Columbia Science Review

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Molecular Gastronomy
Understanding the Science of Cooking

Antibiotic Resistance
Invasion of the Superbugs

Learning to Decode
A Short Introduction to Cryptography

David Helfand
An Interview With Columbia's Most Avid Stargazer

Columbia Science Review

The Columbia Science Review

The Columbia Science Review strives to increase knowledge and awareness of science and technology in the Columbia community by presenting engaging and informative approaches to contemporary science and technology that include, but are not limited to:

- Exploration into contemporary issues of science, including research, policy, and opinion.
- Features on current faculty research.
- Opportunity for students to publish their scientific research.

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Pills Image provided by Bringham and Women's Hospital, Grape Image provided by Nikon Small Worlds Photography Competition, Franklin Image provided by National Library of Medicine

Letters

I am extraordinarily enthused to participate in CSR for my 3rd year in a row now. CSR, for me, serves as a constant reminder that while science may be the greatest and most profound of human endeavors, it remains ever in flux, and ever in need of new minds and new perspectives.

I believe the birth of new cooperation amongst the sciences is perhaps the most exciting event to strike the field in the last decade. Computer scientists labor and research alongside geneticists, chemists and engineers. Physicists have fused their work with that of geologists and biologists. Scientists from every imaginable field and interest continue to form new interfaces of exchange and learning. From astrobiology to paleoclimate studies, to computerized surgery, the fields of science and engineering have never before in recent history been so inextricably linked.

And it is this new collusion of the sciences that I hope will lead us into the 21st century with a greater breadth of understanding about the unity of our natural world. Nature makes no distinction between the false barriers amongst scientific disciplines that we erect for our own convenience. I believe science should be studied fully and comprehensively, lest we find that might see much further than others, but only in a single direction.

Fundamentally, I so passionately believe in the progress of popular science and education because I hold the belief that learning is the most sacred human ability. It is in this spirit that we publish the Columbia Science Review.

~ Jonathan L. Mo, Editor-in-Chief

Only eight years into the new millennium, the sciences have already been presented with many new questions and challenges on topics ranging from the interaction of certain species with the environment to the super-resistance of evolving bacteria to the imminent threat of biological warfare. Indeed, the sciences inform nearly every aspect of our daily lives, with new discoveries being brought forth every day.

As we move into this new age of ever-evolving scientific thought and technological advancement, we must take it upon ourselves to stay informed and educated about the world that surrounds us. It is not only our privilege, but also our duty as human beings, to utilize the highly developed capacity that makes us such a unique species—our minds.

Our minds have and continue to contribute to the world in which we are more interconnected than ever; the globe has become an intricate, intertwining network of vision, innovation and insight. Though vast, this network serves only as a preliminary framework for the infinite possibilities that lie in the future of scientific endeavor and discovery, each of which will help build upon the existing foundation of human knowledge.

Through each issue, our publication hopes to continue strengthening the link not only between students and faculty in the sciences but also between students and faculty across all academic disciplines. It is with this vision that I am pleased to present you with the newest issue of Columbia Science Review.

-Niccola Pérez, President

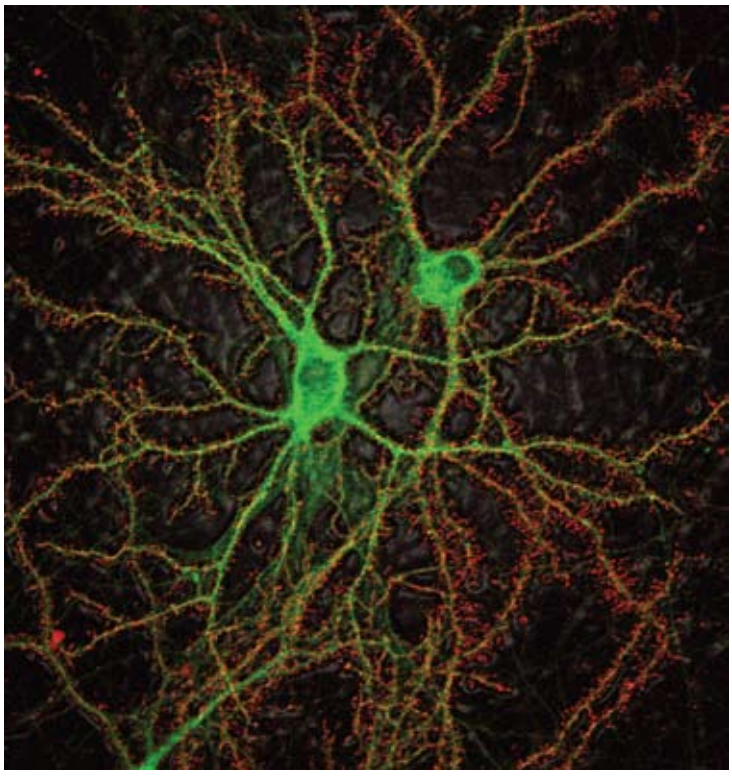
Cocktail Science

Why is Yawning Contagious?

By Ying Li

Whether in class or on the subway, we've all experienced the feeling of wanting to yawn when we see or hear other people yawn. The biological reasons for this phenomenon are still not clear but there are many theories that try to explain the mostly unconscious behavior. One theory suggests that contagious yawning is a result of empathy and helps keep us alert and vigilant. Our brains have evolved to promote behavior that helps groups stay alert and avoid danger. This empathy depends on being able to see things from someone else's viewpoint and so schizophrenics and babies under the age of one won't find yawning contagious. But many different explanations out there and the contagious nature of yawning remains a mystery today.

A Closer Look....



Mature rat hippocampal neurons attacked by Alzheimer's related neurotoxins (100x)

Dr. Pascale Lacor, Northwestern University, Photo courtesy of Nikon Small World

Science Facts and Myths

Try your hand at these 5 questions, then see how your classmates did!*

1) What percentage of Americans believe in intelligent design?

About 51% of Americans believe in intelligent design, according to a poll conducted by CBS News. 13.3% of your classmates guessed close to the right value. Only approximately 15% of Americans believe that humans evolved without the assistance of God. 30% believe that humans did evolve, but God was involved.

2) Where are a slug's sensory organs, its "nose" and "eyes"?

About 27% of your peers got it right. A slug's sensory organs are located on its tentacles. The shorter tentacles are used to smell and its longer tentacles are used to "see". Although a slug cannot see the way humans can, it can tell the difference between light and dark

3) What are the two components of addiction?

40% of your classmates knew this answer. Physical addiction and psychological addiction are the two components. Physical addiction is characterized by building tolerance to a particular substance and can cause withdrawal symptoms when the drug is stopped. Psychological addiction is characterized by a craving or extreme longing for the substance.

4) True or False: You can overdose on caffeine.

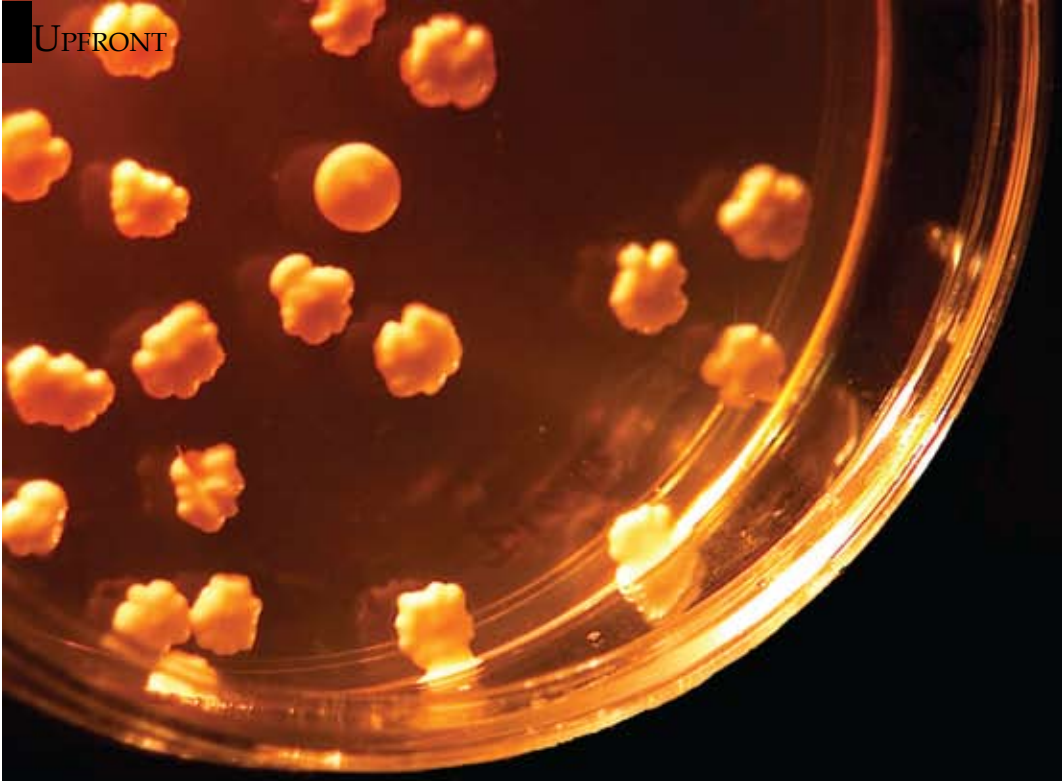
90% of your classmates answered correctly. Symptoms of caffeine overdose includes breathing problems, confusion, convulsions, dizziness, fever, loss of consciousness, and vomiting.

5) Estimate the distance from the Earth to the Sun

40% of your classmates were in the right ballpark. The distance is 150 million km., or 93 million miles.

*This survey was done by randomly picking students in Lerner and John Jay Dining Hall to answer these questions.

By Laika Simeon



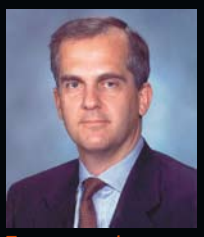
q:

What was your first job? What was the last concert you attended?

Stuart Firestein
Prof, Biological Sciences

"It was a newspaper stand…in the old days you used to stand at the newspaper stand and traffic would come by and people would wave for this paper or that paper and I would run it to their car for believe it or not in those days eight cents…I was probably 13 or 14"

"It just so happens I was at the Kathleen Battle recital at Carnegie Hall"



Julio Fernandez
Prof, Biological Sciences

"I sold sandwiches in high school…ham, mayo, lettuce and tomato…I made them myself"

"I went to War and Peace by Prokofiev or maybe it was The Barber of Seville…I love the opera"

David Helfand
Chair, Astronomy Dept.

"Probably mowing lawns, but the first one I was really in to was being the assistant produce manager of the A&P supermarket in Mattapoisett, Massachusetts where I grew up (at 16)"

"I don't know if you call this a 'concert' but I saw a brilliant production of Lucia with Natalie Dessay"

Darcy Kelley
Prof, Biological Sciences

"I was a TA at an NSF sponsored summer program for high school students"

"Easy Star All Stars at BB Kings"

Life Outside the Petri Dish

Effects of Maternal Food Restriction on Offspring Behavior

By Brittney Dubose

Believe it or not, there may be some aspects of your personality and behavior that are due to certain actions of your mother during pregnancy. Both individuals in and outside the scientific community would agree that maternal and paternal factors affect the phenotype of offspring. Here in Columbia's Department of Psychology, distinguished faculty member Assistant Professor Frances Champagne focuses some of her research on maternal behavior, as well as behavioral neuroscience and epigenetics, an area of biology that looks at the causal relationship between genes and their products. Upon completion of Champagne's lecture course "The Developing Brain," I began a supervised individual research project in her laboratory.

During my first semester working in the laboratory, I helped code open field task videos. Prior to coming to Columbia, Champagne ran a lab in England where she conducted a study in which female mice were given restricted amounts of food before mating. Consequently, the behavior and biology of their offspring was investigated in the hopes of finding an association between maternal food restriction and deficits in offspring behavior. Using observations of play behavior and performance in the open field task, Prof Champagne and her colleagues were able to investigate any associations food restriction may have with certain behaviors. The open field task refers to a form of testing that allows researchers to obtain measurements about animal behavior. The open field apparatus is a box with an open top and a floor divided into 25 squares. During testing, an animal is placed in the lower left-hand corner of the box and videotaped for about 10 minutes. This task provides valuable information regarding the animal's behavior, including signs of fear and anxiety, as well as its degree of exploration. Using a unique open field coding program, I helped track the movements of the animals. While some animals remained stationary, others sped around the box so fast that it was often hard to track their movements.

How is data collected from an open field task relevant to Champagne's study? One important piece of information gleaned from the open field task is the total number of squares crossed by the animal, or in other words, the number of surfaces covered by the mice. The more squares crossed by an animal, the more exploratory and less anxious they seem to be. Another useful observation is the total number of internal squares crossed by an animal. Because new environments may be intimidating, some mice had a tendency to travel solely along the edges of the box out of comfort. In such cases, the animal is considered anxious and less exploratory.

Using a statistical analysis program, Statistical Package for Social Science (SPSS), I compared the control subjects (no maternal food restriction) with the test subjects (maternal food restriction). Interestingly, the test subjects had a significantly lower total number of squares covered score than the control subjects, leading us to believe that food restriction had an effect on the behavior of the offspring. Play behavior and social interaction were also of great interest in this study. Subjects were housed with several others and observed in terms of individual behaviors, such as nest building and grooming, and play behavior with other animals several times a day over the course of a few weeks. Data from these observations, also analyzed using SPSS, were consistent with those of the open field task. Offspring of food restricted mothers were less active and engaged in less play behaviors.

In order to substantiate our findings, we next tried to uncover any biological differences between the two groups. This required sacrificing the animals to extract and freeze their brains. As a research assistant in the lab, I was responsible for sectioning the brains with a cryostat, a machine that runs on a very low temperature, allowing the brain to remain frozen while slicing it into incredibly thin slices. Post doctoral researchers in the lab will study whether or not receptor-binding differences exist between the test and control groups. Neurotransmitter receptors of interest include dopamine, which relates to motivation, pleasure, and salience, and oxytocin, which is released during social interaction.

Animal models can provide a better understanding of what may be occurring in humans since many of their genes are homologous to those of humans. As a result, the ongoing research in Prof Champagne's laboratory is instrumental in improving upon our current knowledge regarding the effects of maternal behavior. Once differences between the two groups in this study have been verified, we will be more confident as to how food restriction affects the social behavior of human offspring.

Petri Dish image from NASA, Helfand Image from Quest University of Canada, all other professor images from Columbia University, Apple picture by Hugo Provoste

Born Outside the Fold

By Jennifer Gillman and Anna Plitt

Years ago, a child born prematurely at 26 weeks would most likely die soon after childbirth, or at the very least, face a long life full of illness. Attempting to save these babies was considered an act of heroism, or perhaps futile optimism. But now, with new improvements in neonatal technology, many of these infants can be stabilized and sent home after months of treatment to live long and healthy lives. As research in neonatal technology continues, investigators are also examining how to grow embryos and fetuses outside of the womb. Will this controversial research be seen as an act of triumph or are the ethical implications too risky?

Estimates suggest that growing a full baby in an artificial womb will be possible in a few years. Nine years ago Japanese researcher Yosinori Kuwabara designed a tank filled with amniotic fluid and an umbilical cord where he developed a 20-week old goat fetus to full term. Another scientist, Dr. Hung-Ching Liu, showed that human embryos can develop attached to a uterus-like chamber lined with human cells.

Researchers attempting to simulate a uterine-like environment must consider the potential physical and cognitive damage on the developing fetuses. At birth, a premature infant's brain is not sufficiently wired, and therefore the rest of its development depends on the environment of a Neonatal Intensive Care Unit, (NICU). Research shows that extremely low gestational age infants are more prone to brain injury and lung disease, and the NICU has been shown to put these premature babies at a higher risk of neurodevelopmental disorders. Until these artificial wombs become fully developed, children maintained in them will face serious medical challenges.

Our bodies have evolved in such a way that the intrauterine environment provides the perfect conditions for fetal development. The architecture of the mother's womb provides the optimal conditions to sustain life. If the child is removed before 37 weeks of gestation, the highly irregular and variable NICU environment can overwhelm and confuse the underdeveloped fetal brain. The natural womb also assists in a child's emotional development. When the child is in the womb, it becomes familiar with the mother's heartbeat, and later learns the sound of her voice. Thus, if a child were to develop completely outside of the mother's womb, there could be psychological consequences due to the absence of this bond.

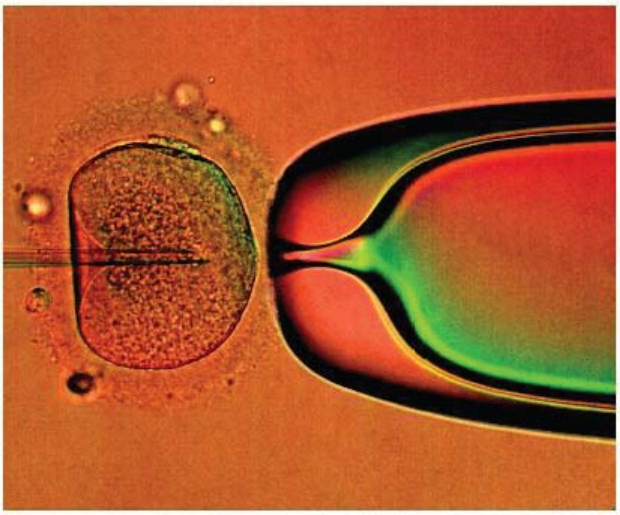
Though the survival-rate of premature babies has improved dramatically, there is a difference between mere survival and healthy living. Frank Duffy of Children's Hospital Boston states, "In the early days of neonatology, just having these babies survive was a miracle. Now it's more or less expected that these 'miracle babies' will survive. We have to help these babies to be comparable to full term infants. That goal is within our grasp." If true, it is our moral obligation to provide these very premature children with health as well as life; we must first develop environments that promote the normal development of premature babies. It is vitally important to improve the outcomes of the children that we know will survive, as opposed to funneling money and resources towards technologies that may lead to more physically and cognitively underdeveloped children.

Still, we may one day see the use of these artificial wombs in our hospitals, and we will have to deal with the ethical consequences. Artificial wombs could one day be considered another alternative to abortion. While the abortion issue looks at the woman's right over her own body, the artificial womb takes the woman's body out of the picture; these fetuses could be born extremely premature and raised instead of being aborted. But of course, the problem would then snowball into the question of how to support these children in our already crowded foster care facilities.

On a more positive note, if regulated appropriately, this form of in vitro implantation could become the sequel to in vitro fertilization and help women who would be otherwise unable to conceive a child, despite its likely high cost. Assuming that the reproductive assistance method would be the most practical usage of artificial wombs, the major ethical priority would once again focus on the well-being and development of the child. This issue is relevant today, and work is being done to improve the environment of the NICU and promote the child's neurological as well as physical development. This step is the key that justifies opening the door to the realm of artificial wombs.

For references see p. 29

deaf by design



By Sara Stream

Through the use of genetic screening, in vitro fertilization, and other medical technology, it is somewhat possible for parents to "design" their children. By using genetic selection, parents can choose certain characteristics for their children before birth, such as blond hair and blue eyes. One aspect of this "designer baby" controversy is concerned with the possibility for Deaf parents to actively choose to have deaf children through genetic selection.

Deaf parents do not view deafness as a physical disability (in which it would simply be referred to as "deaf"), but rather as a shared bond and a common identity among members of the Deaf Community (in which it is referred to as a capitalized "Deaf"). The Deaf Community is based on Deaf Culture, in which strong bonds are formed among Deaf individuals as a result of a common language (sign language) and shared experiences resulting from isolation from the hearing world. Many Deaf parents wish to have Deaf children to ensure that their children will share the cultural, emotional, and social support of the Deaf Community. The ethics of actively choosing to have a deaf child, however, have been questioned.

Although it is highly possible that two Deaf parents will have a deaf child, there are advanced measures which guarantee that Deaf parents will have a deaf child. In vitro fertilization techniques can be used, where embryos are genetically screened and those with the genetic mutations for deafness are selected and implanted into the mother's womb. In a more extreme method, Deaf parents who naturally conceive a child can undergo prenatal genetic testing and if the results show that their child will have hearing, the parents might choose to abort the fetus. In 2004, a Deaf British couple who wished to have a Deaf child underwent genetic testing and found out that they each possessed different recessive gene mutations for deafness and that it would be impossible for them to naturally conceive a deaf child. Medical technology will allow Deaf parents such as these to take further measures to have a deaf child.

Does this medical technology allow parents to provide a unique identity and support system for their child, or does it cause parents to isolate children from the hearing world by giving them a lifelong disability? Francis Murphy, chairman of the British Deaf Association, said in an article from the United Kingdom's Times Online, "If hearing and other people are allowed to choose embryos that will be 'like them', sharing the same characteristics, language and culture, then we believe that deaf people should have the same right." Gedis Grudzinskas, Emeritus Professor of The Bridge Center, a clinic in London that screens embryos, disagrees. "This would be an abuse of medical technology," he said in the Times Online article. "Deafness is not the normal state, it is a disability. To deliberately create a deaf embryo would be contrary to the ethos of our society."

Currently, the British Parliament is deliberating over passage of the Human Tissues and Embryo Bill which includes a clause that would make it illegal for parents using in vitro fertilization to choose an embryo with a genetic defect if other healthy embryos exist. As medical technology advances, the ethics of designing a D/deaf child will remain highly controversial.

For references see p. 29

Baby image by Leonardo DaVinci, In Vitro image from University of Texas

A Short Primer on Cryptography

By Atanas Atanasov

Preliminaries

When young children are first introduced to mathematics, one of the main topics of interest is integers and the operations among them. It is later that they are asked the teacher asks the question, "Are there numbers between numbers?" Its answer gives rise to the whole new universe of real numbers. For the purposes of this discussion, we will confine ourselves to the integers. When a students is first introduced to number theory, they she might initially think that "whole numbers" are easy and that there are no curious problems concerning them — but there is nothing further from the truth. Elementary number theory is a fascinating branch of mathematics, and certainly the most romantic one; K. F. Gauss refers to arithmetic as "the queen of mathematics".

Before going into the subject, let us briefly discuss a few issues of notation. It is universally accepted that modern mathematics is built on top of set theory. One can think of a set as a collection of objects (e.g. fruit, numbers, pastry shops, or functions). We will denote as N and P the sets of positive integers (also called natural numbers)[1] and prime numbers respectively. The sign $\in$ means *element of* or simply *is* (e.g. $3 \in N$ means 3 is a natural number), whereas $/\in$ denotes the opposite (e.g. $2.5 /\in N$ means that 2.5 is not a natural number)[2]. Without further ado, let us chart the basics of number theory.

Remainders and Congruences

Recall a third grade class, when you first experienced division. We were not told that 5/2 = 2.5, but that it equals 2 with a remainder 1. In order to properly think in the context of number theory[3], please forget about the existence of real numbers; think integers, imagine you are back in the third grade. When a number, a, divides another, b, with remainder 0 we say that a divides b and write it $a|b$ for short (e.g. 3|6). When two numbers, a and b, yield the same remainder when divided by some fixed number n, we say that a and b are congruent modulo n and abbreviate it $a \equiv b \pmod{n}$ (e.g. $6 \equiv 21 \pmod 5$). Finally, we call a number prime if it is greater than one and its only divisors (positive) are 1 and itself (e.g. 1, 5 are the only divisors of 5, so $5 \in P$). Otherwise, we call a number composite (e.g. all 1, 2, 5 and 10 are divisors of 10, so $10 \notin P$). Suppose there is a universe whose people are "number-blind" with respect to some fixed number n, so that they cannot tell the difference between two numbers if they are congruent mod n. Then $0, n, 2n, \ldots$ would all be considered the same number, simply called 0, and 1 would be $1, n + 1, 2n + 1, \ldots$, etc. This universe where only remainders mod n are considered, even when adding, subtracting, multiplying, and dividing, is called the finite field of n elements, denoted F_n (e.g. F_{10}, 5+7 = 2). Computers inherently work with 0s and 1s, and this is why elements of F_2 (0 and 1) are called *bits*.

Complexity of Algorithms

Informally, an algorithm means a structured computational method which solves a certain problem. Note that for a given problem there might be more than one algorithm which solves it, possibly with different characteristics. In this section we will get a glimpse of the underlying methods which inevitably appear throughout cryptography, but there. There will be no formal attempt at the subject. When it comes to execution of the algorithm, which is carried out by computers, we are interested in two factors, namely how long it will take, and how much space (memory) it require. These two entities, which are referred to as time and space complexity, are often expressed as functions of the input (or its size).

In order to avoid a lot of dry theory, let's take a practical example. Let A, B, and C be three algorithms taking time N, N^2, and 2^N seconds respectively where N is the input (these are formally referred to as linear,

1 From now on "number" will generally refer to a positive integer unless otherwise stated.

2 Almost every book on elementary number theory and abstract algebra devotes its first chapter to the preliminary notions of naive set theory. For such an account please refer to [2] . For an axiomatic account see [4] . It might also be beneficial to look at [3] (a literary pearl and the winner of Pulitzer Prize) which includes numerous discussions (between Achilles and the Tortoise) on the foundations of mathematics.

3 Please refer to [5] for a more complete introductory account of elementary number theory.

quadratic, and exponential complexities). Suppose we run all three algorithms for $N = 10$ and twice as much. The time A takes will double, that of B will quadruple, and the time of execution of C will be multiplied by a factor of more than 1000. If someone had started C at the big-bang with an input of merely $N = 62$, it would still not have finished executing! Theoretically it is not impossible to compute C, but it is practically unfeasible. The security of cryptography is ensured by functions (problems) which are easy to compute (like A and B), but their inverses are infeasible to find (like C). For example, it is relatively easy to multiply two prime numbers even if they are large, but factorizing an integer whose prime multiples are large is quite difficult. The mentioned example is known as the *factorization problem*. All solutions known are infeasible to compute time-wise, but we have no proof that there is no fast algorithm. Another such pair of easy-hard problems is powering and taking logarithms in F_p for $p \in$

P. Raising a number to some power can be done in time which depends on the logarithm of the power and the square of the length of the number ($(\log p)^3$ in general), but the reverse operation, called *discrete logarithm*, is very slow for large numbers (around 200 digit prime numbers p).

Introduction to Cryptography

Cryptography grew as an attempt to secure information and communications. In *The Histories*, Herodotus describes the first account of people using secret writing: in the fifth century B.C., the Greeks employed obfuscated communication techniques to receive information from Persia about Xerxes' plan to invade them. Despite the long history of demand for such methods, little progress occurred before the twentieth century. Only after people realized how intimately related cryptography is to mathematics and number theory in particular did real advances in the direction of true security happen.

Private Key Systems

If the average person is asked to describe how he or she imagines a cryptographic system, the most common answer involves a two-phase algorithm, one that encrypts the input text (called plain-text) on the basis of some key, text, or number[1], and a reverse operation that decrypts correctly the encrypted plain-text (called cipher-text) provided the same identical key. If the key is not available, it should be infeasible to reverse the operation. This mechanism is called *Private Key Cryptography* or *Symmetric-Key Cryptography*. Let us imagine that Alice and Bob are in possession of a common key, which only they know. Assuming that Eve might wire-tap their phone calls, when Alice calls Bob she always encrypts her messages with the key. On the other side Bob decrypts the received messages using his copy of the key obtaining back the human-readable form. Eve will not be able to understand their conversation, because she would not know the key, and therefore would not be able to decrypt. When Bob speaks to Alice, the same conventions are used. It is understandable why this communication protocol is characterized as symmetric.

Public Key Systems

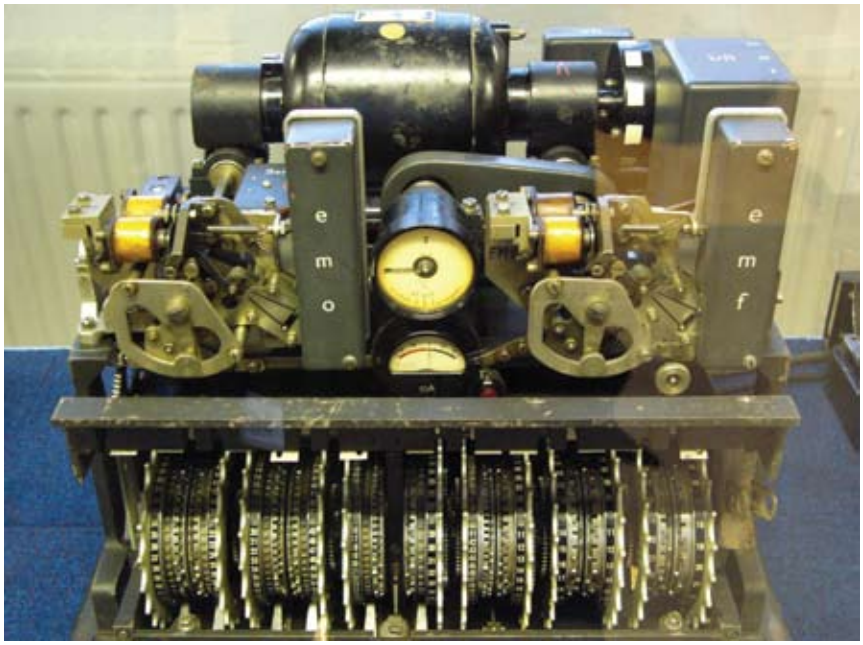
There is one very obvious flaw in the above mechanism. How do Alice and Bob agree on the key and exchange it? If they meet physically then it is very easy to do that. But if they do not, this is not such an easy matter. If Alice randomly generates a key and sends it to Bob, Eve might be tapping the communication line and then she would be in possession of the key too, which in turn means that their communication is not secure anymore. This problem of key exchange is clearly a major threat to the security of communication.

It is not true that two parties are not able to securely exchange keys. However, nobody knew how to perform this operation until recently. The first discovery of such a procedure was in the early 70s at Government Communications Headquarters (GCHQ), the British equivalent of the NSA. Of course, the information was not released into the public domain. Whitfield Diffie and Martin Hellman reinvented the procedure in 1976 which is nowadays currently known as Diffie–Hellman key exchange[2]. The invention of numerous such schemes

1 Plain-text, cipher-text, and keys are often represented in text form (although unreadable) for human and length reasons. On the other hand, mathematics manipulates numbers. Trivial conversion mechanisms are used between textual and numerical representations. These will not be discussed here, and we will predominantly work with numbers for computational and demonstration purposes.

2 See [1] for the original paper.

Image From Door2Door



followed, some of which do not even require a common key but an entangled use of two pairs of keys – one public and one private for each party (the schemes widely used nowadays are of this type). Examples of such are RSA and ElGamal, which fall under the general category of *Public Key Cryptography* systems. The description of these goes beyond the scope of this text.

Diffie-Hellman Key Exchange

In this section we describe the Diffie-Hellman key exchange. To overcome gradually the various technical difficulties, we start by presenting the idea symbolically, which is followed by a short discussion of its realization.

Conceptual Ideas

Although the name refers to the scheme as a "key exchange," there is no real exchange of a single functional key. Conceptually, in the end both parties compute the same key and nobody else is able to do so. Suppose both Alice and Bob generate their own keys, respectively *A* and *B*, which they strictly keep to themselves. They also need to know a transformation function of a key, which is easy to compute but difficult to invert, denoted *T*(key). Alice and Bob exchange their transformed keys in a way that they respectively learn *T*(*B*) and *T*(*A*). Then every party is knowledgeable of its own key and the transformed version of the other party's key. Suppose we also know of a "mixing" operation performed on a key and the transformed version of another, denoted *M*(key, transf. key). Furthermore, this mixing should be symmetric, in the sense that for every two keys *X* and *Y* , we require $M(X, T(Y)) = M(Y, T(X))$. In the above setting, Alice can mix her key with Bob's by computing $K = M(A, T(B))$, and Bob will be able to compute his own copy of the same key by K = M(B, T(A)), which concludes the exchange. We observe that Eve could not compute K, because the only information she has is *T*(*A*) and *T*(*B*), and the mixing procedure requires at least one authentic key which cannot be obtained due to the complexity of inverting *T*.

Realization

The public information necessary for a Diffie-Hellman system is a prime number, *p* (the larger the more secure), and a number g such that $1 < g < p$ for which some additional constraints hold[1]. The private keys of Alice and Bob are respectively the numbers a and b such that $1 < a < p - 1$ and $1 < b < p - 1$ (to avoid security breaches *a*, *b* should not be chosen very close to 1 or $p - 1$ i.e. somewhere in the middle 90%). Then Alice sends to Bob g^a, and respectively receives from him g^b (exchange of transformed versions). Once Alice has g^b, she raises it to the power of her own key to obtain the key $k = (g^b)^a = gab$ (mixing). Similarly Bob computes $k = (g^a)^b = g^{ab}$. Now both parties know the common key $k = g^{ab}$. Yet, Eve has only learnt g^a and g^b which is not enough to compute g^{ab}, unless she can compute the discrete logarithm of one of the values she has to obtain *a* or *b* respectively. It is clear that the security of the scheme depends on the discrete logarithm problem. Modern standards of security require use of a prime number *p* of size about 200 decimal digits. Finding such a *p* and a primitive root for it, *g*, is not an easy task and is beyond our discussion.

Ideas of Security

The security of modern cryptography mainly depends on the difficulty of performing integer factorization, computing discrete logarithms, and solving other similar problems. Choosing long enough keys is one of methods that ensures no third party is aware of the transmitted message.

1. Technically, g should be a primitive root in order to avoid security breaches. A primitive root is a generator for $(Z/pZ)^x$, which is the multiplicative structure behind Fp. In simpler words, g s 4= 1 for any $1 \leq s < p - 1$. The least such $s \geq 1$ is called the order of g, therefore primitive roots have order $p - 1$ which is the size of $(Z/pZ)^x$. For more information on the topic, please consult any introductory text in abstract algebra, such as [2] .

However, computers become faster by the hour, and there is continuous progress on code-breaking techniques (called *cryptanalysis*) which makes most of the keys used 20 years ago utterly insecure. Also, although we described operations in F_p as fast and easy (relatively to the difficult problems), these are quite time consuming considering the large amounts of data (e.g. a secure ElGamal to today's standards requires the raising of a 200 digit number to the power of another 200 digit number roughly for every sentence transmitted). This problem is often addressed using secure communication tunnels (the secure hypertext protocol, *https*, uses a secure channel known as SSL, over the insecure Internet network). We already covered the basics of tunnelling, which is key exchange. In practice, the parties use a public key encryption system to exchange a key and then use a faster private key to transfer large amounts of data (e.g. Data Encryption Standards (DES) which is a block cipher). More sophisticated schemes can also involve a trusted third party which can verify the authenticity of either party (e.g. Verisign).

Having learnt some details about cryptography at a level above the average, one might become increasingly aware of the security threats and ultimately refuse to use various advances of modern society like online payments and internet banking. Paranoia is never a solution! Although minimal threats do exist, the open society we live in is continuously pushing towards better security standards. Another slippery slope is the use of strong cryptography for non-peaceful purposes, and this is what agencies like NSA and GCHQ are trying to control. This is dual position, in the sense that both sides can be argued very extensively and one can hardly ever reach a meaningful conclusion. The best way to address such issues would be to install better awareness of the subject of cryptography, so that people cannot be misled by the numerous sophistic arguments that flow into the public domain.

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A Closer Look....

Margaret N. Oechsli, Jewish Hospital/Heart & Lung Institute/Louisville, Kentucky, Photo courtesy of Nikon Small World

The chemical Phenyl threonine (20x)

A Look Into the Life of David Helfand

"I think it's really important to communicate science to the public since the issues we need to face have so much science content, and the public is so woefully under-informed about science."

~ David Helfand

By Jennifer Hou

Many of his astronomy and Frontiers of Science students may wonder how Professor David Helfand, chair of the Department of Astronomy and codirector of the Columbia Astrophysics Laboratory, became such a captivating teacher. The secret lies in his multiple talents and his love of astronomy.

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While his life story from college on closely parallels the history of modern astronomy, astronomy is not his only interest. As a child growing up in southeastern Massachusetts, Helfand did not have a burning desire to study astronomy. In high school, he was enthralled with theater and acted in several plays. After graduation he entered Amherst College determined to be a theater major, until he took an astronomy course. Although it was mostly by chance that he took the class, it did introduce him to eclipsing binary stars and the enormous amount of information that could be obtained just by looking at the single point of light from these stars getting alternately brighter and dimmer.

Subsequently, he took another astronomy course in his sophomore year during which, the teacher presented all eight students with tickets to Arizona, the center of astronomy in the United States. Aside from enjoying the warm weather in Arizona, Helfand met many prominent astronomers and saw telescopes being built. He was particularly inspired by the director of the University of Arizona Observatory who posed this question to the students: "Suppose you are called before Congress and asked to testify as to why one should use public money for esoteric purposes (astronomy)?" He told the students that the reason for using public funding for astronomy is the same as for funding symphonies, art museums, and opera companies with public money-it is an "essential aspect of being human, and to spend a tiny, tiny fraction of [our] GDP on this thing that satisfies a basic need of humans to explore and understand is culturally significant and important." Helfand went on to the University of Massachusetts to work with astronomers who were building a big radio telescope to observe pulsars, which had been only recently discovered. After completing his Ph.D. there, Helfand moved to New York and to Columbia where he has remained for 31 years. Although science is now his forte, his theater experience and excellence in public speaking serve him well,

Image provided by David Helfand

lending entertainment value to his lectures and helping to make him an even more effective communicator.

While many astronomers choose to become an expert in a certain field and focus on that for the rest of their lives, Helfand has a different philosophy. "I have a more entrepreneurial approach. I have subjects that I have been interested in for a long time like these neutron stars, but if there's a new radio telescope, I'll go pursue that and think of something interesting to do with that rather than stick to my one subject on which I've become the expert." He describes himself as having "an epicurean, hedonistic philosophy. I just go with what feels fun at the moment." After receiving his Ph.D., he turned down three offers to continue to use radio telescopes and instead went to Columbia University to do something totally different by participating in a consortium that was about to launch the first X-ray telescope. This turned out to be a great opportunity for Helfand. Most of those building the new telescope were physicists who were clever at constructing the telescope but knew little about astronomy; it was up to Helfand, the astrophysicist, to decide where to point the telescope. As he recalls, "I wrote many papers on almost every subject in astronomy because almost everything emits X-rays. We were literally seeing the universe with new eyes."

> "[Astronomy is an] essential aspect of being human...To spend a tiny, tiny fraction of [our] GDP on this thing that satisfies a basic need of humans to explore and understand is culturally significant and important."

In keeping with the inspiring words of the director of the University of Arizona Observatory, Helfand feels an obligation to "educate beyond the confines of the university." He taped a series for National Geographic Television and enjoys giving public lectures at various locations throughout the country. Helfand infamously has a tendency to have difficulty turning down speaking requests, admitting that, "I have this bad problem with the word 'no'." As a result, he has, in the last month, presented three different lectures at different locales in Georgia, seven different lectures in California, and a couple of lectures at Penn State. His next project is a series of lectures for the Learning Company, which he will be filming in the fall, allowing him to reach an even larger audience.

Helfand has always been innovative. Seeing that Columbia's Core Curriculum grossly lacked science and math courses, Helfand began advocating a Core science course in 1982, and although several models were proposed, the course did not come into existence until 2003 when a few hundred of the incoming freshmen were sent letters inviting them to take the pilot course, Frontiers of Science; about 85 percent of those invited participated, and the following year the course became part of the Core. According to Helfand, the course is constantly evolving, and the biggest change planned for next year is to give the lectures twice in a classroom instead of a theater.

Another innovative educational activity is Helfand's work with Quest University in Canada on the block system in which students take four courses per semester, but rather than taking the courses together, the students take the courses one at a time for five to six days a week for 3 weeks before going on to the next subject. In addition to helping to design the curriculum, Helfand helped the university hire faculty and last fall taught a course called Our Place in Space and Time.

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Besides astronomy and theater, Helfand's interests extend to cooking. As a child he cooked with fresh vegetables grown on his family's 30 acres of land, as well as with local fish and seafood, but it was not until he started traveling to Europe and expanded his palate that he became determined to cook such food himself. Even without any lessons, he has become a gourmet cook in high demand and recently raffled off a six-course dinner for six. His favorite dish is coquilles Saint Jacques à la Créole, but he does not prepare this often because it takes six hours just to make the sauce. He hopes someday to combine his passions by offering a physics of cooking course.

What are his plans for the future? To this, Helfand replies, "You're assuming I plan, and I don't." You may see him impersonating Galileo, for which he has been growing his beard, during 2009, which has been declared the Year of Astronomy by the United Nations. He may buckle down to write a book revolving around the idea of using isotope ratios to reconstruct history. As he explained why he does what he does to a janitor who marveled at his hard work and dedication, "I do it because I think it's really important to communicate science to the public since the issues we need to face have so much science content, and the public is so woefully under-informed about science."

Invasion of the Superbugs

■ By Amy Huang

Deadly bugs are among us everywhere-they live on door handles, hospital catheters, and human hands. They call for the most potent antibiotics known in the world, and even then, it is not certain how effective these drugs would be. They lurk silently, waiting for someone to walk out of that bathroom without washing his or her hands. They are the superbugs.

From Viruses to Bacteria: The Mechanisms of Resistance

The influenza virus, a primarily seasonal virus, poses a great threat to public health, rapidly transmitting through droplets spread from person to person from sneezing or coughing, and can even infect healthy individuals. Seasonal epidemics kill millions of people, as illustrated by the lethal pandemic of the Spanish Flu in the early 1900's. Inflicting severe hemorrhages on its victims and killing between 50 to 100 million individuals, the pandemic left its mark on humanity as "the greatest medical holocaust in history" (Waring, J.I.). Antigenic shift and drift in the influenza virus produces many serotypes, or subdivisions, of viruses that are created by a series of mutations that alter the surface antigens to varying degrees of virulence, depending on the structure of the surface proteins. For example, H1N1 is the Spanish Flu that claimed millions of lives, while H5N1 is the Avian Flu that continues to spread among birds. Although it remains difficult to determine the next evolving serotype, recent vaccines and antiviral drugs like neuraminidase inhibitors, which work by blocking the viral neuraminidase protein to prevent viral budding and reproduction, make the flu easier to treat and prevent. Like influenza, bacteria exhibit a similar type of evolutionary mechanism; certain bacteria are able to change their physical cellular features in order to elude destruction by antibiotics, while some are naturally resistant to antibiotics. However, a new threat is emerging, as the rampant use and misuse of antibiotics can render certain bacterial diseases virtually untreatable, destroying susceptible strains of the bacteria but allowing the resistant strains to proliferate.

The mechanisms of drug resistance range from drug inactivation to the alteration of target sites, but the etiologies of such a mechanism usually stem from spontaneous mutations of a single bacterium, which can then replicate into thousands of resistant generations. The rate of bacterial mutation is unparalleled by that of any other organism. One such case is *Staphylococcus aureus*, a ubiquitous bacteria responsible for most nosocomial, or hospital-acquired, infections. Antibiotic resistance is not just an emerging problem; it is an ongoing pandemic that has gone largely unrecognized in light of recent influenza cases, and it affects people of every socioeconomic level, race, gender, age, and origin. If immediate action is not taken, the issue of antibiotic resistance can become more problematic than influenza itself, as effective treatments may no longer be available.

Antibiotic resistant strains of common bacteria inflict diseases with similar clinical manifestations as non-resistant strains. However, the lack of effective treatment due to their resistance increases the mortality rate and severity of certain infections, causing many once curable diseases like tuberculosis, gonorrhea, and malaria to become near death sentences. Immunosuppressed patients are most at risk of dying from normal infections, but even individuals with normal immune functionality are unlikely to survive when infected by drug-resistant strains. Additionally, the second-choice medications administered tend to be more toxic and more expensive, but less effective than first-choice drugs. Second-choice medications are used when the first antibiotics that are administered are not effective against the target infection. These

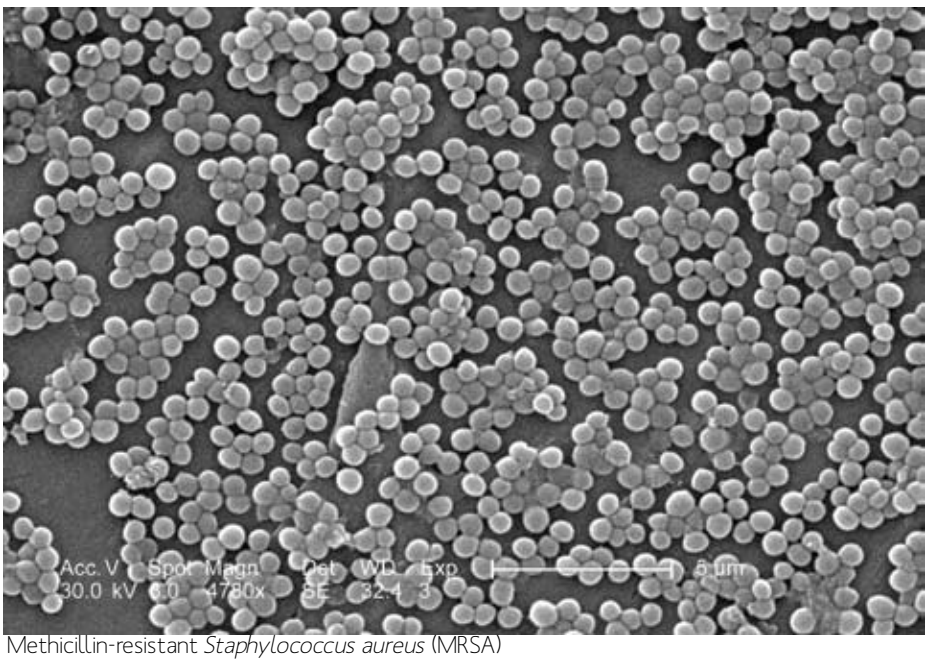
medications run the risk of producing stronger antibiotic-resistant strains that can also overcome second-choice treatments and spread throughout communities.

Infecting by the Numbers: The Statistics of Resistance

Around the world, more than 50% of antibiotics are administered inappropriately or are over-prescribed, leading to high rates of bacterial resistance.6 Many cases of resistance are seen in parts of the world where antibiotics are administered inappropriately or are over-prescribed. The United States is an example of a country where the vast array of medications used to fight infection are rendered ineffective when patients do not complete their course of antibiotic therapy, increasing the amount of resistant bacteria in the body and spreading them to communities. From 2000 to 2005, forty-five cases of pyomyositis, a bacterial infection that forms abscesses in skeletal muscle, emerged in healthy children at the Texas Children's Hospital. Ten of the cases were found to be caused by Methicillin-susceptible *Staphylococcus aureus* (MSSA), while sixteen cases were caused by Methicillin-resistant Staphylococcus aureus (MRSA). A study was initiated to investigate the outbreak, and researchers found that the number of MRSA cases have increased significantly from four in the first year to twelve in the fifth year. The sudden rise in MRSA infections was mainly attributed to lack of hospital staff adherence to basic hygienic procedures, such as frequent hand-washing, wearing gloves and gowns as appropriate, and diagnosing and treating a patient infected with MRSA as quickly as possible to avoid spreading the resistant bacteria.

> "Several Asian countries have the highest rates of antibiotic resistance in the world, with more than 90% of the bacteria no longer responding to first choice medication."

China and certain parts of Asia are encountering similar crises of antibiotic resistant strains of bacteria infecting humans. In 2005, China experienced an outbreak of *Streptococcus suis,* a zoonotic disease spread by pigs, because of the overuse of antibiotics in these animals. Although it is normally treatable and rarely spread to humans, doctors were baffled by the sudden virulence of the bacteria and the recent deaths of thirty-nine people infected with the disease. It has now spread to other regions in China, infecting more than two-hundred people. The World Health Organization states that several Asian countries have the highest rates of antibiotic resistance in the world, with more than 90% of the bacteria no longer responsive to first-choice medications. Doctors in China are worried that the lack of antibiotics administration controls may generate more drug resistant strains over the years. Of all the antibiotic resistant bacteria, MRSA, a strain resistant to methicillin, penicillins, and cephalosporins, is perhaps the most common and problematic. Studies show that approximately 30-50% of populations carry the *Staphylococcus aureus* bacteria asymptomatically, only infecting the body when it is immuno-compromised. The organism can spread endogenously from the external nostrils to an open wound, causing infection. In hospitals, cross-infection can occur as a result of direct or indirect contact with infected individuals. In the case of epidemic MRSA (E-MRSA), a particularly successful strain facilitates the rapid dispersion of bacteria among hospitals. In the UK, cases of MRSA have risen significantly from 1.5% to 20% in a period of seven years, while cases in 2003-2004 have increased by 3.6%. In the U.S., the National Nosocomial Infections Surveillance system (NNIS) reports a 40% increase in bacterial resistance in 1999, as compared to data from 1994-1998, with MRSA accounting for 52.3% of the Staphylococcus aureus nosocomial



Methicillin-resistant *Staphylococcus aureus* (MRSA)

infections. MRSA was originally present in hospitals as a resistant infection, but the disturbing trend of MRSA infecting healthy people outside of a hospital setting has appeared in recent years as "community-associated MRSA" (CA-MRSA).

CA-MRSA: Communities At Risk

CA-MRSA is not only difficult to treat, but also highly infective due to virulence factors that allow the bacteria to invade tissues more effectively, causing deep tissue damage from minor lesions in the skin. These infections are also common in cystic fibrosis patients, who often harbor the bacteria and exhibit fatal forms of MRSA pneumonia. The major histocompatibility complex (MHC) is a large region of genes that play an important role in immunity and autoimmunity, and a region that is affected in a CA-MRSA infection. It has been found that CA-MRSA releases deadly types of enterotoxins, protein toxins that are secreted by bacteria, such as Enterotoxin H and O. These have high binding affinities to MHC type II molecules, causing severe toxic shock-like disorders. The genes that code for the enterotoxins, lukS-PV and lukF-PV, are responsible for acute necrotizing pneumonia, necrotic skin lesions, and the destruction of leukocytes. Other virulence factors, such as the Panton-Valentine leucocidin (PVL) and mecA genes, contribute to the high adaptability and transmission rates of CA-MRSA.

MRSA: From the Hospitals to Abroad

MRSA infections greatly affect the ability for doctors to treat diseases that are already difficult to control, such as necrotizing fasciitis, septicemia, and toxic shock syndrome. Other localized, superficial skin infections are also rendered more difficult to treat. A 2001 research study of 986 hospitals in the United States discovered that patients infected with MRSA are five times more likely to die than other patients. Statistics from these studies present alarming evidence that MRSA creates underlying disorders that raise the mortality rates of certain diseases, lengthen a patient's hospital stay, and raise their medical bill. On average, a MRSA-infected patient had fives times the risk of in-hospital death than a non-infected patient, three times the total hospital charges, and three times the length of hospital stay. Even more startling is the rate at which the bacteria can replicate and transmit, as MRSA can incubate inside of Acanthamoeba polyphagam, a common type of amoeba found in hospitals. Researchers in the UK found that MRSA can multiply 1000-fold inside the organism and disperse through air currents by way of amoeba cysts. This mode of transmission is effective, because the bacteria are protected inside the cysts, while spreading as an aerosol. Additionally, it is possible that the MRSA that are incubated inside an amoeba are more virulent and less susceptible to antibiotics than MSSA incubated inside the amoeba. In one experiment, the mutation frequency for rifampicin-treated MRSA was 10^{-8} in all strains tested.

> "The global increase in resistance to antimicrobial drugs...has created a public health problem of potentially crisis proportions."
>
> --American Medical Association

Although MRSA infections can be treated with vancomycin and teicoplanin, recent cases of resistance to these drugs render treatment extremely difficult. Vancomycin resistant *Staphylococcus aureus*, or VISA, have spread to hospitals in the U.S., Brazil, England, France, and Asia. While cases of VISA infections remain rare, scientists are worried that its rapid rate of mutation and dispersion can lead to outbreaks of the extremely resistant bacteria around the world.

Antibiotic resistance is difficult to combat because of effective bacterial mechanisms that override even the strongest medications and result in severe outbreaks from the lack of successful treatments. Bacteria have evolved to mutate rapidly in response to the utilization of broad-spectrum

antibiotics, such as cephalosporins. In an 11-year study of neutropenia patients in Switzerland, researchers found that between 1983 and 1990, no strains of *Escherichia coli* were resistant to five fluoroquinolone antibiotics., Surprisingly, between 1991 and 1993, 28% of the strains were resistant to all five of the antibiotics. However, the rate of appearance of resistant bacteria depends on the amount of antibiotics administered, or whether certain antibiotics are used in conjunction with others. With many countries' dependence on antibiotics as "miracle" drugs, the rate of drug resistant bacteria is sure to increase within years.

Airplane travel only increases the risk of rapidly dispersing the resistant organisms from their countries of origin to other countries, and exacerbating a pandemic. The emergence of two extremely virulent types of tuberculosis, MDR-TB (Multi drug-resistant TB) and XDR-TB (Extensive drug-resistant TB), fueled World Health Organization conferences in South Africa and calls for stronger preventive measures to control the spread of these strains. Although these types of TB mainly exist in populations with poorly managed TB care and patient non-adherence, plane travel has spread the disease from South Africa and New York City to Paris, Denver, Florida, and Nevada. Drug resistant TB is an especially serious threat to public health in countries with high rates of HIV and insufficient health care resources. Its impact on HIV mortality rates is significant, as illustrated by the 90% mortality rate of AIDS patients with drug resistant TB.

Antibiotic resistant organisms also can easily establish themselves in hospital settings. More than 2 million American hospital patients are affected each year, with 13,300 deaths in 1992. Their ubiquitous nature in hospitals and certain populations correlates with the rapid transmission of the organisms to other communities. The estimated cost of treating and preventing these infections is high, at least $1.3 billion in the United States alone.

Antibiotic Resistance: An Emerging Pandemic

The problem with antibiotic resistance is that it is preventable when measures are taken to ensure that patients complete their course of antibiotics and that doctors do not inappropriately prescribe drugs. However, lack of patient compliance and antibiotic administration controls further the spread of such pathogenic organisms. Antibiotic resistance brings back many once-treatable diseases and transforms them into highly virulent diseases resistant to the most potent antibiotics available. The American Medical Association expresses its concern of the emerging threat of drug resistance in the following: "The global increase in resistance to antimicrobial drugs, including the emergence of bacterial strains that are resistant to all available antibacterial agents, has created a public health problem of potentially crisis proportions." If measures are not taken to prevent the transmission and emergence of antibiotic resistant bacteria, the ongoing pandemic will indeed rise to crisis proportions.

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Picture by Sweta Agrawal and Ying Li

The Philosopher's Stove:

Molecular Gastronomy and the Science of Food

Cross section of a grape (*Vitis vinifera*) (10x)

By Sweta Agrawal

A brilliant chef is a lot like a brilliant scientist: not only do they both need a keen understanding of the basics of their craft, but they must also possess an ability to improvise and invent, experimenting with new techniques, concepts, or flavors. Their tools are similar, be it chemicals or foods (foods are, after all, chemicals), Bunsen burners or gas stoves, incubators, water baths, or ovens, and they face many of the same enemies: bacteria and mold.

Many renowned scientists have also been avid food lovers: take for example Seymour Benzer, famous for his work with fruit fly behavioral genetics. Benzer was especially in love with exotic foods, and would bring ingredients like ostrich eggs into his lab and cook them in a beaker set over a Bunsen burner. And, when working with fruit flies that had a tendency to develop brain defects, Benzer named each mutant after some food that resembled the shape of the fly's lesions. Other noted food-loving figures include Francis Bacon, who is remembered more as a philosopher and proponent of the scientific revolution than a scientist. Bacon (his very name cannot help but remind you of food) met an untimely death when he was inspired to try to use snow as an aid to preserve meat. After stuffing a fowl with snow, Bacon caught a deadly form of pneumonia that quickly ended his life, though not before Bacon actually tried eating the half frozen bird, hoping it would somehow delay his death. Needless to say, it did not work.

But for all this, cooking has still always been placed in the realm of art or tradition, at most being considered a sort of "mysterious alchemy" by which foods are magically turned into sumptuous pies, gravies, and roasts. Recipes are typically passed on by word of mouth, and often include little truisms or culinary conventions for the chef's benefit: add salt to pasta before boiling it, mayonnaise will fail when prepared by menstruating women, and many other

strange tricks and superstitions have accumulated over the years through culinary trial and error.

Recently, however, a group of scientists and chefs have taken a special interest in the science underlying food and cooking. Preparing a stock does, after all, involve a lot of chemistry and physics. Heat convection, conduction, denaturing proteins, Maillard reactions, colloidal suspensions, phase changes—they all contribute to the success of the most basic recipes. This interest in the science of cooking is now often referred to as "molecular gastronomy" and is the brainchild of two men in particular: the biochemist Herve This (pronounced "Tees") and the late Oxford physicist Nicholas Kurti.

The Hungarian-born physicist Nicholas Kurti was the first to demonstrate the possibilities of molecular gastronomy in a presentation to the Royal Society of London in 1969 entitled "A Physicist in the Kitchen," during which he is often purported to have said, "I think it is a sad reflection on our civilization that while we can and do measure the temperature in the atmosphere of Venus, we do not know what goes on inside our soufflés." During his presentation, Kurti demonstrated such wonders as the digestive powers of proteins in pineapple juice, the cooking of sausages by connecting them across a car battery, and a Reverse Baked Alaska (hot inside, cold outside) made in the microwave.

Herve This, when discussing the inspiration that led him to investigate the science of cooking, always tells the following story: one day, he was looking through a magazine when he noticed a recipe for a cheese soufflé. The recipe called for 6 eggs but gave a very curious instruction: "add the eggs two-by-two, no more, no less." Intrigued, This invited his friends for dinner and tried to make the soufflé for them. "Because I was a rational man," he says, "I tried to put the eggs in all at once… it was a disaster." At the time, This took his experiments with the cheese soufflé as proof that eggs really did need to be added two-by-two, though he had no idea why. Looking back, This realizes that in fact the disaster was probably due more to his inexperience with soufflés rather than some scientific phenomenon. The same experience is probably why the "two-by-two" wives' tale continues in many French soufflé recipes. Recipes are the result of trial and error by chefs, and when they come across a success, they tend to remember the details of the situation that led to that success so they can repeat it, much like a football player continuing to wear the same dirty pair of socks over and over again, or a tennis player eating the same breakfast before every big game.

> The discovery of a new dish confers more happiness on humanity, than the discovery of a new star.
>
> -- Jean Anthelme Brillat-Savarin

Since his soufflé disaster, Herve This has dedicated a large part of his research to the compiling and testing of such cooking truisms, which he likes to call "culinary precisions," in an effort to simplify recipes by getting rid of all the superstition and untruths. These culinary precisions formed the bulk of his PhD thesis, which was the first PhD in "molecular gastronomy" ever earned. This also went on to coin the term "Molecular and Physical Gastronomy" with the help of Nicholas Kurti, which was later shortened to "Molecular Gastronomy" after Kurti's death. This has since written several books on what he likes to call "the science of deliciousness." He is best known for his work with eggs, including the discovery of the perfect temperature for cooking an egg, around 65°C, at which the white, but not the yolk, coagulates. This has gone on to collect more than 25,000 culinary precisions, and has overhauled many culinary axioms including the ideas that searing meat seals in the juices, that the cooking time for roast meats depends on weight, and that haricots verts need to be immersed

in cold water immediately after cooking in order to help preserve their bright green color.

This is also well known for developing a formal system of classification of what happens when different kinds of ingredients (such as solids, liquids, or gases) are cooked in different ways, like mixing, frying, whipping, baking, and so forth. In this system, for example, puff pastry becomes ((S1/S2)0.5 ((W/O)/S3)0.5) 729, a formula which means little to us, but which can greatly help chefs or scientists when studying foods and their compositions. This system, for example, can demonstrate that 451 French sauces essentially fall into 23 different types, but most importantly, allows for the creation of brand new sauces and dishes. In an exciting demonstration on the possibilities of this system, This randomly generated a formula describing the physical microstructure of a previously nonexistent dish, then asked chef Pierre Gagnaire to plug real ingredients into it. The result was a bitter orange, scallop, and smoked-tea concoction which delighted Gagnaire's customers.

We can begin to see how molecular gastronomy has not just been a topic for scientific journals or academia; rather, many chefs have actually begun to apply this new knowledge to their cooking, giving rise to a new trend in haute cuisine called molecular cooking[1]. Noted molecular chefs include Ferran Adrià of El Bulli (Girona, Spain), Grant Achatz of Alinea (Chicago) and Wylie Dufresne of wd50 (New York City). These chefs have used molecular gastronomy to develop foods that use techniques like vaporizing foods with lasers, developing hot foams, using chemicals like sodium alginate and calcium carbonate to make edible "spheres" of liquid, deep frying mayonnaise, and even developing edible menus using an inkjet printer adapted for inks made from vegetables and fruits. These restaurants try to provide truly unique culinary experiences, exploiting the discoveries of scientists to develop whole new methods of cooking and new textures or ways of eating food. Of course, all of these chefs are quick to say that they are not "molecular chefs;" science is only one aspect of their cooking. Nevertheless, the influence of molecular gastronomy on their cooking is unmistakable.

This, however, does not aim to just change haute cuisine. He genuinely hopes that his discoveries can someday lead to the development of new dishes and new methods of cooking that people can use in their own homes. Many of the techniques that came out of his and other related research have already made their way into common kitchens, like the use of a water bath and vacuum sealer to cook meats at low temperatures to a juicy perfection (also known as sous vide). Renowned Food TV personality Alton Brown is yet another example of the use of science to help non-professional cooks understand how to cook better and more confidently. Moreover, a large portion of This's book, *Kitchen Mysteries: Revealing the Science of Cooking*, is dedicated to understanding how a common household tool like the microwave works and how it can be used to cook in new ways. At other times, This also discusses how to make a successful soufflé, braise, or bread simply by being

1 Herve This is at great pains to distinguish molecular gastronomy, the scientific investigation of cooking, from molecular cooking, the actual application of the discoveries of molecular gastronomy. One he cites as science, the other as technology.

Picture by Saroja Bangaru

more aware of the reactions that take place and their results. Most of all, he asks us to understand food in new ways, as not simply mixes of oils, spices, vegetables, and meats, but also as solutions of lipids, proteins, and water, demystifying what have always been traditionally considered difficult techniques reserved only for the most skilled of chefs. This is thus fascinating not only in his commitment to a scientific understanding of one of the most fundamental aspects of our lives, but also for his firm belief that food should not be relegated to the domestic sphere of tradition and superstition, but should be actively acknowledged, developed, and understood.

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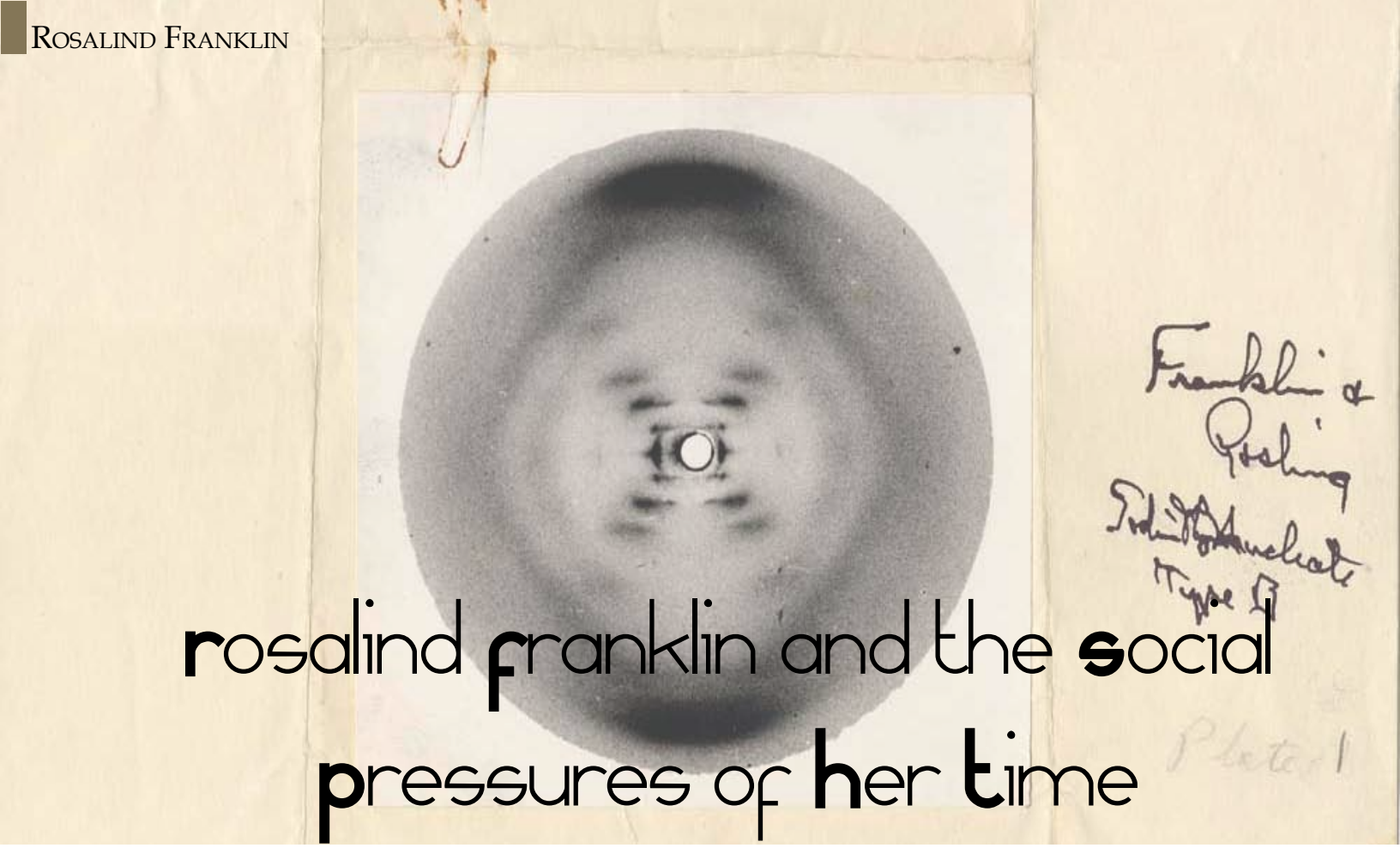
But if you are beginning to think that This means to take the love and passion out of food, reducing it to what we think of as "dry science" or a system of rules, you would be very much mistaken. This is a passionate foodie, who loves to cook for his friends and will spend hours talking about food. His research reflects this deep understanding of food and its importance in our lives. Recently, he has decided to take on the project of understanding how love, be it the love of the cook for diners, of diners for the cook, or everyone for each other, affects our tastes.

Or, you can just take a look at the glossary of his book, Kitchen Mysteries, which opens with the following: "Aaah!: The cry of delight guests utter when the first dish arrives. The sleight of hand responsible for the most beautiful 'aaahs' cannot be explained in terms of physical chemistry." Or, the other very endearing entry, "Béarnaise: One of the crown jewels of French cooking (I have a weakness for it; don't tell my wife!)"

Interested in learning more about molecular gastronomy? I would recommend any of This's books, though unfortunately, very few have been translated into English. In particular, Kitchen Mysteries: Revealing the Science of Cooking is an incredibly enjoyable read, and the breadth of foods and techniques it covers is amazing. He dedicates at least one paragraph, if not an entire chapter, to every major course, food group, or technique, ranging from a simple discussion of when to add salt to a crash course on making the perfect stock. You can also try reading Harold McGee's On Food and Cooking, written by a food scientist from the United States. And finally, NYU is home to the newly founded Science Cuisine Collective, a group of chemists, biologist, physicists, and food enthusiasts from all over the city that meet every so often to discuss food and the science behind cooking and eating.



rosalind franklin and the social pressures of her time

By Alexandra Polsky

Rosalind Franklin, working at King's College London for a short eighteen months from 1951 to 1953, made important contributions to the question surrounding the structure of DNA, the hereditary information found in all organisms. She discovered the B form of DNA, the compact double-helical structure we typically see, which occurs in crystal form upon hydration of the molecule. Franklin also succeeded in capturing X-ray crystallographic images of both the A and B forms of the molecule and her images of the B form, specifically the famous "Photo 51," were integral pieces of experimental evidence, among many other theoretical considerations, that lead James Watson and Francis Crick to the publication of the correct structure of DNA in 1953. Her untimely death in 1958 at the young age of 37 made her ineligible for a share of the Nobel Prize awarded in 1962 to Watson, Crick, and her coworker at King's College, Maurice Wilkins, with whom she never had even a cordial working relationship. But, despite her ineligibility, no great lengths were made to even recognize her contributions to this cornerstone discovery. Instead, her role was either ignored or outright belittled.

An analysis of Franklin's notes was written in 1968 by Aaron Klug, who worked with her once she left King's College in 1953, and it is apparent that Franklin was indeed very close to determining the structure of DNA by herself. Upon seeing Watson and Crick's first model that showed the phosphate backbone on the outside with the bases pointing inwards, she immediately accepted the structure as correct, further proof of her intimate understanding of the parameters for the correct solution. As her friend Anne Sayre wrote in her biography of the discovery, "...[Rosalind] was a very good scientist who knew her subject and could not help but recognize the perfect solution when she saw it. It was, come to think of it, one of the best compliments Crick and Watson ever received"

Franklin herself was probably unaware of the central role her own data played in Watson and Crick's deciphering of the structure. The tragic irony is that she was pleased the model confirmed her own work, but she had no idea that that was because it actually incorporated her work. For in February of 1953, only a few months before Watson and Crick, Wilkins, and herself all published their papers side-by-side in the April 1953 issue of *Nature*, Wilkins had (without Franklin's permission, and probably to spite her because of their less-than-warm relationship) confided to Watson that he and his assistant Crick were duplicating Franklin's work without her knowledge. Wilkins then proceeded to show Watson the stunning X-ray diffraction photographs of the crystal of B form DNA that Franklin had produced. The effect was dramatic, and, as the story is told, Watson immediately

recognized that the structure of the B form must be double-helical. However, Watson and Crick were not as quick to give Franklin her due credit. In their April 1953 *Nature* article, published three pages before Franklin's article in the same issue, they wrote, "We were not aware of the details of the results presented [in the following communications] when we devised our structure...," a lie which Watson admitted in *The Double Helix*.

So the question can be asked, if Franklin had been alive, would her contribution to the project have earned her a share in the 1962 Nobel Prize in Physiology or Medicine?

In a retrospective article published in *Nature* in 1974, Crick wrote, "If Watson had been killed by a tennis ball I am reasonably sure I would not have solved the structure alone, but who would?" The rhetorical question is rather poignant because this is exactly what Rosalind Franklin was doing—trying to solve the structure alone—and by no fault of her own.

> "If Watson had been killed by a tennis ball I am reasonably sure I would not have solved the structure alone, but who would?"
>
> --Crick, 1974

It has been long acknowledged that the key to Watson and Crick's successful solution of the structure was the candid, open, and informal nature of their collaboration as well as their differing scientific backgrounds that complimented one another so well. They understood the theoretical requirements of the molecule, namely that it had to act as a template for synthesis of the components of living things and that it have some way of duplicating itself. They used these elements of theory to fit together experimental evidence, something which no other group working on the structure was able to do.

As Judson writes, "Rosalind Franklin...had no such collaborator. It is evident from her notebooks that she needed one." Klug's analysis of her notes proves that she was focused purely on the experimental data, circling back and forth between believing the structure was helical and believing it was not. She based her thoughts solely on the minute calculations of the Patterson synthesis, a formula used for interpreting X-ray diffraction patterns, and had none of the theory, the biological or genetic implications of the molecule, in mind. She was solely concerned with its structure. Franklin was a crystallographer, and so it is not surprising that, without a collaborator to help her contextualize her research, she would not be interested in much else besides the molecular dimensions of DNA.

So why did Franklin lack such a collaborator? Before coming to King's College, she worked in France, where she was known for her ability to foster successful and warm professional relationships, so she was clearly capable of the frankness and openness required for such a relationship. Yet the culture in France afforded women much more equal treatment at that time. During the time Franklin was engaged in her research at King's College, the main cafeteria there was not open to women, and instead there was a separate, much smaller room in which the female staff was permitted to eat their lunches. In this context, then, Franklin's lone, and ultimately unsuccessful, struggle toward solving the structure suddenly made perfect sense. So much of science, and the success of a scientist, is based on facts and ideas learned through casual interaction, camaraderie, and operating in an environment where the scientist is able to ask candid questions of colleagues. An environment such as this must have fostered Watson and Crick's successful relationship. Yet Franklin's environment demonstrated that she was not valuable outside of what she could produce on her own, and she was therefore forced to work in such a way.

To attempt to answer the question, then, whether Franklin would have also shared the prize had she been alive in 1962, is difficult. Friends, coworkers and historians have all written passionate arguments that the way she was treated when alive certainly indicates that she would have been disregarded in the case of the Nobel Prize as well. But then again, her contributions to the structure of DNA might actually have been rather minor. She was unaware of the potential significance of the discovery, and her work was one-sided, purely experimental, and uninterested in theory. Watson and Crick not only proposed a structure in April of 1953, but they also commented on the "genetical implications" of the molecule and proposed a loose theory for a copying mechanism, one which turned out to be not far from the truth. Franklin's article in the same issue of *Nature* is purely interested in calculations.

It is still debatable whether she would have shared the prize. But no one can doubt Franklin's brilliance, which is, if anything, proven by how close she was to the solution working purely on her own. She was a victim of a social environment supremely unwelcoming to women, forcing her to work in a fashion least conducive to scientific discovery—isolated, unhappy, and alone.

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Image from Oregon State University, Special Collections, the Valley Library

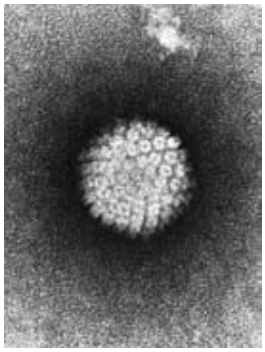
GARDASIL®
A GUARD AGAINST HPV

■ By Laika Simeon

By now we have probably all seen the commercials and advertisements for Gardasil®, the recently released vaccine for Human papillomavirus (HPV). When the vaccine was made available in 2006, there was both elation, due to its public health implications, and apprehension, due to its ethical implications, for the outcome of its administration. But in order to fully understand the controversy, it may help to explain what HPV is.

What is HPV?

About 20 million people in the United States are infected with HPV. HPV is a group of more than 100 different types of viruses, about a third of which can be transmitted through sexual contact. Viruses are nonliving (although there is some debate about this), subcellular particles made up of a protein coat and DNA or RNA. They function by invading a live host cell and commandeering the cell's mechanisms for its own production. HPV viruses can cause cervical cancer, lesions, and between about one third to one half of cancers in the vulvar and vaginal regions, as well as genital warts. The four types of HPV which Gardasil® protects against are among the five most common strains, 6, 11, 16, and 18. Together, they cause about 90% of genital warts cases, while HPV 16 and 18 cause the majority of cervical dysplasia cases, which leads to pre-cancerous changes in cervical cells.



Facts about Cervical Cancer

Cervical cancer is the second most common type of cancer in women, after breast cancer. Approximately 470,000 new cases of cervical cancer are diagnosed each year, and causing around 233,000 deaths per year.. Like many other STDs such as HIV and herpes, you can test positive for HPV and pass it on to your sexual partners without exhibiting symptoms. Because HPV is a virus, it cannot be cured, but it can be treated. When the virus causes visible changes in the tissue, treatment options are available. Options for women include waiting for the tissue to heal on its own; cryotherapy, freezing the altered cells with nitrogen; conization, or removing the affected sections of tissue; and Loop Electrosurgical Excision Procedure (LEEP), removing the altered cells with a mild electrical current.

What is Gardasil®?

Gardasil® is a quadrivalent vaccine, meaning that it associates with the four homologous chromosomes during meiosis against HPV types 6, 11, 16, and 18. It is made with purified virus like particle (VLPs), which are particles made from viruses but which lack viral nucleic acid. Therefore these particles elicit the same response as the viruses but do not lead to infection.

Gardasil® consists of VLPs in a liquid suspension (containing aluminum, sodium chloride, L-histidine, polysorbate, sodium borate, and water) and is administered through injection. It is injected 3 times to the upper arm or thigh over a 6 month period. It is typically most effective in women between the ages of 9 and 26. Gardasil® is not completely effective in women who already have one type of the HPV strains but will protect them against the remaining types.

Controversy

There have been many mixed opinions about Gardasil®. Lawmakers in all 50 states have been attempting to make the vaccination mandatory for all 9 year old girls. Currently, no state in America has a mandatory vaccination policy except for Virginia. This outraged many religious leaders who felt that a vaccine would give children a false sense of security and promote sexual promiscuity. Linda Klepacki, a member of Focus

on the Family, a Colorado based conservative Christian group, effectively expresses the sentiment of moral conservatives against the vaccine, saying, "You can't catch the virus, you have to go out and get it with sexual behavior. We can prevent it by having the best public health method, and that's not having sex before marriage." Some opponents are worried because the drug is "too new." Texas was the first state in which there was an initiative to make the vaccine mandatory for all 6th grade girls. A counter bill in the Texas House to prevent the initiative received 118 votes for and 23 votes against, preventing the health commission from instituting a mandatory vaccine. Representative Dennis Bonnen, who didn't support a mandatory vaccine, said that "we did not want to be the first in offering young girls for the experiment to see if this vaccine is effective or not."

On the other hand, some people feel that the number of lives that could be saved and the prevention of HPV related conditions outweigh all potential negatives. When the efficacy of the vaccine was tested against a placebo among subjects who tested negative for HPV prior to the study, the vaccine correlated to a 93-100 % decrease in cases of genital warts, cervical dysplasia, and vaginal interepithelial neoplasia, a precursor to vaginal cancer. When it was tested against a placebo among subjects who didn't necessarily test negative for HPV, there was a 39% decrease in type 16 or 18 related cervical dysplasia, a 69.1% decrease in type 16 or 18 related vaginal interepithelial neoplasia, a 46.4% decrease in type 6, 11, 16, and 18 related cervical dysplasia, and a 68.5% decrease in types 6, 11, 16, and 18 related genital warts cases.

One thing that cannot be denied is the huge impact of this vaccine, demonstrated by the lengths government and private sectors have gone to make the vaccine available to all women. Even though most states do not currently have a mandatory vaccination law, Gardasil® is still available to people between the ages 11 and 26. Most health insurances will cover Gardasil® and there is a federal program set up to distribute the vaccine to women and teens without health insurance. In New Hampshire it is free to all girls between the ages of eleven and eighteen. At some clinics, such as Sanders Family Medicine in Concord, the demand is so high that there is a waiting list.

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Flight of the Albatross

a Tale of Successful Wildlife Conservation

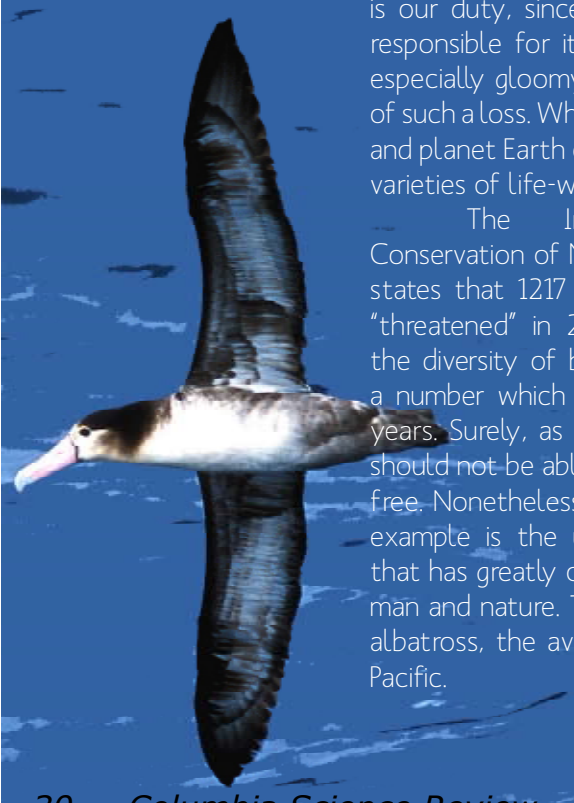
"'God save thee, ancient mariner!
From the fiends, that plague thee thus!--
Why looks't thou so?'--With my cross-bow
I shot the ALBATROSS"

-Samuel Taylor Coleridge

By Alan Daboin

The loss of something precious should be avoided at all costs. Yet it appears, at least on a global scale, that not all humans believe this. After all, many animals are in danger of following in the steps of the dinosaurs and dodos towards complete extinction. And why would anybody want to witness such a thing? Extinction is one of the most disheartening occurrences in nature. Furthermore, the preservation of biodiversity is our duty, since we are, after all, a species responsible for its own actions. As such, it is especially gloomy when people are the cause of such a loss. Why should we deprive ourselves and planet Earth of the inherent richness in the varieties of life-whether on land, sea, or air?

The International Union for Conservation of Nature and Natural Resources states that 1217 bird species were considered "threatened" in 2007. Picture for a moment the diversity of birds making up that number, a number which has only increased with the years. Surely, as this number gets larger, man should not be able to get away from this scot-free. Nonetheless, there is still optimism. One example is the uplifting story of an animal that has greatly overcome adversity from both man and nature. This animal is the short-tailed albatross, the avian monarch of the northern Pacific.



Overall, there are 22 recognized albatross species in the world. Despite their large size, albatrosses are agile fliers, true kings of the skies. One species, the wandering albatross, has a record wingspan of about 3.5 meters (close to 12 feet). Albatrosses are also seabirds with a diverse diet supplied by the ocean. In addition, they rarely, if ever, lay more than one egg a year. That egg they do lay, however, can be surprisingly large. In one photograph from a research team at Wake Forest University, an albatross egg is seen to be as tall as a can of soda. The same team also had some information concerning the curious way albatrosses feed their babies. They do so by a process of regurgitation where the parent's catch enters the mouth of the offspring. When referring to these animals by group, you can call them a "flight," "crookery," and "weight" of albatrosses. Based on all this information, it is fair to judge these birds as considerably unique.

Physically speaking, short-tailed albatrosses are visually dazzling. They appear to have a distinctive mien of royalty; with a golden-colored head and nape, it is not hard to associate it with a crown of sorts. Its pink beak is slightly hooked towards the end and possesses a blue tip. The general plumage is bright white with some black on the wings and tail. The legs and webbed feet are pale blue. It is a behemoth

Black-browed albatross

of a bird, the largest in the Pacific, and measures about three feet long with a wingspan of about seven feet.

The short-tailed albatross likes eating a wide assortment of seafood, ranging from fish eggs to squid to crustaceans. They are surface feeders and they will travel almost 2000 miles away from their breeding grounds for food. Their lifespans are equally impressive. They live for an extraordinary length of time, from 12 to 45 years on average, according to the Midway Atoll's National Wildlife Refuge. A high proportion of this time must be spent flying, as their time on land is limited to nesting.

This brings us to the breeding habits of the short-tailed albatross. The National Audubon Society says that pairs of the bird are monogamous unless one of the two dies, whereupon a new breeding pair may form. Both members of the pair, the male and female, may sit upon the eggs during incubation, which takes a little over two months. They both feed the chicks as well. These chicks move on and leave their nests a few months after birth.

The geography of the species has played such a large part in its history. The short-tailed albatross is generally found in and around the areas of Japan and Hawaii. The largest colony, one of only two, is found in the former's Torishima Island. The area is volcanic, meaning that at any moment a large part of the population can be decimated.

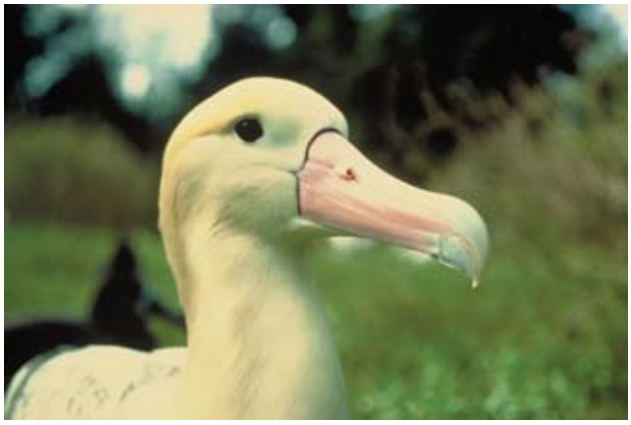
Why exactly has this bird been in such great danger? One major threat has been hunters in Japan, who once desired albatross feathers. There were once millions of short-tailed albatrosses before hunters reduced the population by five million birds, followed soon by a catastrophic volcanic eruption in 1939 that essentially led to the species being considered extinct by the end of World War II. Yet somehow, quite incredibly, there are about 2600 short-tailed albatrosses today, and their rate of growth is outstanding, about 6-8% yearly.

The reasons for this success are manifold. Part of it is legal, as the birds are now protected under Japanese law. A lot of the credit, however, should go to Hiroshi Hasegawa, an ornithologist with a longstanding interest in the short-tailed albatross. In a radio interview many years ago, he said, "It is my dream to save the short-tailed albatross on the Earth." Hasegawa has gone about accomplishing that goal by creating a new colony on the same volcanic island, but on a better side, one with more vegetation and slopes less steep than those on the side of the volcano. This is in part because more vegetation was needed for a permanent breeding ground. Birds were fooled into thinking it was a real breeding site using

Above image and image to the left provided by Save the Albatross Campaign

sound effects, and soon thereafter the success followed.

Similar efforts have been undertaken by the Yamashina Institute for Ornithology, which worked with Hasegawa. In February of 2008, instead of tricking birds on the same island to move to a new breeding site, 10 short-tailed albatross chicks were literally moved to Mukojima Island, as the two other colonies, Torishima and Senkaku, despite all efforts, have proved not to be the best place for the birds. The Mukojima birds will be raised there by researchers.



Nevertheless, everything is still not perfect. There are still considerable threats to consider, such as driftnet and longline fisheries, which are a problem for many seabirds like the short-tailed albatross. Other problems include oil pollution and other issues that Japan and the United States will hopefully solve soon. Measures are already being taken to protect seabirds in general. For instance, in February 2008 New Zealand's fisheries minister announced more humane measures than those previously in place thanks to the efforts of many bird supporters.

Thus, this unusually positive comeback story shows us two things: first, that incredible and fascinating animals are under threat for reasons both natural and man-made. Second, that even if an animal is considered extinct because of nature as well as human intervention, we can still accomplish great things for the sake of biodiversity by working hard, creatively, and passionately like Hiroshi Hasegawa. Of course, if this proves too complicated and too demanding, we can always help out in the little ways which collectively allow us to live in a planet with more animals like these that make our Earth more beautiful and full of life.

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The Albatross Project at Wake Forest University. <http://www.wfu.edu/biology/albatross/atwork/atwork.htm>

Audubon Magazine. <http://audubonmagazine.org/birds/birds0801-webExclusives.html>

Alaska Sea Grant. <http://seagrant.uaf.edu/news/97AS/10.30.97Albatross.html>

Save the Albatross. <http://www.savethealbatross.net/thelatest/thelatestitem.asp?newsid=75>

Whatbird.com. <http://identify.whatbird.com/obj/506/overview/Short-tailed_Albatross.aspx>

Australian Museum Online. <http://www.amonline.net.au/factsheets/wandering_albatross.htm>

Natural History Magazine, April 2008

facts

Phoebastria albatrus breeds on Torishima, Japan, and the Senkaku Islands. Its marine range covers most of the northern Pacific Ocean and there are some records of the bird in the Sea of Okhotsk, though it has not recently been found in the Sea of Japan. It typically occurs on shelf and shelf break waters and has been recorded along the coasts of Japan, eastern Russia, South Korea, China, Taiwan, Alaska, the west coast of North America, and the Northwestern Hawaiian Islands. Post-breeding birds from Torishima follow one of two general migratory patterns. Firstly, they migrate to the east coast of Japan, and then either fly offshore of the continental shelf and north to the Aleutian Islands, or they remain in waters around Japan for several months before heading north.

source: nternational Union for Conservation of Nature and Natural Resources Red List of Threatened Species

Are Antioxidants the Answer to Emphysema?

By Victor Thompson

Abbreviations: COPD, chronic obstructive pulmonary disease; TNF, Tumor Necrosis Factor; GPX1, gluthione peroxidase 1; PP2A, protein phosphatase 2A; JNK, C-Jun NH2-terminal kinases; p-JNK, phospho-JNK; DNA, deoxyribonucleic acid; CD, cluster of differentiation; TLR4, toll like receptor 4; MD2, Lymphocyte antigen 96; FAN, factor associated with neutral sphingomyelinase; RNA, ribonucleic acid; SOD, superoxide dismutase; CuZnSOD, copper zinc SOD

Cigarette smoke is one of the major causes of chronic obstructive pulmonary disease (COPD), a condition characterized by nonreversible difficulty in breathing. 20.8% of all American adults (45.3 million people) (1) and about 23% of high school students smoke cigarettes (2). In 1998 COPD accounted for about 110,000 deaths (3) in the United States. Despite these statistics, minimal progress has been made in translating research findings into improved therapies. Cigarette smoke-induced inflammation is a central factor in the destructive processes that cause this detrimental condition. Along with its many other medicinal values, antioxidants have also demonstrated potent anti-inflammatory properties in the lung and are thus able to inhibit cigarette smoke-emphysema (4).

Antioxidant gene expression is increased when overwhelmed with the products of cigarette smoke (5). Every puff of cigarette smoke exposes the lung to more than a trillion free radicals (6). This significantly increases the imbalance between the presence of highly reactive forms of oxygen and our biological system's capability to readily detoxify the reactive intermediates or easily repair the resulting damage. The surplus of reactive oxygen species leads to lipid peroxidation and protein, carbohydrate, and DNA damage in the respiratory tract, which induces apoptosis (programmed cell death) and enhances inflammation. The Tumor Necrosis Factor (TNF) signaling pathway in lung epithelial cells is believed to play a key role in the disease (7). Oxidants initiate TNF signaling through a reaction cascade by causing TNF to bind to the TNF-R1 receptor (8), which activates the kinase enzyme JNK. Activated JNK in turn activates c-JUN, which induces cytokines (intercellular chemical messenger proteins released by white blood cells that facilitate communication among immune system cells) that are responsible for the inflammatory response (9). Oxidants also inactivate PP2A (10,11), a serine/threonine phosphatase that affects TNF signaling by dephosphorylating p-JNK and c-Jun. Counteracting oxidative stress with an adequate addition of lung antioxidants, capable of bonding with and thus neutralizing free radicals within the body, may be an effective method to deal with the problems of emphysema.

The body's natural metabolic processes expose all cells to oxidative stress. Cigarette smoke also produces reactive chemicals like hydrogen peroxide that play a major role in oxidative stress damage. GPX is an enzyme family with peroxidase activity whose main biochemical role is to protect the organism from oxidative damage. GPX1 is located in the cytosol and mitochondria, which are two main cellular compartments involved in apoptotic signaling (12). It detoxifies hydrogen peroxide into water and is one of the most important antioxidant enzymes in human beings. The aim of this study was to determine if the enhanced expression of the human gene GPX1 within the lungs of mice could prevent the development of emphysema and, if so, to figure out how.

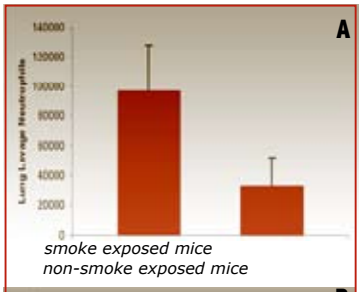

Figure 1: *Glutathione Peroxidase-1 Decreases Smoke Induced Neutrophil Influx*

Oxidative stress plays a major role in the development of COPD. The lung is continuously in direct contact with oxygen from the air we breathe and as a result is subject to more oxidative stress damage than other organs of the body. The

Albatross image from US Fish and Wildlife Servcie, Smoke image from Cancer Research UK

lung naturally contains an effective network of antioxidants that work to protect itself from damage caused by reactive oxygen species. However, cigarette smoke causes a large chemical imbalance between free radicals and our body's natural ability to detoxify these harmful chemicals, resulting in conditions like COPD. Treatment studies have demonstrated mixed results on the benefits of antioxidants for this detrimental condition. Studies have shown that there is a positive correlation between dietary intake of antioxidants and lung function (14) and that antioxidants decrease smoke induced oxidative damage in animals (15) and humans (16). However, in a clinical study N-acetylcysteine, a precursor of glutathionine that suppresses cytokines and cancer cells, had no affect on disease progression or exacerbation rate (17). There are many possible explanations as to why there are variable results, such as the specific antioxidant chosen for the experiments. This study demonstrated not only that a 3.9% increase in GPX1 activity within the lung decreases lung macrophages and neutrophils, but also how this increase in activity decreases inflammation in response to chronic smoke exposure.

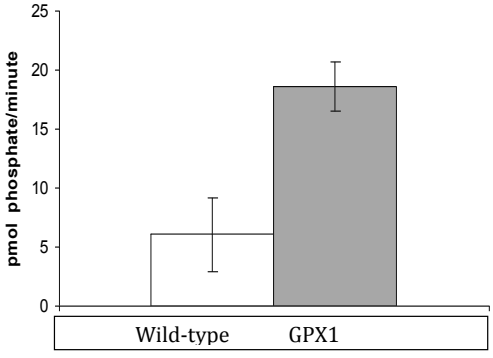

Figure 2*: Increased PP2A Activity in GPX1 Transgenic Mice*

Neutrophil granulocytes are the most abundant type of white blood cells in humans and are an integral part of the immune system. Although these phagocytes are normally found in the blood stream, during inflammatory responses to bacterial infection, they leave the blood stream and rapidly migrate toward the site of inflammation in a process called chemotaxis (18). Macrophages help to get rid of necrotic debris and dust in the lungs. These macrophages tend to stay at strategic locations like the lungs to ingest foreign material such as dust and pathogens (19). This is why neutrophils and macrophages are credible biomarkers for inflammation, and the marked decrease in smoke-induced neutrophil influx (Fig 1A) and

smoke-induced macrophage influx (Fig 1B) in the GPX1 transgenic mice demonstrate the positive effect of this gene on inflammation. These results strongly correlate with a recent study that showed that after one year of cigarette smoke exposure, (6 hours/day, 5 days/week at 250 mg/m3) wild-type littermate mice developed emphysematous changes in their lungs while the smoke exposed transgenic GPX1 mice preserved lung architecture.

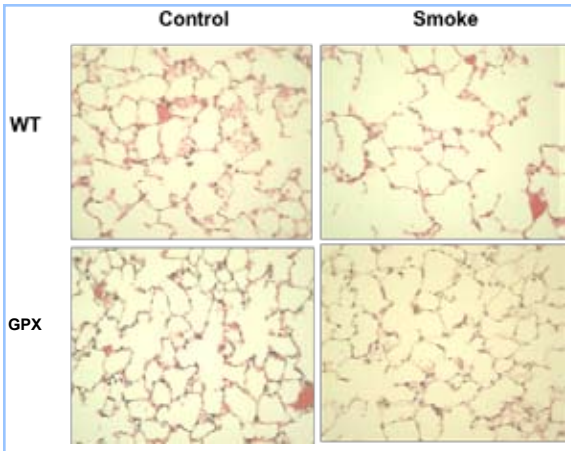

Figure 3*: GPX1 Expression Prevents Cigarette Smoke-Induced Emphysema.*

TNF, a well known inducer of JNK (20), is a key initiator of smoke induced inflammation (21-23). JNK stimulation enhances the influx of neutrophils and macrophages in response to lipopolysaccharide exposure (24). TNF is also a well known inducer of FAN. FAN stimulates N-Smase, which increases ceramide levels and activates PP2A, which then inactivates both JNK and c-JUN. A recent study demonstrated through Western blot analysis that a decrease in functioning PP2A increases JNK activation (20). The present study, also through Western blot analysis, demonstrates that GPX1 decreases JNK activation. These two pieces of information led to the belief that GPX1 expression protected against smoke induced changes in lung architecture by increasing PP2A activity, which decreases JNK activation. The present study proved this hypothesis; there was a remarkable increase in PP2A activity in the GPX1 transgenic mice (Fig 2). It must be specifically the activity of PP2A and not the amount of PP2A that increases because the levels of PP2A RNA isolated from the lungs of wild-type littermate and GPX1 transgenic mice at baseline and after one day following a six hour smoke exposure did not differ significantly (n = 8 in each group; data not shown).

Results of this study indicate that the transgenic expression of GPX1 prevented cigarette smoke-induced lung inflammation and emphysema. GPX1 mediates its anti-inflammatory effects by altering the TNF signaling pathway; the antioxidant induces an increase in PP2A activity, which then inhibits the activation of JNK. Thus these results not only denote the importance of glutathionine peroxidase, but they also show how GPX works to reduce emphysematic processes.

In the future, experiments will be done to determine how GPX1 works to increase the activity of PP2A. Where COPD is concerned, an even greater decrease in inflammation and emphysema would be more beneficial. These results are consistent with a previous study that showed that the antioxidant CuZnSOD effectively counteracted the smoke-induced increase in oxidative damage, protease expression, and inflammation that occurred in smoke-exposed mice and prevented the formation of emphysema in two separate animal models of the disease (26). SOD is the primary enzyme to defend the lung from the damaging effects of superoxide. It does this by converting superoxide into hydrogen peroxide, which can then be broken down into water by antioxidants such as the one of this study, GPX1. Therefore, we predict that if the correct amounts of both antioxidants GPX1 and CuZnSOD are transfected into mice, an even greater decrease in inflammatory damage will be demonstrated.

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