Columbia Science Review

Vol. 9, Issue 2: Spring 2013

Fostering Compassion in Medicine

The God Particle
How the Higgs Boson Shapes the Universe

The Secret Life of Plants
Vaccines of the Future?

Our Curiosity Knows No Bounds
Mars and the Curiosity Rover

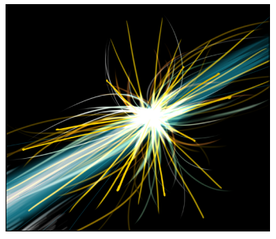
The Columbia Science Review strives to increase knowledge and awareness of science and technology within the Columbia community by presenting engaging and informative articles, in forms such as:

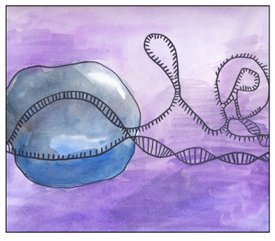
- Reviews of contemporary issues in science
- Faculty profiles and interviews
- Editorials and opinion pieces

Sources and credits for this issue can be found online at www.columbia.edu/cu/csr.

Contact us at csr.spreadscience@gmail.com
Visit our blog at csrspreadscience.wordpress.com

Columbia Science Review



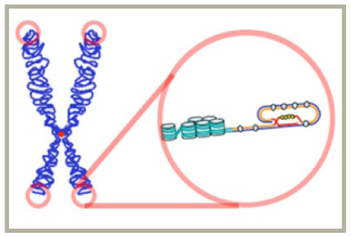


Selby Byashimova
Jenna Lemonias
Diane Wang
Joanna Diane Caytas

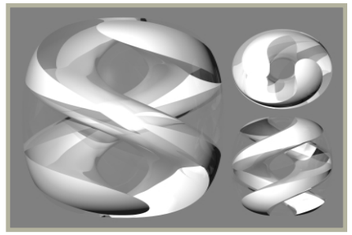
Cocktail Science

Today, the US has imported roughly 80% of Active Pharmaceutical Ingredients (APIs), where 40% of these APIs are "finished drugs" from low- and middle-income countries, such as Mexico and Thailand. The vast majority of these "finished drugs" are generics—copies of the original drugs, but under other names and cheaper. In the United States, those who cannot afford brand-name drugs have no choice but to purchase generics, which could be life-threatening. Unfortunately, the government cannot regulate the production of these generics, even though the factories that produce generics have continuously produced low-quality pharmaceutical products, which can lead to death or drug-related health complications. Furthermore, whether it is a new or familiar drug, all drugs require long-term, continuous monitoring of drug safety because side effects and complications could appear after several years. For instance, doctors needed nearly 50 years to detect a link between aspirin and gastric ulcer development, and scientists needed almost 10 years to determine the link between combined oral contraceptives and the development of venous thrombosis.

Expectant mothers discouraged by the lack of evidence showing that exposure to classical music in utero will make their children smarter might be uplifted by recent results indicating that some birds can relay information to their unhatched chicks. Scientists at Flinders University in Adelaide, Australia recently reported that fairywren mothers teach their unhatched chicks a specific note that the chicks later sing back to them when seeking food. Young fairywrens, native to Australia, include the identifying tone in their call for food as a type of password. The mother fairywrens listen for the password to distinguish their own young from two species of cuckoo birds that are known to lay their eggs in fairywren nests. The mother fairywrens can avoid feeding chicks that are not their own because the cuckoos spend less time in the egg than the fairywrens and do not have time to learn the password. This result is the first evidence that learning can take place in the embryonic stage. Though similar evidence for human learning has not yet been discovered, humans can at least take comfort that they do not have to teach their children the equivalent of a secret handshake to identify their young as their own.



Want to increase both the length and quality of your life? Perhaps the key is to improve the health of your telomeres. Telomeres are "caps" at the ends of chromosomes, playing the vital role of protecting important DNA sequences every time cells divide. It has been known that the effect of aging is due to the shortening of our telomeres as cells divide over and over in our lifetimes. Shorter telomeres are associated with the development of age-related illnesses, such as heart disease and cancer. Researchers at Carnegie Mellon University found that telomere length not only plays a role in determining our longevity, but also affects the health of the young and healthy. In their study, they measured the telomere lengths of 152 healthy adults between the ages of 18 and 55. Afterward, the subjects were exposed to a virus causing the common cold. Two-thirds of the subjects became infected, with a link between shorter telomeres and infection rate. The researchers speculate that telomere length is a marker in disease susceptibility, and that maintaining telomere health can lead to overall well-being. How exactly can you keep your telomeres long and healthy? While the length of your telomeres is predetermined by genetics, there is evidence that getting plenty of omega-3 fatty acids may slow the shortening process. Along with diet and reduced stress, you may be on your way to a healthier and longer life.



While provisional nature and falsifiability are axioms of our notion of science, so is causality. Betting against Einstein has proved exceptionally risky for more than a century. But recent independent discoveries raise the possibility that Einstein's General Relativity Theory may require an overhaul. In September 2011, CERN measured neutrino speeds minimally in excess of light. While the errors cannot be reliably excluded yet, another similar result was observed in 1987 with neutrinos from an extragalactic event, Supernova 1987A, arriving hours before photons originating from the same event. The OPERA experiment at the underground Gran Sasso Laboratory in Italy reported in September 2011, from data collected during 2009-2011, the measured velocity of a muon neutrino to be in excess of the speed of light. Then again, in May 2012 researchers at the Green Bank Telescope in West Virginia observed Pulsar J0348+0432 with 2.04 times solar mass. General Relativity categorically excludes the possibility of such a result. It is important to eliminate logical pseudo-contradictions: Though special relativity declares impossible for an object with any mass to move at the speed of light without consuming infinite energy, it does not rule out the existence of an object that always moves in excess of the speed of light. Such hypothetical "tachyonic" particles have not been quantized. If tachyons transmit information faster than light, they would violate causality according to special relativity, which is one of the current frontiers in quantum computing experiments.

Fostering Compassion in Medicine

Lukas Matern
Illustration by Allison Scott

In capturing the poignant tragedies and triumphs of the daily hospital environment through a literary medium, narrative medicine aims to better students' capacities to register and respond to emotional cues.

As a result of the growing push toward health initiatives with a more "human-centered" focus – even despite today's financially and legally turbulent healthcare climate – physicians, nurses, and hospital staff encounter ever more challenges in their efforts to balance the efficiency of treatment with the need to cultivate strong rapports with those in their care. All too often, the number of capable doctors may be dwarfed by the influx of patients requiring personalized attention. For young physicians especially, the issue of staff shortages is then further compounded by the inherent psychological and physical demands of fighting one's way up through the hospital hierarchy to establish a career. Amid the cascade of demands competing for the rising health professional's attention, the vital task of creating a fully effective and meaningful connection with each patient, of building the vibrant relationship between the provider and the recipient of medical care, may be forgotten entirely.

The notion of the jaded doctor is nearly as old as the medical profession itself. And indeed, as medical students, interns, and residents pass through the rigors of modern clinical training – performing menial "scut" tasks, working late to memorize mercilessly vast quantities of information, encountering the keen dramas of medical practice on a daily

basis — they may be sacrificing a basic competency: the ability to empathize with their patients.

A number of studies have documented neophyte physicians' propensities toward employing techniques of distancing and depersonalization to ease the emotional toll accompanying hands-on work involving death and disease. Out of perceived necessity, many young doctors begin to hold back from investing themselves in their patients' clinical outcomes. They close themselves off from an adequate appreciation of the pathological horrors that may wreak havoc upon the lives of the afflicted and, most grievously, keep themselves from attaining a thorough understanding of the patient as a "whole person." Simply put, the physician may subconsciously come to view patients merely as the sums of their observable symptoms, neglecting to account for their personal accounts and histories in the process. Though some sources point out that empathizing too deeply can be detrimental to quality of care, the consequences of removing oneself from a patient's story, letting important details go unseen, are ultimately far more disastrous. It is through this common error that the holistic doctor-patient relationship — or, indeed, the opportunity to formulate a truly effective and comprehensive treatment plan — may be all but completely forsaken.

The famed pathologist and medical educator William Osler once remarked: "The good physician treats the disease; the great physician treats the patient who has the disease." Unfortunately, given the realities of our current medical education system, beleaguered doctors frequently seem to find this particular brand of "greatness" impracticable.

How, then, is the essence of this singular bond to be recaptured? A growing body of evidence amassed over the last two decades has allowed investigators to make the case for a revised medical training process — namely, one which integrates a literary component into its curriculum. More and more experts, many of whom are both respected physicians and writers themselves, now agree that a complete educational regimen for the physician should incorporate exercises in the dissemination and detailed examination of novel perspectives. Doctors of the twenty-first century must be able to understand the experiences, backgrounds, and emotional states of their patients, especially as these relate to their specific diagnoses. And narrative medicine, proponents argue, provides the most effective vehicle for instilling this ability in up-and-coming physicians.

A slew of new investigations, such as the study conducted by Dr. Johanna Shapiro at the University of California Irvine, have discovered that sensitivity to patients' feelings decreases markedly over the course of a doctor's training. By gathering extensive questionnaire assessments, Shapiro and her team found that the standard four years spent in a modern medical school are indeed frequently depriving students of their abilities to relate emotionally to the individuals placed in their care. In the same study, however, they discovered a powerful impact: a single discussion-based course in narrative medicine could improve the levels of empathy in these physicians-to-be by a significant margin. Shapiro and her colleagues emphasized that fostering this genuine compassion required "participating deeply in another's experience" — and that cultivating an intimate awareness of an individual's situation calls for the joint involvement of "emotion and intellect." In capturing the poignant tragedies and triumphs of the daily hospital environment in a literary medium, then, supplementary narrative medicine courses aim to better students' capacities to register and respond to emotional cues.

Widespread recognition of narrative medicine's positive influences on patient care has been growing, albeit at a relatively modest pace. In recent years, initiatives like Columbia University's Graduate Program in Narrative Medicine have carved out spaces of their own in the medical landscape, holding conferences, workshops, and special "rounds" to foster appreciation of patients' distinctive stories. Other efforts, such as the medical humanities program run by Dr. Richard S. Panush at the Saint Barnabas Medical Center in New Jersey, encourage both doctors and patients alike to chronicle and share their clinical experiences with others. While such attempts to infuse the medical profession with the power of the narrative are innovative in their systematic approaches, they also pay a quiet homage to the legacies of physician-writers such as Anton Chekhov and William Carlos Williams — prominent literary figures who infused their works with inspiration from the medical world.

Closely interwoven with the burgeoning efforts of narrative medicine advocates are the problems of medical ethics. Moral philosopher and ethicist R. S. Downie describes literature and the arts as particularly efficacious in enabling students to "experience" complex scenarios without actually encountering them firsthand. Instead of being thrust into the clinical wards armed with little more than rote medical knowledge, the presentation of narratives would provide young physicians with insights extending beyond the merely scientific — and, ideally, a newfound respect for the impacts of disease on human life. As Downie states: "Whereas the medical and social sciences develop understanding of disease processes and typical behavior, literature can remind us that what is scientifically typical occurs in unique forms in individual patients." As reflected by the dilemma of empathy loss in medical students, a purely technical foundation proves insufficient when confronted with the realities of treatment—no two patients are quite the same, and each individual is more than just a case to be "solved."

Ultimately, successful work in medicine remains firmly rooted in human trust. Healthcare is perhaps especially profound in the sense that professional expertise in the field requires a uniquely close bond between patient and provider, and it therefore remains crucial that each party builds a mutual understanding through an honest appreciation of the other's position. By strengthening their abilities to connect with their patients, a new generation of doctors may be cultivated—physicians more completely equipped to provide for the physical, mental, and emotional well-beings of their respective communities.

Adrian Meyers
Illustration by Hannah Hyunji Park

The God particle

How the Higgs Boson Shapes the Universe

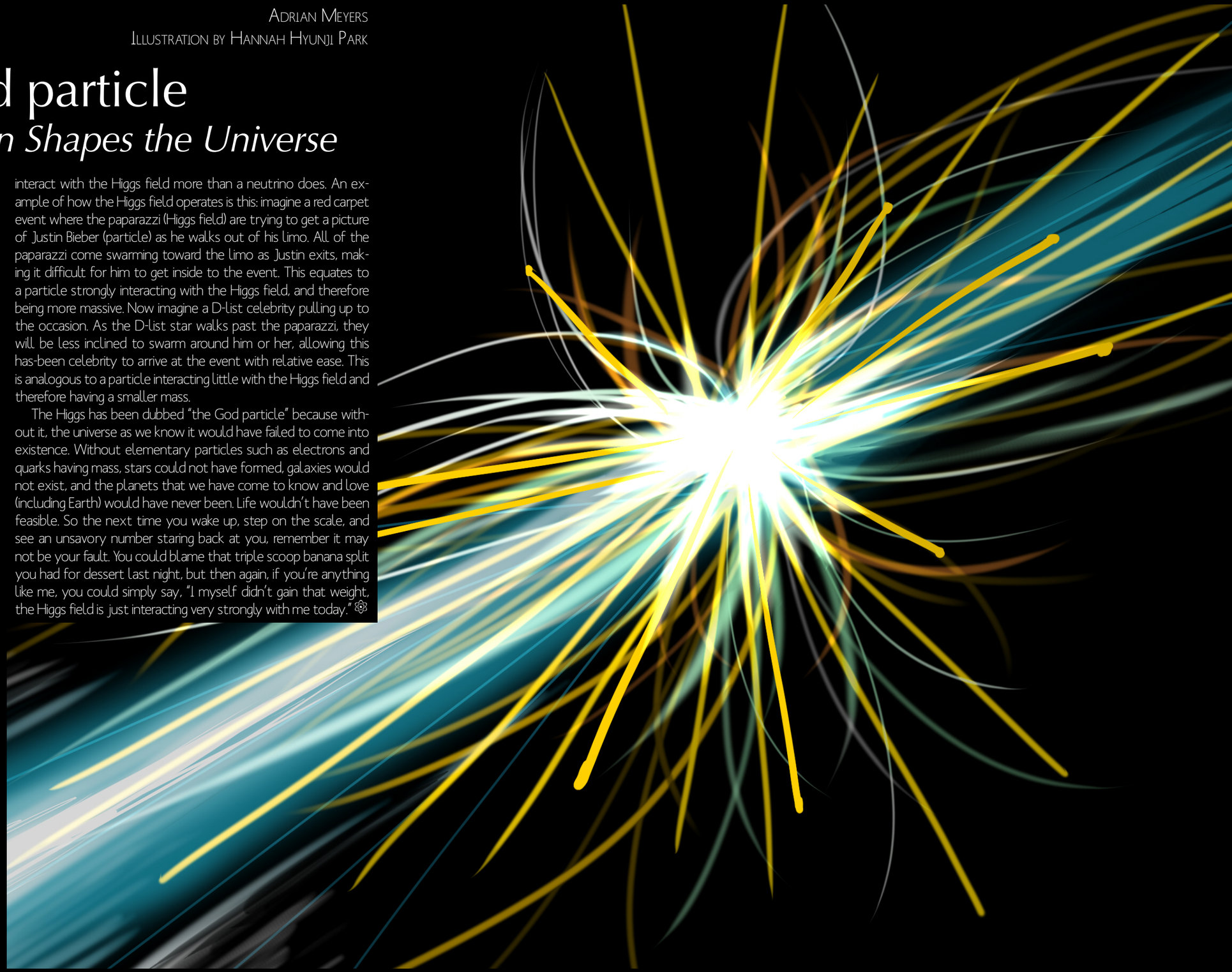
It has happened to almost all of us at some time or another—we have stepped on the scale hoping to see a significantly lower (or perhaps higher) number. Most of us have a general idea of how mass and gravity work and realize that in order to slim down or bulk up we have to lose or gain the necessary pounds for the change. Now imagine your long-lost twin standing next to you on a separate scale. He or she is the same exact height, shape and size as you, but as you look down at the number on his or her scale you realize that you weigh over 100 times more than your twin! Making sense out of this disparity is no easy feat for the mind. This is the type of dilemma that challenged physicists for quite some time.

For years, there was a problem with the Standard Model theory, which explains the phenomena that occur between all known subatomic particles. The predicament was this: according to the predictions of the Standard Model, particles that make up normal matter in the universe (e.g. electrons and quarks) should not have any mass. Obviously, this was a huge flaw in the Standard Model because humans, chairs, cars, and every non-force carrying piece of matter have mass. This is where the Higgs Boson comes in to save the day—in order to accommodate for this inconsistency, the Higgs particle was added to the Standard Model. This alleviated non-force carrying particles, such as electrons, of their "masslessness" while saving half a century of particle physics from being discarded in the process.

So what exactly is the Higgs Boson, how does it give particles mass and why are scientists making such a big fuss over it, with some even dubbing it "The God particle"? The excitement is not over the particle itself, but actually the field which it produces. In classical physics, we learn that fields affect particles. For example, we are all aware of what a gravitational field does to a ball thrown in the air—it causes the ball to fall. We can clearly decipher which part of the ball/gravity system is the matter part (the ball), and which part is not (the gravitational field). However, according to the Standard Model and quantum mechanics, fields such as those created by the electromagnetic force are simply large collections of their corresponding "force carrying particles." This means that an electromagnetic field is simply a conglomeration of photons. In the same manner, the Higgs field is simply a sea of Higgs Bosons. This Higgs field permeates throughout the whole universe and without it, life as we know it would not be possible.

Now here comes the cool part—how massive a particle is depends on how much it interacts with the Higgs field. This means that since an electron has more mass than a neutrino, it must interact with the Higgs field more than a neutrino does. An example of how the Higgs field operates is this: imagine a red carpet event where the paparazzi (Higgs field) are trying to get a picture of Justin Bieber (particle) as he walks out of his limo. All of the paparazzi come swarming toward the limo as Justin exits, making it difficult for him to get inside to the event. This equates to a particle strongly interacting with the Higgs field, and therefore being more massive. Now imagine a D-list celebrity pulling up to the occasion. As the D-list star walks past the paparazzi, they will be less inclined to swarm around him or her, allowing this has-been celebrity to arrive at the event with relative ease. This is analogous to a particle interacting little with the Higgs field and therefore having a smaller mass.

The Higgs has been dubbed "the God particle" because without it, the universe as we know it would have failed to come into existence. Without elementary particles such as electrons and quarks having mass, stars could not have formed, galaxies would not exist, and the planets that we have come to know and love (including Earth) would have never been. Life wouldn't have been feasible. So the next time you wake up, step on the scale, and see an unsavory number staring back at you, remember it may not be your fault. You could blame that triple scoop banana split you had for dessert last night, but then again, if you're anything like me, you could simply say, "I myself didn't gain that weight, the Higgs field is just interacting very strongly with me today."



The Secret Life of Plants

Radhika Gupta
Illustration by Allison Cohen

Plants may seem unassuming, but they hold the power to transform vaccines and preventive medicine as we know them today.

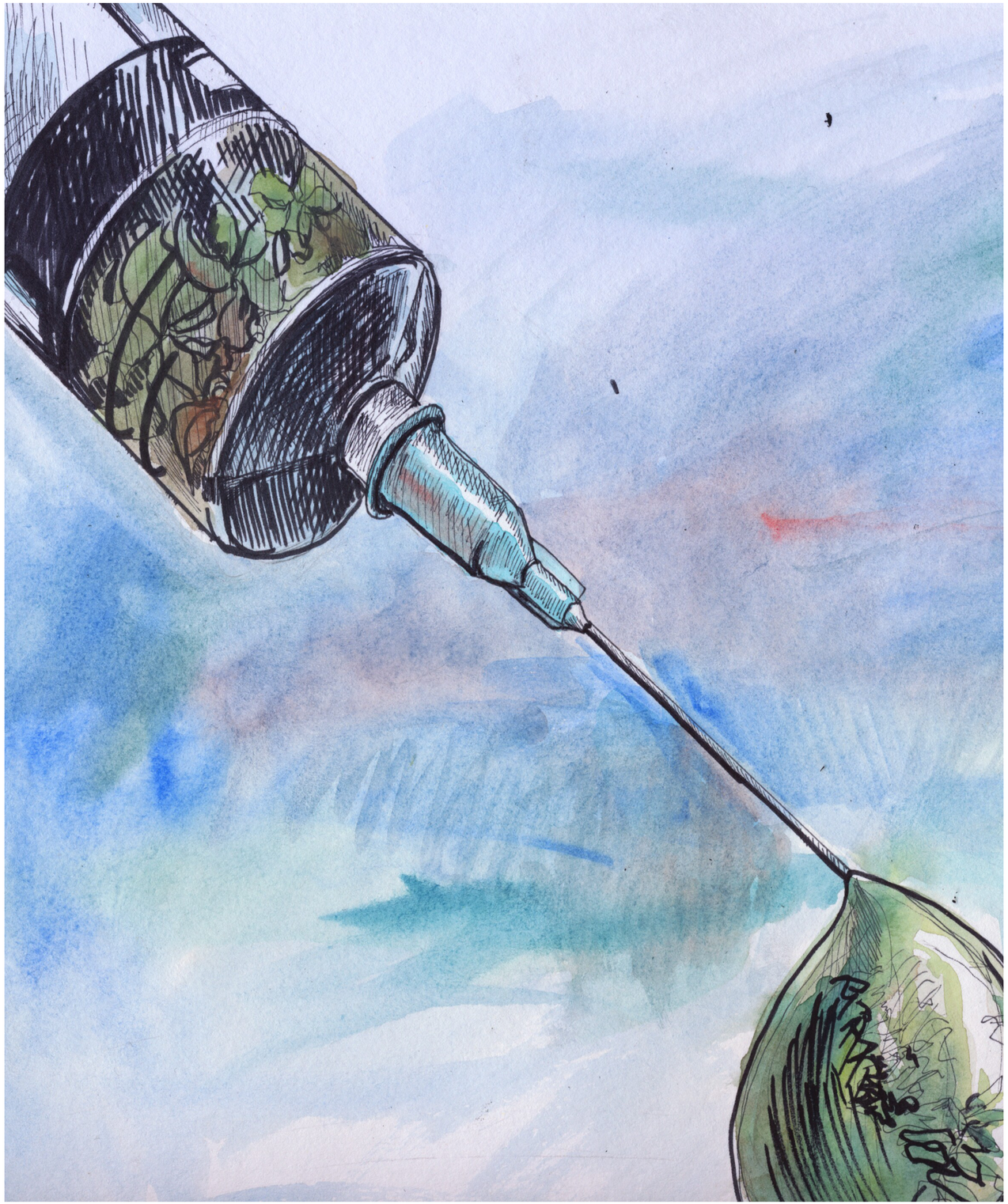
It's a familiar scene: a small child is crying as a nurse prepares to administer an injection that contains a vaccine, which will protect the child from various diseases such as malaria or diphtheria. The vaccine is most likely egg-based—that is, the vaccine was made by growing an inactive version of the virus in the chorioallantoic fluid or ovalbumin of chick embryos from which the resulting viral replicates are later administered. Most of the vaccines used today are created using the egg-based approach, but this process is not ideal since many people are allergic to eggs and the process is time consuming and costly.

For these reasons, alternatives to egg-based vaccines are emerging in research labs all over the world. One such substitute is cell-based vaccine production. In this approach, a virus is inserted into a laboratory-grown cell line and later multiplies. This method solves the problem of procuring specialized chicken eggs, but it is still quite expensive.

However, another effective and cheaper method comes in the form of plant-based vaccines. These vaccines use plants as the medium by which to grow antigens—in this case, viral proteins antigens, Using plants eliminates the need for fermentation, extensive purification, refrigeration, transportation, and sterile injection, which are all necessary for egg-based and cell-based vaccines and which contribute to their higher prices. Because of the ease and magnitude of plant growth, this approach is proving to be promising for vaccine production.

In plant-based vaccines, researchers introduce viral vectors into a plant and direct it to produce a specific protein. This can be done in two ways: stable genetic transformation and transient expression. The main difference between these two processes is the way in which they enable the plants to produce the viral proteins that cause the vaccine to work.

Stable genetic transformation involves altering the genetic line of the plant by integrating recombinant DNA into the genome of the nucleus or chloroplast.



This can be done in two ways. The plant can be infected with a plant pathogen that has been engineered to transport DNA into plant cells. A biolistic method can also be used, where plant cells are bombarded with DNA that is coated on microscopic particles of gold. In both processes, the plant is then allowed to grow, creating larger quantities of the proteins needed for proper vaccination. These proteins are later harvested. In stable transformation, once the plants' genomes have been transformed, the subsequent generations of the plant will also have these qualities, based on the rules of Mendelian inheritance. As the mass of the plant grows, so does the mass of the antigen, or viral protein, thus creating a steady supply of vaccines.

In transient expression, a recombinant plant virus (a virus which has DNA from multiple different viruses) that carries the viral protein gene is introduced into the plant, inducing the plant to express a certain viral protein that determines the characteristics of the vaccine. Transient expression generally causes a higher level of expression, but it is inconvenient because each plant has to be individually imbibed with the virus. The plants are then freeze-dried, ground up, and distributed. After it is ingested, the plant vaccines travel to the stomach, where their cell walls are broken down by microbes that inhabit the small and large intestines. The contents of the plant cell, including the vaccine antigens (viral proteins), are then released into the blood stream. From there, these vaccines act similarly to traditional ones: they are identified by the immune system in small quantities. The immune system is then able to recognize viruses it was previously exposed to and destroy them in the future, thus protecting the vaccine recipient from illness.

Though the effect of a plant-based vaccine in the body is similar to that of other vaccines, they offer many benefits. These vaccines do not need to be refrigerated nor sterilely injected and pose less of a contamination risk than current mainstream types of vaccines. This all helps to reduce the total costs associated with the production and distribution of the vaccines. Overall, plant cultures grow faster and at a lower cost than egg or cell-based cultures, which make them a more feasible and efficient method of vaccine production. Plant based vaccines have numerous implications on global health and show much promise. Current research has shown that plant-made vaccine antigens against malaria have been successful in helping immune systems in mice remember pathogens they were previously exposed to. Because of the lowered cost associated with plant-based vaccines, their use can improve access to vaccines globally and presents a promising future for preventive medicine.

Our Curiosity Knows No Bounds

Josephine McGowan
Illustration by Allison Scott

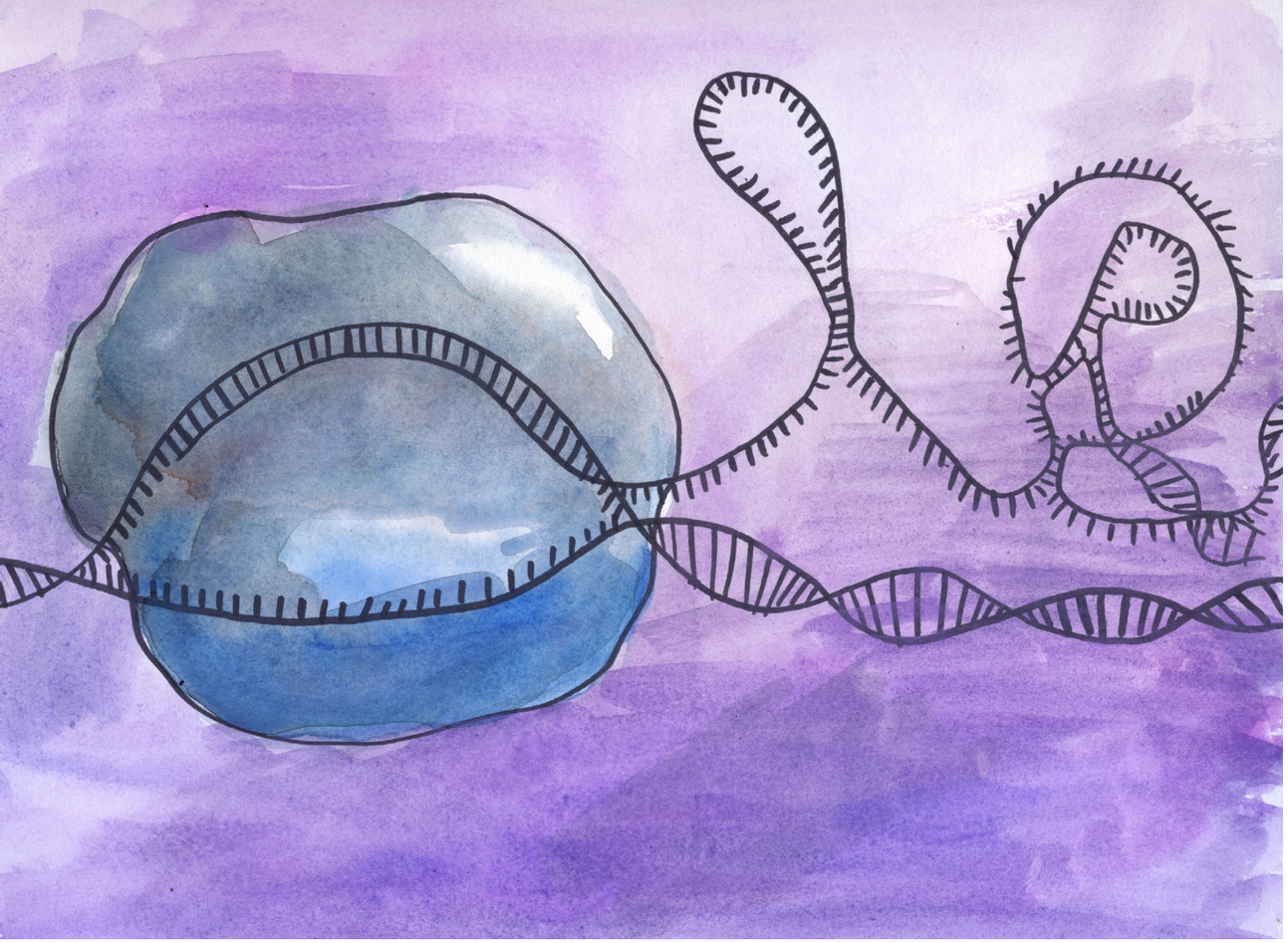
Curiosity about our cosmological surroundings is pervading the universe. At the moment, it centers on a fiery, barren landscape both mysterious and perplexing. This "Red Planet," the planet Mars, was dubbed by the Egyptians in the 28th Dynasty of the New Kingdom as the "Horus of the Horizon": a human with the head of a hawk. Past the sooty skies of our sparkling city, the Curiosity rover, which landed recently on the Gale Crater, glides the perfectly desolate planet—no hawks or humans, unfortunately. Its two-year mission aims, according to NASA's definition, to "understand whether Mars was, is, or can be, a habitable world." Twitter updates (@MarsCuriosity) drift past computer screens to follow its discoveries and to ascertain the feasibility of this lofty operation across the world. The powerful Mars Hand Lens Imager (MAHLI) camera sends us photos of the terrain and of the rover in action. Curiosity elicits high hopes of adventure and possibility, as it almost seems armed with the zeal of Wall-E, its robotic doppelganger.

The plight of this Curiosity rover is not novel. Percival Lowell, an early astronomer of the seventeenth century, fixed his gaze on the bright red dot and its flickering, lively movements, which he thought were canals, later turned out to be windblown dust shifted by seasonal changes. The orbital dance that Mars and Earth engage in offers the most energy-efficient opportunity to send a vehicle to Mars every 26 months, as it is the shortest distance a vehicle may make. The precision of each vehicle's six month voyage through space is impeded by innumerable factors, dust storms especially; it is no wonder the success rates for all attempts is about 47 percent. Vikings 1 and 2 from the U.S. in 1976 gathered soil samples, treaded rocky boulders, and photographed massive volcanoes, while our Pathfinder in 1997 explored the terrain before losing contact. Thousands of years of contemplating the haunting and speckled void above has inspired meticulous calculations, defining Mars as the desert-like and copper-colored counterpart to Earth. The search for life on the planet has elicited the harshest of criticism, and the sci-fi genre, breeding movies such as "Mars Attacks!" featuring ghastly, malevolent creatures of the imagination. Still, our innate inclination to look beyond, to the hypothetical ends of the universe, and possibly even further if such a concept exists, inspires us to continue exploring.

With this insatiable desire for exploration, the future of our relationship to this red beacon is difficult to pinpoint. Data retrieved from the Phoenix Mars Lander in 2008 suggested that the thin atmosphere can indicate whether water existed on this planet. A meteorite from Mars found very recently in the Sahara, suggests that 2 billion years ago, there very well may have been water on the planet. Where did it all go? Could life have been possible with the discovered composition? Could there be worlds we have not yet conceived in our imaginations, emanating from the history of our neighboring planet? Are there microorganisms of times past embedded in the landscape that our rovers have not yet explored? These are the questions that astronomers are attempting to answer with their exploration. NASA intends to send another rover very similar to Curiosity in the summer of 2020. Though the mission is not exactly defined as the search for life presently on Mars, astronomers still aim to map the geological patterns and the planet's history.

However, NASA may face an 8.3 percent cut in funding for the fiscal year and may be facing even more in the next eight years, impacting the search for exo-Earths, possible organic compounds, and evidence of planets that were once habitable. An article titled "Cosmic Cliff" featuring the Kepler space telescope funding for its search for Earth-like worlds and supernovae (dying stars) stated that NASA receives less than 1 percent of the federal budget, and it has been so since about 1975. In a meeting of the American Astronomical Society, members noted that our universe, brimming with about seventeen billion galaxies, contains about seventeen billion planets the size of Earth within those galaxies. The seemingly infinite vastness elicits disconcerting yet fantastic possibilities. In our precarious existence, it is difficult to shed our money towards lofty adventures when our own habitat is so bleak. Yet, it is so necessary to push our galactic limits further, if only to understand it more completely.

Famous astronomer and poet of cosmological wonders Carl Sagan recorded a warning and a heartfelt wish to future Mars explorers from his workplace in Ithaca, New York. In the comment, he said that we may be in Mars because "the gates of the wonder world are opening in our time...[or] because we have to be, because there's a deep nomadic impulse built into us by the evolutionary process." In a hopeful tone, he ends by saying, "whatever the reason you're on Mars is, I'm glad you're there. And I wish I was with you." Echoing John F. Kennedy's promise to the nation that we would land on the moon before the 1960s ended, Sagan's quote implies a promise that our society is capable of interplanetary exploration. As the Curiosity rover treads onwards on the Red Planet, surpassing the expectations of its lifetime, astronomers tirelessly work to shape the dust and star stuff of the universe into something we can all understand. Despite skepticism and failure, one can only look to the future with awe and curiosity.



Alyssa Ehrlich
Illustration by Allison Cohen

Copy Rights

On the Ethical Implications of Gene Patenting

As scientists continue to unravel the genetic code through DNA sequencing, it is becoming increasingly possible to diagnose and treat—or perhaps even cure—the countless diseases and disorders that afflict us. Many researchers and clinicians set out to discover and decode disease genes in the hopes of benefiting society as a whole: they aim to increase collective scientific understanding, and eventually inform novel therapeutic techniques. Scientists make these discoveries by first isolating genes, and then performing DNA sequencing, or mapping out the precise order of nucleotides that comprise a gene. Each new gene discovery made with this altruistic purpose in mind constitutes one step closer to reducing the suffering caused by human illness.

However, not all scientists who actually discover genes are so benevolent. Consider the case of researchers employed by a for-profit biotech company that may be more concerned with monetary gain than with patient health. These particular gene discoverers would rather claim a DNA sequence as their intellectual property and patent it than share this newfound information in order to fuel progress in medical science and facilitate the treatment of sick individuals. Although the notion that a naturally occurring genetic sequence—a "product of nature" that no human being can rightly claim credit for having "invented"—could be lawfully patented might seem absurd to some, over the past twenty years, thousands of genes have been patented. This issue, and the ethical implications that arise from it, have recently received greater attention due to a highly contested court case regarding gene patents. In this case, a lawsuit against the diagnostic company Myriad Genetics was filed by the American Civil Liberties Union (ACLU) in 2009, and reached the United States Federal Court of Appeals in the summer of 2012.

To the dismay of the ACLU, many medical professionals, and several patient advocacy organizations, on August 16th, 2012 the appeals court upheld Myriad Genetics' right to hold patents for sequences to the BRCA1 and BRCA2 genes. Mutations of the BRCA1 and BRCA2 genes account for most heritable forms of breast and ovarian cancer, and can be detected by Myriad's genetic test, termed "BRACAnalysis." Given the results of the court's ruling, only Myriad's laboratories—which are located in Salt Lake City—will be legally allowed to test for variations of these genes, thereby securing an effective monopoly for the biotech company. Opponents of gene patents argue that proprietary licenses to perform diagnostic DNA testing raise the cost to the patient and limit access to life-saving medical care. Myriad can charge as much as $3,340 for each BRCA test, and even though most academic medical centers are able to run these tests themselves in-house at a much lower cost, due to the BRCA patent, DNA samples must be sent to Myriad's laboratories in Utah.

The price of the BRCA test is far more reflective of Myriad's desire to make a profit than the actual cost incurred in carrying out the diagnostic procedure. Furthermore, recent advances in DNA sequencing technology continue to reduce the cost of genome sequencing, but Myriad's testing fees have not been correspondingly lowered. Recently implemented genome sequencing machines, such as Ion Torrent Systems' Ion Proton, can sequence a person's entire genome for as little as $1,000 in less than 24 hours. But so long as Myriad's patent is upheld, the company can continue to set an arbitrarily high price.

Myriad's legal patenting of the BRCA gene has several other disadvantages for patients. Shipping samples to Myriad's laboratories unnecessarily lengthens the time between being tested and receiving results. Consequently, the onset of treatment will ultimately be delayed for the patients in need of these tests—women suffering from an inherently aggressive form of breast cancer. Furthermore, those patients with health insurance not accepted by Myriad are unable to legally receive these potentially life-saving tests, unless they are willing and able to personally pay exorbitant fees.

It must be conceded that these same arguments, which appeal to the public utility of prohibiting gene patents, can also be made against patenting pharmaceutical drugs. However, the latter is generally a far less disputed practice. Thus, like advocates of pharmaceutical patenting, advocates of gene patenting claim that these patents may actually benefit society in the long run. Without enforceable patents, there would be less incentive for companies to invest massive amounts of time and money in order to discover these disease genes.

What makes the ethical issue of gene patenting unique is not whether the practice is helpful or harmful to society. Rather, this case also raises the question of whether gene patenting adheres to the defined purpose of patent law. The judge in the Myriad case ruled that DNA sequences were patentable entities, on the basis that "… when cleaved, an isolated DNA molecule is not a purified form of a natural material, but a distinct chemical entity." Yet the logic here appears to be faulty, as not all distinct chemical entities are the proper subjects of patent law. Genes clearly do not meet the Patent and Trademark Office's explicit criteria for patentable living matter as "non-naturally occurring manufacture or composition of matter – a product of human ingenuity – having a distinctive name, character, [and] use." Arguments in favor of gene patents may often be vain attempts to justify misappropriations of the law, a fundamentally juvenile "finders keepers" mentality intended to ensure the monetary gain of some at the cost of patient welfare.

Serendipity Machine

ARI TURKIEWICZ
ILLUSTRATION BY VANGIE SHUE

Imagine writing a research project proposal that rested on randomly mixing chemicals together and crossing your fingers with the hope of discovering new and amazing chemistry. Indeed, many of the world's best inventions, such as Post-it Notes and penicillin, have come about by accident, but such a proposal would probably not get the warmest reception. The trouble is that such fortuitous accidents are few and far between. However, one research group at Princeton University has taken just this approach, albeit on a grand scale, through a process termed accelerated serendipity, and they have already seen positive results.

One of the focuses of the David MacMillan group at Princeton is organocatalysis, or the development of organic molecules that speed up the rates of reactions without being consumed. The synthesis of new organic catalysts by rational design has proven to be one of the more challenging fields of chemistry, as it is often difficult to predict what will endow a molecule with catalytic properties for a given reaction. The alternate approach, synthesis by empirical observation—more commonly known by its less glamorous name, trial-and-error—is hampered by the large amount of material and time that must be invested. This is where accelerated serendipity comes into play. MacMillan made the leap that serendipity is not entirely random, but is rather probabilistic and occurs with some statistical regularity. Therefore, by stripping trial-and-error of its intensive time requirements, one could run a sufficiently high number of chemical reactions to appreciably increase the odds of chancing upon a new discovery. The only remaining issue is how to achieve that critical volume in practice.

In an effort to expedite the discovery of new catalytic agents, the Merck Center for Catalysis at Princeton University has employed a machine capable of running and analyzing a few hundred random chemical reactions simultaneously, and up to roughly 1000 every day. The machine capable of this magic is the aptly named Accelerator Synthesizer, designed by the Swiss engineering firm ChemSpeed Technologies. The Accelerator Synthesizer is equipped with nearly 200 parallel reactors, each capable of handling all aspects of reaction preparation, environment regulation, purification, and preliminary product analysis.

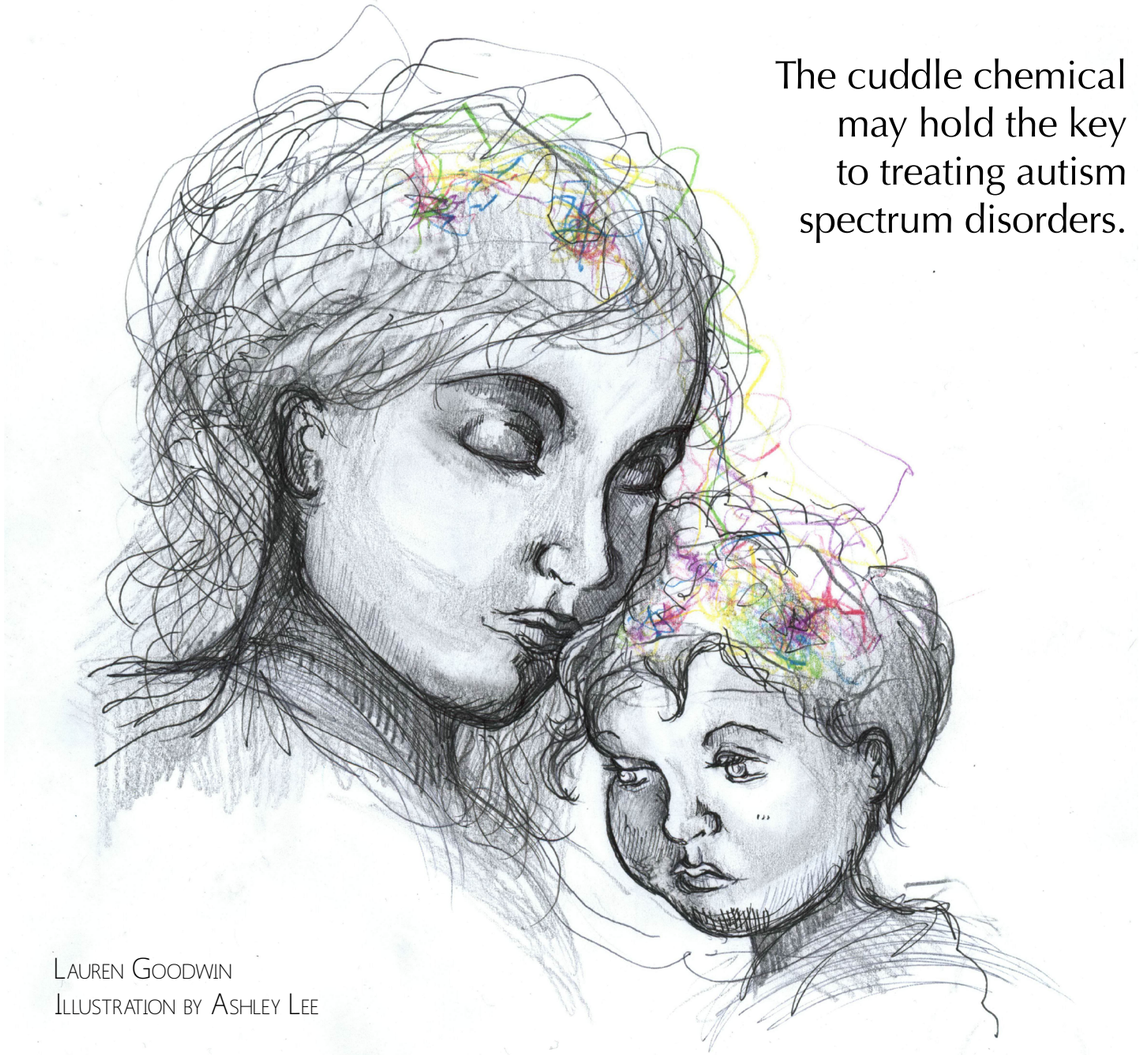
The machine operates by examining every pair-wise combination, including self-matches as a control, of a pool of substrates that are expected to be nonreactive with respect to one another given the current body of known chemical reactions. Aside from the presumed nonreactivity, no other factors are used in selecting the participant chemicals in order to preserve the randomness of the process. Different catalytic systems are introduced to each reactor with the hope that the catalysts induce these otherwise nonreactive partners to actually react. Analytical techniques including mass spectroscopy and gas chromatography are then brought to bear on each reactor to see if a reaction took place. For those reactors where a reaction did occur, products are screened using automated software and molecular databases in order to identify the products and determine whether they are unanticipated.

Fortuitous accidents are few and far between—this is where accelerated serendipity comes into play.

The researchers of the MacMillan group decided to focus their attention toward the relatively new and unexplored field of photoredox catalysis - the development of light-activated catalysts - considering that the potential for new discoveries should be high. The ever-versatile Accelerator Synthesizer supplies a fluorescent light source for each reactor in order to activate these light-sensitive catalysts. In a stunning proof of concept, the Accelerator Synthesizer was able to identify a new photoredox catalyzed process successfully after the observation of an unexpected coupling product, specifically an amine with a newly attached functional group. By optimizing such parameters as the solvent system and choice of catalyst, and generalizing the process to a wide variety of substrates, the researchers have provided for an easy, high-yielding, and robust method to functionalize amines. Amines, which are derivatives of ammonia, play a major role in biology. Therefore, this process can be utilized in the design of pharmaceuticals, many of which are designed to mimic or interact with amines found in the human body.

The success of the MacMillan group in discovering new catalytic pathways has demonstrated that accelerated serendipity is both a viable and promising approach for identifying new roles for existing catalysts. By discovering new reactions and mechanisms, it furthers the boundaries of reaction chemistry itself. Indeed, the day may not be far off when the Accelerator Synthesizer becomes the first machine to win the Nobel Prize for the next great breakthrough in the field of chemistry.

The Role of Oxytocin in Social Behaviors



The cuddle chemical may hold the key to treating autism spectrum disorders.

Lauren Goodwin
Illustration by Ashley Lee

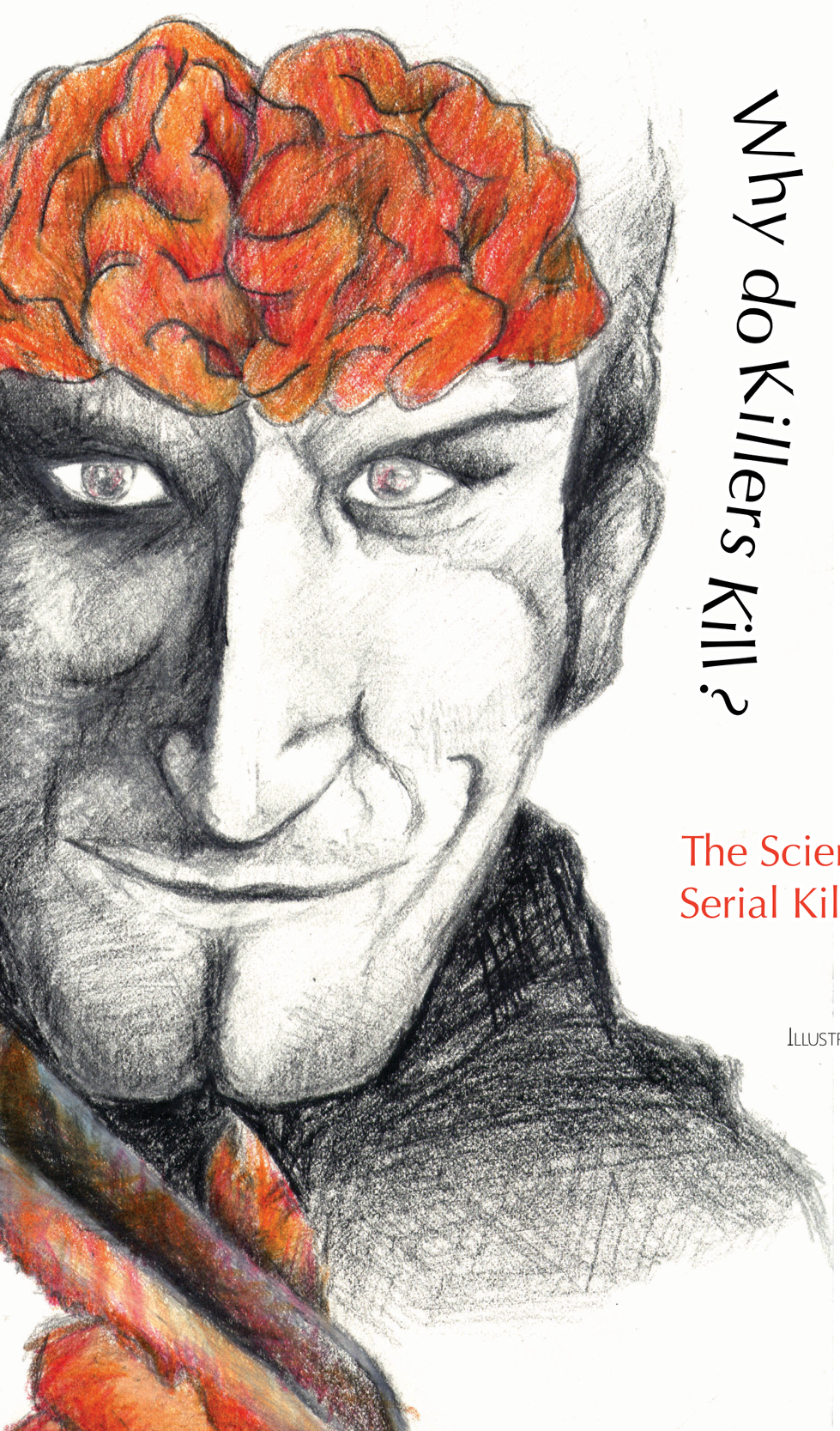
Everybody cuddles. From humans, dogs, bunnies, to even alligators. But researchers believe it is this very "cuddle chemical," known as oxytocin (OT), that may be implicated in the etiology of autism spectrum disorders (ASDs). Autism spectrum disorders (ASDs) are a broad spectrum of heterogeneous neurodevelopment disorders consisting of autistic disorder, pervasive development disorders, Asperger's disorder, Rett syndrome, and childhood disintegrative disorder. ASDs are characterized by severe impairments in social interaction, communication, and restricted stereotypic interests, which manifest in early childhood. The Centers for Disease Control and Prevention estimates that within the United States, 1 in every 88 children has an ASD, more than a 20% increase in prevalence since 2009, with ASDs now affecting tens of millions worldwide.

Since Leo Kanner first described ASDs in 1943, little progress has been made in either identifying the pathophysiology behind these disorders, or developing a specific, reliable treatment. Due to the wide range of maladaptive social processes exhibited by autistic individuals, researchers have begun to examine the neurobiology of social attachment in order to identify causation for the pathology behind autistic symptoms and to develop novel treatments for these disorders. Since the neurohormone oxytocin has been implicated in playing a crucial role in social processes, many researchers have speculated about the role of OT in autism and its potential use as an effective treatment for autism spectrum disorders. Animal models of OT suggest that this neuropeptide modulates social and emotional behaviors such as maternal behaviors, attachment behaviors, social recognition, social exploration, trust, aggression, anxiety, and fear responses. In a study by Professor Michael Meaney at McGill University in Montreal, researchers demonstrated an association between the central administration of OT and virgin female rats nurturing young pups, which they would normally find aversive since maternal behavior in rats is initiated only after parturition. This study was then built upon using prairie voles, one of the few species in nature that forms lifetime monogamous relationships between reproductive partners. This means that if the female prairie vole dies, the male does not seek a new partner. In the wild, a virgin female or male prairie vole will often adopt stray pups, raising them as his or her own. Researchers found the unique behavior exhibited by prairie voles is due to the high density of oxytocin receptors in the nucleus accumbens and amygdala regions. Prairie voles have more receptors than humans or chimpanzees, causing an addiction to social behavior not exhibited by other species.

In order to examine the relationship between oxytocin and autism spectrum disorders in humans, researchers have developed intranasal oxytocin. Intransal OT is a spray that is squirted into the nostrils and enters the brain through the incomplete blood brain barrier at the olfactory region, which is the site where the nasal cavity meets the brain. An array of functional magnetic resonance imaging (fMRI) studies, which measure neural activity by detecting associated changes in blood flow, have illustrated that intranasal OT in humans may be a potentially powerful treatment approach. Intranasal OT increases prosocial behaviors and decreases social fears, which may be due to the effect OT has on the amygdala region. Previous fMRI studies have illustrated that decreased amygdala activation is correlated with genetic hypersociability and aggressiveness, while amygdala hyperactivity is associated with asocial behavior and social phobias. Peter Kirsh of the National Institute of Mental Health administered intranasal oxytocin to healthy male participants during a double-blind fMRI study. The results of this study indicated that as compared to the placebo, oxytocin significantly depressed amygdala activation. Additionally, the connectivity between the amygdala, brainstem, and midbrain regions was reduced in participants that received intranasal oxytocin. This reduced activation is thought to play a central role in increasing social interactions and trust while reducing social anxiety.

In recent news, during the International Meeting for Autism Research 2012, Yale Child Study Center presented preliminary results from their double-blind placebo-controlled pilot study on children and adolescents diagnosed with ASDs. In this study, researchers administered a single dose of intranasal oxytocin and used fMRI to observe its effect. Researchers found that intranasal oxytocin decreased amygdala activity while increasing brain activity in regions known to process social information, such as the medial prefrontal cortex, temporal parietal junction, fusiform gyrus, and superior temporal sulcus. This study represents the first crucial step towards devising more effective evidence-based treatments for the core social dysfunctions that encompass autism spectrum disorders. Yale Child Study Center ascertains that intranasal oxytocin will aid to regulate social behavior and cognition in children and adolescents suffering from ASDs. Based upon this pilot study, a 12.6 million dollar NIH funded clinical trial called SOARS-B, the Study of Oxytocin in Autism to improve Reciprocal Social Behaviors, will be underway in early 2013 at centers in Boston, New York, Seattle, Nashville, and North Carolina. This double-blind placebo-controlled study will monitor children's social skills, communication skills, and stereotypy after the administration of intranasal oxytocin over a period of six months. This study will also attempt to identify genetic, immune, and blood plasma differences between children in the experimental group who receive the oxytocin treatment and children in the control group who do not.

At this point, many questions about the pathology behind autism spectrum disorders and potential treatments have been left unanswered. But, SOARS-B promises hope for individuals and families affected by ASDs throughout the United States and the world. There is no doubt that the results of this study will bring researchers one step closer to finally understanding and devising treatments for these disorders.



Why do Killers Kill?

The Science behind Serial Killers' Brains

Alisha Maity
Illustration by Kimberly Shen

Are you one of the millions of *Dexter* addicts nationwide? What makes this amiable serial killer so interesting is that, despite his seemingly normal exterior, he is somehow motivated to commit violent acts of murder. The complex relationships between genetic predisposition and the effects of a poor environment make it very difficult to evaluate the culpability of criminals. Modern technological advancements have made access to brain scans and genetic sequencing of criminals common in judicial courts. These scientific observations boil down to an alarming conclusion. Could a passion for killing stem simply from an unfortunate combination of genetic mutations?

Surprisingly, the idea that a killer is not to blame is not too far-fetched, scientifically speaking. Scientists have examined criminals for biological anomalies, among them, changes in the part of the brain that makes ethical judgments and mutations of particular genes that regulate anxiety.

For many years, scientists have known that the orbitofrontal cortex (OFC) located in the frontal lobe of the brain is responsible for ethical and moral behavior in humans, as well as impulsive behavior. PET scans of the brains of criminals have shown that the majority of criminals either have damage to or lack completely, this area of the brain. In the field of genetics, violence has been traced to one gene in particular, the monoamine oxidase A (MAO-A) gene. This gene is a regulator for the release of serotonin, a neurotransmitter that has a calming effect on the body. The deficiency of MAO-A relates to enhanced aggression and antisocial behavior.

Recently, UCLA scientists Mikhail Simkin and Vwani Roychowdhury have mathematically modeled the actions of a serial killer, noting the similarities between time lapses in acts of criminality and the time between seemingly random occurrences of events like earthquakes, avalanches, and stock market crashes. In normal brain activity, the firing of a single neuron leads to a cascade, which is the firing of multiple neurons. Once a neuron has fired, it requires a period of rest time (a few milliseconds), called a refractory period, to be able to fire again. Thus, the brain is unable to repeat an activity because it cannot respond to a stimulus for a defined refractory period. This series of neuronal "steps" can be used to predict how many neurons will be induced to fire over time. Based on when his murders took place, the scientists proposed a model for neuronal activity. By running this simulation they found that there was a correlation between the timing of murders and firing of neurons in the brain. This particular threshold of neuronal excitation may be exceeded every few days or every few years, explaining the variability in the actions of serial killers.

These scientists also graphed one killer's time between murders and discovered that there is a power law distribution that represents this relationship. This distribution is the same one that is found in the time lapses between epileptic seizures, and many other natural events, which suggests that criminal actions are motivated by natural aspects of criminals' brains. But does this render serial killers and sociopaths scientifically blameless for their actions?

While these studies succeed in explaining the scientific side of criminality, the creation of a serial killer cannot be explained so easily. Beyond bad genes and a damaged OFC, a societal trigger, such as childhood abuse, is usually necessary for a normal human to be converted to a violent killer. Over a 30-year period, scientists at the University of Otago in New Zealand examined the MAO-A gene in combination with sexual or physical abuse. They found that when individuals with low MAO-A gene expression experienced childhood abuse, they consistently behaved with hostility and antisocially as adults. Another group of scientists at Yale University performed this same experiment, and found that the MAO-A gene also affects vulnerability towards stress, demonstrating the degree of interconnection between genetic expression, brain activity, and environmental cues.

Could a passion for killing stem simply from an unfortunate combination of genetic mutations?

An unlucky combination of these three factors is the best way to explain the existence of serial killers. As such, it is interesting to examine the legal complications of serial killer activity when the lines between nature and nurture are blurred. Changes are being made, and new precedents are being set. Recently, a serial killer named Bradley Waldroup was accused of second-degree murder with the possibility of receiving the death penalty. However, because of his lawyers' defense that he had a deficient MAO-A gene and had also suffered childhood abuse, he was cleared and convicted of voluntary manslaughter instead. This new form of law, dubbed "Neurolaw," attempts to reconcile discoveries in neuroscience and existing legal rules. For instance, the degree of blame that should be placed on patients who have neural disorders is diminished. However, whether this additional information will allow for a more unbiased form of justice, or will improperly cloud the decision-making of juries is still in question.

The character Dexter's desire to kill is a complex phenomenon that is not and may never be completely understood. If you ever thought the ethics of culpability was a difficult topic, the emerging findings of neuroscience have made it much more complicated.

Columbia Science Review

www.columbia.edu/cu/csr