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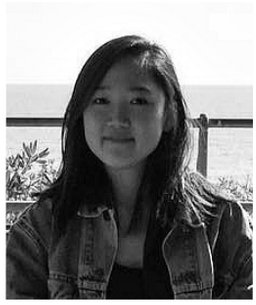

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A Message from the Chapter President...

Dear Triple Helix Readers,

In your hands is the work of a talented group of writers, editors, and designers who want to share with you their passion for the interdisciplinary study of science. Personally, I believe that science is not an exercise in intellect but an exercise in empathy. Despite the highly technical and at times brain-boggling research that is foundational to this endeavor, what we make of it is ultimately human, reflecting the hopes, dreams, and crises facing us as a species. Therefore in understanding the interdisciplinary nature of science, we understand the intersecting forces that shape our world and the people around us.

The key to using this science to change the world lies not only in knowledge and application. It also lies in the ability to cogently communicate these ideas —as well as their complex societal implications. Dialogue at the intersection of science and society has educated and empowered the public, inspired career paths, and spawned fantastically daring solutions to problems that engage the world's greatest intellects. In this tradition, your peers in The Triple Helix have documented their exploration of diverse subjects spanning law, ethics, genetics, psychology, technology, and gender.

Have a look. And remember, stay curious and never stop questioning.

Sincerely,
Amy Meng
Chapter President

A Message from the Editor-in-Chief...

Dear Readers,

The Triple Helix is a journal that explores the intersection of science and society. We examine how scientific progress may actually be implemented in real, volatile, unpredictable human populations. We probe the ethical dilemmas that exist in the gray area between research and real world application. We ask questions, we break boundaries, and we offer these mind bytes to you, dear reader. When you delve into our articles, please understand that you are only glimpsing a page of the whole story; in fact, we hope that these articles spark your curiosity and push you to dig deeper than what is encompassed here, so that what you read here remains with you long after you set this journal down.

And as for me, the editor-in-chief, what do I hope? Well, as a neurobiology major and English minor about to embark on a study abroad adventure to Australia before battling the monster that is medical school applications, I hope that you learn something new and share it, so that someone else can learn something new too. That's what I think this journal really is: a creative avenue to learn about exhilarating science from the unique perspective of your fellow students. This way of disseminating information outside of a classroom setting is, I think, pretty cool, and has the potential to be pretty powerful.

Oh, and I also hope that you enjoy reading this journal as much as I enjoyed bringing it to life, with the help of my talented writers and diligent editors.

Sincerely,
Mae Grewal
Chapter Editor-in-Chief

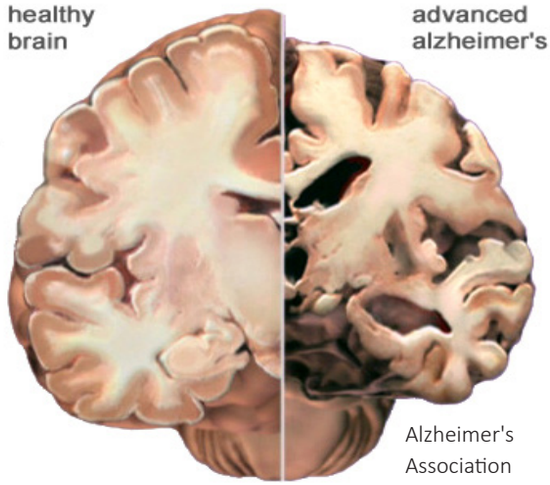
Blame it on the Epigenetics?
The Epigenetic Mechanism that May Influence Alzheimer's Disease

by Mae Grewal

Modern technology is able to peer into organs, cells, even organelles with powerful MRI machines and microscopes, sequence the entire human genome and compare it across populations rapidly with GWAS studies, and even test the blood of a mother-to-be to determine what sort of life her unborn baby might have with prenatal screening. Yet when it comes to pinpointing the pathology of diseases affecting the organ that developed all these incredible tools, the brain, scientists are stuck. Though many neuropsychiatric and neurodegenerative disorders like Alzheimer's disease have been classified for symptomatic diagnosis, they elude precise genomic definition. This is possibly due to a factor only recently being considered in the etiology of these neuro-circuitry diseases: epigenetics.

The sequencing of the whole human genome led to a push in modern research to link every human disease to a physical mutation on a chromosome. However, the DNA sequence is not the only factor that affects the protein end-product. Epigenetics considers the expression of genes based on how available that sequence of DNA is to transcriptional machinery. For example, CpG methylation makes chromatin less available by methylating cytosine nucleotides that precede guanine nucleotides; conversely, histone acetylation involves adding acetyl groups to the histone proteins that DNA is wrapped around to dissociate the DNA and make it more available for transcription. Furthermore, small RNAs, like micro RNAs, can influence the translation of post-transcriptional mRNA by binding to a complementary region and signaling that RNA molecule for degradation. Through such mechanisms, epigenetics alters the proteins found in cells in ways that only looking for chromosomal mutations would not match up with. Thus, an individual with a mutation correlated with a neurodegenerative disorder may escape the disease if epigenetic mechanisms are preventing that mutation from being expressed in the quantity necessary to disrupt normal circuitry function. The degree of epigenetic influence may also explain the wide spectrum of severity associated with neuro-circuitry diseases like Alzheimer's. Alzheimer's disease usually manifests later in life and is characterized by the slow but progressive process of forgetting. Those afflicted will first experience a short-term memory loss which can accumulate into disorientation, mood swings, lack of interest in activities that were previously enjoyable, and problems with language. These symptoms have a tendency to isolate the patient and make them feel very alone in their experiences, which results in them pulling away from family and and society. Eventually, a gradual loss of bodily function

> *"The degree of epigenetic influence may also explain the wide spectrum of severity associated with neurocircuitry diseases like Alzheimer's."*



Alzheimer's Association

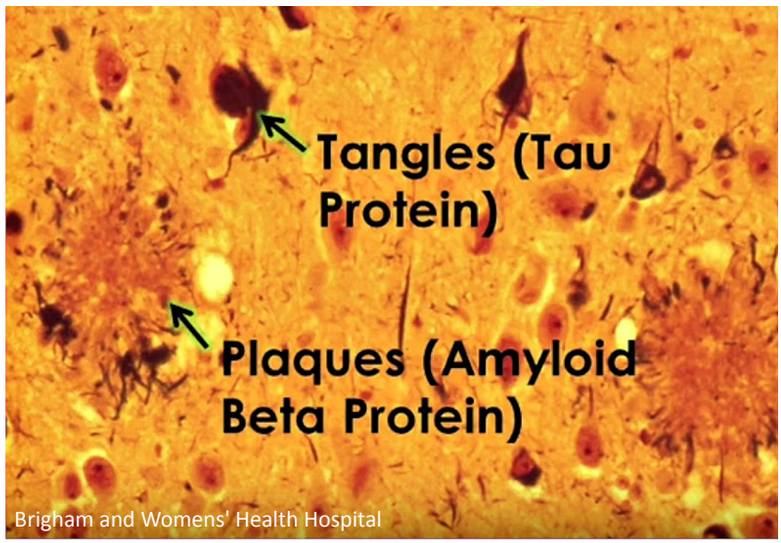
will lead to death, typically 3-9 years post-diagnosis [1]. The molecular mechanisms behind the progression of Alzheimer's disease have been determined, even if the trigger, be it genetic, environmental, or epigenetic, has not. MRI's have shown that the symptoms of Alzheimer's disease are accompanied by the accumulation of plaques and neurofibrillary tangles in the brain. These are the result of an inappropriate isoform of secreted product of the amyloid precursor protein (APP). The gene for APP lies on chromosome 21, which is triplicated in Down Syndrome and explains why nearly all Down Syndrome patients exhibit Alzheimer's symptoms as early as age 40. There are three different proteolytic enzymes that can cleave APP; cleavage by the beta and gamma enzymes sequentially yields amyloid beta (Aβ). The disease state is produced when the gamma enzyme cleaves in a slightly different location to produce a longer isoform of Aβ. Once secreted, this isoform is not able to be degraded easily by apolipoproteins, and thus it accumulates in the extracellular space in the brain to produce neurofibrillary tangles and plaques. These plaques create a toxic environment for nearby neurons, inducing neuronal death. It is still unclear as to how exactly this toxicity is mediated—various hypotheses suggest that amyloid derived diffusible ligands bind to receptors, like death receptor 6, on nearby neurons and alter their synapses to disrupt neuronal communication and induce the withering of the entire circuit and cortical atrophy [1]. Genes associated with an increased risk for Alzheimer's include different alleles of the apolipoprotein gene that result in less effective degradation of Aβ [1]. Of course, all of the genes identified as correlated with Alzheimer's are only predictors of increased risk; no gene or set has yet been marked as causal, likely due to the fact that epigenetic influences on disease manifestation have only been recently characterized.

Brigham and Womens' Health Hospital

Indeed, something besides genetics has to be afoot to explain the existence of a pair of monozygotic twins discordant for Alzheimer's disease. Post-autopsy immunochemistry on the subjects revealed decreased methylation in the Alzheimer's twin. Colocalization fluorescent studies indicated that in the normal twin, methylation was seen in the neurons, aastrocytes, and microglia; in the Alzheimer's twin, the lack of methylation extended to all three types of cells as well [2]. Bakulski's research team took this revelation even further by determining exactly which genes might be hypomethylated in Alzheimer's patients. They performed a gender-matched genome-wide DNA methylation discovery across over 14,000 genes in 25 Alzheimer's patients and their normal controlled counterparts. They isolated over 900 methylation sites across 918 genes and determined the maximal difference in methylation to be around 20%. The gene that they dubbed the strongest link to Alzheimer's was transmembrane protein 59, whose promoter region was hypomethylated in Alzheimer's patients by an average of 7.3%. The protein product of this gene is involved in APP shedding, and is a key point of regulation in the formation of Aβ peptides [3]. Hypomethylation of this gene would result in increased expression of its protein product, which would yield more Aβ peptides from APP. If an individual also carries a mutation for an apolipoprotein or for the gamma cleaving enzyme that results in the longer isoform, this individual is very likely to develop Alzheimer's. However, an individual who possesses those same mutations but is normally methylated in this promoter region is less likely to develop Alzheimer's; even if they do develop the disease, it will be less severe due to the epigenetic control of Aβ peptide formation. This is just one example of how epigenetics might influence neural circuitry and function, working in conjunction with other mutations to ultimately manifest different severities of a neurodegenerative disease like Alzheimer's.

CpG methylation is not the only mechanism through which epigenetics may have a hand in Alzheimer phenotypes; histone modifications, especially histone acetylation and deacetylation, may also play a substantial role. Zhang's research team used a selected-reaction-monitoring (SRM)-based

targeted proteomics scan to quantify the levels of histone acetylation in Alzheimer's and aged control brains. After confirming their results with a Western Blot, they reported significantly lower levels of acetylation in the temporal lobe of Alzheimer's brains as compared to control brains [4], possibly due to histone deacetylation (HDAC) hyperactivity. To determine whether this was in fact the case, Su's research team observed the effects of HDAC inhibitors like lithium and valproic acid on APP transgenic mice modeled for Alzheimer's. These mice overexpress a human APP with a mutation that results in the age-dependent accumulation of Aβ plaques. Control transgenic mice were administered water, while the treatment groups were administered either sodium chloride, lithium chloride, or valproic acid. Both lithium and valproic acid treatments significantly reduced the total amount of Aβ peptides, and the amount of the longer isoform. This correlated to a decreased plaque burden in the brains as well [5]. Fischer's team further showed that HDAC inhibitors could lead to the sprouting of new dendrites in the brain, which restored access to lost long-term memories. The team injected sodium butyrate, an HDAC inhibitor, into mice modeled for hippocampal brain atrophy and neurodegeneration, and found that these mice had regained access to long-term fear memories-- demonstrated by freezing behavior-- compared to saline-administered controls. They also observed a correlated increased MAP-2 and synaptophysin immunoreactivity in these mice, as well as an increased level of synaptic acid and dendritic marker proteins, suggesting the formation of new dendrites as a result of the HDAC inhibitor [6]. Thus, HDAC inhibitors that exert an epigenetic control could be a promising new line of therapy to consider in assuaging neural circuitry issues and delaying the degenerative phenotypes of Alzheimer's disease.



The epigenome and how it affects neural circuits is more complex than just making DNA available for transcription via demethylation and acetylation; it also involves the regulation of post-transcriptional pre-translation mRNA via miRNA. Gene expression does not guarantee a protein product as miRNA can bind to complementary regions on the mRNA transcript to signal it for degradation before translation can occur. Liu's team performed research on senescence-accelerated mouse prone 8 (SAMP 8) against SAMR1 mice controls. SAMP 8 mice are associated with age-related memory and learning deficits and are therefore used as age-associated Alzheimer's models. Through real time RT-PCR analysis, they determined that APP protein levels do not match the APP mRNA levels in the hippocampus of the SAMP 8 mice as they should in the control, suggesting aberrant post-transcriptional regulation. Bioinformatics and RT-PCR revealed that this regulation could be due to mi-R16, mi-R144, mi-R195, or mi-R383. Co-transfection of the 3'-UTR of the APP gene with a luciferase reporter into a 293 ET cell line revealed that mi-R16 overexpression reduced luciferase activity and thus must be the main miRNA regulator of APP mRNA. Through immunohistochemistry and in situ hybridization, they further showed that where APP protein levels were increased in the hippocampus of the treatment

"The epigenome affects the level to which mutations that disrupt neural circuitry are manifested, so that even if an individual possesses a certain set of mutations, it is not guaranteed that those mutations will produce an effect."

mice, mi-R16 levels were abnormally low [7]. Thus, the deregulation of mi-R16 could lead to the overproduction of Aβ peptides as a direct result of the accumulation of APP. While it is still unclear as to how mi-R16 is deregulated, this is a poignant example of how post-transcriptional epigenetics can still affect neural circuits. Because of this, mi-RNA also show promise in terms of drug therapies for Alzheimer's disease. Administering extra mi-R16 to appropriate brain regions to boost the levels back up to normal could help temper the molecular mechanisms by which Alzheimer's results.

Clearly the level to which genes are expressed, as mediated by methylation, acetylation, and miRNA, is just as important to maintaining a healthy neural circuit as is a mutation-free genome. The epigenome affects the level to which mutations that disrupt neural circuitry are manifested, so that even if an individual possesses a certain set of mutations, it is not guaranteed that those mutations will produce an effect. This added layer to disease manifestations makes understanding the development of degenerative neural circuit disorders, like Alzheimer's, much more difficult. Delving into how the interactions between epigenetics and genomics produce varying severities of a disease, and then how best to tackle treatment, be it on the epigenetic, genetic, or even proteomic level, is within the realm of personalized medicine. This certainly should be the focus of future research in order to provide the best therapy possible to the wide variety of individuals— with even more disparate underlying causes— afflicted with these diseases. Ultimately, epigenetics is the emerging frontier of truly cracking open the underlying causes of neuropsychiatric diseases like Alzheimer's disease.

"Delving into how the interactions between epigenetics and genomics produce varying severities of a disease, and then how best to tackle treatment, be it on the epigenetic, genetic, or even proteomic level, is within the realm of personalized medicine."

Mae Grewal is a junior in the college, majoring in Neurobiology, minoring in English, and hoping to pursue a career in medicine. She hails from Phoenix, Arizona, and will be studying abroad in Sydney, Australia in the Spring of 2017.

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Capital Punishment: Honoring Dignity

by Brendan Desimone

Aside from debating for or against the ethical existence of capital punishment, improvement of its operations in the United States is an unequivocal priority. The death penalty has evolved significantly over time in the United States. According to Cornell University Law School's Legal Information Institute, current analysis of the Constitution's prohibition on "cruel and unusual punishment" prescribes some flexibility in determining what kinds of executions are considered constitutional [1]. This premise has caused an evolution of execution methods over time, as standards change. All 31 states which permit capital punishment specify lethal injection as the primary means of execution, but there are four other de-jure methods of execution: electrocution, firing squad, hanging, and gas inhalation [2]. In some states, sentenced convicts have the choice among some or all five means mentioned [3]. While reform has taken place to preserve the dignity of those sentenced to death, the mores of modern society prevent the most dignified execution possible from occurring. This notion of preserving dignity requires that no undue suffering is exacted on the sentenced other than death. Lethal injection is the modern standard in humane executions because it mitigates any loss of dignity when compared to feasible alternatives.

As the primary cause of questionable practices in the execution of capital punishment, the European Union's embargo on the export of key drugs used in lethal injections to the United States prompted hastily-conceived workarounds that place those sentenced to death at risk of suffering with no dignity. This policy came into effect in 2012 [4]. Now, the industry standard is to refuse to sell and prohibit distributors from selling to United States prisons. Due to the increasingly small number of executions annually administered, most states stockpiled enough drugs to outlast the shortage until around 2014 [5]. The assumed course of action has been to use compounding pharmacies, which can manufacture any made-to-order drugs, to fabricate near facsimiles of the previously used drugs or entirely new alternatives; however, these pharmacies often do not face the same rigorous regulatory processes traditional pharmaceutical manufacturers endure.

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New protests on the supply-side of the lethal injection industry threaten the continuing existence of morally sound executions. The American pharmaceutical industry has withdrawn from involving its products in carrying out capital punishment [6]. Two notable U.S. manufacturers involved in this protest are Hospira and Pfizer, which have placed restrictions on the distribution of their products and in some cases withdrawn them from the market [7].

"While reform has taken place, the mores of modern society prevent the most dignified execution possible from occurring."

This retreat has caused states to improvise by instituting untried and ill-formed procedures. Now, boutique-style compounding laboratories are consulted to replicate unavailable established drugs and derive new lethal compounds for lethal injection, and their names are legally kept secret in most states [8]. These labs have virtually no oversight, and their products face no vetting or approval before being authorized for use on those sentenced to death [5]. By not adhering to standards established by the FDA, prisoners who are subject to death by these drugs are placed in more danger of a malfunction. Also, some professional organizations within the medical community, like the American Pharmacists Association and the International Academy of Compounding Pharmacists, are calling for all medical professionals to remove themselves entirely from the process [8]. This stance is flawed because executions occur at the discretion of the government, not of medical employees of the state who aid in this end, for employees can be replaced and the absence of medical professionals can do more harm than good. These protests endanger prisoners' humanity to a greater degree than they effectually preserve it.

The drug substitutes, while almost chemically identical to the original drugs, are slightly different. The procedure for lethal injection can be attained with either a combination of three or two drugs, or just one drug. The three and two phase injections begin with an anesthetic, sometimes a paralytic and end with a lethal drug that stops the heart; for the one drug solution, a lethal dose of an anesthetic or barbiturate is used [2]. Most compounding pharmacies attempt to replicate the barbiturates used to anesthesize because, given industry embargoes, this compound is the most difficult of the three to procure. And since these drugs are manufactured by compounding pharmacies, they are not required to be tested in accordance with FDA safety guidelines [5]. One instance of such a substitute, an entirely new chemical, was used in an execution in Ohio after the Ohio prison system requested that a compounding pharmacy furnish the array of drugs used in a two drug procedure. The anesthetizing drug did not function properly and caused the sentenced man to suffer for 25 minutes while "gasping for air" as the lethal component slowly worked [9]. This would be an example of what the constitution terms a "cruel and unusual punishment" because, while the death penalty is legally accepted in the United States, further torment violates essential human dignity and is not considered constitutional by the Supreme Court [1]. Due to a lack of vetting and oversight by the United States government, the existing procedures for synthesizing new alternatives place the inherent dignity of individuals at risk.

"The United States has an obligation to maintain human dignity, even in cases of capital punishment."

The United States has an obligation to maintain human dignity, even in cases of capital punishment. As such, it must intervene in the manufacturing of any compounds used in executions to ensure a functioning lethal injection is furnished without any of the adverse side-effects that cause unnecessary suffering. A new system ought to be instituted to prevent the sourcing of lethal injections from tainting the dignity of those sentenced. One apparent way to fulfill this requirement would be to increase the FDA's power over the actions of compounding laboratories. FDA oversight would allow for the humane development of new drugs for use in lethal injections because these new drugs would have to be vigorously tested to ensure that they function effectively when needed. Because of the complex pharmaceutical interactions involved in executions, the testing process would need to establish that the new drugs would function exactly as the previous ones did, because testing an entirely new family of drugs on prisoners could potentially cause slow or cruel deaths. Oversight in the form of thorough testing to prove that new drugs mimic the effects of those already in use is therefore nec-

essary to minimize any unduly cruel punishment.

At executions, medical personnel have a responsibility to ensure the dignity of the sentenced. The sentencing of a person to death must be perceived as, in itself, killing. Therefore, the role of practitioners of medicine is to minimize discomfort. While some professional groups claim that medical personnel should refrain from involving themselves in executions, they are nevertheless uniquely qualified to administer injections and supervise. If their replacements were less educated and less willing to help reduce suffering, they would not attempt to protect the dignity of those sentenced. Just as in war, medical professionals do not cite the actions of those warring as cause to abandon caring for even the most vicious warriors on the verge of death, medical professionals cannot leave those sentenced to death without some agent acting on the behalf of the sentenced to preserve dignity whenever possible. The hippocratic oath, the document cited by opponents to capital punishment justifies actions that are for the "benefit of the sick" [10]. No such phrase as "do no harm" is a part of the modern hippocratic oath [10]. The hippocratic oath only levies a duty to help. Those on death row are not strictlyspeaking sick, but their lives are similarly in peril, and healthcare professionals need to help whoever they can, including those irrevocably condemned to death.

While the premise that capital punishment in any form violates human dignity may or may not be true, certain means employed in pursuit of capital punishment have the potential to violate human dignity. The purpose of capital punishment is to render dead those justly sentenced in modern society. As such, the particular method and specifications of an execution should only fulfill the end of taking a life, without going beyond that and introducing unnecessary suffering. The use of compounding pharmacies places untested drugs in the hands of prison systems, and those being executed are the first test subjects of the new drugs. New policies must protect the dignity of those on death row by placing quality control on the pharmacies that ensure those sentenced are not in risk of suffering because of a malfunctioning drug. To exacerbate matters, some amongst the medical community claim that medical personnel have no place in executions. This stance exposes those sentenced to unwarranted and cruel punishment that could be inflicted by less well-trained replacements. All associated with capital punishment have a duty to honor the dignity of those sentenced to death, and any action which compromises that dignity violates the inherent worth of life– even though that death is inevitable and compulsory.

Brendan is from Beverly, MA. He intends to major in Science, Technology, and International Affairs. He is also a freestyle skiing coach.

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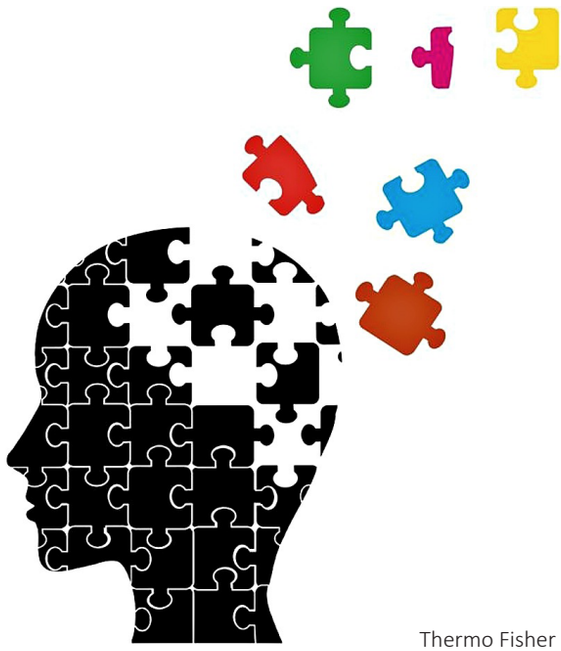
Flipping the Switch: Lights Out for Alzheimer's?

by Alexandra Brunjes

Alzheimer's disease is an incurable neurodegenerative disease whose pathology has long plagued the scientific community; its causes are unknown, its treatments are generally ineffective, and its effects are devastating. Alzheimer's affects an estimated 5.1 million Americans [1]. Its symptoms include memory loss, cognitive impairment, and intellectual disability caused by the deterioration of brain cells and neuronal connections. The ultimate prognosis is multiple organ failure leading to death, but arguably the most difficult part of the disease is the incredible toll it takes on the patient's loved ones. Although treatments are available, they serve only to ameliorate symptoms and are unable to prevent onset or halt the disease's progression. Although Alzheimer's primarily affects those over the age of 65 – in fact, the chance of developing Alzheimer's doubles every five years beyond this age – there are also approximately half a million Americans suffering from early onset Alzheimer's or another form of dementia [1]. This makes Alzheimer's research an incredibly important field to explore.



Thermo Fisher

Given that there are no medications able to cure Alzheimer's or cease its progression, the treatments currently available are targeted at lessening the severity of symptoms during the disease's early stages [2]. Although effective, these drugs only work for a limited time. The medications that treat memory and cognitive impairment, for example, alter chemical signal transmission in the brain, which means that they only work when neurons are signaling properly. Thus, when the disease's progression leads to significant enough neuronal death, these medications can no longer help patients [2]. In addition to long-term ineffectiveness, all current medications for Alzheimer's have side effects such as nausea, vomiting, headaches, and loss of appetite [2]. While this is primarily due to the nature of medication, it is ultimately rooted in our lack of understanding of the disease and thus inability to develop treatment that properly targets its underlying causations. In response to the plethora of problems related to Alzheimer's and its widespread impact, many scientists are devoted to researching the disease. One promising area being explored is research surrounding the protein neuroglobin. Neuroglobin (NGB) is a neuronal globin protein that is heavily expressed in the brain and retina and has been shown to have neuroprotective capabilities [3]. This property makes it a prime candidate for neurodegenerative research. Its classification as a "globin protein" means that it can reversibly bind oxygen [4]. This capability allows globin proteins to play many important roles in animals, bacteria, plants, and fungi [5]. Likely the most familiar globin protein is hemoglobin, the protein on red blood cells that carries oxygen from the lungs to the rest of the body.

Research has also confirmed the presence of NGB in the brains of rats, mice, and zebrafish, so it is highly conserved across species, which enables scientists to look at the brains of a few diff-

erent animals during research. However, while these discoveries are certainly fascinating and merit further research, the aspect of NGB that is currently drawing the most attention – and arguably has the most potential – is its role as a neuroprotectant.

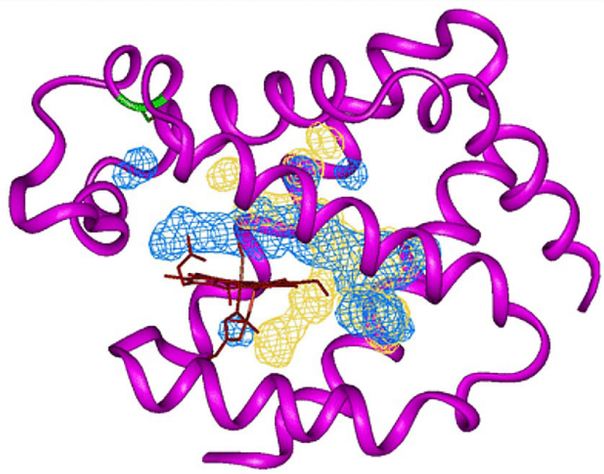
In recent years, NGB has been shown to have a neuroprotective role that becomes evident in brains affected with stroke, oxidative stress, amyloid-beta plaque toxicity, hypoxic-ischemic injury, and, most importantly for this article, Alzheimer's disease [3-4]. A 2007 study done *in vivo* (on a living organism, in this case mice) showed NGB overexpression to protect against beta-amyloid induced neurotoxicity [5]; beta-amyloid is a plaque that builds up in unhealthy amounts in the brains of Alzheimer's patients and causes damage. This same study also found that NGB protects against the transgenic Alzheimer's phenotype [5], which is the observable expression of symptoms in Alzheimer's mutant mice.

> *"In recent years, NGB has been shown to have a neuroprotective role that becomes evident in brains affected with stroke, oxidative stress, amyloid-beta plaque toxicity, hypoxic-ischemic injury, and, most importantly for this article, Alzheimer's disease."*

NGB expression has been shown to vary as a result of age and sex, as well as the specific variant of the gene that an individual has; a 2010 study found that groups with a high risk for developing Alzheimer's had a NGB gene variant that resulted in decreased expression of the protein [6]. Thus, even if people in these groups were experiencing natural NGB upregulation in response to disease, due to their risk factors it would likely not be enough to prevent neurodegeneration, and would lead to faster onset [6].

While NGB is known to be a neuroprotectant, the mechanisms underlying this ability are still largely unknown [7]. One plausible mechanism is NGB's involvement with mitochondria. Mitochondria are essential for brain function in part because neurons need a lot of energy, and mitochondria are the powerhouse of the cell [7]. Subsequently, mitochondrial dysfunction is often involved with the pathogenesis of neurological problems, because as mitochondria cease to function, they stop being able to give neurons energy and thus the neurons begin degenerating. Recent research has shown that NGB upregulation preserves mitochondrial function by conserving ATP production [7]. This suggests that NGB may be an indirect neuroprotectant; instead of directly helping degenerating cells, it may just help mitochondria, which in turn keep cells alive and functioning. In another study done in 2013, researchers observed mouse cortical neurons and found NGB overexpression to result in improved mitochondrial function [7].

Therefore, one of the most exciting discoveries made about NGB is that it can be up or downregulated as needed in response to disease. For example, after looking at NGB levels in the brain tissues of subjects both with and without ischemic stroke, which is a sudden loss of blood flow to the brain, researchers in a 2016 study found NGB presence to be increased in those who had had strokes [8]. Previous research also showed that NGB knockout leads to worsened outcomes for hypoxic/ischemic brain injuries [5]. These results support the notion that NGB is a neuroprotectant, as they indicate that NGB is upregulated in response to the stroke; they also demonstrate the brain's ability to recognize trauma and trigger upregulation. If scientists find a safe way to intervene



Neuroglobin 3D Structure (Synchotron)

and chemically upregulate NGB, they could potentially prevent brain damage in other stroke patients.

The upregulation seen in response to stroke also happens during Alzheimer's progression. A 2010 experiment found that NGB was upregulated in the temporal lobe during early Alzheimer's disease progression, demonstrating that it reacted to the neuronal death caused by the disease [6]. Additionally, when compared to healthy people, they found that patients with Alzheimer's had a 23% increase in NGB expression [6]. The problem with the protection caused by NGB is that it only lasts for a certain amount of time; as the disease progresses, NGB stops being overexpressed and instead drops back to its original levels and ceases to help the brain. Although NGB ultimately is downregulated during disease progression, the knowledge of its ability to respond to neuronal degeneration by changing its expressed levels has served as a launching point for research into the functionality of NGB as well as other endogenous proteins.

"The problem with the protection caused by NGB is that it only lasts for a certain amount of time."

While lab-created medication is a perfectly suitable treatment for numerous diseases, many researchers instead focus on finding ways to induce the body's own mechanisms as treatments. In this vein, multiple studies have suggested that studying the activation of endogenous neuroprotectants could be a very beneficial area of study, as it could lead to the development of effective therapies against a variety of neurological problems [5]. Thus far into NGB research, the chemicals that have been shown to have an upregulating effect include cinnamic acid, valproic acid, and 17B-estradiol [5,8]. Further exploration into their efficacy could potentially lead to them being incorporated into medications that treat neurodegenerative diseases.

The most recently published study on NGB came out in early October, and it discussed an incredibly exciting discovery: there is a genetic "switch" that controls NGB's up and downregulation. Researchers in the study found a cell type-specific loop to be responsible for regulating NGB [3]. After confirming this ability, the team used a technique to fully remove the region of DNA from the NGB gene in order to observe its effects [3, 10]. The removal of the DNA region caused the NGB to be turned off, suggesting that this portion of DNA is able to control the expression of NGB [3, 10]. This is a monumental discovery: if we could use this knowledge to find a way to control that switch, we could potentially use gene therapies to turn on neuroprotection and turn off Alzheimer's progression. This could halt neurodegeneration; this could cure Alzheimer's.

"There is a genetic "switch" that controls NGB's up and downregulation. If we could use this knowledge to find a way to control that switch, we could potentially use gene therapies to turn on neuroprotection and turn off Alzheimer's progression. This could halt neurodegeneration; this could cure Alzheimer's."

Although NGB research has been fascinating and informative, it does have some significant bioethical implications. For example, right now research is in the early stages and is focusing on NGB in animal brains. Beyond the ethical issue that many people harbor about animal research, as studies continue and more solid conclusions are formed, eventually trials will be conducted on humans. This approach has a variety of obstacles: researching NGB in humans would necessitate chemical interference with brain functions, which is inherently dangerous, and if ineffective could likely shorten the lifespan of research subjects. Research would likely also focus on preventing the disease, whichmeans it would require giving treatments to patients in its very early stages; if a person knows that they have very little memorable life left, it is unlikely that they will want to spend it participating in a potentially dangerous trial.

Even when our NGB knowledge bank becomes more comprehensive and concrete, there are still many steps we must take before treatment can be broadly implemented. However, until we reach the point where we must do human research, current studies still have a lot of ground to cover. Researchers at Harvard Medical School are looking into NGB knockout in order to observe its effects on normal brains as compared to ischemic brains; they also want to continue exploring cinnamic acid and look at its role in animal stroke models. Many other scientists who have published research on NGB are conducting experiments that confirm their results and build upon their conclusions. Additionally, NGB research has further opened the door to exploring more genetic factors and working to better understand the roots of diseases as opposed to simply the symptoms; many researchers are investigating a variety of genetic factors and endogenous protein activity. However, no matter the lab or the researcher, the ultimate goal is to be able to understand NGB well enough that medical interference can be used to manipulate its properties and allow it to be a treatment for devastating diseases. There is a long way to go, but research thus far is showing promise. Alzheimer's has the ability to steal lives; NGB may be able to save them.

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Gendered Impacts of Climate Change-Related Events on Health

by Kate Jin

Climate change is a widely studied and well-researched issue that has severe consequences for global health. Though many studies examine its effects on human health, particularly in developing regions, and its differential effects on the health of women and men, relatively little has been done to analyze these gendered effects [1]. Because a gender perspective remains of peripheral interest in climate change and health studies, it is important to emphasize the need for gender-aware solutions when deciding on management and mitigation programs and policies. The consequences of climate change will continue to worsen if leaders and decisionmakers neglect to assume a gendered approach in mitigating climate change impacts.

> *"The consequences of climate change will continue to worsen if leaders and decision makers neglect to assume a gendered approach in mitigating climate change impacts."*

Climate change has a two-fold impact on health: 1) climate change increases the severity of natural disasters, drought, and disease; and 2) climate change diminishes people's abilities to cope with these events. These impacts are felt strongly in developing regions of the world, but even among these populations, women are disproportionately affected [2].

To elaborate on the first impact of climate change on health, extreme weather events such as tropical storms and droughts are becoming more intense and frequent. According to the World Health Organization, the number of reported weather-related natural disasters around the world has more than tripled since the 1960s, and most deaths (~60,000 each year) resulting from these disasters occur in developing countries [3]. Additionally, climate change contributes to the spread of infectious disease by creating optimal environments for malaria-carrying mosquitos and increasing the numbers of cholera-causing bacteria [4]. According to various studies, climate variability played an important role in initiating malaria epidemics in the East African highlands and accounts for 70% of variation of recent cholera series in Bangladesh [5-6].

The second impact—people's decreased ability to cope with extreme events—is closely connected to the first because natural disasters often rob people in developing regions of valuable resources and assets by diminishing food and water availability, in addition to forcing people from their homes. For example, increasingly variable rainfall patterns can negatively impact freshwater supplies [4]. The resulting lack of safe water for drinking, cooking, bathing, and other household use can compromise hygiene, increase rates of malnutrition, and increase the risk of waterborne disease [7]. Furthermore, water shortages can amplify into water scarcity and then drought, which could lead to food insecurity and famine, ultimately leaving populations ill-

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equipped to handle natural disasters or other shocks [4].

Droughts are not the only concern when it comes to climate change and global warming—on the other side of the spectrum, floods are increasing in frequency and intensity as well. The consequences of floods can be devastating. Floods contaminate freshwater supplies, heighten the risk of waterborne diseases such as cholera, and disrupt the supply of medical and health services [4,7]. Moreover, damaged homes and property drive people to migrate to villages that are overcrowded and foster disease [2].

Though climate change affects all countries in all parts of the world, its impacts will be felt differently among regions, generations, age classes, income groups, occupations, and genders [2]. Developing countries bear the brunt of climate-related impacts on health because they lack the resources necessary to cope with natural disasters compared to other countries, qualifying these countries as vulnerable populations [8]. Groups that are especially vulnerable, such as the poor, will be disproportionately affected. This is significant because women constitute 70% of the world's poor, which means that even among the already disadvantaged group of impoverished populations, women are especially at risk [2,9].

The increased risk women face manifests clearly in the gender gap that is apparent in the aftermath of natural disasters. In a sample of 141 countries over the period 1981 to 2002, researchers found that natural disasters and their aftermath kill more women than men on average, or kill women at an earlier age than men [2]. For example, the cyclone disaster in Bangladesh of 1991 killed 140,000 people, a staggering 90% of which were women— that is 126,000 women [9]. These figures can be explained by the fact that more women than men are homebound as they look after children and property, and many women die while waiting for relatives to return home to accompany them to a safe place [10]. Additionally, women face increased risk of contracting illness and disease, whether because of natural disasters or otherwise [11].

"The cyclone disaster in Bangladesh of 1991 killed 140,000 people, a staggering 90% of which were women."

It is crucial to note that gender-based vulnerability does not derive from a single factor, nor is it a result of women being the "weaker" sex, but reflects historically and culturally specific patterns of relations in social institutions, culture, and personal lives" [2].

It is common in many countries to view women as second-class citizens. This is clear in the aftermaths of natural disasters, in which women and children are 14 times more likely to die than men during a natural disaster [12]. According to the International Union for Conservation of Nature, there is strong evidence that gender differences in deaths from natural disasters directly correlate to women's economic and social rights [9]. When women are considered second-class citizens, it follows that men are likely to receive preferential treatment in rescue efforts, leaving women to suffer more from food shortages and lack of other resources in the aftermath of disasters [9]. This helps to explain why 90% of the people killed in the 1991 cyclone disaster in Bangladesh were women.

"Gender-based vulnerability does not derive from a single factor, nor is it a result of women being the "weaker" sex, but reflects historically and culturally specific patterns of relations in social institutions, culture, and personal lives."

Unfortunately, women are disadvantaged not only in natural disasters, but also in epidemics exacerbated to climate change. For example, cholera is an equal-opportunity infection, but it is not gender-neutral [13]. As climate change increases the risk of disease outbreak for all, there could be gender-differentiated impacts due to the aforementioned historically and culturally specific patterns of relations in social institutions, culture, and personal lives [2].

There exist two outstanding cultural and social norms that are contributors to the vulnerability of women in the face of climate change-related events: 1) women have limited or reduced access

to resources and services than men, and 2) women are the victims of widely internalized sexism and are forced to fulfill societal gender roles. These factors are closely linked and reinforce one another. The vulnerability and adaptive capacity of any person is dependent on a variety of assets which include natural resources and land, information and local knowledge, technology, power and decision-making potential, education, health care, and food [2]. The more assets one has, the less vulnerable they are and the better they can cope with shocks and stresses, such as droughts or floods. Conversely, greater deficiencies in assets are conducive to greater insecurities such as food insecurity and unreliable access to medical care [14].

Data from around the world indicate that women tend to have less or limited access to such assets as physical, financial, social, and natural capital [2]. This is evidenced by studies that have found that the consequences women face from and following natural disasters are more severe when the socioeconomic status of women is particularly low, as experience highlights that the most "socially excluded and those least able to gain access to or control strategic resources during and in the aftermath of a natural disaster [2, 15]. On the opposite side of this, studies have shown that in countries where women are comparable in status to men, natural disasters affect men and women almost equally [11].

As a specific example that showcases gender inequality, women in some communities in Bangladesh are deprived of the capacity to cope with disasters by being kept in positions that are dependent on the man of the household. This is done by denying women the right to make major decisions and restricting their ability to access information from the outside world, which “directly prescribes women’s vulnerability to disaster” [2]. These women are sheltered from the world outside of their homes, so unless their husbands alert them of an impending natural disaster, they have no hope of escaping injury and possible death.

Underlying the first factor of limited access to safety is the deep-rooted issue of societal gender roles. Gender roles are “learned behaviors in a given society or community that condition which activities, tasks, and responsibilities are perceived as male and

Women Deliver

female" [16]. Women are often disadvantaged asa result of gender roles. In most cases, men are able to focus on a particular productive role and play their multiple roles sequentially, whereas women must play their roles simultaneously and balance competing claims on time for each of them [16]. This plays into the limited resources women have access to, including time as a valuable resource. The gender-based inequalities that are fostered by traditional gender roles limit women's access to assets, which makes them more vulnerable to shocks and stresses [12].

To revisit the impacts of climate change on disease outbreaks, various studies have shown that climate variability played an important role in initiating malaria epidemics and cholera series [5-6]. It is crucial to recognize that this increase in outbreaks due to climate change could have gender-differentiated impacts because women have *less access* to medical services than men, and women's workloads increase as they fulfill their *gender roles* in spending more time caring for the sick [9,17]. To reiterate, women are vulnerable not because they are the "naturally weaker" sex, but because women and men face varying degrees of vulnerability due to their different gender roles.


Manipadma Jena/IPS

Many of women's responsibilities in their gender roles have been implied in the examples above. Specifically, women's roles include fetching water, handling and treating water, gathering firewood, preparing food, and caring for sick family members, among many others. Additionally, these roles are not limited to adult women; these responsibilities are shared by young girls as well.

Furthermore, certain social norms follow gender roles. During mealtimes, food is served first to the husband, then to the children, and finally to the wife. This becomes problematic when there are shortages of food, as this coping strategy leaves little to no food for women so they often become under- and malnourished [18].

Speaking in the broadest of terms, the best way to alleviate the vulnerability of women—and by extension, populations—in developing regions is to eradicate poverty in these regions. The most vulnerable people are those in poor rural areas, whose low resilience and dependence on natural resources expose them to potentially devastating impacts from even minor changes in environmental conditions [19]. Because the adverse effects of climate change disproportionately affect poorer communities, it would be best to institute solutions that help alleviate poverty. In strategizing and implementing these solutions, it is absolutely essential to keep in mind that the vulnerability of women to natural disasters is socially constructed and gender-specific [11]. The factors that keep women disadvantaged compared to men—limited access to resources, restricted rights, no voice in decision-making—are rooted in gender inequalities reinforced by gender roles [2]. Therefore, it is critical to overcome these barriers first in order to eliminate the gender-differentiated health effects of climate change.

Various measures can be taken to alleviate the vulnerability of women. Possible actions include: improving access to skills, education, and knowledge; improving disaster preparedness and management; supporting women in developing a voice in decision-making; developing policies to ensure equal participation of women in climate change adaption initiatives; providing women access to land and credit; and many more [2]. The purpose of these actions is to raise the socioeconomic status of women living in developing regions to levels comparable to that of men, because studies have shown that in countries where women

are comparable in status to men, natural disasters affect men and women almost equally, and that consequences of natural disasters are especially severe for women of particularly low socioeconomic status [2,11].

It is also important to collect sex-disaggregated data for all programs and projects that are implemented in order to ensure that sound, holistic information is collected. Additionally, it is important to implement gender mainstreaming, in which gender perspectives and gender equality are a central focus of all activities from the inception of any project [20].

Taking these steps will ensure an integrated and gender-sensitive approach based on sound knowledge and strategies, which are invaluable in building the resilience of the most vulnerable to the impacts of climate change [18]. Ensuring that access to the key determinants of human health, including clean air and water, sufficient food and adequate shelter, is not impeded by societal norms and gender inequality for women will be essential in moving forward. Ensuring that access to the key determinants of human health, including clean air and water, sufficient food and adequate shelter, is not impeded by societal norms and gender inequality for women will be essential in moving forward [3].

Kate Jin is an Environmental Biology major (COL '17) from Tenafly, NJ. She is currently studying the sociality of bottlenose dolphins and was consistently attacked by the same emu while conducting fieldwork in Australia last summer.

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Nano: The Future of Medicine

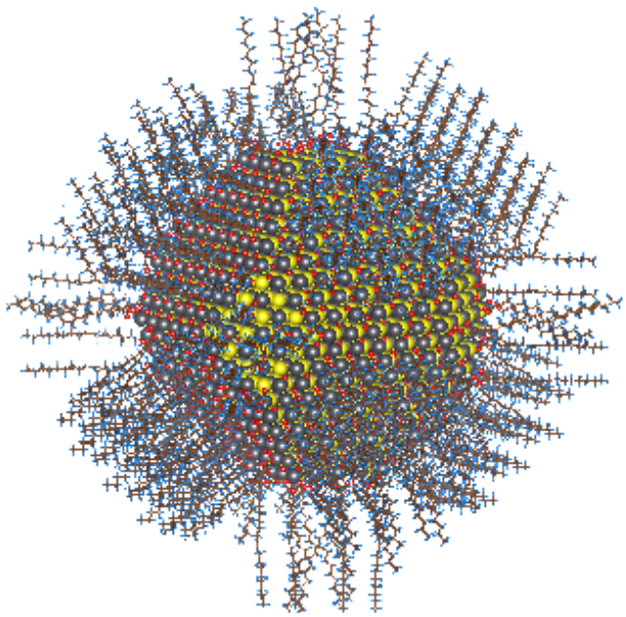
by Patrick Mulcahey

In recent years, “nano” has become a buzzword of science. Over the past fifty years, huge leaps in our ability to measure the world at the atomic level have permitted scientists from all disciplines to gain a greater understanding of our world. This interdisciplinary collaboration between scientists has led to the development of the fields of nanoscience and nanotechnology. While these studies have permitted scientists a greater view of our universe, there are potentially revolutionary applications of nanotechnology in the medical field. While there are many possible applications of nanotechnology in medicine, there will be inevitable social consequences of the development of these technologies. These consequences will create ethical questions that scientists, philosophers, and policy makers will have to grapple with going forward as these technologies develop and grow.

"Although nanotechnology is a field of study that is young and relatively undeveloped, it has the potential to greatly enhance our understanding of the material world and our ability to create innovative devices for application in various fields."

Nanotechnology is a recently emergent field of science. The central ideas and concepts of nanoscience were first presented by famed scientist Richard Feynman at a meeting of the American Physical Society on December 29, 1959 [1]. In particular, he described how scientists would one day be able to control individual atoms. The actual term “nanotechnology” was first coined approximately a decade after Feynman’s famed talk by Professor Norio Taniguchi. Finally, in 1981, scientists were first able to visualize individual atoms via scanning tunneling microscopy. Scanning tunneling microscopy (STM) uses a very fine probe to detect idiosyncrasies of electric current at the substrate surface to provide high-quality images of minutely small particles; a technique like STM must be used instead of optical microscopy because certain objects such as atoms and some nanoparticles are smaller than the wavelength of visual light [2]. Although nanotechnology is a field of study that is young and relatively undeveloped, it nonetheless has the potential to greatly enhance our understanding of the material world and our ability to create innovative devices for application in various fields.

One of the greatest potential applications of nanotechnology is in the field of medicine. Nanotechnology currently represents one of the vanguards of medicine; while some technologies, such as nanoparticles, are already in mainstream use in medicine, other technologies, like "nanobots" that make repairs at the cellular level, are still in development. Drug delivery is one of the fileds that is very pro-



Structure of a nanoparticle that could be used in drug delivery (Jing Zhou)

mising for nanotechnology [3]. For example, nanoparticles that deliver chemotheraputic medications directly to cancer cells are a topic of current research. The group of Robert Langer at the Massachusetts Institute of Technology, for example, synthesized nanoparticles made of polymers coated with parts of RNA molecules, which serve to guide the nanoparticles to the tumor sites to deliver the cancer drug [4]. These nanoparticles successfully eradicated tumors in a mouse model of prostate cancer. One of the greatest challenges for this research is to engineer nanoparticles that go to specific parts of the body; while Langer did this successfully with parts of RNA, other scientists are trying to do this using the physical properties of the nanoparticles including size, shape, and charge. While there is certainly a great deal of research and engineering to be done in cancer nanotechnology, it remains full of promising solutions to medical problems.

Another possible field of application for nanomedicine is neurology, the study of the nervous system. As one of the most delicate systems in our body, any disturbance or degradation of the nervous system can yield potentially disastrous results, as seen in neurodegenerative diseases. Nanotechnology actually may be able to serve in a neuro-protective or neuro-engineering capacity [5]. By delivering the necessary cellular materials for repair, nanoparticles may be able to facilitate and even direct the repair of brain or spinal cord tissue. For example, conduits, or channels for the delivery of water, composed of nanomaterials such as polysaccharides like chitosan, have been used to facilitate nerve repair in cases where surgery is unreasonable. While there still remains a great deal of research that must be done to understand the intersection of nanotechnology and neurology, the ability to encourage and control tissue regeneration in the brain and in the spinal cord could lead to effective treatments for combating presently incurable neurodegenerative disorders marked by widespread tissue degradation, such as Alzheimer's and Parkinson's disease. Furthermore, while spinal cord injury remains a common disability with no established cure, the potential to the repair nerves of the central nervous system offers hope to all who are afflicted.

Undoubtedly, nanotechnology holds great promise in medicine. As scientists progressively come to an understanding about the diversity of nanomaterials available, nanomedicine will surely expand exponentially as a way to approach health issues from cancer to the brain. However, behind all of this advancement, there are significant social consequences. The cost of these nanotechnological solutions in medicine will be great, a reality that may only exacerbate the national and global inequalities in health care. Furthermore, nanotechnology research in medicine may spur potentially unethical applications of nanotech in military and corporate spheres.

"However, behind all of this advancement, there are significant social consequences."

In order to understand the potential social impacts of nanotechnology, philosophers and scientists alike must understand four distinctive features of working at the nanoscale. At the level of nanotechnology, the properties of the material cannot be extrapolated from just its chemistry; an understanding of its physical properties is absolutely necessary [6]. In particular, Robert Sparrow, a professor of bioethics at Monash University in Victoria, Australia, writes that in order to work effectively with nanotechnology, scientists must understand how physics affects an object's chemistry. This trait of nanomaterials may impact how materials are regulated; as assessments of safety and risk may have to be completed for each individual material rather than on a large scale basis. The other three qualities Sparrow assigns to emerging nanotechnologies are "ubiquitous, invisible, and 'slippery.'" As research on nanomaterials continues and technology progresses through the 21st century, indeed, nanotechnology will be everywhere. Furthermore, nanotechnology will be invisible to the public in that many consumers will not be aware that they are using nano-based products. Finally, the 'slippery' element of nanotechnology refers to the difficulty federal agencies will have in regulating nanomaterials as scientists and engineers create new technologies every day.

While advances in nanotechnology will inevitably lead to innovation in medicine, Sparrow warns read-ers that such progress will almost certainly come with unseen costs and consequences. Initially, he writes, nanotechnology-based therapies, such as those developed for cancer or neural regeneration, will most likely be only available in wealthy, industrialized nations [6]. Furthermore, the concentration of nanotechnology-based therapies will most likely be confined to only the wealthiest of Western nations, and while eventually, developments in material synthesis and device fabrication may drive costs down, they will still be notably high in the foreseeable future. Certain ethicists believe that the emergence of nanotechnology will create a similar "divide" that the tech revolution has created. The "haves" of society will have greater access to technology (and thus information, vital service, etc.), while the "have-nots" will remain in poverty [7]. The costs of nanotechnology and nanotech-based therapies may also put an undue strain on centralized health systems. This creates an ethical dilemma for central authorities: the funding of medical nanotechnology research may yield incredible advancement and create effective treatments for certain conditions; however, as the widespread demand for such innovations increases, the burden of the cost will be put on the same central authority funding the original research.

In addition to the social consequences of the advancement of medical nanotechnology, there are other consequences that could arise as the field of nanotechnology grows. First, nanotechnology has potentially deadly applications in military technology [6]. Because most of the funding for nanomaterials research comes from the United States Military, citizens can expect that much of the emergent nanotechnology will be used for military applications. Across the board, ethicists agree that there can be very little positive social benefit to applying nanotechnology in a military setting. In a military setting, there is always a potential for a nanotechnology arms-race to occur [7]. In addition to the military element of nanotechnology, there is a corporate element to its development as well. [6] As corporations funnel large amounts of money into nanotechnology development, how can citizens be assured that private enterprises will use such technology beneficently? Scientists, policy makers, and philosophers will have to grapple with such questions in the future in order to make responsible, informed decisions about the wellbeing of society.

Unquestionably, nanotechnology is a field that holds great promise for society, especially in its potential applications to medicine. As scientists gain a better understanding of how materials work at the nanoscale, researchers and engineers will be able to create innovative solutions to tackle the seemingly unsolvable problems of our age, such as cancer and nerve damage. Already, nanotechnology has proven its use in delivering vital cancer drugs to tumor cells and facilitating the repair of nerve tissue. While these medical advances are truly amazing, there will be significant social consequences of nanotechnology. Nanotech in medicine may only exacerbate the inequalities of health care quality within and between nations of the world; furthermore, high costs of such technologies may put undue strain on national health systems. Additionally, the military and corporate branches of nanotechnology development pose difficult ethical questions for scientists, ethicists, and policymakers alike. Ultimately, humans must take responsibility for their discoveries and creations and exercise prudence in order to maximize the potential of nanotechnology.

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Self-Disclosing to Decrease Loneliness and Improve Relationships Within College-Age Populations

by Angela Wong

Though everyone experiences loneliness during their lives, young adults report higher rates of feeling lonely often (12%) and feeling depressed due to loneliness (53%) [1]. It is not surprising, then, that loneliness is a problem on college campuses. College students experience loneliness at a reported rate of 30% [2].

Loneliness results when one feels disconnected from others around them. However, loneliness is more than a transient emotion, for it carries significant physiological and psychological repercussions. Many students, seeking camaraderie, join a multitude of student clubs and organizations. But due to demanding coursework and other responsibilities that college students shoulder, it is easy for one to feel spread thin when he or she becomes overcommitted. Students, instead, should seek quality over quantity of relationships. Conversations that incite feelings of closeness are what bring two people together. In other words, many students experience loneliness when they have less of these types of interactions and more of superficial interactions that simply scratch the surface. Thus, students should actively seek and foster deeper relationships by practicing self-disclosure, the concept of revealing personal information to others. Research has indicated that the more one self-discloses, the less likely he or she is to feel lonely, and that self-disclosure promotes genuine interpersonal relationships [3]. By striving towards genuine and heartfelt relationships, college students can both prevent and lessen feelings of loneliness.

Loneliness commonly results when one feels alone, isolated from others, or unsupported [4]. It correlates with the size of the gap between what one expects and what one experiences in their relationships [5]. Influenced by portrayals of college by popular media, many young adults envision college as a vibrant social atmosphere. These students, however, may end up facing difficulties finding their place in this new environment. They may feel lonely and isolated for varying periods of time. Many students simply push their emotional well-being aside, believing that their loneliness will eventually subside. For some, their loneliness extends into other psychological issues. Studies have indicated a correlation between depression and a lack

Scientific Chicago

of confidence in addition to "paranoia, alienation, external locus of control, aggression, and potential suicide" [6]. Loneliness has also been shown to have various physical manifestations in the hormonal, cardiovascular and immune systems [6]. Some scientists even believe loneliness to be as detrimental to one's health as smoking, obesity, and excessive alcohol consumption [4].

Put simply, loneliness hurts. However, if one recognizes it as an issue within his or her own life, loneliness can also be a useful signal that his or her current relationships are lacking in some way. It can mean that one is having fewer or less satisfying relationships than he or she desires, for research has shown that loneliness is "as much a function of the intimacy… of one's social intercourse as the sheer quantity of time spent in the presence of others" [5]. Feelings of intimacy are largely dependent on the ability of individuals to discuss personal and private matters with another person. In fact, above all other factors, people attribute their loneliness to a lack of these opportunities [5].


Healthday

By increasing the frequency of these opportunities, one will develop more meaningful relationships, better cope with difficult situations, and access social support. Self-disclosure, the practice of disclosing private matters to another individual, has been shown to improve the quality of relationships and lessen feelings of loneliness. This effect takes root even during initial interactions, for when one reveals personal information to someone else, he or she is more likely to like that person. It is true that people are more likely to share intimate details about their lives to those they initially feel a connection to, but research has also shown that people like others more as a result of self-disclosure [7]. Self-disclosure continues to play a role throughout a relationship's development [2]. In a study with undergraduate students, strangers who engaged in reciprocal self-disclosure reported more "positive evaluations of their partner…than two people who did not divulge as much" [7]. However, it has been shown that the emotions charging one's words often cause more impact than their factual content [8]. The more emotional self-disclosures are, which "lie more closely at the core of [one's] self-definition," the more satisfying people report their interactions to be [2]. It is the act of baring oneself authentically that improves sincere relations by fostering a sense of trust.

"Some scientists even believe loneliness to be as detrimental to one's health as smoking, obesity, and excessive alcohol consumption."

Self disclosure penetrates superficial barriers to improve the quality of interpersonal relationships and reduces stress, which is often paired with loneliness. Particularly for college students, who frequently experience these negative emotions, opening up to others can improve both their mental and physical health. In spite of the demonstrated benefits of self-disclosure and emotional vulnerability, barring oneself can be easier said than done specifically for college

students. This population experiences a myriad of stressors stemming from alterations in lifestyle habits, increased workload, and new responsibilities that come with the flux of every semester. However, the paradox of self disclosure--the act of rendering oneself vulnerable--is that it may actually make one stronger. While life is relatively stressless, college students should not feel pressured to make a boundless number of friends. Instead, they should invest time into cultivating deeper relationships. When times get stressful, then students can fall back on their social network. Self-disclosure can be more than a means by which to develop personally satisfying relationships. Since all members of a social network will benefit from the support that it provides, self-disclosure has the potential to positively improve campus-wide emotional and physical outcomes.

"However, the paradox of self disclosure--the act of rendering oneself vulnerable--is that it may actually make one stronger."

Angela Wong is a sophomore in the College, majoring in Biology of Global Health and minoring in Chinese. She is interested in studying health disparities and their social determinants, particularly in Asian American communities.

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The Genes They Carried

by Benjamin Bryant

The wars in Iraq and Afghanistan have once again focused the attention of the American public on the mental health effects of combat. Since 2001, approximately 2.5 million US Military service members have been deployed to combat zones around the world [1]. Advancements in military medicine for the treatment of trauma have enabled more wounded service members have survived otherwise fatal injuries. Additionally, improvements in equipment such as body armor and armored vehicles have greatly reduced the incidence of gunshot wounds and injuries from other projectiles, resulting in a reduction of overall fatalities. Furthermore, blast injuries, primarily resulting from improvised explosive devises (IED), have become increasingly survivable [1].

"The changing nature of warfare, as well as improvements in lifesaving equipment, has resulted in a large and growing cohort of individuals who have been exposed to biomechanical head trauma, blast or otherwise, and survived to live with its complications."

The IED is the most effective asymmetrical weapon that an enemy force of the United States has to inflict casualties on US forces, making it a prominent weapon of the war. IED injuries, primarily blast related concussion, have made mild traumatic brain injury (mTBI) the signature injury of the war. The changing nature of warfare, as well as improvements in lifesaving equipment, has resulted in a large and growing cohort of individuals who have been exposed to biomechanical head trauma, blast or otherwise, and survived to live with its complications [2].

In this article, the genetic and environmental components of mild traumatic brain injury will be explored. An overview of the epidemiology of mTBI will be covered, followed by a focused look at the role of the apolipoprotein E (APOE) gene as a risk factor for being susceptible to long term complication from mTBI, as well as the APOE gene's involvement in the brain's neuroplastic healing process following injury.

The purpose of this article is to propose a theory based upon correlation, for which a causal link could eventually be proven or disproven. Approximately, 20% of the 2.5 million the service members deployed to a combat zone since 2001 experienced at least one mild traumatic brain injury during their deployment. Of that population, 15% report suffering from persistent symptoms resulting from their mTBI [1]. The theory proposed in this paper is that the 15% of veterans reporting long term symptoms is directly related to the 15% prevalence of the APOE4 gene in human populations. In other words, the vast majority of veterans suffering from persistent symptoms due to their mTBI are most likely carriers of the APOE4 gene.

An Improvised Explosive Device (IED) (RF System

The Epidemiology of Mild Traumatic Brain Injury

Mild traumatic brain injury is commonly referred to as a concussion. It is an injury to the brain that occurs when a force causes the brain to impact the inside of the skull. The term "mild" is used because traumatic brain injuries (TBI) are graded on a scale from mild to severe. Under this hierarchy mild denotes a non-life threatening injury while severe means that brain death is likely.

The Centers for Disease Control reports that mTBI has a prevalence of 700 per 100,000 in the United States. This means that it is extremely common. Automobile accidents represent the primary reason for most mTBIs in the United States followed by workplace accidents, assaults, and sports injuries. TBIs are diagnosed on the Glasgow Coma Scale (GSC) which is a neurological scale designed to give healthcare professionals a decision support tool for making a diagnosis [3]. The scale considers consciousness, ocular, verbal, and motor status in determining the severity of the brain injury. Mild TBIs are characterized by losing consciousness for fifteen minutes or less, unequal pupil sizes, sporadic ability to keep the eyes open, diminished verbal and motor skills and the inability to understand and follow instructions.

Having established that mTBI is a significant public health problem in the United States, the condition is of particular importance to the US Military and Veterans health systems. Various studies indicate that between 15-22% of all service members that have deployed to combat zones since 11 September 2001 have experienced an mTBI [1]. The majority of these brain injuries are a result of blast wave proximity. Blast waves initially travel at approximately 7,000 meters per second, and despite the use of helmets and body armor their force can still be devastating. The blast radius of a one hundred pound bomb is approximately 100 meters. Anyone within this radius is likely to suffer a mTBI or worse injury.

The military also uses the GCS to diagnose TBIs. In the National Defense Authorization Act of 2008, in response pressure from veterans service organizations citing a growing body of evidence that mTBI may be responsible for early-onset long-term cognitive decline, Congress created the Defense and Veterans Brain Injury Center (DVBIC), and ordered

"The vast majority of veterans suffering from persistent symptoms due to their mTBI are most likely carriers of the APOE4 gene."

the military to begin administering the Automated Neurophysiological Assessment Metric (ANAM) Test to all service members prior to their deployment [1]. The ANAM is a computer-based test designed to be given on a mass scale and is used to determine a baseline level of mental cognition for an individual. Then if the individual suffers from a mTBI, when they return from their deployment they will take the test again, and the two scores are compared. The ANAM scoring scale ranges from +1.000 to -1.000, high to low, with a score of zero set as the average score of human cognition. The average composite score for all healthy military service members is +0.095±0.006, before and after deployment. While the average score for service members that have experienced an mTBI was -0.347±0.008 [1]. This is a key piece of evidence in showing that mTBI causes significant cognitive decline within the first year of injury. However, a large body of evidence has consistently shown that two years or more after a mTBI most people show no signs of cognitive decline [3]. These two seemingly conflicting bodies of evidence can be reconciled by the apolipoprotein E gene, and its functions in brain neuroplasticity and healing.

The Apolipoprotein E Gene

Although the environmental contribution of mTBI is fairly obvious, military medical researchers have often wondered why service members under the same blast conditions may have substantially different long term health outcomes - the difference being that the majority of people improved while some people did not. This confounded the military, and even led to charges of cowardice or malingering.

Modern research, compiled in a recent systematic review in the *Journal of Brain Injury,* has shown that both age and the type of APOE allele are key determining factors of whether or not mTBI patients will experience early onset cognitive decline

[3]. While many studies disagree on the importance of the APOE gene, most agree that people under the age of 25 are far less likely to fully recover from mTBI than those that are older [3]. This is counterintuitive to most types of healing, but makes sense considering the fact that 25 years of age is the approximate age at which the brain completes its major developmental process.

The apolipoprotein E (APOE) allele is located on chromosome 19 and is a 299 amino acid protein. The gene has two common single nucleotide polymorphisms (SNP) in its promoter region which impact its gene expression. The first SNP is at A-491 T and is known as the APOE2 allele. The other is at G-219 T and is known as the APOE4 allele. All three alleles APOE2, APOE3, and APOE4 have a prevalence of 7%, 78%, and 15% respectively. These alleles produce six genotypes; three homozygous APOE2:APOE2, APOE3:APOE3, APOE4:APOE4, and three heterozygous APOE2:APOE3, APOE2:APOE4, and APOE3:APOE4 [4].

The APOE3 allele is considered the neutral form, and both APOE2 and APOE3 are considered codominant [4]. Under normal conditions APOE glycoprotein is the primary lipid transporter in the central nervous system (CNS). The transporter and the lipids that it moves play an important role in maintaining synaptic integrity and function, promoting neural recovery and repair, and modifying and regulating inflammatory responses after central nervous system trauma. The APOE2 allele produces a protein that completes these same functions, but does not bind as well to neuronal and glial cells surface receptors [4].

The APOE4 allele is recessive and its prevalence in the human population is estimated to be 15%. In addition it has been identified by several studies as being associated with poor outcomes following mTBI, and an increased risk of Alzheimer's disease [5]. The reason why APOE4 is associated with poor outcomes following mTBI compared to APOE3 and APOE2 is unclear. The leading theories are that since APOE3 is responsible for neuronal repair the APOE4 protein may simply be less effective at neuronal repair. Another study reviewed in the Handbook of Clinical Neurology has shown that APOE4 was responsible for increased [Ca2+] in the brain following mTBI. The [Ca2+] in brain cells normally increases following mTBI. It follows the same pathway as in Alzheimer's disease, and instead of being regulated as it should be by APOE3, APOE4 allows the [Ca2+] to increase unregulated which leads to plaque developing in the brain [4].

Unfortunately, the scientific evidence linking APOE4 to cognitive decline in mTBI, Alzheimer's Disease, and chronic traumatic encephalopathy is not conclusive. What is certain is that the APOE gene is not the cause of a simple Mendelian genetic disorder in which familial susceptibility to traumatic brain injury or the other aforementioned diseases is passed down from generation to generation [4]. The truth is that the body's response to traumatic brain injury is polygenic.

Neuroplasciticity, Recovery, and Further Study

Neuroplasticity is a broad term that refers to the brain's ability to heal or change into adulthood, as opposed to the prior belief that the brain is rigid after development. For the 85% of people that have the APOE2 or APOE3 alleles, the APOE glycoprotein that transports lipids in their central nervous system will function properly. For most people that suffer from an mTBI the prognosis is a full recovery within two years [1]. This is great news for most service members and veterans that suffered from a blast-related mTBI and are worried about their future prospects.

Correlational evidence is available and growing that the APOE4 allele does not perform this lipid transport function properly following a mTBI. The thesis of this paper is that the 15% of veterans reporting long term symptoms is directly related to the 15% prevalence of the APOE4 gene in humans. The genes they carried into battle directly influenced their health outcomes. The military is a randomized representative sample of the American population which is essential for proving causation above mere correlation. Further study of these veterans is warranted because as a cohort they may be key in discovering all that is yet unknown about how APOE4 is related to neural degenerative diseases.

Moreover, a persistent challenge of veterans seeking to re-integrate themselves into civilian society is finding employment commensurate with their skills and abilities, and staving off the perceptions of employers of mental instability or weakness due to their experiences in combat. A key asset for all veterans is that they are trainable. The military assigned them a job to learn, with little consideration of their aptitude, and the service member was expected to learn the job and quickly become proficient. This trainability, or rather the ability to learn, is the primary reason why many corporations hire veterans. This has been the prevailing paradigm in American society since its beginning, but most notably since the modern American society emerged following the Second World War. This is when the first GI Bill of Rights was enacted to finance the higher education of veterans following the war. Many neuroplasticity studies show that the best therapy for staving off cognitive decline, regardless of injury or not, is to challenge the brain with learning [6]. In this way the GI Bill may very well be the best therapy that we can offer our veterans.

A Personal Statement

It has been five years since I returned from Iraq. My memory of the experience has faded over time. Which I suppose is for the best. I was a first lieutenant, 25 years old, and I was the Executive Officer, second in command, of my company of 105 soldiers.

The IED that I experienced detonated at night. I was leading a dismounted patrol, and an engineer unit that had a route clearance mission thought it might have found an IED, but was not sure, and was asking for security assistance while their “Buffalo” vehicles cleared the obstacle. As I moved towards the engineer’s position to link up with their leader the bomb exploded. My vision went from normal, to white, to black. I could feel that the blast had knocked me down, and every sound was muffled. I had lost my ability to hear. My vision returned first within 20 seconds, then my hearing returned within minutes. The Buffalo was badly damaged, but everyone in the engineer crew survived, although they almost certainly also had mTBIs.

An Apache gunship that was supporting the mission claimed that it had identified the triggermen for the bomb. I regrouped with my platoon, none of them were injured in the blast, and we pursued the insurgents. At this time I was skeptical that the helicopter pilot could have identified the triggermen. Then the two guys he had us follow started shooting at us, which erased my doubt. The fifteen of us pursued the two insurgents for a couple of blocks into a slum area of Baghdad. Eventually the two entered a building and we surrounded the building. We notified the Iraqi police to come to our location, and after a brief standoff the two insurgents surrendered. They were kids, and could not have been older than sixteen.

Despite getting blown up, the operation was a huge success. There was no loss of life, and the Iraqi people got to see the Iraqi police force act competently. This was one of the main achievements listed in my Bronze Star citation, among a few other events in which we unfortunately did lose a few US Soldiers.

I suffered from four mTBIs during my ten years on active duty. Three were from getting punched during fights, and the fourth was from the aforementioned explosion. Because of this the Veterans Administration has deemed me a 50% disabled veteran. I have often wondered if getting hit in the head so often has made me mentally slower. In my most depressed moments of the past year, I have wondered if I am wasting my time in trying to become a doctor. Usually then I just tell myself that it is hard for everyone.

The biggest impact that I have noticed on my life that I think is mTBI related is that I now have a much greater appreciation for restful sleep. Sleep is when the brain heals, and it is when we learn. Both of which my brain needs to do a lot of. Beyond mTBI there is also certainly a complex relationship between post-traumatic stress, current daily stress levels, sleep, physical activity, depression, happiness, and nutrition.

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FEATURED BLOG POST

Genomic Diversity - Jumping Genes

by Angela Wong

Recent discoveries may help shed light on what makes us all unique, and why even identical twins can be so unlike each other [1]. These findings have large implications on not only what distinguishes us from one another, but also on what sets *Homo sapiens* apart from other eukaryotes. In a sense, these factors simultaneously define and unite us.

LINE-1 retrotransposons (L1s), also called "jumping genes," are small pieces of DNA that have been known to insert genetic information throughout the genome. Effectively "jumping" around the genome, they amplify themselves which causes regulatory DNA to be copied and shuffled [2].

Present in most healthy neurons, L1s are a source of genomic diversity in the brain. Variations between neurons within the same brain suggest that they "function slightly differently from each other," says the study's senior investigator, Rusty Gage.

Due to L1s and other factors, each neuron contains around 1,500 unique mutations [3]. Diversity of neurons, which process and transmit information in the brain, impacts the brain's functionality [1]. Additionally, at least a third of the 20,000 different genes in the human genome are expressed in the brain—the highest proportion of genes expressed in the human body.

According to latest studies, L1s can also remove large chunks of DNA, affecting the genome even more significantly than previously thought. Evidence has shown that neurons from those with schizophrenia and Rett syndrome have above-average levels of L1 variations within their genomes. Researchers at the Salk Institute believe that these findings will further the understanding of their role in the genome, and they plan to continue exploring the role of L1 variations and how they impact both brain function and illness [1]. Other scientists conducted a phylogenetic analysis of more than 500 species from widely different branches in the tree of life to examine the diversity of L1s, which are thought to be "tightly constrained, homologous, and ubiquitous elements with well-characterized domain organization" [1]. They found that in recent times, the growth of L1 elements in mammalian species have diverged from lineages in other plants and metazoans, animals with cell differentiation. This illustrates that both gradual evolution and rapid bursts of activity in species can substantially alter genomes [2].

These two studies highlight the significance of L1s in the expression of characteristics that make each one of us unique, as well as uniquely human.

Latin American Culture Club

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FEATURED BLOG POST

The "Birth" of a New Procedure to Prevent Mitochondrial Disease

by Marissa Stepler

Commonly known as the "powerhouses" of the cell, mitochondria provide the vast majority of energy required for cells to function, grow, move, and thrive. Mitochondria self-replicate and have their own DNA, but only 37 of the approximately 3000 genes needed for mitochondrial function are found in mitochondrial DNA. The majority of genes contributing to mitochondrial energy generation, nucleotide synthesis, hormone production, and the many other functions of the mitochondria are located in the nuclear chromosomal DNA of each cell [1].

When the "powerhouses" of the cell fail, cellular health and function drastically decrease, often leading to cell dysfunction and death across numerous different cell types and tissues. In mitochondrial disease, this dysfunction occurs due to inherited or spontaneous mutations in nuclear genes encoding proteins involved in mitochondrial function or mitochondrial DNA. Mutations in nuclear genes can be inherited from either parent. However, because, in a fertilized embryo, all cytoplasm and mitochondria are provided by the egg, mutations in the mitochondrial DNA of a child are inherited solely from his mother. Furthermore, a mother's mitochondrial DNA mutation may occur in a small enough percentage of her total mitochondria that she remains unaffected, yet the mutation may be lethal when passed on to her children [3].

So if a mother knows she carries a mitochondrial DNA mutation, how can she prevent the transmission of the mutation to her children? Recently, researchers have addressed this problem through a new variation on in vitro fertilization (IVF) called three-parent IVF [2]. In this procedure, instead of using an egg from a single female donor and sperm from a single male donor, eggs from two female donors – one from the mother and one from a female donor lacking mitochondrial DNA mutations – are used. When a cell, such as an egg cell, undergoes DNA replication, the dividing chromosomes are pulled apart by microtubule spindles before being separated into two daughter nuclei. In three-parent IVF, a technique called spindle transfer is used to extract the spindles and their attached chromosomes, which are then injected into the healthy donor egg from which the spindles have been removed. This new combined egg is then fertilized with the father's sperm, resulting in an embryo which has maternal and parental nuclear DNA but healthy donor mitochondrial DNA [2].

While this IVF method has been previously tested in primates and mammals, it was not attempted in humans until recently, when the procedure was used by a mother who had a mitochondrial gene mutation which results in Leigh syndrome, a lethal neurological disorder. After two of her previous children inherited the disease, the mother underwent spindle transfer three-parent IVF, which resulted in a successful pregnancy and birth of a healthy baby boy.

Although considered controversial in some circles, three-parent IVF seems to be a powerful and effective method for preventing some inherited human mitochondrial diseases. As technology continues to advance, this procedure may be used to prevent other inherited disorders related to mitochondria and organelle dysfunction. Currently, this breakthrough procedure offers hope for parents carrying mutations in mitochondrial disease-related genes and for scientists researching organelle-related diseases.

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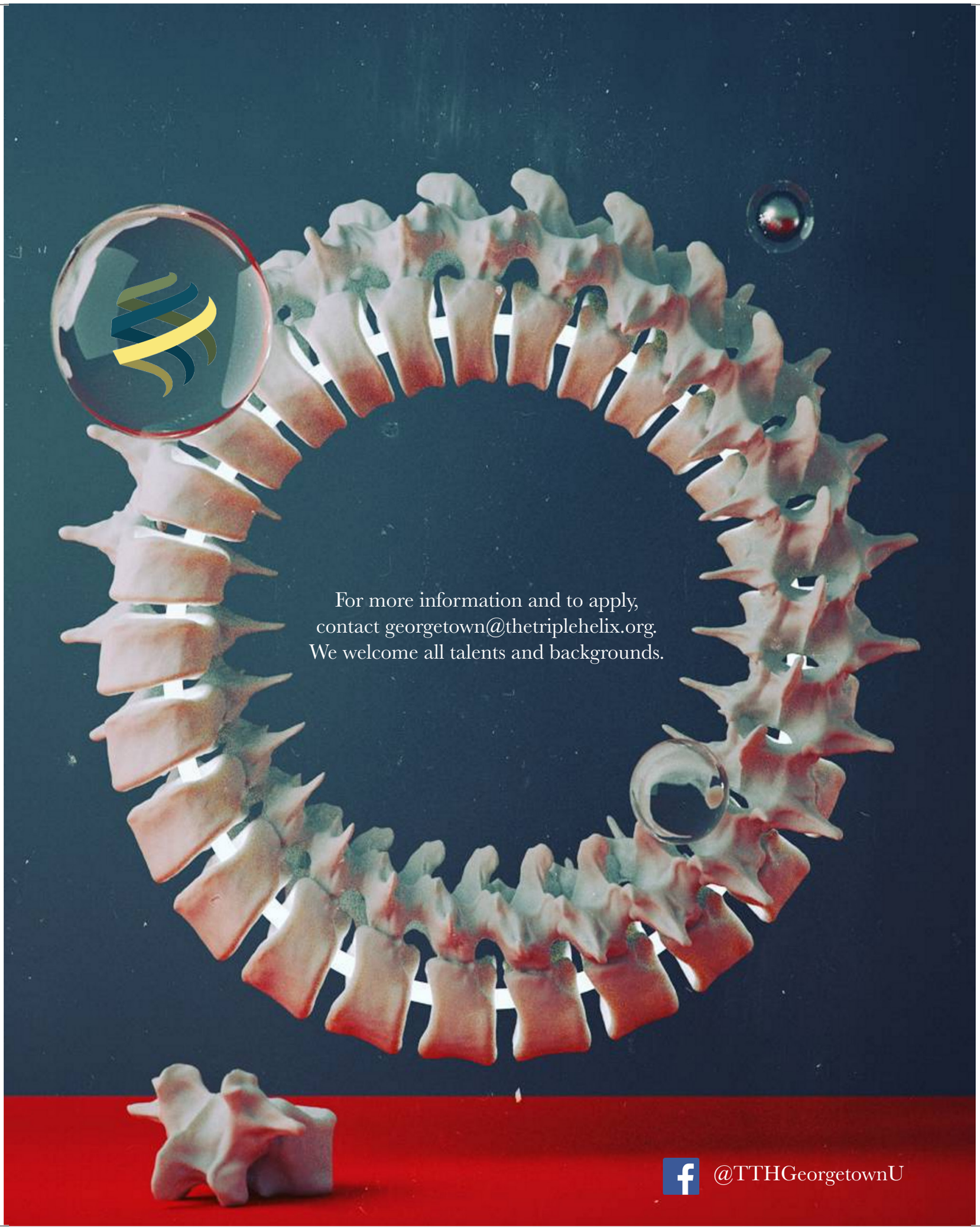
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