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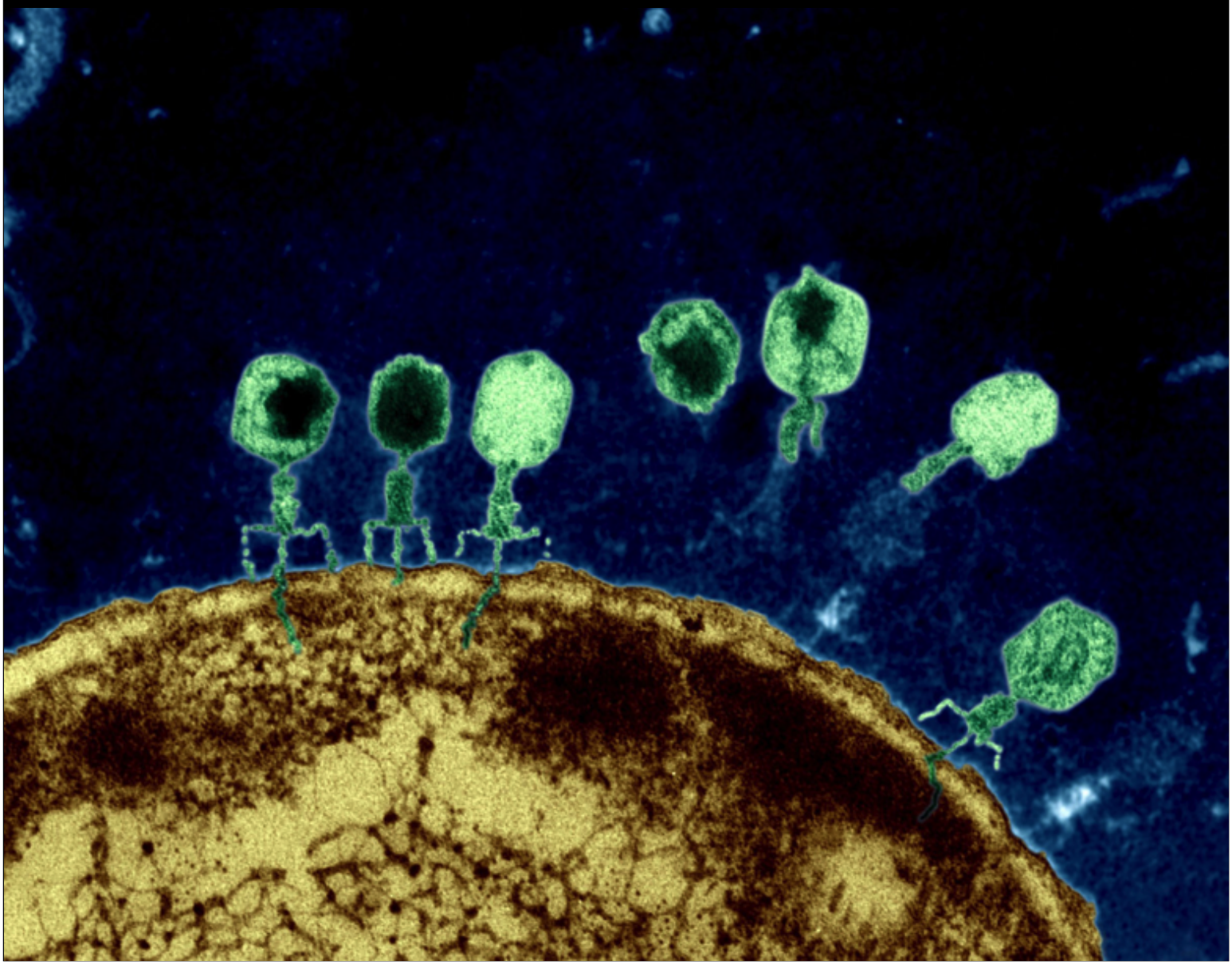

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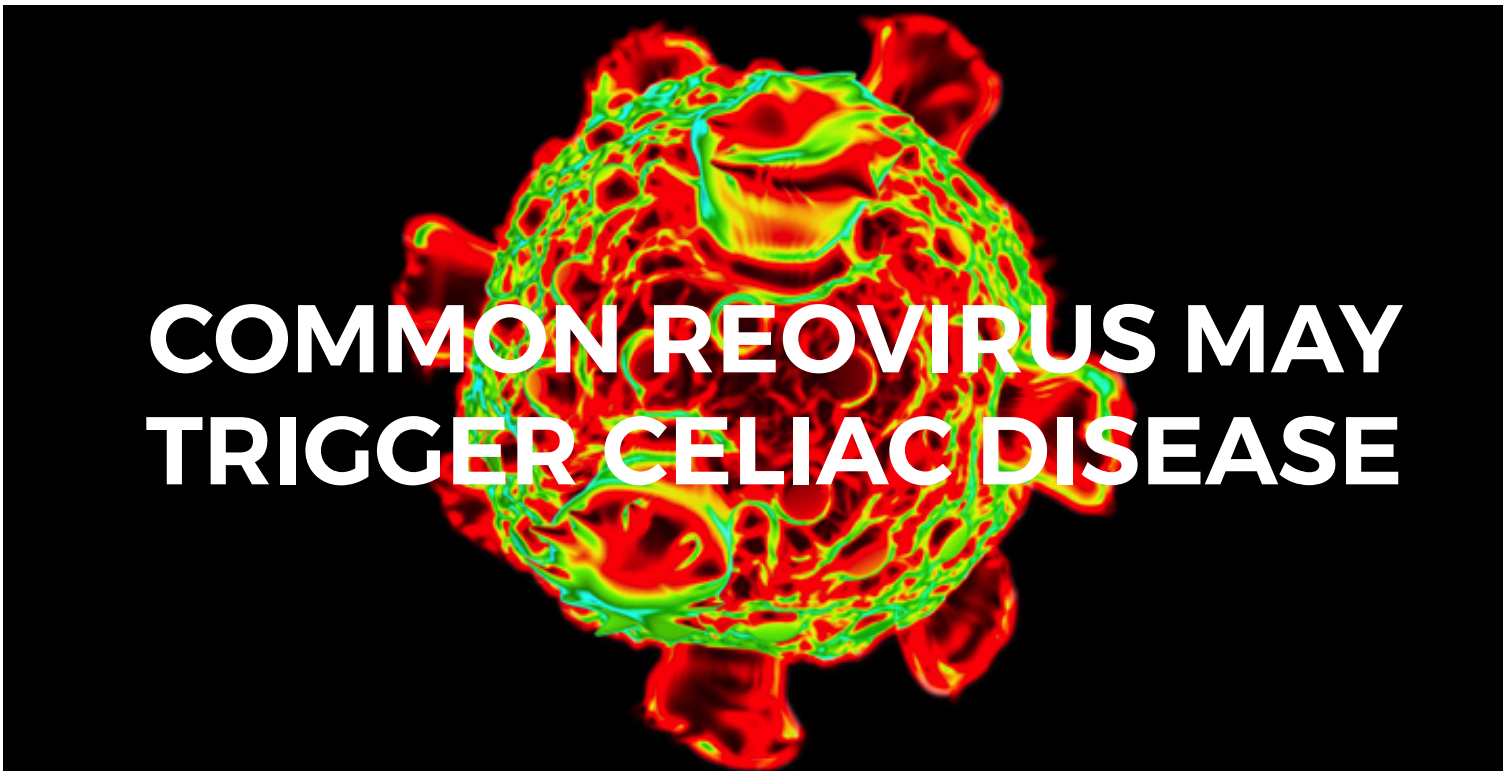


COMMON REOVIRUS MAY TRIGGER CELIAC DISEASE

Illustration of a Reovirus

https://www.sciencenews.org/article/common-virus-may-be-celiac-disease-culprit?tgt=nr

by NICOLE YAO '18

A common and typically harmless virus may cause celiac disease, a recent study suggests. Celiac disease—also known as coeliac disease, celiac sprue, non-tropical sprue, and gluten sensitive enteropathy—is a severe genetic autoimmune disorder characterized by an abnormal immune response to the protein gluten. When people with this disorder consume gluten, which is found in wheat, rye, and barley products, their immune systems mount an attack on the small intestine. These attacks damage the villi which are miniscule, hair-like projections that line the small intestine and are primarily responsible for nutrient absorption. Without properly functioning villi the body cannot effectively absorb nutrients from food. Such a condition can lead to anemia, early onset osteoporosis, infertility, and even certain cancers and neurological disorders.

According to the Celiac Disease Foundation, approximately 1 in 100 people worldwide are thought to have celiac disease. An estimated two and a half million people in America remain undiagnosed and unaware of their disease, which can lead to long-term health complications. Celiac disease is hereditary. Those with immediate relatives that suffer from celiac disease have a 10% chance of developing it themselves. Currently, the only treatment for celiac disease is a gluten-free diet.

A recent study conducted by an international team of researchers in early April discovered that a common human intestinal reovirus may cause celiac disease. Reoviruses are a family of viruses that can have a wide range of hosts and typically affect the gastrointestinal system or the respiratory tract. Injecting particular strains of a reovirus, specifically T1L, into mice tricked the animals' immune systems into treating gluten as if it were a dangerous pathogen instead of an innocuous food particle. According to Terence Dermody, a virologist at the University of Pittsburgh, and his colleagues, the

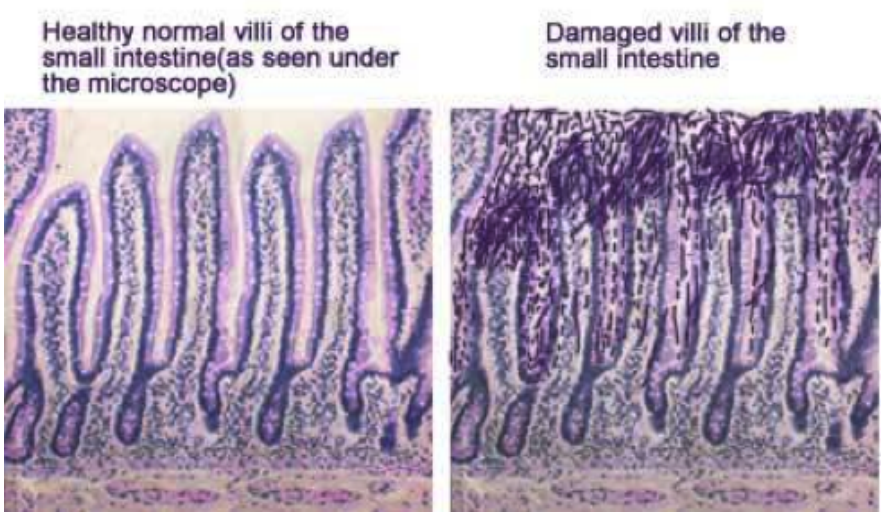
> **"This study clearly shows that a virus that is not clinically symptomatic can still do bad things to the immune system and set the stage for an autoimmune disorder"**
>
> **- Dr. Bana Jabri**

reovirus blocks the immune system's ability to allow "non-native" substances such as food proteins to pass through the body peacefully. Instead, the virus triggers a damaging inflammatory response.

The key interaction between the virus and the body's immune system is thought to happen in the mesenteric lymph nodes, where gluten first meets the dendritic cells. Dendritic cells, professional antigen-processing cells, are responsible for conducting the immune system's response to foreign substances entering the body.

Researchers also found that the reovirus T1L stimulates activity of the enzyme tissue transglutaminase. In those afflicted with celiac disease, this enzyme enhances the ability of gluten to trigger an inflammatory immune system response. Dermody and his fellow scientists observed that people with celiac disease have higher levels of reovirus antibodies than those without the disorder.

Interestingly, reoviruses which are viruses that pack their RNA genomes in multi-layered capsids instead of lipid envelopes, are not deadly. In fact, almost everyone has been infected by a reovirus and survived without any lasting or obvious effects. But researchers found that a reovirus infection, coupled with exposure to food containing gluten, may trick the immune system into treating the food protein as an enemy. "This study clearly shows that a virus that is not clinically symptomatic can still do bad things to the immune system and set the stage for an autoimmune disorder, and for celiac disease in particular," commented Dr. Bana Jabri, the director of research at the University of Chicago's Celiac Disease Center. "However, the specific virus and its genes, the interaction between the microbe and the host, and the health status of the host are all going to matter as well," she added.



https://celiac2051.wordpress.com/cause/

The issue of whether vaccines could effectively prevent celiac disease has also come up in light of this recent study. Scientists must conduct further research to conclude if T1L or other viruses are the real triggers of celiac disease. With that information, a vaccine could be developed to block the development of celiac disease in children at risk. Jabri states, "During the first year of life, the immune system is still maturing, so for a child with a particular genetic background, getting a particular virus at that time can leave a kind of scar that then has long-term consequences. That's why we believe that once we have more studies, we may want to think about whether children at high risk of developing celiac disease should be vaccinated." Vaccines offer a potential chance to prevent the development of a harmful disease that is impacting millions of people around the world.

The study's findings were published in *Science* on April 7, 2017.

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CRISPR/CAS9
FROM BACTERIUM TO BIO LAB

by KATE SPENCER '20

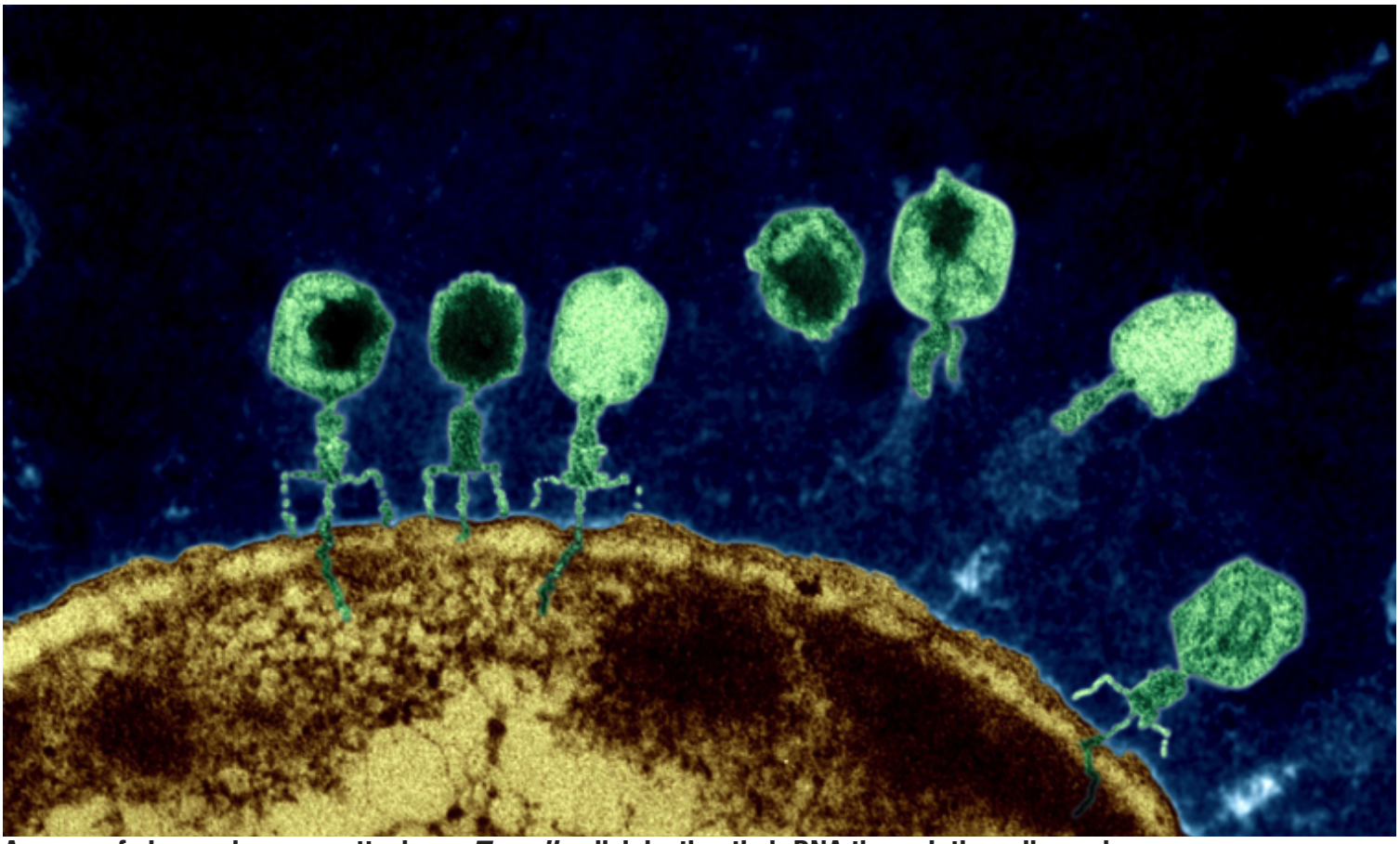
With its ability to alter DNA with great precision, CRISPR/Cas9 has become a revolutionary tool in the biotech community. CRISPR, which stands for clustered regularly interspaced short palindromic repeats, was initially discovered in the late 1980s. Despite its newfound applications, CRISPR has been used by bacteria for eons. Recently, scientists have been racing to collect samples and conduct experiments to further examine CRISPR/Cas9 systems.

The CRISPR/Cas9 system contains three important components: a guide RNA, Cas9 endonuclease, and template DNA. Scientists transfect organisms with the guide RNA, which is complementary to the DNA sequence of the gene that scientists want to modify. Once the guide RNA is inside the organism, the Cas9 endonuclease attaches to form a complex. Then, the complex creates a double strand break in the DNA that will be edited. The cell naturally repairs this double strand break by one of two methods: either homology-directed repair or nonhomologous end joining. Homology-directed repair is when the cell repairs itself using the template DNA that is supposed to be inserted. On the other hand, nonhomologous end joining is when the broken ends of the DNA sequence are "shaved off" such that the ends are blunt. Then, the cell reconnects the blunt ends of the broken strand together to fix it—a method that often leads to unpredictable mutations. Scientists hope that homology-directed repair happens so that the engineered template DNA sequence can be incorporated.

CRISPR works naturally in bacteria as a form of immunity against invaders. Initially, when a phage, or virus, injects genetic material into bacteria, the bacterial cell cuts out the viral DNA using this system. If the phage returns, a segment of the bacteria's RNA connects to the phage DNA and the Cas proteins cut at that location, disabling the phage DNA. Scientists observed that bacterial cells that had been exposed to a certain phage developed immunity to that strain of virus since the complementary RNA molecules remained. As a result, researchers recognized that the CRISPR/Cas9 system worked similar to the adaptive immune system.

Researchers at the dairy food company Danisco exhibited CRISPR's potential after their widely published experiment in 2007. A researcher named Rodolphe Barrangou at North Carolina State University explains, "It was not just discovering a cool system, but also uncovering a powerful phage resistant technology for the dairy industry." The research is expected to impact the dairy industry by helping to fight viruses and determine if food poisoning cases are linked.

Despite CRISPR's vigorous phage-fighting ability, viruses can often evolve to better defend themselves against the systems. As a phage genetically morphs, it turns into forms that CRISPR/Cas9 systems can no longer recognize, or it develops weapons to fight against them. In a 2015 experiment conducted by microbiologist Joe Bondy-Denomy and Alan Davidson at the University of Toronto, phages were found to have developed small proteins that bonded and interfered with the CRISPR systems in the bacterium *Pseudomonas aeruginosa*. Since then, anti-CRISPR genes have



A group of phages, in green, attacks an *E. coli* cell, injecting their DNA through the cell membrane.
Twilley N. The New Yorker. 2015 Feb 26 http://www.newyorker.com/tech/elements/phage-killer-viral-dark-matter

been found in other phages and other interloping DNA forms. Another experiment at the University of California, Berkeley, uncovered a phage that created its own CRISPR system to invade cholera bacteria. CRISPR systems, through their powerful yet simple defense mechanisms, have been found to shape their surrounding ecosystems. Microbial communities, such as the ones inside the human body, contain many dynamic CRISPR systems and phages. Because of the use of CRISPR in ongoing defense systems, new phage populations appear through genetic changes, in an effort to adapt to the immunity of the CRISPR systems.

The diversity within CRISPR systems is a reflection of the experience of the bacteria rather than where it develops. One would expect CRISPR systems to differ from one geographical location to another. However, according to Rachel Whitaker, a University of Ilinois at Urbana-Champaign microbial population biologist, there is no sign that CRISPR systems that are close together spatially are any more alike than systems across the world. Through studying patients with cystic fibrosis and taking samples of *P. aeruginosa*, Whitaker found no close matches within the sets of CRISPR systems, despite their expected encounters with similar phages.

Scientists are currently investing heavily in further research on CRISPR systems. Fellow at the University of California, San Francisco, Alexander Marson explains, “The potential [for CRISPR] is enormous. The rate of application and development is astounding, from basic science right through to clinical applications.” As a result of their revolutionary ability, CRISPR systems have already seen major development within the scientific community and beyond.

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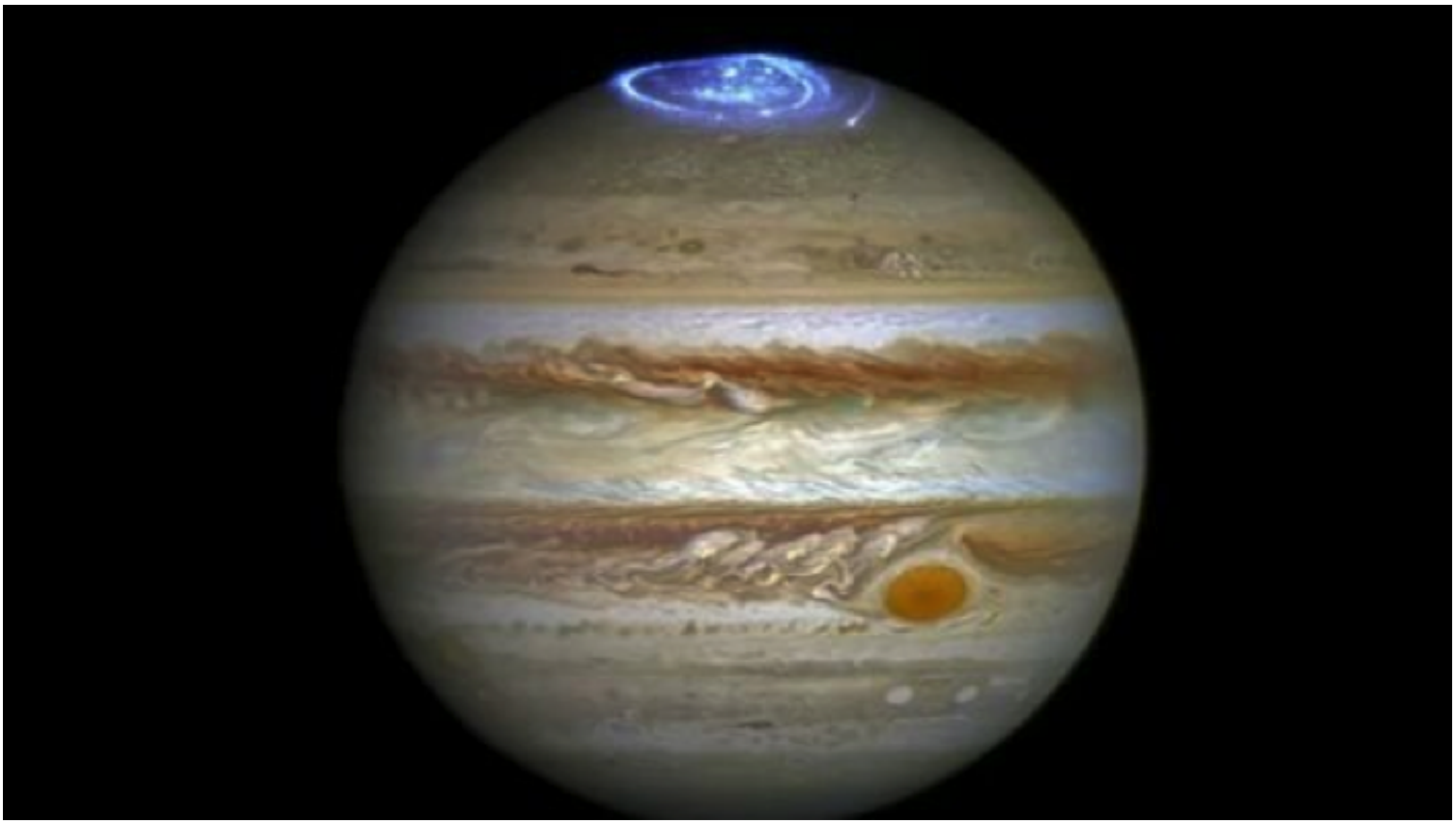


Jupiter's northern aurora, shown in this Hubble Space Telescope image, may help generate the newly detected "Great Cold Spot" in the planet's atmosphere.

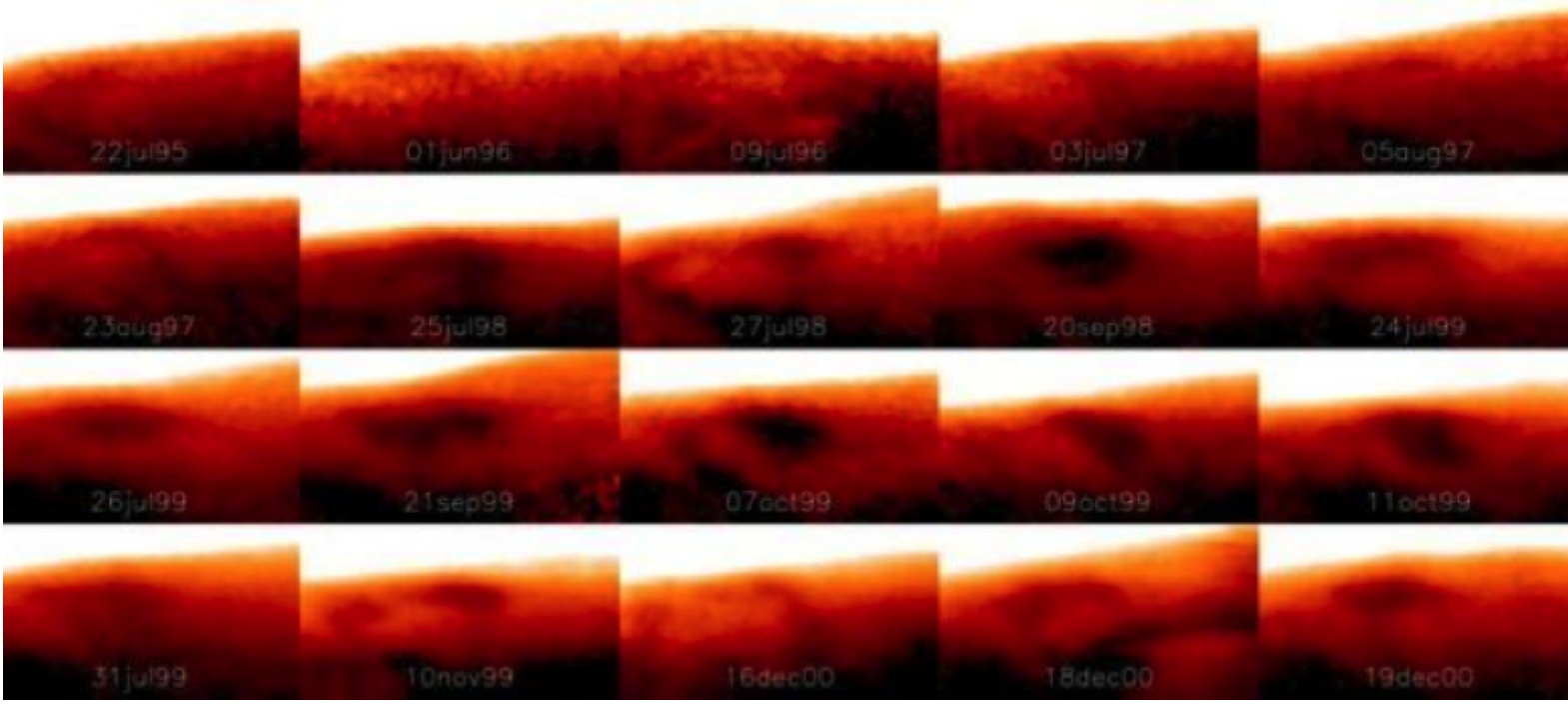
Yeager A. Science News. 2017 April 12 https://www.sciencenews.org/article/jupiters-great-red-spot-has-company-meet-great-cold-spot

INTRODUCING JUPITER'S NEWLY DISCOVERED "GREAT COLD SPOT"

by LILY DING '20

One of the most prominent features of Jupiter's surface is the Great Red Spot. However, this iconic red gyre now has some company: the Great Cold Spot. The Great Cold Spot was officially discovered by astronomers from the University of Leicester on April 11th, 2017. At 24,000 kilometers in longitude and 14,0000 kilometers in latitude, the Great Cold Spot is around the same size as the Great Red Spot when in its largest form. It also appears to be a weather system, similar to its red cousin.

Astronomers have been monitoring this spot unintentionally for decades. While the Great Cold Spot cannot be seen with the naked eye, it is visible on infrared readings as a dark oval on top of Jupiter's bright upper atmosphere. Tom Stallard, a planetary scientist at the University of Leicester, and his colleagues first noticed the spot using the Very Large Telescope in Chile to study an ion of hydrogen in Jupiter's atmosphere. To their surprise, they noticed a region that was consistently around 73°C cooler than its surroundings.



This series of images from the University of Leicester illustrate how the Great Cold Spot changes dramatically in shape and size on different days.

https://astronaut.com/jupiter-now-great-cold-spot-go-great-red-spot

The scientists compared their findings to data obtained at Hawaii's NASA Infrared Telescope Facility. This comparison revealed that the spot has been in the exact same place for years. Interestingly, scientists have photographs of the spot from decades ago. By combing through over 13,000 images, including those taken by the InfraRed Telescope Facility, scientists discovered that the appearance of the spot seemed to be changing.

Upon further investigation, researchers noticed that the Great Cold Spot changed in size, shape, and darkness over time. Stallard noted, "Sometimes it is clearly a spot and sometimes it's not so prominent." He continued, stating, "The Great Cold Spot is much more volatile than the slowly changing Great Red Spot, changing dramatically in shape and size over only a few days and weeks." This shape shifting is speculated to arise because the Great Cold Spot is connected to an "influx of energetic particles into Jupiter's atmosphere from the Jovian moon, Io, that generates auroras." Auroras are natural electromagnetic phenomena that produce reddish-green lights in the sky. On Earth, these auroras are capable of creating vortices in the atmosphere that are cooler than their surroundings. Scientists speculate that the Great Cold Spot was created in a similar way. The Great Cold Spot may be a swirling weather system that waxes and wanes as the intensity of Jupiter's northern aurora changes.

When asked about his next steps, Stallard stated, "The detection of the Great Cold Spot was a real surprise to us, but there are indications that other features might also exist in Jupiter's upper atmosphere. Our next step will be to look for other features in the upper atmosphere, as well as investigating the Great Cold Spot itself in more detail." The discovery of Jupiter's Great Cold Spot demonstrates that there are countless aspects of the solar system that remain a mystery.

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http://melissavandyke.com/wp-content/uploads/2015/09/code.jpg

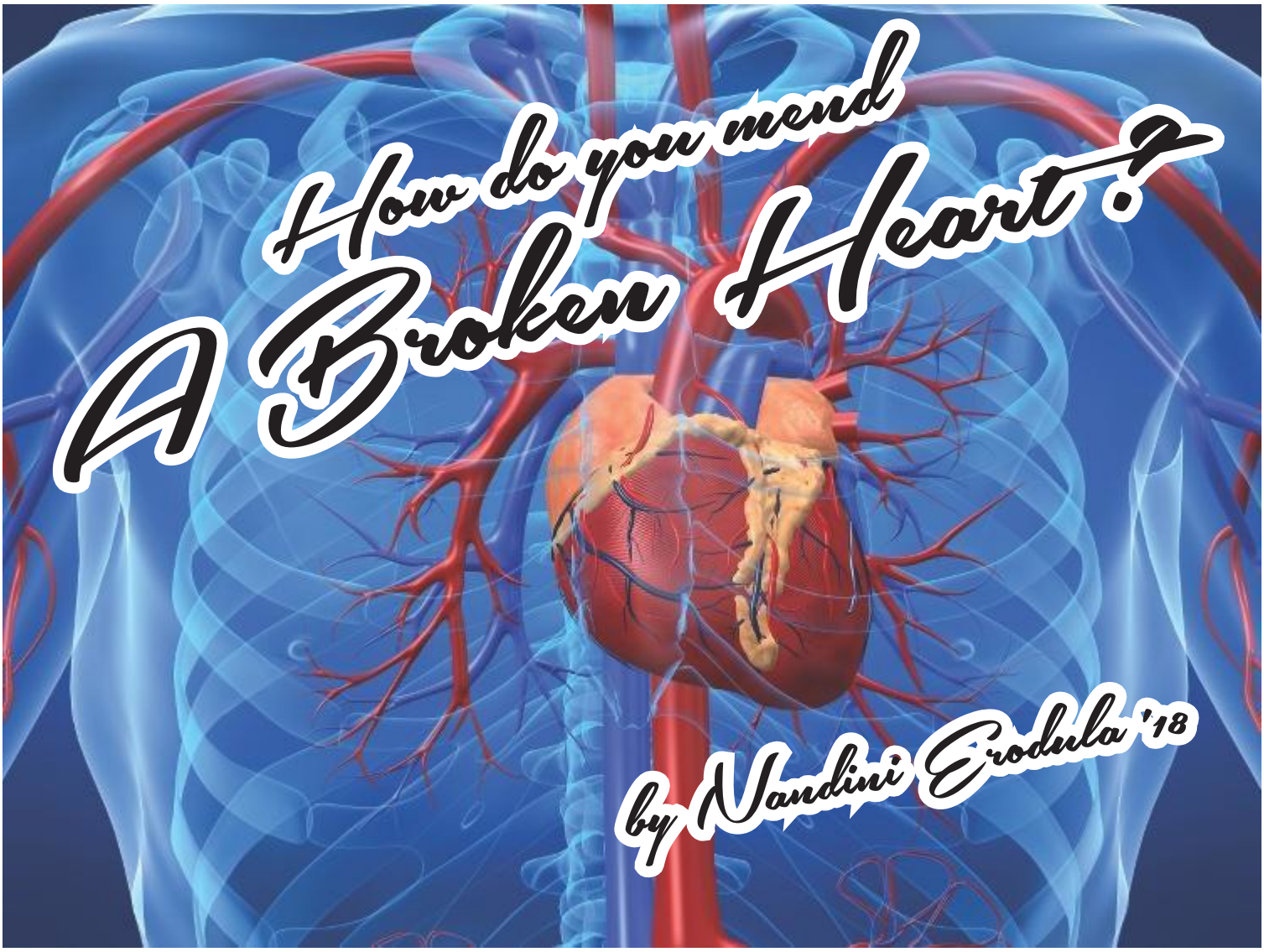
by HUONG PHAM '19

In her third year at Choate, Mrs. Healey, originally from New Hampshire, currently serves as both a math and computer science teacher. She teaches both geometry and an impressive array of computer science courses, ranging from Introduction to Programming to iOS Programming and Web Development.

Mrs. Healey's initial interest in computer science was sparked during a high school course in HTML. "I lost track of time, and it didn't feel like work," commented Mrs. Healey about the first course she took. Despite her interest in the field, there was a period where her passion for the subject diminished. She cites one major reason as the dullness of lectures on hardware and technical networks, which cuts off computer science's charm of creativity. As a result, after graduating from college, Mrs. Healey travelled and taught English in France for a year. However, when she returned to the United States, there weren't many positions open for a foreign language teacher. In contrast, computer science and math teachers were in high demand. Mrs. Healey found a school in New York that had a curriculum in which computer science studies were interwoven with art. The creativity and logical thinking involved in this interdisciplinary curriculum rekindled her childhood interest in computer science.

Reminiscing on her time teaching at New York, Mrs. Healey still recalls many of the assignments she gave to students. For example, they were able to create paper dolls and shapes in Photoshop and were given the opportunity to put together their own websites built using HTML and JavaScript. Fascinated by the course material, Mrs. Healey stayed and taught in New York for seven years.

Seeing students learning and being able to compile their own lines of code captivates Mrs. Healey. She describes her favorite part of teaching as observing "someone who struggles at the beginning but is able to solve the problem." Mrs. Healey is driven by her desire and passion to help students see the beauty and power of computer science.



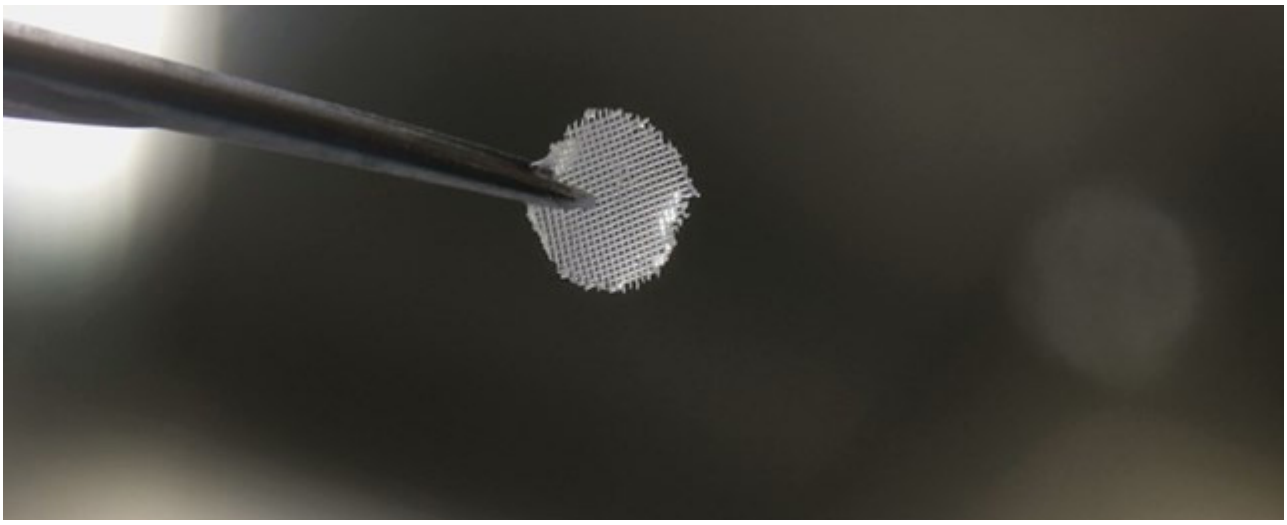
http://theindianweekly.com.au/wp-content/uploads/2017/04/tech.jpg

Heart disease is the leading cause of death in the United States. According to the American Heart Association, one person in the United States has a heart attack every forty seconds, and more than 360,000 people die from a heart attack each year.

Heart attacks occur when the buildup of fat, plaque, or cholesterol stops the flow of blood to the heart muscle. As a result, cells in the heart begin to die due to a lack of oxygen. Heart attack patients suffer from a "broken heart" because of the damage done to the heart muscle. The body will eventually heal the heart in about eight weeks after the attack, but there may be a severe loss of function and a slower rate of pumping blood than usual. Scar tissue forms around the damaged area, and the human body cannot replace the dead cells to help the heart recover fully.

To address this problem, biomedical engineering researchers at the University of Minnesota sought to create a way to replace those heart muscle cells by mimicking the structure of heart tissue using a laser-based 3D-bioprinting technique. Their method involves using stem cells taken from adults to create a cell patch, which can be attached to the heart to promote the growth of cardiac muscle cells. In the lab, the researchers discovered that cells began to grow and beat together simultaneously in the dish used to create the cell patch.

The researchers tested the cell patch by inserting it into a mouse after a simulated heart attack. After observing the mouse for just four weeks, they found that the patch had worked well inside the mouse, as measured by an increase of function in the heart. Since the patch is made of cells and structural proteins of the heart muscle, the mouse's body was able to absorb the



A 3D-bioprinted patch made from cells and protein native to the mouse heart in which it is to be placed. This patch was fabricated at the University of Minnesota, Minneapolis.
www.kare11.com/news/breakthrough-3d-printed-patch-could-help-patients-after-a-heart-attack/431438388

patch without the need for further surgery. “We feel that we could scale this up to repair hearts of larger animals and possibly even humans within the next several years,” remarked Brenda Ogle, an associate professor at the University of Minnesota.

With this cell patch, these researchers have advanced even further in the treatment of heart disease, one of the most deadly conditions around the world. They have developed a way for a human to potentially avoid further heart failure induced by a heart attack. And finally, they have provided a potential solution to mend a broken heart.

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The Science of CHEESEMAKING

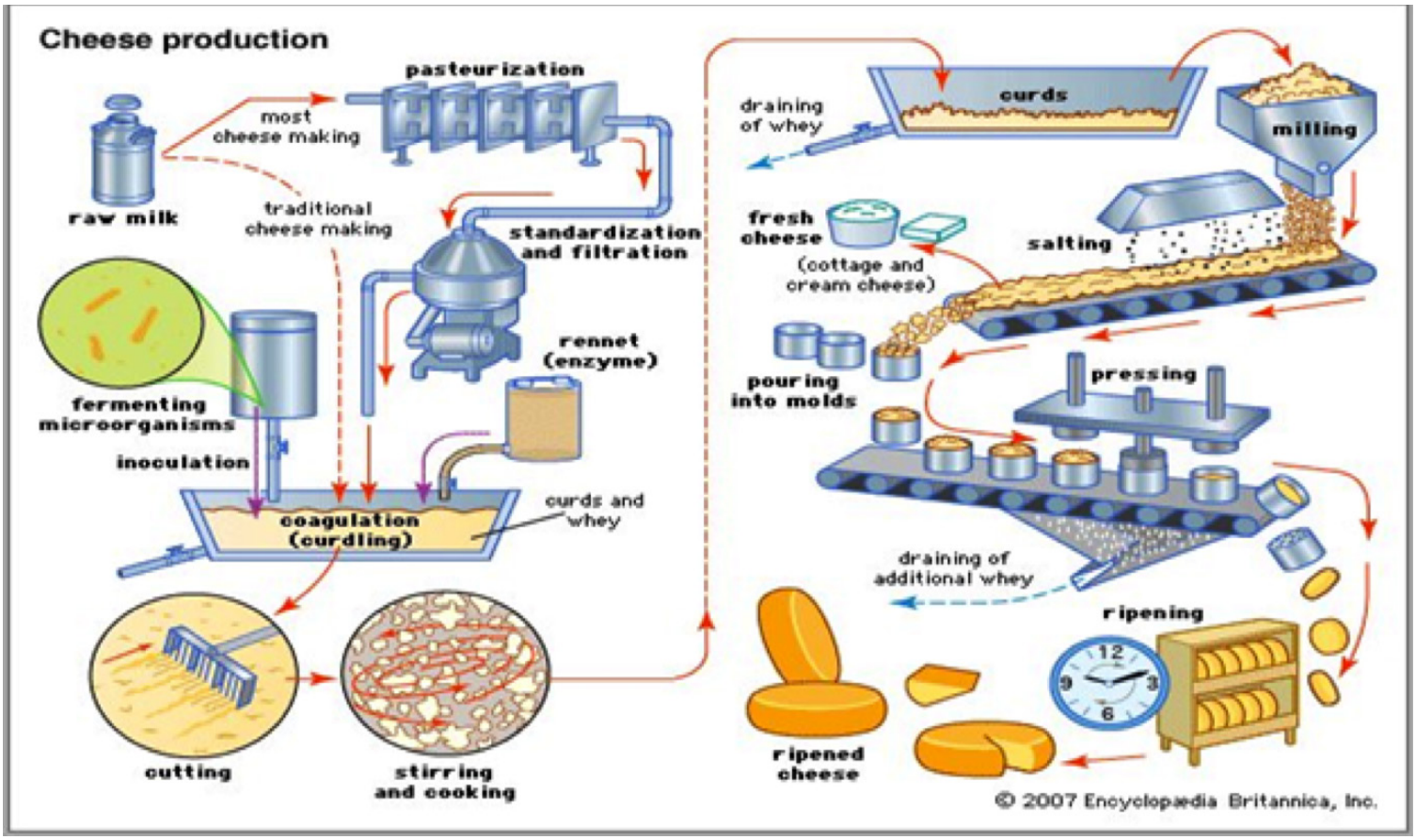
by VINCENZO DINATALE '19

From American to mozzarella, cheese is a staple for many cultures across the planet. People have made cheese for thousands of years using milk from cows, sheep, and goats, and have developed cheese varieties often distinguished by the region in which they originate. However, many do not realize that science, above all else, is key to understanding how and why cheese comes in so many different forms.

Milk is the primary ingredient in the cheese-making process. Cheese requires a lot of milk as input relative to the amount of cheese produced: about ten pounds of milk are required for one pound of cheese. To guarantee safety, the milk is typically pasteurized, meaning it is heated to a very high temperature so that all the harmful bacteria are killed.

Once the proper amount of milk is obtained, starter cultures, which are a specific type of bacteria, are added to the heat-treated milk. The bacteria turn the milk sugars into lactic acid. Cheese types are often characterized by their pH level, and the amount of lactic acid produced by the starter cultures determines the pH level in the cheese. The acidity of a cheese is essential in distinguishing its flavor from others.

Then rennet, which contains a milk clotting enzyme known as chymosin, is used to coagulate the milk and a custard-like substance is formed. Milk is full of proteins, most of which form into the casein micelle.



Small portions of the casein micelle are negatively charged and therefore repel each other. Because of this repulsion, milk remains a liquid. The chymosin removes the negatively charged portions of the proteins, and the proteins can join together with the milk fats, forming solid chunks.

In order to separate the liquid and the milk solids, the mass is then cut into small pieces. The liquid is called whey and the solids are referred to as curds. When larger curds are cut, they are usually cooked at low temperatures for softer cheeses such as ricotta. Small curds are cooked at high temperatures for harder cheeses such as parmesan. The larger curds retain more moisture.

Once this step is complete, the curds are stirred until a specific firmness is reached. The desired consistency of the curds depends on the type of cheese being made. After all the whey is removed, a solid compact curd is left behind. It is then pressed for three to twelve hours, depending on the size of the curd. The pressing process is essential for determining the curd's size and shape.

Finally, the pressed curd is cured to establish a specific flavor and texture. The curd is placed in a room where humidity and temperature are controlled, and the curd may age in it for as little as a few weeks or as long as a few years. Soft cheeses like ricotta and mozzarella are eaten fresh and are not aged at all, while hard cheeses such as parmesan do undergo this aging process. The breakdown of casein proteins in the cheese is responsible for its transformation whereby a mixture of amino and fatty acids is left behind.

Science is involved in all aspects of the cheese-making process. Cheesemakers rely on it to produce various textures and flavors to satisfy consumers around the world. Next time you encounter a slice of cheese, be sure to appreciate its scientific significance.

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Header Illustration by Huffington Post

MANDELBROT, ESCHER, BACH:

The Math of Musical Fractals

by SAM MARKOWITZ '17

If you've ever taken a physics class, you would know that every sound wave has a certain frequency, a number of oscillations per second. This frequency determines the pitch that we hear. Higher frequencies produce higher pitched notes. Tuning methods are based on the relationships of these frequencies. Just Intonation, one of the possible tuning methods, tunes every note with respect to the frequency of the note defined as C. Using this, we can do some cool experiments in music programs. We can do this in Pro Tools, Ableton, GarageBand, or another program that is similar.

First, take a four measure phrase from any song. Repeat that phrase by copying and pasting it multiple times. Then, condense the repeated phrases into four bars. By doing so, you have condensed two of those phrases into the duration of one of the original. Repeat this process over and over again until you hear only a single synthetic sounding note. You can change its duration by simply copying, cutting, and pasting it.

Now we can produce all of the other pitches that may be used in the phrase. Below is a table listing all of the frequency relationships between pitches. Let us try to produce the D pitch. Because the ratio is 9:8, take the C pitch that we produced earlier and condense it by a factor of 8/9. Every other pitch can be produced similarly. Pitch frequencies normally relate to each other by the number of crests of the sound wave that pass the listener in any given second. Instead, we are creating frequencies that relate to each other by the number of phrases that pass by in any given second. From here, every pitch can be prolonged, shortened, and reorganized to produce the same exact melody.

Using this process, we have created a musical fractal, an idea or concept that contains itself inside of itself. The most popular fractal is the Mandelbrot set. It looks very simple at first, but as you zoom in, you can find patterns of the whole thing repeated again. Similarly, you can take this musical creation, slow it down by a large factor, and then hear the same exact melody. Technically, you could do the same thing again, and produce a third layer. I personally haven't tried this, but it certainly isn't out of the realm of possibility!

You can also do a few other things in these music editing programs. Take a bass drum hit, cymbal crash, or the sound of some other non-pitched instrument. Have it play one note on every beat, and then speed it up in a similar manner as described above until it is only one continuous pitch. You can then take the same instrument and have it play, let's say three times for every two times that it does in the initial track. Then, when sped up, you should hear a perfect fifth interval. In this way, every interval is really just a very fast polyrhythm. Try to experiment and see what other cool occurrences you find!

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Pitch	C	D	E	F	G	A	B	C
Ratio	1:1	9:8	5:4	4:3	3:2	5:3	15:8	2:1

Table based on data taken from https://en.wikipedia.org/wiki/Just_intonation