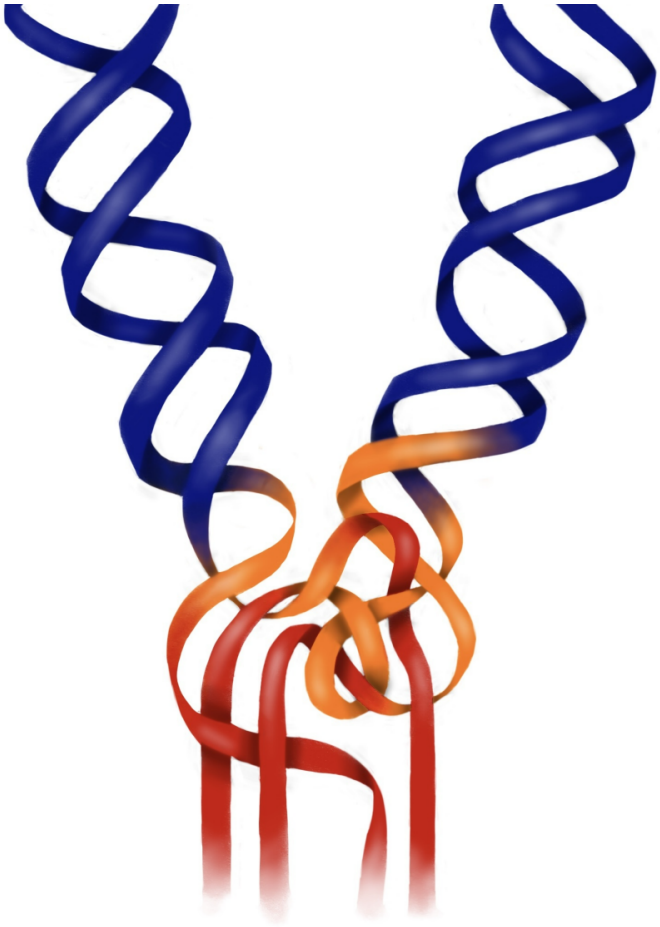
by Tej Ramachandrula, Biological Engineering '25

Imagine that it's your 30th birthday and after years of your parents asking about when you're finally going to get married, they take it upon themselves to set you up with someone: your cousin. In the United States, most of us laugh at the absurdity of marrying our cousin, but in many Middle Eastern, Sub-Saharan African, and South Asian cultures, this practice is highly prevalent. Consanguineous marriage (CM) is the practice of marrying a blood-related individual who is a second cousin or closer; however, the large majority of cousin marriages occur between first cousins, especially between a man and his father's brother's daughter (FBD) [1]. This type of marriage persists because it ensures that property and financial assets stay within the family, offers the security of marrying daughters to trusted spouses, and strengthens the paternal dominance in a lineage [2].

Seeing that the social consequences are generally constructive, what are the genetic consequences of FBD marriages? Examining the average shared DNA between relatives, researchers have found that we share about 50% of our genetic material with our siblings and parents, 25% with our aunts/uncles, and about 12.5% with our first cousins which is a significant, yet reconcilable amount of DNA to share with a spouse [2]. A singular and isolated union between cousins slightly inflates the probability of a harmful recessive trait being expressed in the next generation. Fortunately, one instance of CM can be easily reversed by introducing new genetic material and re-establishing heterozygosity in the next generation [3]. However, more significant issues arise as cousins continue to marry cousins within a family, each instance shrinking the available gene pool for the next generations. This creates a significant lack in genetic diversity which has two main effects — decreased resilience to disease and environmental changes, and the propagation and expression of dangerous alleles in a population.

In a study published by the Journal of Molecular Genetics and Genomic Medicine, researchers conducted an experiment at Hamad Medical Corporation, a tertiary center for the diagnosis and management for certain genetic disorders, on 599 Qatari families with certain indicators of genetic and nongenetic anomalies. Of this group, consanguineous marriages were observed in 397 (66.2%). The study found that "consanguineous marriages had significantly higher risk of Autosomal Recessive disorder compared to nonconsanguineous marriages" with about 50% of consanguineous marriages having autosomal recessive conditions compared to 20% of nonconsanguineous marriages [4]. Interestingly, the researchers found that the expression of recessive alleles was mainly observed in the autosomal chromosomes, meaning that, at least in this population, recessive sex-linked disorders are not propagated through cousin marriages.

Another study conducted on the risks of CM in Bangladesh found that the mortality rate of children under 5 years of age was significantly higher in CM families compared to non-CM families. Moreover, there was an observed increase in both child mortality rate and miscarriage with increased levels of inbreeding, or how closely related the parents are to each other. It was also discovered that CM is associated with the incidence of heart diseases, bronchial asthma, sickle cell anemia, and hearing defects. Despite the tragic effects that CM has had on the population, researchers noticed that "the general attitude and perception toward CM were rather indifferent, and very few people were concerned about its genetic burden" [1]. This qualitative remark has two potential implications: those affected by the genetic consequences of CM have either not been made aware of the threat it poses or that they are aware, but do not value the greater health of their community above the preservation of a harmful tradition. Yet, both studies agree that consanguineous marriages are a large risk to the populations they're practiced in, and that greater social and public health initiatives need to be taken to mitigate the prevalence of genetic diseases.



Artwork by Samantha Smith '26

One particularly analytical perspective proposed the idea that CM has certain biological advantages in a population claiming that "the consequence of consanguineous marriages is an upsurge in the number of homozygous diseased individuals with fewer chances of mating and reduced chances of survival, therefore evolutionarily confining the transmission of disease alleles to future generations and encouraging its elimination from a population" [5]. From a purely functional perspective, the idea of containing recessive diseases within a single community to promote its removal from an entire population seems like an effective course of action. However, even if the immense social and humanitarian issues that this idea presents are put aside, the isolation of a recessive allele is a temporary solution to a reliably imperfect DNA replication process that inevitably results in another mutated allele appearing within the population just as quickly as the first was eliminated.

While we have yet to discover a method for treating genetic conditions directly, there are measures we can take to reduce the harmful effects they have on public health, starting with the reduction of consanguineous marriages. This type of cultural change does not solely require widespread awareness campaigns and policy at the government level restricting CM; it needs time — time for people to shift their values towards their collective health and away from archaic traditions.

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The Vaccination Crisis: How You Can Help

by Flavia Scott, Human Biology, Health, and Society '24

As the world prepares to enter year three of the COVID-19 pandemic, the question on everyone's mind is simple: "when will this be over?" Experts hope that the U.S. population could eventually reach the threshold required for herd immunity, but the new strains of COVID-19 make that pathway very difficult. Thus, the most viable option according to many virologists is mass vaccination [1]. However, as of June 2022, only 78.0% of the U.S. population has received at least one dose, which lags behind other countries with comparable infrastructure, such as Canada (86.7%) and England (80.0%). Only 87.8% of those in the U.S. who have received the first dose have also received their second dose (68.5% of the total population) [2]. This percentage also declines for every subsequent booster [2]. Given that the protection offered by the vaccine and booster shots wanes every few months after the shots are received, it is imperative that a significant portion of the population receives the boosters to maintain the maximum possible degree of immunity. It is easy to feel powerless in the face of such a monumental task, but there are ways to get involved and help stop the spread. Even at Cornell, there are ways to improve the public health of the community.

So what can we do? Well, as with almost any issue related to the pandemic, it is complicated: those with a lot of power and public trust like Dr. Anthony Fauci appear on network television to answer and assuage concerns, national organizations like the WHO take to the internet and social media to provide essential information, and, at the local level, volunteers staff phone banks and take to public gatherings to do tabling and hand out pamphlets.

The biggest hurdle that everyone faces is vaccine hesitancy, ranging from general concerns about the safety to the myriad of rumors circulating regarding the development and efficacy of the vaccine. The unvaccinated are not a monolith either; they range from self-proclaimed "anti vaxxers" to those who go to lengths to distance themselves from the term [2]. There are also some who eagerly get other vaccines and refuse the COVID-19 shots, as well as those who happily receive the COVID-19 vaccines and refuse to get others [3]. With such a range of concerns, it makes sense that any approach to mitigate the woes of the unvaccinated would need to include human connection, patience, and knowledge.

At Cornell, these skills are being put into practice with organizations like Vaccination Conversations with Scientists (VaCS). They hold weekly phone banking sessions, run regular public Q&A sessions, and engage with the community at local events by tabling. When the pandemic made it difficult for Grace Marshall to volunteer, she turned to VaCS. Grace, a Research Support Specialist at Cornell, has been volunteering with VaCS and co-chairing the phone banking committee for nearly a year. She states that "[it's] a good way to connect with people in this sort of limited capacity that were able to... reach out to some areas around Tompkins County with less healthcare resources." She says that while there's a wide range of opinions towards the

Artwork by Flavia Scott '24

vaccine, the vast majority of the residents she's spoken with have been incredibly polite. Grace says the most difficult concerns to address have been when someone believes the death of a relative is linked to the vaccine: "They would ask me how 'many deaths are caused by the vaccine' and...you can't find that number because no one has...in all of the studies, no one has died because of the vaccine." To address these issues, Grace would always offer condolences and empathize with their fears. She found that this approach is often more effective, because it creates a human connection. Leading off with facts is not always the right answer: "if they really believe that someone they know died because of the vaccine, it seems a little insensitive to talk about [talking points] like numbers of people who have swelling in their arm or something."

The COVID-19 pandemic has presented the healthcare system with one of the toughest challenges it has had to face in decades. No matter where an individual stands in their personal stance on vaccination, we are united in our exhaustion with the pandemic

and our hope that things will once again return to some semblance of normalcy. If you are interested in helping with the effort, or even just connecting with others to understand different opinions in an increasingly polarized world, perhaps you could try something like VaCS. As Grace says, the phone calls teach both the caller and receiver: "Even if I'm not able to change people's minds I think it's been interesting for myself to just learn about other perspectives and also try to impart a little bit of knowledge too."

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What Modern Outbreaks Can Teach Us About Public Health

by Anjali Anbu, Global & Public Health Sciences '26

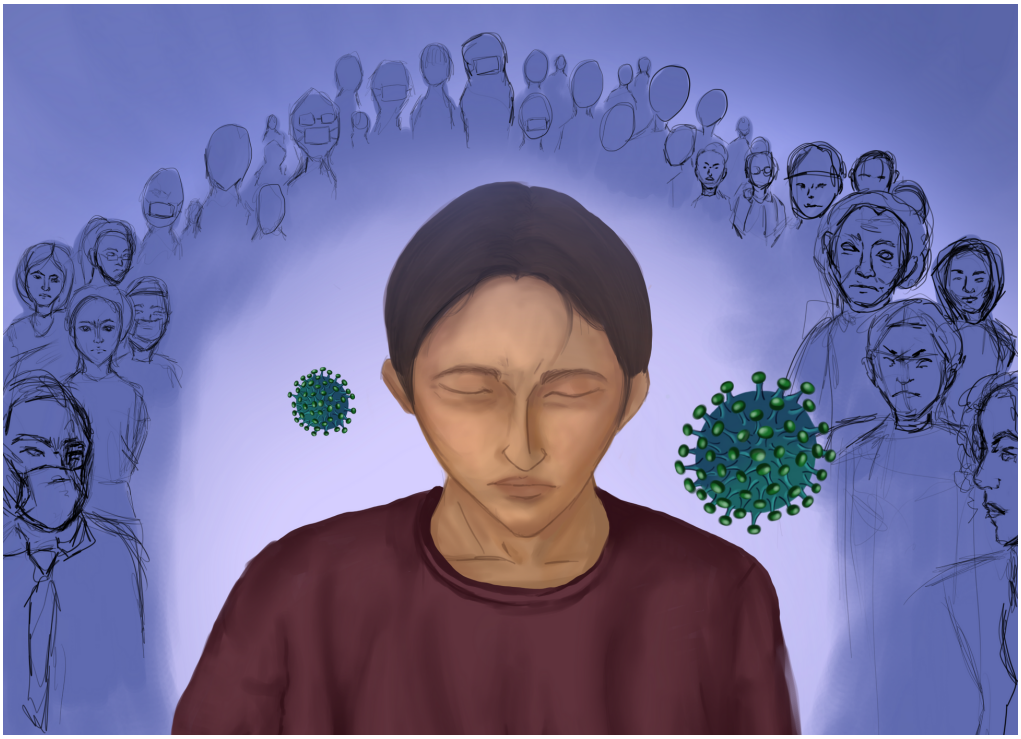
Today, most people who stay moderately up-to-date regarding the spread of monkeypox know the same core facts: contraction is typically accompanied by a smallpox-like rash, it can spread through close contact with bodily fluids, and sexually active queer men make up a significant number of known cases. But when the World Health Organization (WHO) first began publicly commenting about the rise of monkeypox as a potential global public health emergency, official publications were careful about the language used to describe specific at-risk populations. Its bi-monthly epidemiological assessment update, for example, consistently refers to the body of cases as "mainly but *not exclusively*...identified amongst men who have sex with men (MSM)," and its facts sheet about monkeypox does not mention queer populations at all [1] [2]. Indeed, at the second meeting of the International Health Regulations (IHR) Emergency Committee of the UN – a collection of global public and community health advisors to the WHO Director-General – the committee members were unable to come to a consensus about even declaring an international emergency due to, in part, this same concern [3].

The international spread of monkeypox, which was declared a Public Health Emergency of International Concern by the WHO in July 2022, comes hot on the heels of the truly ubiquitous COVID-19 pandemic, for which public health communications took a vastly different approach. Programming from governments and international bodies encouraged people to empower themselves against the coronavirus, and a robust program towards personal risk assessment accompanied this effort. Written everywhere, in every PSA and infographic, was the message: "Individuals with pre-existing conditions or who are over 60 years of age may be at greater risk of contracting COVID and developing serious symptoms." Every other news broadcast seemed to contain updates like: "Increased fatalities among older populations leave care homes and senior living facilities at risk." Practices including social distancing, mask-wearing, and even wiping down groceries prevailed before spread via surfaces could be confirmed. Officials appeared less wary about making statements that could be rolled back, and empowerment surrounding personal risk and protection were seen as key staples of the pandemic response effort.

What, then, was suddenly the problem?

Lessons learned from the HIV/AIDS epidemic, which started in the US in 1981, provide important context for the current government response to monkeypox. When clusters of rare opportunistic infections (infections common in people with weakened immune systems) among MSM communities were linked to Acquired Immunodeficiency Syndrome (AIDS) in 1982, the disease had already killed over 100 people, the majority of whom were sexually active queer men. But AIDS was not called AIDS in the early 1980s: by May 1982, the New York Times had already established the strange outbreaks of rare infections as "GRID" (Gay-Related Immune Deficiency), associating the disease closely with homosexuality for decades to follow [4].

Over the next several years, the association of AIDS with homosexuality had extensive and widely fatal impacts nationwide,



Artwork by Ishani Chopra '24

with over one hundred thousand deaths by 1989. In his famous 1983 call to action, "1,112 and Counting," gay rights activist Larry Kramer writes, "There is no question that if this epidemic was happening to the straight, white, non-intravenous-drug-using middle class, [grant money already held by the National Institutes of Health] would have been put into use almost two years ago, when the first alarming signs of this epidemic were noticed....there would have been... such an outcry from that community and all its members that the government of this city and this country would not know what had hit them."

It is undeniable that slow progress towards research into a treatment and/or a cure for HIV/AIDS is attributable to public stigma against homosexuals and intravenous drug users. By extension, the critical difference between COVID-19 and monkeypox may also be the communities they impact. This begs the question: when a distinct history of medical prejudice against marginalized communities exists, is it acceptable to frame a disease in this way, even if it's true?

Beyond HIV/AIDS, stigma has been used to great effect in public health to change populational behavior. One need only look towards movements stigmatizing tobacco usage in the United States for evidence of stigma contributing to positive health outcomes. Since the 1970s, smoking rates have fallen from 37.4% to 13.7% as a result of what is considered one of the most successful stigma-based public health behavioral campaigns of all time [5].

However, even if the health outcomes can be positive, is stigma a constructive strategy for continued beneficial change? HIV/AIDS would suggest otherwise. Ongoing studies about the continued impacts of HIV/AIDS stigma speak to decades of internalized shame among queer populations, dividing gay men over HIV-positivity status and impeding access to care for all [6] [7]. Even in the "successful" case of American smokers, shame may have been misattributed to users rather than a controlling industry: tobacco users report an increased sense of isolation and shame that makes it difficult to get support, successfully quit, or talk about condition-specific struggles with addiction [8].

Indeed, the utilization of stigma as a method for population health-based behavior control consistently results in significant barriers to assessment and treatment that are difficult to overcome [9]. Consequently, when designing a long-term strategy, stigma should undoubtedly be avoided—an idea that certainly guided the WHO's messaging about monkeypox, and which will continue to be emphasized going forward in future public health emergencies and pandemics.

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Scientific Development is Creating a "Super-Race." Are We Ready?

by Anna Hayek, Biology & Society '25

Have you ever dreamed of possessing a science-fiction character's powers? For instance, the ability to memorize anything by just uploading the information into your brain just like Neo from the Matrix? While this may seem like a far-fetched dream, thanks to rapid scientific advancements, our limited human abilities seem to have new horizons. Without realizing it, we are on the verge of transitioning into a world we are not ready for.

With a tiny microchip in the brain and a quick thought that comes to mind, modern nanotechnological developments such as Neuralink enable us to have full control over our body. By interpreting neuronal signaling and decoding neural activity, these microchips can convert our thoughts into actions [1]. Sounds simple, right? Being able to work out just by thinking about it? Neuralink has got you! But is this what we want our future to look like? Let's take a pause and understand where our blind-trust in science is guiding us.

Co-founded in 2016 by Elon Musk, Neuralink's original purpose was to treat neurological disorders like spinal cord injuries and Parkinson's Disease [2]. However, it seems that this new avant-garde science is now pivoting towards a human enhancement technology. A recent survey by the Roper Center suggests that most Americans are, in fact, sensing the danger of these scientific developments. In 2019, more than half of the participants (53%) believed that scientific developments have equal positive and negative outcomes [3].

By merging biological intelligence with artificial intelligence, Neuralink is clearly elevating the human species into a trans-human species. As its use expands, this science is developing faster than our ability to understand it [4]. While this technology may be legal and scientifically approved, it still has to pass the ethical, moral, and safety test. Because of Neuralink's overall procedure and potentiality to create social inequalities between members of a society, we must draw a line between what "should" exist and what "can" exist.

The idea of inserting a microchip inside the skull might fascinate some, but it is clearly dramatized to look like individuals walking around with thousands of wires inside their brains. Yet while it may sound like a science-fiction movie, it could be our near future.

The problem does not stop there. Another moral consideration is the disproportionate access to this technology. Just like any other neurosurgery, the implant seems to be reserved for people who are able to pay for it.

Because only a certain branch of society will be able to afford this transplantation, some individuals will outperform others in terms of mental and physical abilities. Social discrimination will not only be based on race, ethnicity, and gender, but also on the differences between biological and bionic brains. Are you ready to live in a society growing at two different rates?

Artwork by Joan Rong '25

Being an algorithm-based technology, it is clear that microchips possess the characteristics of any computer or software: the ability to read, translate, and generate information . And just like all technologies, they too can be hacked [5]. But in this case, it is not a simple file or document being scammed, it is the flow of your thoughts! Can you imagine someone hacking your brain? As soon as the microchip enters your brain, this scenario is likely to become possible. Are you ready to jeopardize your

brain's safety?

While he has quite literally proven to us that the Moon is his limit, it seems that Musk's excellency in many domains helped him maintain a prestigious and influential position. As the Elite Cues Hypothesis [6] suggests, Elon Musk is regarded, by many, as a source of accuracy which explains the blind-trust in his innovations. However, is he the one to trust in the neuroscientific context? Are we hyped-up because of the technology itself or because it's Elon Musk's idea? With this, the big question remains: are we ready for this type of scientific development? The answer is yours.

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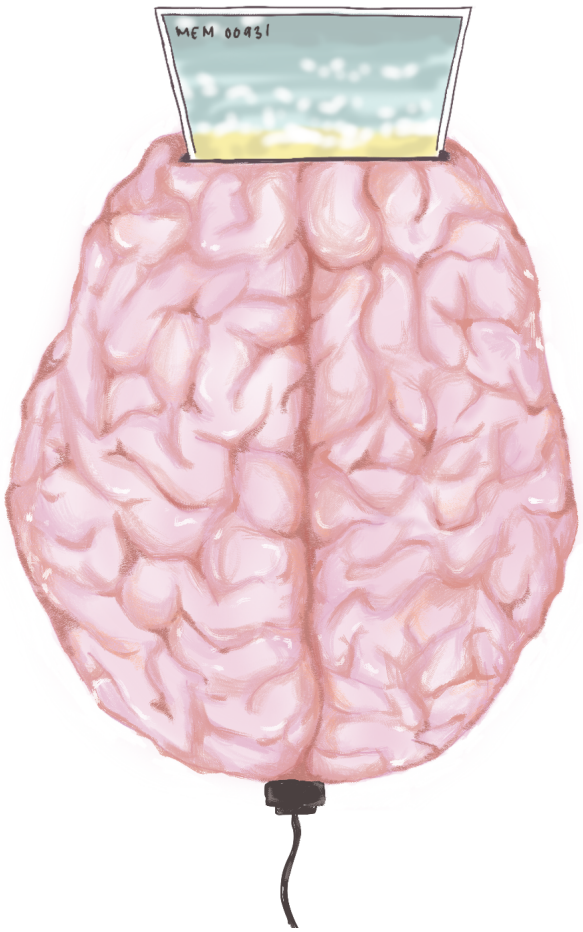
Mind Control in the Name of Medicine?

by Anika Kumar, Human Development '22

We've all encountered the theme of mind reading and mind control in sci-fi novels and films. But with technological progress skyrocketing over the past decade, could these far-fetched, dystopian scenarios become our new reality? Scientists have already created systems that control brain waves and neurotransmitters to communicate with paralyzed patients, restore limb function, and even reduce depressive symptoms. However, new devices are currently being developed at an unimaginable speed and focus on overall human enhancement, such as IQ boosts, that extend beyond the therapeutic benefits of brain manipulation. While such a reality may sound appealing in theory, relinquishing human autonomy to artificial intelligence comes with a plethora of ethical concerns.

One revolutionary advancement that scientists have already developed includes brain-computer interface (BCI) technology, which is important for reading and translating brain wave signals to restore or replace functions of people with neuromuscular disorders. Scientists have been able to build sophisticated AI algorithms to translate information directly from brain activity into computer-generated speech. In one study conducted by



Artwork by Ashley Chopra '24

Angrick et al. (2019), researchers used electrocorticography, a method of measuring brain waves by placing electrodes directly on the surface of the brain, to create neural recordings [1]. These recordings supplied the necessary information to decode the process of speech production in the individual to eventually reconstruct the intended speech audio. Such research aims to create new speech functions for those suffering from conditions like amyotrophic lateral sclerosis (ALS) and strokes. Other applications of BCI technology have involved utilizing brain signals to control cursors, robotic arms, prostheses, wheelchairs, and other devices [2]. Hong et al. (2020) successfully trained amputees and paralyzed individuals to use thought and visualization to control the movements of their prosthetic arms [3]. Studies like this showcase the ability to read and translate brain waves into commands for devices that facilitate human function.

While BCIs have led to substantial progress in the medical field, an important question remains: where do we draw the line when it comes to neural data collection? In one study by Haynes et al. (2007), when participants were asked to choose between two sets of tasks, decoding activity from the prefrontal cortex predicted their choices with a 71% accuracy rate [4]. Human thoughts and intentions become more accessible with the advancement of brain-reading technologies, and as a result, privacy concerns and the fear of non-consensual manipulation are on the rise.

Beyond simply reading and recording neural signals, could tools like BCIs actually be used to *control* experiences in the brain and human behavior at large? Scientists are exploring a number of new technologies and techniques to help patients control their brain waves and nerve cells to treat a variety of behavioral issues and mental illnesses. One such technique is the use of neurofeedback to retrain brain wave patterns as a treatment for sleep disorders and behavioral conditions like ADHD [5]. In one study, Lim et al. (2019) investigated the effectiveness of a BCI-based attention training program in helping patients identify and control ADHD-associated brain wave patterns [6]. The researchers collected EEG data to monitor the brain waves of participants as they played a computer game, and the speed of the game's avatar would increase in response to the detection of waves associated with high attention levels. Through such positive reinforcement, participants successfully learned to identify and control their attention levels, and their ADHD symptoms were reported to have improved [6]. Moving beyond the use of reward-based reinforcement, another non-invasive technique known as transcranial magnetic stimulation (TMS) has been used to control the experience of emotions by releasing powerful pulses of electromagnetic radiation through a person's skull to directly excite particular brain circuits [7]. This technique can treat brain-related conditions like depression and obsessive-compulsive disorder. Along similar lines, yet another new tool called Opto-vTrap was recently developed to control the mind through the use of infrared radiation [8]. By using a single light source, researchers were able to control the release of neurotransmitters, allowing them to manipulate emotion and behavior at a chemical

level. The technique successfully reduced fear memories in mice, and researchers believe that future applications could also aid in epilepsy treatment, muscle spasm treatment, and skin tissue expansion technologies [8].

Although new methods and devices designed to restore function for those that are disabled seem beneficial, they walk a fine line between therapeutics and enhancement. For example, a device known as Neuralink, which is an implantable brain chip currently being developed by Elon Musk, aims to counter the effects of neurological diseases like Parkinson's disease and restore mobility to people with spinal cord injuries [9]. However, another major goal of Neuralink is to enhance human performance in terms of game experiences, telepathy, cognitive abilities, and symbiosis with artificial intelligence [10]. The neuronal activity collected by devices like Neuralink is the same activity that encodes our personalities, emotions, memories, decisions, actions, and the entire individual human experience. By surrendering this data to a separate entity, we run the risk of sacrificing human autonomy and simplifying our existence into pieces of recordable data that can be manipulated for profit-seeking purposes.

Could controlling social behavior with such devices help us achieve an ideal world and strengthen human potential, or would such a phenomenon create a dystopian future built upon an imbalance of power and unequal access to critical human data? How would we decipher between true human experience and neurologically manipulated thoughts and emotions? What types of "enhancement" would be prioritized, and who would ensure the ethical use of BCIs? Could these technologies actually be used to produce harmful effects on human behavior? While these questions enter speculative territory, it is critical to consider the future impacts of developing devices that read and control human behavior.

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Sex Difference Research: Neurosexism or Necessary?

by Aindri Patra, Biological Sciences '25

"A gendered world will produce a gendered brain," Gina Rippon, a British neuroscientist, proclaims. Famous for her books, The Gendered Brain and Gender and Our Brains, Rippon claims that there is no validity to the research on the biological basis for differences between male and female behavior. Yet, researchers continue to pursue sex difference research — why?

Since the 19th century, research results, such as the "missing five ounces" of the female brain, are used to tout the narrative of female inferiority [1]. Scientists used neuroimaging to argue that women have higher emotional processing, in turn saying that men have more white matter than women, allowing them to better focus on one single task and women to better multitask [2]. Every year, dozens of papers are published on the sex differences between men's and women's brains. Researchers often use these findings to make arguments in favor of an unequal society, that women are better fit for certain behaviors than men are, perpetuating stereotypes about women, also known as neurosexism. Neurosexism is a term employed to inaccurately justify the differences between men and women using biological factors. Given how easy it is to manipulate scientific research to promote harmful stereotypes, is there even a need for sex difference research?

In the aftermath of such claims, others began to study whether there truly is a difference between traditionally male and female brains. In 2010, Cordelia Fine, a British psychologist, published a book criticizing the idea of an innate difference between male and female brains, arguing instead that societal expectations and values have socialized us through the years, leading to these gendered behavior differences that we see [3].

However, while science and neuroscience research has historically been used to undermine and perpetuate harmful stereotypes against minorities, studying sex differences can be crucial. For instance, the presence of certain hormones, such as estrogen or testosterone, during development can have different effects on gene regulation in various animals [4].

The sex of the patient could affect their prognosis, which can shape the treatment they receive. For example, research on multiple sclerosis (MS) in mice found that pregnant females had protection from the disease because of a biological disease modifier of pregnancy, a key finding the researchers wouldn't have noticed if their research was only conducted in male mice. Sex differences, if studied with the right intentions and presented in an objective and factual manner, can be beneficial in understanding more behind these differences. It could allow for research to be conducted as accurately as possible [5]. MS is just one example among countless diseases where males and females have different prognoses. For instance, stroke is another good example of how scientists have found that drugs that work in women don't always work in men.

This type of sex difference research focuses on understanding the difference in the biological basis of disease rather than the difference in behavior. This is a key distinction to be made. Biological focus makes it easier to separate sex differences from the gender norms placed by society — as Fine argues, the reasoning for the behavioral differences between the two sexes.

Artwork by Ishani Chopra '24

Ultimately, an underlying biological difference between the two sexes leads to the different effects of the same disorder [6]. Medicine cannot follow a one-size fits all approach, as every person is different, including on the biological level.

Women and men are not the same, but a difference doesn't mean that one is better than the other. *Difference should not and does not mean inequality.*

While this is true, scientists must be cautious about the language they use to describe their research and the results they find, because it can be very easy for those results to be misconstrued and represented. This issue extends beyond discrimination against women; the process and portrayal of scientific research can directly affect the transgender community [7]. The language used to associate certain traits with a particular sex or gender draws attention away from the true biological mechanism. We have to realize that many of the traits associated with one sex or the other and the categorizations of genders are largely socially constructed.

Precise language must be used when researching sex differences "that focuses on the variables themselves" while "acknowledging that people express these variables in ways that may not conform" [7]. Scientists in the past have allowed for societal norms to cloud the way that they interpret and present their research, which is what led to the sexist spin of sex difference research.

The dangers that studying sex differences can pose — including the opportunity for misuse — often permeate much of the work in the scientific field. It remains important for the researchers to identify the differences between each person and the potential impact of their sex while still being careful with how their research is presented and the language that they use. Sex difference research can easily be warped to fit the narrative that members of society would like to promote; it is imperative that scientists be vigilant in their research, while also presenting their findings clearly to avoid harmful misinterpretations.

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The Overturn of Roe v. Wade and Surrogacy

by Yoojin Jung, Human Development '23

On June 24th, 2022, the U.S. Supreme Court overturned Roe v. Wade, a monumental court decision that had previously given women the right to abortion and autonomy over their own bodies. With the overturn of such landmark legislation, this news received worldwide attention. The federal settlement retracts women's rights as well as the health and lives of their babies. This decision stirred controversy among the public and is debated due to its consequences on mothers and families across the U.S. Moreover, this decision has affected the less-talked-about issue of surrogacy.

Artwork by Fiona Reilly '26

Unlike the overturn of Roe v. Wade, the issues that arise with surrogacy have not received enough attention from both the public and at the federal level. With ever-advancing technology, the number of surrogacy arrangements has been increasing [1]. According to Bandelli, "the number of transfers for [Assisted Reproductive Technology (ART)] cycles using gestational carriers [has] more than doubled, from 2,251 in 2006 to 4,725 in 2015" [2]. Even with the consistent increases in ART procedures including surrogacy, it is oftentimes not included in the agenda for women's rights and women's movement. Moreover, there are no proper regulations and legislation on surrogacy at the federal level, except for the proposal for an updated Uniform Parentage Act (UPA) by the Uniform Law Commission (ULC). Though the demand for attention and resources for surrogacy is increasing, the current resources are not sufficient for the procedures to take place. Such lack of resources will negatively affect same-sex or infertile couples since the lack of proper legislation and regulations may pose risk in carrying out a safe surrogacy process.

In terms of the effect that the overturn of Roe v Wade has on surrogacy, the current U.S Supreme Court decision worsens the already complicated issues concerning surrogacy. One of these issues includes the ongoing debate on its ethics. According to Bandelli, there are two sides to this debate: "an abolitionist front" and "the regulatory or reformist front" [2]. The abolitionist front believes that surrogacy should be banned as they see it as "a violation of human rights and commodification of women and children" [2]. On the regulatory, or reformist, front, there are those who are in support of surrogacy and there are those who are not in support of it. However, both parties believe that surrogacy is "an opportunity to achieve the individual desire of having a baby and at the same time to participate in others' reproduction process" [2]. Such strong opposite views make it challenging to move forward with combating other issues that arise as a result of surrogacy.

Other possible issues that arise with surrogacy involve surrogacy contracts and decision-making during surrogacy. In addition to the biological parent or parents, there is another actor in the play, the surrogate, or the gestational carrier, who is carrying the baby. In the case of making decisions regarding abortion, there is a question of who has the right to terminate \ the pregnancy. Again, the lack of surrogacy-related legislation and regulations puts different actors in vulnerable positions.

There are no specific legislations and regulations for surrogacy contracts at both the state and federal levels. According to Bradley, there is a "large disparity amongst states as to the effect and enforceability of surrogacy contracts" [1]. There are states that do not have relevant laws and regulations regarding surrogacy contracts. Without the necessary policies in place for these contracts, the states put both the surrogate and intended parents in difficult positions, as the surrogate receives compensation for surrogacy and they also carry the child for the intended parents. Proper regulations should be in place for surrogacy contracts so that both parties are able to fairly carry out their roles and undergo a safe surrogacy process.

The recent overturn of Roe v Wade negatively affects surrogacy in the U.S. as it further burdens various aspects regarding surrogacy from surrogacy contracts to decision-making during surrogacy. To minimize such issues, there needs to be proper legislation and regulations both at the state and federal levels that can allow for a more organized, efficient process for all.

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Unmet Needs: Addressing Barriers to Mental Healthcare

by Ishan Shah, Human Biology, Health, and Society '24

The numbers speak for themselves– Over 50 million Americans or 1 in every 5 Americans were experiencing a mental illness in 2019-2020 [1,4]. In 2021, over 5.4 million Americans took a mental health screen, a 103% increase from the previous year and a slightly below 500% increase from 2019 [2]. About 12.1 million people reported experiencing serious thoughts of suicide, and over 1 in 10 American youth are experiencing life-impairing depression [1]. Simply put, it is apparent that the state of mental health in our country is alarming. While mental health conditions were becoming increasingly prevalent to begin with, the pandemic's effects on people's health, financial situations, and social interactions only accelerated this growth. As the pandemic continues, people report heightened mental distress and seek mental health care at unprecedented rates. The situation regarding mental health in our nation is only worsening, but this is not where the issue stops. Mental health disorders disproportionately affect minority populations, and treatment is harder than ever to utilize due to a number of barriers.

Not only is the nation's state of mental health declining, but also there is not an adequate infrastructure of mental health providers put into place. Over one-third of people in the US live in Mental Health Professional Shortage Areas, places with less mental health providers than is needed to meet the needs of the population [5]. It is predicted that the US "will be short between 14,280 and 31,109 psychiatrists in a few years [4]. Because of this shortage of providers, people in the US often find themselves having to wait for a couple months for an appointment. This has led to nearly 40% of Americans suffering from anxiety, depression, substance use disorder, or other mental illnesses to not receive any treatment forms [6]. The lack of accessibility to adequate mental health care is not exclusive to the US. The World Health Organization estimates that 75-85% of serious mental disorders in developing countries were untreated [3]. To address the shortage of treatment providers, many have called for the opening of new psychiatry residency slots to increase the number of trained physicians, but funding for these programs is difficult to allocate on a state and government level. Insurance companies also contribute to the disaster, as most plans cover little to no mental health services, causing this treatment to be more expensive for the patient and also more difficult for providers to offer a comprehensive care plan [7].

These issues, amongst many others, are amplified for minority populations, as cultural and socioeconomic barriers prevent them from accessing sufficient treatment options. In general, ethnic and racial minority groups are less likely to seek mental health care than whites [8]. With respect to cultural barriers for minority populations, the primary concerns are stigmas surrounding mental health disorders, care providers, and treatment methods. Stigmas can lead to potential patients declining or avoiding treatment, worsening the symptoms of their conditions, as they can lead them to feel more isolated and hopeless [8]. In some Asian and Hispanic cultures, having a diagnosed mental illness is

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thought to look bad upon families and is often considered embarrassing or weak. Only 4% of Asian Americans, compared to 26% of whites, would seek help for a mental illness from a psychiatrist or specialist [8]. While it is clear that stigma contributes to the inequalities in mental health, mistrust and overall health status are other major barriers to mental healthcare for minority populations. A few studies have shown that African Americans and Latinos reported a significantly higher rate of mistrust in physicians and care providers than their white counterparts, citing prior experiences where they believe they were mistreated by a physician [8]. Furthermore, the burden of illness is higher for minority populations, and they are more likely to suffer from chronic illnesses. While this in itself is a major issue, chronic illness is recognized as a risk factor for mental health disorders, contributing to the gap in mental health care in our nation.

Many entrepreneurs have taken on the challenge of combating these serious issues in mental healthcare through various projects, startups, and businesses. Startups such as Meditopia ($18.3M Series A funding), NUE Life Health ($26.3M Series A), and Lyra Health ($910.1M Series F funding), increase accessibility to services through a mediation app, offer ketamine therapy through a subscription service, and increase mental health service utilization by employer-provided mental health coverage, respectively [10]. These are few of the many rapidly growing startups in the mental health space that are critical in addressing the various barriers to mental health treatment. While these companies will help to improve the overall situation, some entrepreneurs have taken a more specific approach in targeting minority mental health issues. To address the distrust in care, Kevin Dedner founded Hurdle and, in 2021, raised a $5 million series seed to accelerate his project [9]. Hurdle is a technology service that measures cultural responsiveness and provides appropriate training for therapists [9]. In other words, the company is designed to create a system in which all people can receive treatment from therapists who understand their backgrounds. Another startup project working to combat mental health issues within minority populations is Shine, an app founded by Marah Lidey and Naoimi Hirabayashi, which provides content specifically geared towards Black, LGBTQ+, and women's mental health. Lidey, Hirabayashi, and their team, which is over 80% people of color, have raised $1 million in venture capital funding [9]. These ideas are just the beginnings to a force of heavily needed solutions to the mental health crisis in the US. Americans must continue on the path to developing an innovative mental healthcare system that addresses the various barriers preventing the receipt of adequate mental healthcare for all.

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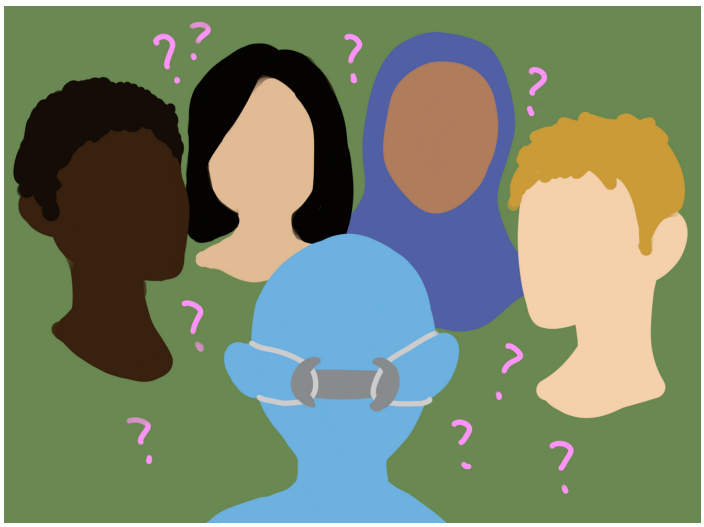
Understanding Cultural Humility In U.S. Healthcare

by Amina Khan, Biological Sciences '22

Communication between physicians and patients presents an issue for one in five individuals receiving healthcare in the United States. [1] This percentage rises to an alarming 27 percent among Asian Americans and 33 percent among Hispanics. [1] Furthermore, population admixture in the US is accelerated now more than ever. [2] How do we then address the issues that arise when healthcare providers treat patients with cultural values which present an obstacle in delivering their treatment plan? Research on patient-centered care has shown that the proper use of language has improved the quality of healthcare through cultural sensitivity, [3] and consequently, through increased patient engagement. [4]

Culture encompasses a multitude of behaviors that are composed of material and non-material aspects that humans have used to communicate with each other as a tool for survival. [3] Over generations, these survival tools have evolved into adaptive behavioral strategies that differ amongst peoples, societies, and subcontinents. [3] In healthcare, culture plays an integral role in the perception of the patient experience as it allows for the separation of objective disease from subjective stress through its influence on diagnosis and treatment plans. [3] The area of diverse complications arises from the range of transforming behaviors, traditions, restrictions, norms, rituals, and political beliefs. [3] Consequently, these shifts in ideas result in major challenges when healthcare providers work with patients from a variety of cultural backgrounds. Although a universal approach that encapsulates all cultural differences would be ideal, this is simply not feasible due to culture's very complexity. [3] This makes competency something akin to trying to capture a fleeting bubble.



Artwork by Angela Yuan '24

In order to understand cultural competency in healthcare, we must define it. Cultural competence includes four facets: cultural awareness, attitudes, knowledge, and skills. [3] In this theory, ompetence is something that can be achieved through a finite understanding of culture. It implies that an awareness and mastery of diverse backgrounds is sufficient to allow for communication between the patient and provider. However, this may also lead to stereotyping and standardization of ethnic groups. Contrastingly, cultural humility emphasizes a process-oriented approach to understanding at-risk groups and the social disadvantages that lead to poor health outcomes. [3] It involves an "intrapersonal and self-reflective dimension as well as an interpersonal dimension that includes respect for others, lack of superiority, and a focus on others rather than self." [3] Cultural humility requires an in-depth understanding of one's own background and how it influences their perspective and formation of knowledge. [4]

Cultural humility in healthcare actualizes as the ability to understand the beliefs a patient communicates by supporting and validating decision-making in regards to screening, treatment, and care options. [4] This care must meet the social, cultural, and linguistic needs their patients possess. Most importantly, this process is ongoing and requires an ability to collect health-related information and respond in a way that displays an intrinsic motivation to hold space for a conversation about the patient's needs. [4] Consequently, the increase in patient engagement validates and increases patient contribution to the decisions being made regarding their health. Claiming to achieve competence in any cultural background is untrue and potentially harmful to patients. [5] Thus, an appreciation of implicit bias demonstrates the need to prioritize the development of cultural humility to begin to create more efficient patient-provider experiences.

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Uninsured, Sick, and Afraid: Realities of Undocumented Immigrants

by Synnie Cao, Global & Public Health Sciences '24

In recent years, the idea of universal health care has gained global momentum, with many countries adopting this model as a national goal. Universal healthcare entails "people obtaining the health services they need without risking financial hardship from unaffordable out-of-pocket payments [1]." It also ensures "financial risk protection, access to quality essential health care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all [2]." Yet, this goal has been unattainable thus far in countries around the world. In the United States, as of 2020, there are over 22.1 million undocumented immigrants in the U.S. About 4 in 10 undocumented immigrants are uninsured, making undocumented immigrants the largest group of uninsured individuals in the country [3]. The lack of coverage hindering undocumented immigrants contributes to healthcare affordability and access barriers, affecting the health outcomes of the growing undocumented population. When considering universal healthcare, we must consider the large numbers of undocumented and uninsured immigrants across the United States.

Undocumented immigrants have had a pre-existing history of discrimination in different sectors of society making it unlikely and unable for them to seek help as an underrepresented group in the US. During the recent COVID-19 pandemic, many undocumented immigrants lost their jobs, resulting in the loss of employer or union-covered health insurance. Moreover, most undocumented immigrants work low-wage jobs that do not offer employer-sponsored coverage. Currently, across the United States, undocumented immigrants are ineligible for coverage through the Affordable Care Act (ACA) Marketplace, Medicare, Medicaid, as well as the Children's Health Insurance Program (CHIP). Only six states—California, Illinois, Maine, New York, Oregon, Washington, and Washington, DC—provide CHIP to children of undocumented immigrants [4]. Although there has been controversy surrounding funds used for public benefits aiding undocumented immigrants, it fails to take into account the billions of dollars and local taxes contributed by undocumented immigrants. According to research conducted by New American Economy, undocumented immigrants contributed $20.1 billion in federal taxes and $11.8 billion in state and local taxes in 2018 [4].

There are many coverage limitations and obstacles undocumented immigrants face in searching for insurance options and affordable healthcare access. Yet, the available options do not cover visits and medications that may not be deemed "necessary." For example, in New York and other states, one available option for undocumented immigrants is Emergency Medicaid. While Emergency Medicaid requires hospitals to treat patients during emergencies, regardless of ability to pay, this coverage only provides medical payment for emergency medical care and service. For example, heart attack, kidney dialysis, labor, and cancer treatment. However, Emergency Medicaid does not cover ongoing medical care and routine health services, preventing undocumented immigrants from accessing preventative health care [5]. Only prescription drugs associated with emergency medical care are covered. Certain prescription drugs that do not meet these standards include proton pump inhibitors for GERD, blood pressure medications, and insulin for diabetic patients.

Limited insurance coverage affects the health outcomes of undocumented and uninsured immigrants and their access to proper healthcare services. Although immigrants usually have healthier chronic disease profiles compared with the U.S. population, the risk of developing a chronic disease increases over time as mentioned by Dr. Colleen Payton [6]. Amongst immigrant populations, there is a lack of knowledge about chronic disease management and a lack of preventive care within communities. This may be a barrier to seeking care in a timely fashion contributing to an increased risk of developing chronic diseases. Immigrant populations in the U.S. are at increased risk for hypertension, diabetes mellitus, cardiovascular disease, and mental health issues. Undocumented immigrants, in particular, face structural, economic, and linguistic barriers that contribute to these adverse health outcomes [7]. This population also faces stressors related to their undocumented status including fear of deportation, discrimination, and stigma within society, which contribute to poor physical and emotional health. Especially during the Trump administration, this fear resulted in families avoiding health programs and seeking medical care. As of now, undocumented immigrants depend on Federally Qualified Health Centers (FQHCs) that provide primary health care, dental, mental health, and pharmacy services that operate on a sliding-scale basis. They also rely on free health clinics operated by volunteer medical students, physicians, and private donations, However, this preventative care is limited as patients do not have access to specialty services for specific health concerns [8].

Moving forward, policy solutions must be made to expand access to health coverage for immigrants. Additionally, policy solutions should consider rebuilding trust and reducing fear to support the well-being of immigrant families. Proposed solutions at the federal level may include
expanding Emergency Medicaid coverage to cover preventative healthcare services, medications, and equipment. Recently, certain states have attempted to expand Medicaid and CHIP coverage. Advancements during the Biden Administration included Navigator programs that provided insurance enrollment assistance to individuals [9]. However, these interventions and policies must involve communities to rebuild trust and reduce fears of utilizing these services. There also is a need to promote outreach and assistance to help uninsured families be aware of their health insurance coverage options. These outreach programs should

2 recognize the racial and ethnic compositions of uninsured demographics and focus on addressing underlying barriers including poor health literacy, unawareness of rights, and fear of stigma. While universal healthcare in the United States requires complex policy implementations and logistical barriers, we cannot define this goal as universal if undocumented immigrants are excluded.

Artwork by Flavia Scott '24

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Federal Versus State Long-Term Care Funding

by Christopher John Arroyo, Health Care Policy '24

Everyone is aging, but not everyone fully utilizes programs such as Medicare, Social Security, and Medicaid that most people pay into. In 2019, only 10% of Medicaid beneficiaries were 65 or older [1], but long-term care (LTC) and Medicare payments made up 22.3% of Medicaid's $728 billion dollars of expenditures in 2021 [2]. Thus, Medicaid made up 42.1% of all domestic spending on long-term services and supports (LTSS) spending [3]. Further, 70% of people will need LTSS in some form [4].

LTC policy has been a concern in health care since the 1980s, when the nursing home industry was rapidly growing. We almost saw the Affordable Care Act (ACA) include the Community Living Assistance Supports and Services (CLASS) Act—which would have established a public LTC insurer—though it was not found to be economically sustainable in the long-run. Other than $139 billion in annual LTC spending by Medicaid [2], the other major quantifiable cost of the current system is submerged: unpaid, informal caregiving. This unpaid labor, along with its opportunity costs, amounted to an estimated cost of $67 billion in 2013 [5]. This is not to mention the largest cost faced by the status quo, loss of life and quality of life for our older adults. Though sweeping national reforms for LTC have not been successful, more initiative may be possible at the state level.

Though the ACA passed in 2010, some key provisions were either never implemented or repealed at some point. Title VIII of the ACA, the CLASS Act, was officially deemed not to be implemented in 2011 and repealed in January of 2013 [6]. The CLASS Act's attempt to create a public LTC insurance market would function similarly to Worker's Compensation, where everyone who pays in may become eligible to utilize the insurance. The CLASS Act would require that individuals pay an average monthly premium of $123 for a potential average daily benefit of $75 as a direct cash support, or at least $50 per day admitted in an LTC facility or utilizing LTSS [6]. These premiums would be adjusted by age, but not by health status. Benefits were also to be triggered given that the individual was suffering from a cognitive impairment or at least two or three limitations in their activities of daily living (ADLs).

The essential problem of the CLASS Act was that paying into the program was voluntary rather than compulsory. The CLASS program was likely made voluntary so as not to mount more opposition against the ACA's constitutionality or palatability; the ACA already intended to eliminate the uninsured population via the individual mandate, which was constitutionally upheld by the taxing power of Congress. A mandatory CLASS Act likely could have been held constitutional on the basis of the General Welfare Clause, however, the basis of other compulsory social programs. Thus, the CLASS program was doomed to suffer from adverse selection and a downward spiral, with costs and premiums rising and few healthy workers opting to pay into it.

In recent years, California, Hawaii, Maine, Michigan, and Minnesota have implemented regulatory reforms to their LTC markets, studied potential reforms, voted on reforms, and even attempted some of these larger reforms. The most successful individual state action came out of Washington, however, in 2019, with the state currently working to implement a universal LTC insurance program with exemptions only for some veterans and people who have already purchased a private plan. The WA CARES Fund is planned to collect contributions starting July 1, 2023 and to begin paying benefits July 1, 2026. The CARES Fund is intended to work as a bridge between Medicare and Medicaid in LTC funding, creating a dedicated pay-for for LTC in Washington and offsetting the state's Medicaid cost. The CARES Fund has a lifetime maximum benefit of $36,500, which is enough to pay for 20 hours of care per week for a full year. This is described as the average level of utilization of long-term, at-home care for Medicaid users [8].

Instead Medicaid remained the primary payer of long-term care for the elderly. LTC has had a place in Medicaid since its inception in 1965, where Medicaid was set to pay for institutional LTC while Medicare would not. This was a large contributor to the rise in nursing home utilization, creating the basis for proposed LTC reform since the '80s and many reforms to nursing homes. In 1981, home and community-based services, including non-medical supports, were added onto Medicaid's benefits to act as a substitute for nursing homes and hopefully save money. Legislation in 1987 expanded these services for frail older adults and increased appropriations to prevent elder abuse in nursing home settings. The final major expansion was a 1990 piece of legislation that allowed Medicaid to pay for a beneficiary's Medicare premium given that they could not [7].

Artwork by Flavia Scott '24

LTSS funding may become a reality once it is clearly cost-saving. This is a difficult position to reach, as LTSS is geared towards people who do not have many economically productive years ahead of them. Effectively, the government is incentivized to let these older adults die and prioritize other populations. The U.S. health care market is rapidly growing and represented 19.7% of GDP in 2020 [9]. Investing in LTC programs and infrastructure may arguably be cost-saving in this regard, through the new jobs and markets it can create.

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Advancement of Prosthetics

by Lauren Peysakhova, Biological Sciences '26

The loss of a limb can have a significant impact on a person's life. We depend on every aspect of our body and any missing part can impede our lives. Limb amputation can happen as a result of trauma or disease. Prosthetics are devices that are designed to replace the missing body part and improve a person's quality of life by restoring normal functions. The quality of prosthetic limbs has improved greatly over the past several years but they remain expensive and treatment is rigorous.

There are many different types of prostheses, with each patient receiving one that specifically fits their needs. When deciding upon prostheses, a person needs to understand their economical capabilities and their functional needs. A passive device is a lightweight prosthetic and is designed to look like the body part it is replacing but has minimum function otherwise.
A passive prosthetic is also static, meaning the device has no movable parts and is useful for bimanual tasks [1]. Having minimal movement, this prosthetic is the cheapest and most affordable option.

Artwork by Phoebe Ahn '22

Body-powered devices, on the other hand, are operated by a harness or cable and can be compared to a bike break in terms of activation. To operate a body-powered prosthesis, a patient would use other parts of their bodies to manually adjust the device. Being one of the cheaper prosthetic options, there is also a sacrifice for fine motor skills and precision [2].

The last type of prosthetic device is an externally powered device or the myoelectric device. This device is the most practical, however, it is the most expensive and takes a lot of time to get adjusted to. Externally powered prostheses provide movement in the joints without the need for movement from other parts of the body. A sensor in the prosthetic can obtain electrical signals from the muscles and translate those signals into movement, allowing the patient to have a greater resemblance of life before amputation [3].

The materials required for the creation of the prosthetic depends on the type of prosthetic that is being manufactured. The more lightweight a prosthetic, the more convenient it is for the patient. Thus, most prosthetics use plastic, rubber, wood, titanium, or aluminum. It is also important to note that prosthetics are individualized treatments, with each person's amputation varying. To make the prosthetic, there needs to be a measuring of the stump. These measurements need to be accurate so that the prosthetic fits well and is close to resembling the original limb. After obtaining measurements, the mold is made to fit the patient using a thermoplastic sheet. Acting as a simulation, the prosthetic is generated using the help of the mold [4]. Customizing and creating the prosthetic can take anywhere from 3 to 6 weeks, with an additional minimum of 18 weeks for physical therapy [5]. There are currently no standards for prosthetic testing and creation, however, prosthetic companies use their techniques to ensure that patients receive good-quality prosthetics that will last for a minimum of 5 years [4].

Rehabilitation is one of the most difficult parts of the journey of recovering a lost limb. Once the prosthetic is obtained, a patient needs to see a physical therapist for at least 6 months [6]. However, there are many other issues in addition to getting used to having a faux limb. These issues can be pain in the limb, back pain, instability, irritation in the skin, fear, socket discomfort, or generally reduced mobility. Because adjusting to a prosthetic is incredibly difficult and demoralizing, the patient needs to have a strong support system. The recovery time can last much longer than six months and the patient will have a lifelong need for doctor visits [7].

Although prosthetic technology has been rapidly evolving, there is still a long journey for prosthetics to become more affordable and have a larger range of motion. In 2012, Easton LaChapelle met an 8-year-old girl who had a bulky passive prosthetic with incredibly limited mobility. The parents were paying $80,000 for the prosthetic plus additional doctor visits and replacement

prosthetics, which cost $160,000 altogether. Amazed at this huge expense for a prosthetic that did not simulate the quality of life as well as an externally powered prosthesis, Easton LaChapelle created a way to 3D print more affordable prosthetics costing between $5,000-$10,000 [8]. Prior to Easton LaChapelle's innovation, there was not a lot of competition in prosthetic pricing because it was a very limited field. However, with Easton LaChapelle's 3D printing and increased mass production of higher-quality prosthetics, prosthetics are becoming more readily available and affordable. Lachappelle continues to work on decreasing the cost of the prosthetic while incorporating a greater range of features [9].

Prosthetics still have a long way to go to become more reasonably priced and give patients an easier recovery process. However, with new advancements, greater options, and more information, amputee patients can continue living their everyday life with support from their family and friends.

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SSRIs: Surprising Science Raises Issues

by Ananda Kalukin, Biological Sciences '26

A media firestorm ignited last summer when a team of researchers led by University College London psychiatrist Joanna Moncrieff and her team published a paper in the journal *Molecular Psychiatry*. The paper, entitled "The serotonin theory of depression: a systematic umbrella review of the evidence," rapidly became one of the most-discussed pieces of scientific literature in the world and garnered substantial coverage in the mainstream press. The topic of the paper, depression, is a serious and widespread disorder that affects 5% of the world's population, causing crippling symptoms such as chronic sadness, despair, and a lack of motivation [1].

Specifically, the *Molecular Psychiatry* paper sought to determine whether the serotonin theory of depression — which postulates that depression is caused by reduced levels of the neurotransmitter serotonin — was accurate [2]. Serotonin is a neurotransmitter that affects numerous aspects of the human brain, including perception and mood, so a link to depression seemed plausible [3,4]. Moreover, some of the most prescribed antidepressants are selective serotonin reuptake inhibitors (SSRIs). SSRIs are theorized to function in the brain by disabling serotonin transport proteins, which remove serotonin from synapses. Therefore, using SSRIs should increase serotonin availability in the synapses and thus treat depression. To evaluate the theory, Moncrieff and her team performed a meta-analysis, examining the conclusions of dozens of papers. Ultimately, the researchers determined that there was no substantial evidence of a relationship between low serotonin levels and depression [2].

These results surprised the public since they seemed to invalidate the use of SSRIs. However, many scientists were unsurprised by the findings. Although the paper's authors allege that the serotonin theory of depression commonly appears in public and educational discourse, other experts counter that it has never been widely accepted within the scientific community [2,4,5]. Depression is an extraordinarily complex disorder that affects many regions of the brain and originates for a wide variety of reasons. Scientists have postulated many causes for depression, some physiological, some environmental, and some social. Aside from biological factors, we know that depression can occur from life events, such as after birth (known as postpartum depression) or as the result of childhood events [1]. Moreover, scientists know that serotonin is involved in a diverse array of physiological functions, and its role in our health cannot be oversimplified [3]. As a result, some researchers criticized the paper for unnecessarily disproving an already-discredited theory, but the debate is still raging. A recently published primary study performed brain scanning on depressive patients and once again implicated diminished serotonin as a factor in depression, though Moncrieff and other scientists criticized flaws like low sample size [6].

However, despite all of the disagreement, one widely accepted point was revealed: scientists do not fully understand how either depression or SSRIs work [4]. What does this mean for the millions of adults who are taking these medications? Fortunately, studies show that SSRIs are effective and on par with alternative antidepressants. Experiments with adults with moderate to severe depression show that using placebos, roughly 20-40 patients out of 100 show improved symptoms after a few weeks. In comparison, roughly 40-60 patients out of 100 improve when treated with SSRIs or other antidepressants. Furthermore, antidepressants including SSRIs can also prevent relapses. Relapses occur in about half of patients on placebos within 1-2 years, but in less than a quarter treated with medication preventatively [7]. So even though we don't understand how SSRIs work, we know that they do work in many cases. Although the idea of taking a drug which is not fully understood may seem unpalatable, it's important to remember that we can still establish its safety and effectiveness. Even aspirin was used for many decades before scientists discovered its mechanism of action [8]. Thus, we need to ensure that there is no stigma around SSRI usage.

Artwork by Angela Yuan '24

One of the most critical impacts of the Molecular Psychiatry paper was challenging prevalent false beliefs about depression. Up to 80% of the public believes that depression originates from a simple "chemical imbalance" [2]. This misconception is dangerous — it promotes the false narrative that drugs are the best, and only, answer. While we should not ignore the potential benefits of

SSRIs, it is vital that we prescribe them carefully, and use them in conjunction with other effective treatments [5]. For example, non-psychiatric approaches like cognitive behavioral therapy (CBT) may be even more helpful than using medication. CBT and other therapies can get at the root of problems underlying depression, helping people cope with feelings and experiences by changing the way they think [8]. Furthermore, combined psychotherapy and medication treatment were found to improve depression remission by 20% over medication alone [9]. Patients should always be encouraged to explore therapy in addition to medication and determine what treatment regimen works best for their specific needs.

Overall, the Molecular Psychiatry paper reminds us that we have a limited understanding of both SSRIs and depression itself, which is a serious challenge to formulating effective treatments. Going forward, we need more research to understand the nature of depression and how it affects our biology. It is also vital that we elucidate the impacts of both serotonin and SSRIs within our bodies. With deeper knowledge, we can increase the effectiveness of medication and other therapeutic strategies. Research will revolutionize our understanding of depression, but we must always keep an open mind about new findings.

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Why Did We Evolve to Have Migraines?

by Hayley Striegel, Zucker School of Medicine '25, Human Biology, Health, and Society '20

Migraine is a debilitating condition that affects more than 10% of people worldwide [1]. Historically, conditions that are disadvantageous to a species decreased in prevalence to the rate of spontaneous mutation. Migraine, despite being disadvantageous to the humans who suffer from it, has not decreased in prevalence at all in the millions of years it has existed, but seems to be increasing in prevalence. With this information in mind, scientists have to suppose that there is an evolutionary advantage to migraine, either in survival or reproduction [2]. The question is — what advantage could there be? By examining the behavioral and neurological correlates of migraine, we can begin to theorize.

Trigger-Mediated Explanations

Have you ever had a headache after drinking a glass of wine? A popular theory for migraine's evolutionary benefit is that it helps us detect toxins in our diet. There are two proposed mechanisms: if a migraineur (migraine sufferer) eats something toxic and gets a headache, they may choose to avoid the food in the future, whereas healthy people will continue to eat the food and may suffer toxic effects; or, a migraineur who eats something toxic and gets a migraine may vomit, eliminating the toxin [2]. This effect is seen in the fact that alcoholism is less common in migraineurs [3]. The effect is stronger for red wine than vodka, as it contains other molecules that may be headache triggers, most importantly histamine [4]. If less toxic food and drink makes it through the stomachs of migraineurs, it makes sense that this would favor their survival, perhaps by reducing cancer risk or preventing acute poisoning [2].

A migraine makes you want to curl up in a quiet, dark room, but why is that? Studies have begun to demonstrate that migraineurs are much more sensitive to visual, auditory, and odor stimuli than healthy controls [2,5,6], not only during migraine attacks but also between them. Interestingly, this seems to lead to an increased ability to process visual stimuli [7]. "This probably results in such behaviors as increased attention to environmental sensory stimuli

Artwork by Janice Indajang '25

such as light, noise and odors, an increased ability to detect and avoid threats in the environment, and a preference to avoid novel or unfamiliar (and therefore dangerous) environments" [2]. These behaviors could be advantageous for survival, from primitive scenarios like hunting and avoiding being hunted to modern scenarios like avoiding a car crash.

Common triggers of migraines include lack of sleep, hunger, and stress [8]. It is not hard to imagine how this could induce behavioral changes in a migraineur to include adequate sleep, regular mealtimes, and lower stress levels. It also makes sense how these behavioral changes could improve overall evolutionary fitness, both reproductive and survival. This theory has not been adequately studied, but it makes intuitive sense, so future research on the topic might help elucidate whether trigger avoidance has conferred an evolutionary benefit to migraineurs.

As a Trade-Off

Cystic fibrosis and sickle cell anemia demonstrate a "heterozygote advantage" pattern in which, while homozygotes experience a debilitating disease, heterozygotes experience few symptoms and have the benefit of being immune to malaria. It is thought that "headache heterozygotes" might experience a similar advantage with increased CNS excitability while having few to no headaches [2]. In a study of the family members of migraineurs, visual responsiveness was significantly increased, which could confer a survival advantage [9].

It is also thought that, since evolution is unidirectional, the development of our higher brain could have been constrained by existing structures like the brainstem. This is likely the reason that the brainstem is unable to suppress excessive excitatory inputs from the higher brain [2]. This mismatch between older and newer structures creates the pain that migraineurs feel but was worth the trade-off because we were able to further develop a highly evolved brain. Supporting this theory, only several instances of headaches have ever been described in another species: one great ape, an orangutan, and a dog [2,10].

Considering genetics, a single nucleotide mutation in the TRPM8 gene, a gene encoding a cation channel, has been implicated in migraine. Recently, scientists investigated the distribution of this allele among populations and found that it was much more common in people living at a high latitude – 88% in those living in Finland vs. 5% in those living in Nigeria. It seems that, in addition to increasing propensity for migraine, the mutation also conferred protection from the cold, and as such the gene was positively selected for in northern populations [11]. Scientists still do not understand why the traits became linked in the first place.

Other Theories

A final theory, which focuses on reproductive fitness, supposes that since migraine improves with pregnancy in many cases, it may have incentivized pregnancy and lactation for female migraineurs. This fits with two facts: migraine is much more common in women than men, and the highest prevalence of the disease is between the ages of 25 and 40 — also the peak reproductive period for women [2].

Conclusions & Future Research

While the evolutionary origins of migraine are still poorly understood, multiple compelling theories have emerged to explain why it might have been advantageous either in survival or reproduction. Future research should attempt to elucidate the connections between other migraine-associated genes and populations, more specifically characterize common migraine triggers, and understand the neurochemistry of migraine attacks in order to identify drug targets.

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The Future of Male Contraception in a Post-Roe Society

by Shruti Nagpal, Global & Public Health Sciences '25

On June 24, 2022, the Supreme Court of the United States overruled Roe v. Wade, the famous 1973 court case recognizing the Constitutional right to abortion [1]. The ruling has sparked changes across the nation with several states tightening their abortion regulations in accordance with the Supreme Court, making abortion less accessible for those who may need it.

With safe abortions no longer serving as an option for pregnancy termination, greater stress has been placed on the need for safe and effective contraception. Contraception currently exists in many forms, but numerous studies show that most forms of effective female contraception can be very dangerous to users.

The most well-known and commonly used contraceptive today is the oral birth control pill. In fact, the NIH finds that "approximately 25% of women aged 15 to 44 who currently use contraception reported using the pill as their method of choice" [2]. The oral pill is a hormone-driven contraceptive, typically containing estrogen and progesterone, that is designed for females and taken daily. Studies show that it is about 93% effective [3], but it results in a number of concerning side effects. According to Paula Cohen, professor of genetics at the College of Veterinary Medicine at Cornell University, the oral pill may result in blood clots, cardiovascular issues, and an increased risk of developing breast cancer [4]. Additionally, the oral pill, like most other common forms of effective contraception, is often controversial because it places the burden of preventing pregnancy on women and limits male responsibility [5].

It's time for society to focus its attention on male contraception.

Male contraception offers an up-and-coming, safe alternative to current birth control methods. Although an understudied field, male contraception has begun to show promising results for pregnancy prevention.

Researchers with the American Chemical Society have developed a non-hormonal contraceptive pill that targets the retinoic acid receptor alpha (RAR-α), a protein involved in sperm formation, in mice. The pill contains a compound called YCT529 that has an inhibitory role on RAR-α. Through veterinary clinical trials, the researchers found that YCT529, when ingested orally for four weeks, dramatically reduced sperm counts and was 99% effective in preventing pregnancy. No side effects were presented, and the mice were able to reproduce again 4-6 weeks after discontinuing the treatment [5]. In light of these positive results in mice, the researchers are in the process of beginning human clinical trials to future test the prospective contraceptive.

Another male contraceptive with recent, promising results is called Nestorone®/Testosterone gel, or NES/T. NES/T is a hormone-based product in the form of a clear gel that minimizes sperm production. The user would apply the gel on each shoulder blade daily. If a user stops using the gel, their sperm levels will return to normal in about four months [6]. The gel has proven effective and safe in Phase 2 of the study, and researchers are hopeful that it will continue to produce results that will allow a Phase 3 study [6].

Researchers at Cornell University are also working on developing a form of male contraception that targets sperm production. Currently, they are identifying the genes that control meiosis in mouse models. [4] With this information, the researchers intend to install a reliable and reversible "on/off switch" on the mice genes using genome-editing technology [4] which would have the ability to successfully regulate spermatogenesis. The research study is in Phase 2, and researchers are optimistic about the data to come, including results regarding the side effects of the contraceptive, if they exist.

In a post-Roe world, it is more important than ever that individuals have access to contraceptives if they choose to engage in sexual activity. It is also critical that women are not left to carry the responsibility of preventing pregnancy and suffer the side effects of common contraceptives on the market. Male contraception has the potential to integrate a greater sense of fairness in society and ensure the well-being of all of the individuals in a relationship. Great innovation is to come in the field of male contraception.

Artwork by Constance Newell '24

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The Future of Precision Oncology: Bioinformatics Solutions and Challenges

by Sarah Lim, Psychology '24

Cancer is a leading cause of death worldwide, accounting for one in every six deaths globally [1]. In particular, advanced and metastatic cancers are notoriously difficult to treat because they are no longer resectable through surgery, which is the mainstay of treatment for most solid cancers [2]. In such cases, alternative therapies, such as chemotherapy, radiotherapy, and immunotherapy, are administered independently or in combination to reduce and potentially remove the tumor. For years, patients diagnosed with the same type of cancer received the same lines of therapy. However, this 'one-size-fits-all' approach to cancer treatment often yields drastically different outcomes for each patient and entails severe side effects, reducing the patient's quality of life. Thus, there is an increased need for the active implementation of precision oncology in clinical practice [3].

Precision oncology is the "use of therapeutics that are expected to confer benefit to a subset of patients whose cancer displays specific molecular or cellular features" [4]. Adopting the precision oncology approach enables oncologists to tailor therapies to the unique biology of the patient's tumor, which improves the diagnosis, prognosis, and treatment of the disease. Unfortunately, precision oncology has only been adopted to a limited extent in the clinical setting despite its potential benefits. However, advances in sequencing technologies and bioinformatics methods, coupled with sophisticated information systems for managing biological Big Data, may offer unprecedented opportunities for the realization of precision oncology [5].

The fundamental idea behind precision oncology is to develop a highly targeted and personalized treatment based on the molecular characteristics of each patient's tumor, which is not new [3]. For instance, cancer biomarkers (e.g., mutational cancer driver genes and protein overexpression) are frequently used to make diagnostic and prognostic predictions. The introduction of high-throughput sequencing technologies such as next-generation sequencing (NGS) in cancer research has enabled oncologists to identify and validate a range of genetic alterations, such as single-nucleotide variants (SNVs), copy number variants (CNVs), insertions and deletions (indels), and gene fusions [6]. Today, the expansion of sequencing technologies beyond genomics, including epigenetics, transcriptomics, proteomics, and metabolomics, has led to an exponential rise in the number of targetable tumor-specific molecular alterations identified through molecular profiling [4]. In turn, bioinformatics techniques play a central role in the integration and analysis of molecular profiling results, which, together with other relevant clinical data, such as the patient's treatment history, comorbidities and complications, radiology imaging scans, and family information, form the basis for therapeutic decision-making by oncologists.

While bioinformatics systems are an essential tool for the large-scale processing of complex clinical data, much work remains to transform the massive volumes of data into real-life treatment recommendations tailored to each patient. An article by Servant et al. (2014) describes an ideal bioinformatics workflow for precision oncology. First, scientists profile patient-derived tumor biopsies (e.g. through microarrays, NGS, immunochemistry, etc.) to assess for mutations and other genetic aberrations. Profiling results are then processed using bioinformatics pipelines to extract relevant information about the tumor, which is then integrated into a shared information system. The system should enable end-users to make queries for real-time data retrieval (e.g. raw and processed data, clinical phenotypes of the patient, etc.) and match treatments to specific targetable molecular alterations. Finally, artificial intelligence (AI) systems should be applied to the bioinformatics pipeline to combine the raw findings from molecular tests with existing clinical data to predict the therapeutic benefits the patient can realistically expect [7].

Several challenges must be addressed to incorporate the bioinformatics workflow into the everyday decision-making by oncologists, namely the lack of adequate technology for the large-scale curation and interpretation of biological Big Data. Unlike other forms of data, biological data is inherently hierarchical and heterogeneous; it exists on multiple levels (e.g. molecules, cells, tissues, organs, whole systems) and in various forms (e.g.,

Artwork by Flavia Scott '24

sequencing data, clinical data, imaging data, behavioral data) [8]. To handle such complex datasets, oncologists must determine how data parameters will be defined to make the data comparable and interpretable for therapeutic decision-making [9]. Data standardization will therefore be an absolute prerequisite for achieving this goal. Furthermore, to accelerate the mainstream use of precision oncology in clinical care, an integrative database of patient-level oncological data must be established [9]. The database should enable real-time access to longitudinal patient data showing the tumor profile, disease progression, treatment pathways, and health outcomes of comparable patient cases [9]. Healthcare organizations, including hospitals, cancer centers, and clinical laboratories, should make a collective effort to facilitate efficient data sharing across institutions and national borders while maintaining strict standards for data quality, privacy, and security [9].

Although leveraging the full potential of precision oncology requires more significant reform, it is without a doubt that the importance of precision oncology will grow immensely in the coming years. The development of cutting-edge bioinformatics systems for storing, processing, and exchanging molecular data and real-world clinical results will play an integral role in the broad adoption of precision oncology in clinical practice. These technologies may pose new challenges in data analytics and governance, which should be addressed through robust data management practices and ongoing assessment of relevant policies. Nevertheless, bioinformatics solutions to precision oncology will help oncologists better understand their patients' disease and make more informed decisions, especially in the treatment of rare cancers for which limited therapeutic options and preliminary clinical trial data are available.

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Physician-Scientists: Bridging Research and Medicine

by Jerome Dovan, Human Biology, Health, and Society '23

Though they occupy an uncommon niche, physician-scientists are critical contributors to the field of biomedical research. This workforce consists of individuals who operate at the interface of clinical medicine and science, and despite only accounting for 1.5% of the physician workforce today, physician-scientists make up an enduring group of science trailblazers [1]. In fact, physician-scientists account for nearly 40% of Nobel Prizes in Physiology or Medicine and are responsible for landmark discoveries including DNA's genetic role, antibiotics like penicillin, and induced pluripotent stem cells [2][6]. The label physician-scientist may lead some to assume that these individuals simply spend half of their time in either the research lab or the clinic; however, the reality is that a physician-scientist's work is founded on the symbiotic relationship between both realms. Trained in both scientific research and medical science, physician-scientists have the tools, experience, and knowledge to take on diverse roles. For example, some may utilize their clinical knowledge to initiate projects investigating clinical mysteries, in turn developing new therapies and treatments, or optimizing existing diagnostic tools [3]. Others may take on unique roles such as advising scientific and research teams, organizations, and even policymakers [7].

For the physician-scientist in training, there are a myriad of career paths that exist. For instance, physician-scientists in academic research often lead self-sufficient research groups consisting of graduate students and postdoctoral fellows. In this line of work, specific qualities that might help a physician-scientist to succeed include leadership as well as originality and creativity when approaching projects [3]. Outside of academia, some physician-scientists may engage in industrial research. This line of work generally entails building a target product profile, which identifies a drug's properties such as the disease states it treats or the route by which it should be administered [3]. Though physician-scientists in industry can take on a multitude of different roles, most will enter a firm as a clinical investigator with a primary focus of collaborating within clinical development teams. Their day-to-day role can vary depending on the stage of the project, ranging from basic scientific and preclinical advising, leading the selection of chemical compounds for clinical trials, providing counsel to teams designing the clinical trial, and bridging communication between laboratory scientists and clinicians [3]. From there, physician-scientists commonly take on major leadership roles, making up as many as 70% of chief scientific officers for pharmaceutical companies [2]. Outside of industrial research, which tends to emphasize commercial outcomes, academic research is much more concerned with discovery. As such, the biomedical research physician-scientists pursue is diverse, encompassing basic, translational, and clinical research. Furthermore, some will even branch out into non-biomedical research fields like epidemiology and health services, looking into the impact of healthcare on patient outcomes [4].

Following the countless and ever-growing career opportunities for physician-scientists, there are numerous different training paths a physician-scientist might undergo. The most common training path by far, however, is the MD-PhD dual degree program which is specially designed for those looking to become physician-scientists. Trainees on this track typically undergo eight years of comprehensive training in both medicine and research, working towards a medical degree (MD) and a doctoral degree (PhD) [5]. For the budding physician-scientist, there are many benefits to this training path: an integrated curriculum, a streamlined training path, the ability to build a network of mentors and future collaborators, and the waived medical and graduate school tuition (plus an additional stipend depending on the program). Nevertheless, while this training path is highly recommended for individuals interested in a future career as a physician-scientist, it is not the only possible path. Physician-scientists may instead choose to obtain a master's degree or participate in non-degree-awarding research

Artwork by Waverly Shi '25

during or after their medical training [4]. Historically, the latter option entailed undergoing postdoctoral training as a research fellow for an extended period. More recently, however, resident training programs have sprung up, such as the UCSF Resident Research Training Program (RRTP) and the Yale Research-in-Residency Program (RIR), offering a synchronous research training program for residents interested in expanding their research careers.

Ultimately, the profession of physician-scientist encompasses a diverse range of career paths within the medical and biomedical research fields. The expanding possibilities for nontraditional training programs for physicians aspiring to do work in research are leading to an ever-growing variety of different professional careers. As the healthcare field continues to be driven by greater innovation and discovery, this group maintains a critical role in bridging science with clinical medicine and patient care. With this, the increasing accessibility of training and career trajectories is a reason for excitement as more individuals will be encouraged to enter the physician-scientist career pipeline.

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Host-Directed Therapeutics: Ideal Targets and in vivo Approaches

by Constance Newell, Biological Sciences '24

The spread of COVID-19 and its subsequent variants illustrate the urgent need to develop combative therapeutics that can quickly identify and attack emerging viral threats. Vaccines, such as mRNA-derived ones, represent the most effective method of viral control [1]. However, all current antivirals directly target viruses by inhibiting their protein functionality, exerting an intense selective pressure that encourages the fixation of drug-resistant mutations within the viral population [1]. Furthermore, viral-directed vaccines are specific, limiting their pan-viral efficacies and the possibility of repurposing for emerging diseases. Vaccine hesitancy, suboptimal efficacy, and the emergence of resistant viral strains exemplify the necessity for alternative antiviral treatments.

Introduction

A promising alternative to traditional vaccines are host-directed therapeutics (HDT). Viruses, like parasites, rely on host cell machinery to survive and replicate. HDTs utilize viruses' host dependency to disrupt viral perturbation, targeting essential host factors for viral replication. These host factors are ideal targets for therapeutics because they will not mutate under selective pressure, lowering the possibility of viral resistance through escape mutants. Furthermore, many viruses share host-dependent factors for replication, so HDTs could potentially increase pan-viral treatment efficacies [1].

However, HDT's implementation requires an extensive understanding of virus-host interactions and the identification of specific genetic regulators of viral infection and replication. Advancements in high-throughput genomic screening with CRISPR have identified various host-viral factors. Furthermore, safe regulation of these factors *in vivo,* remains a challenge. This paper explores promising host-pathogen interactions and the implementation of HDT in vivo.

Modulation of Sialic Acid

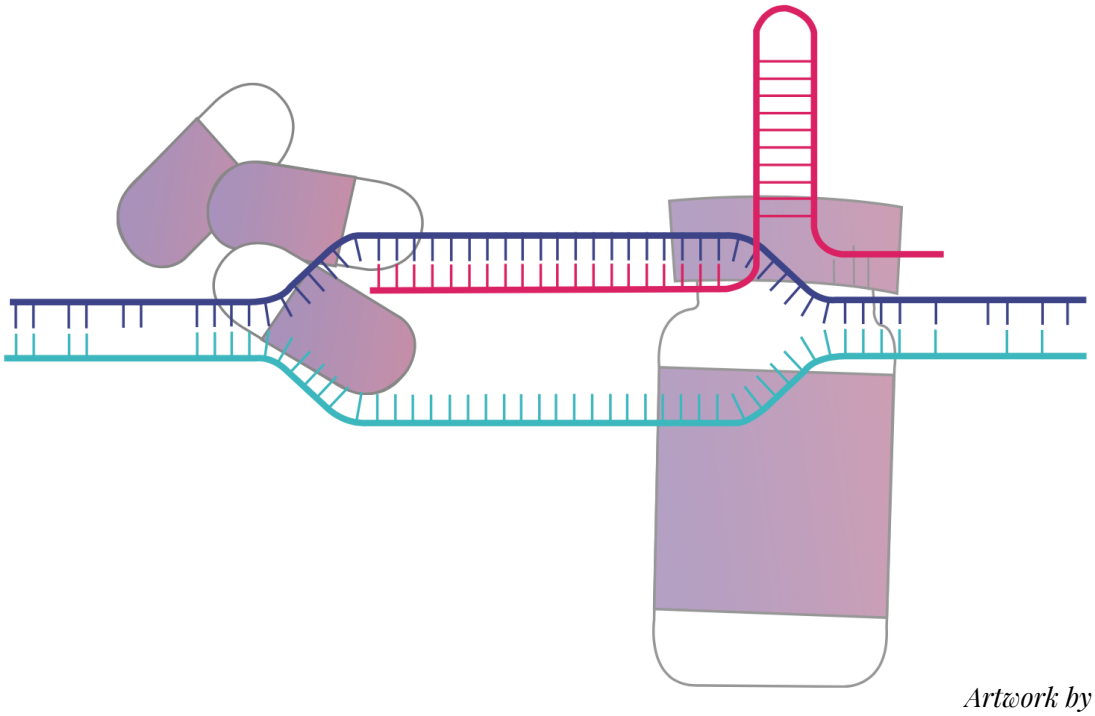
Viruses enter a host through cell surface receptors. Each specific receptor binding site determines its host range and pathogenicity. Sialic acid linked to glycoproteins is a primary receptor for pathogen binding. SLC35A1 and SLC35A2 are sialic acid transporters, and the complete knockout of these genes results in total surface sialic acid removal without increasing cell toxicity [2]. The transporter loss makes sialic acid unavailable for glycosyltransferases and prohibits viral cell entry.

Modulation of Transmembrane

After binding to sialic acid surface receptors, viruses travels through the cell's transmembrane proteins. Transmembrane protein IGDCC4 plays a crucial role in influenza virus internalization into host cells [3]. In one such study, CRISPR/Cas9 gene knockout of transmembrane protein IGDCC4 in mice revealed reduced replication of N5H1 in lung epithelial cells without adverse effects on the mice [3].

Modulation of Endosome

After viral endocytosis through receptor-mediated transmembrane protein, acidification of the resulting endosome releases the viral genome into the cytoplasm. Accordingly, functional ATPase and endosome assembly components were shown to be essential host factors for viral release [2]. In one study, knockout of functional V-ATPase precludes viral endosomal escape [2]. The three proteins, WDR7, CCDC115, and TMEM199, were V-ATPases co-factors and facilitated V-ATPase assembly onto the endosome [2]. Functional loss of these factors led to lysosomal biogenesis and incoming endosome over-acidification, prohibiting viral entry, and increasing invading virions degradation [2].



Artwork by Ashley Kim ' year

In Vivo Modulation

Even with identification of promising host factors, safe modulations of these factors *in vivo* remain a major challenge. Modulating factors are often too broad and run the risk of off-targeting elsewhere in the host, leading to undesirable consequences. A recent study that used mRNA lipid nanoparticles to deliver CoV-2 spike genes as a COVID-19 vaccination strategy was shown to be safe and effective [4]. Although use of mRNA delivery was sufficient in some cases, generally mRNA delivery is highly transient, with maximum efficacy peaking and fading within 48 hours [4].

Self-amplifying RNAs (saRNAs) and CRISPR-mediated gene activation (CRISPRa) may provide a more lasting alternative [5*]. saRNA's are RNA replicases that are derived from self-replicating alphaviruses. Upon delivery, translation of saRNA produces replicases which multiply copies of the original RNA strand [5*]. This replication mechanism induces an immune response at a lower dosage and is shown to have prolonged protein expression of up to 60 days [6*]. Long term expression can also be achieved through delivery of CRISPRa with associate viral vectors. Synthetic CRISPR transcription factors can modulate target genes *in vivo* and it has been shown that removal of VP64 from CRISPR notably decreases gene activation. Therefore, fusion of a transcriptional factor, such as VP64, to a nuclease-dead Cas9 should upregulate gene expression [7*].

CRISPR can also be used to down regulate genes through CRISPR interference and Cas13a. CRISPR interference is composed of a KRAB transcriptional repressor domain fused to a dead Cas9[7*,8]. CRISPRi's are less toxic than Cas9 because they do not cause a double stranded break in the DNA. However, disruption of gene function is more sensitive to guide RNA selection than Cas9 and often results in incomplete gene silencing [7]. It has also been shown that Cas13a can successfully downregulate influenza and SARS-CoV-2 RNA in the respiratory epithelium of animal models [13]. In mice, Cas13a was shown to degrade influenza RNA while in hamsters, Cas13a reduced viral replication and symptoms [12,13*]. These findings suggest that RNA mediated targeting can be an effective and safe way to modulate host genome.

Conclusion

Host-directed therapies provide a promising alternative to traditional viral-directed vaccines. Genome-wide CRISPR screens and meta-analysis studies have identified various ideal host-dependent factors for antiviral targeting. Furthermore, these factors exhibit high efficacy in vivo with minimal host toxicity after being modulated by multiple strategies. Future studies will optimize these factors and identify other antiviral targeting candidates. A better understanding of viral-host interactions will provide molecular insight for broad-spectrum antiviral therapy development against viral infections.

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