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Picture by Richard Lee

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MISSION STATEMENT

The Emory Undergraduate Medical Review (EUMR) publishes a semesterly journal that features faculty and student-authored articles on cutting-edge medical issues. Our interdisciplinary articles span various clinical fields and are peer reviewed by medical professionals from more than a dozen leading academic institutions, including Emory University, Yale University and the Mayo Clinic.

In addition to our publication, EUMR hosts various medically-related events on campus, including collaborations with the School of Medicine. Our projects have been featured by Emory's News Center and have caught the attention of former President Sterk.

LETTER FROM THE EDITOR

Dear Reader,

As per tradition, we will try to keep this short and sweet.

It has been almost two years since we began online learning and as Spring 2022 draws to a close, the word that best captures this moment is "bittersweet." This semester marks the end of both our tenure as Co-Editors in Chief and the end of our first-ever, full spring semester as juniors at Emory University.

At the same time, we are proud of the efforts of our Editorial Board and feel that our team has accomplished more than ever before. We onboarded four new contributing writers for the first time in the spring and were impressed by how quickly they learned the ropes. Together, with their more senior contributing writer peers, they were able to produce publications of the highest quality in our Open Access Journal. Similarly, our staff writers delivered another staggering 12 articles for publication in this issue as well. We hope you enjoy topics ranging from chimeras to the science of segregation. We owe our advisory board a huge thanks for offering their invaluable feedback for another semester and are thrilled to announce the addition of Dr. Ken Houk from the University of California – Los Angeles to the team.

A principal goal of ours when we began our roles as Editors in Chief was strengthening intergenerational relationships between members in EUMR and without skipping a beat, the events team worked diligently this semester on our inaugural Alumni Panel covering Medical Misconceptions in Media, featuring Dr. Maheen Nadeem ('16), Dr. Adit Gadh ('16), Daniel Bujnowski ('20), and Anirudh Pidugu ('20).

In the spirit of connecting with EUMR alumni, Class of 2022, we wish you the very best in your endeavors and hope that you stay in touch! To the new executive board, we know you will take EUMR to new heights and we will always be a resource for you in the coming year. All the best and we hope you enjoy a great summer.

Cordially,

Anjanay Nangia & Richard Lee
Editors-in-Chief
EUMR 2021-2022

Proteolysis targeting chimera: A novel small molecule cancer therapy

ETHAN ESSENFELD
Staff Writer

Company	Agent	Target	Indication	Stage
Arvinas	ARV-110	Androgen receptor	Prostate cancer	Phase 2
	ARV-471	Estrogen receptor	Breast cancer	Phase 2
	ARV-766	Androgen receptor	Prostate cancer	Phase 1
Bristol Myers Squibb (Celgene)	CC-94676	Androgen receptor	Prostate cancer	Phase 1
Kymera	KT-474	IRAK4	Atopic dermatitis, HS	Phase 1
	KT-413	IRAK4, Ikaros, Aiolos	MYD88-mutant DLBCL	IND 2H 21
	KT-333	Stat3	Liquid and solid tumors	IND 4Q 21
Nurix	NX-2127	BTK, Ikaros, Aiolos	B-cell malignancies	Phase 1
	NX-5948	BTK	B-cell malignancies	IND 2H 21
Dialectic Therapeutics	DT2216	Bcl-xL	Liquid and solid tumors	Phase 1
Foghorn Therapeutics	FHD-609	BRD9	Synovial sarcoma	Phase 1
C4 Therapeutics	CFT8364	BRD9	Synovial sarcoma, SMARCB1^{-} tumors	IND 2H 21
	CFT8919	EGFR L858R	NSCLC	IND mid-22
Cullgen	CG001419	TRK	Cancer	IND pending
Proteovant	NA	Androgen receptor	Prostate cancer	Preclinical
	NA	Stat3	Cancer	Preclinical

EGFR, epidermal growth factor receptor; NSCLC, non-small-cell lung cancer; DLBCL, diffuse large B-cell lymphoma; HS, hidradenitis suppurativa.

Figure 1. Table demonstrating current uses of PROTAC technology in cancer therapy and each example's current progress in clinical trials.

Cancer is infamous for being difficult to treat. Scientists worldwide are tirelessly working on the next breakthrough in cancer treatment, amassing a total of 167 billion US dollars devoted to cancer research in 2020 and a predicted 206 billion in 2022 (Oncology Spending Worldwide 2011-2022, n.d.). Their work is difficult not only because cancer mutates and spreads rapidly, but also because each cancer type must be approached differently. Current treatments are not always effective, especially when they are not started at the early stages of the cancer, and often have unmitigated risks with patients having to endure potentially debilitating side effects. However, in 2001, scientists discovered a promising new cancer therapy known as proteolysis targeting chimera (PROTAC), which utilizes natural intracellular ubiquitination and proteasome-mediated protein degradation (Sakamoto et al., 2001). Two decades of intense research, including numerous drug development processes currently as far as phase II clinical trials, have produced strong evidence to suggest that PROTACs may become a universal cancer treatment modality due to their widespread application.

Two decades of intense research...have produced strong evidence to suggest that PROTACs may become a universal cancer treatment...

PROTACs are unique in that instead of attacking tumors directly, they indirectly flag cancer-causing proteins for proteasome degradation using E3 ubiquitin protein ligase (Law & Tung, 2009; Tanaka, 2009). The E3 ubiquitin protein ligase is not the only required component of ubiquitination, or the process of attaching a ubiquitin protein to the cancer-causing protein, resulting in the degradation of the protein. The entire ubiquitination process requires two enzymes: E1 activating enzyme and E2 ubiquitin conjugate enzyme. The E1 activating enzyme primes ubiquitin and is then bound to the E2 ubiquitin conjugate enzyme. The E2 enzyme is then bound to the E3 ligase which is the only ligase in the ubiquitination process capable of binding to a cancer-causing protein for degradation. Afterwards, the E3 ligase facilitates the transfer of ubiquitin to the bound protein (Paiva & Crews, 2019). PROTACs that bind to the targeted proteins will result in the proteasome targeting the protein of interest for degradation. This happens because the ubiquitin will be transferred from the E3 ubiquitin protein ligase to the protein bound to the other side of the PROTAC. The ligase and protein are connected with what is known as a linker molecule (Ocaña & Pandiella, 2020). Proteasomes are the protein complexes responsible for the degradation of other proteins within the cell through proteolysis, in which amide bonds between amino acids are broken. When this occurs, the protein will unfold and stop functioning, which can benefit the host cell if the protein was previously misfolded to perform the wrong function. PROTACs take advantage of this process by bypassing the cell's system of identifying proteins that need degradation and instead introduce the already-made E2 ubiquitin conjugate enzyme to faulty, cancer-causing proteins with an E3 ligase. The intrinsic ubiquitination process can malfunction, potentially leading to cancers because malfunctioning proteins will not undergo proteolysis. PROTACs potentially fix this by bringing the E3 ligase, and thus ubiquitin, to the proteins that need to be degraded for the

overall health of the cell.

While most drugs are only capable of targeting one protein to treat a disease, PROTACs can be modified to target any specific protein. PROTACs are ternary complexes, or three different molecules bound together. The two major components are a small molecule ligand that binds to a targeted protein, known as a warhead ligand, and a small molecule ligand that binds E3 ubiquitin protein ligase, known as an anchor ligand. These two ligands are bound to a small linker molecule. Each of the three components in PROTACs can be any compound from a large set of possibilities, and each unique combination addresses different cancers or other disease-causing proteins. While all E3 ligases contain E2 ubiquitin enzymes, they are varied in structure. The three main types of E3 ligases are RING, HECT, and RBR which are all classified by their structure and mechanism for transporting ubiquitin to the protein of interest. RING E3 ligases, or Really Interesting New Gene, is the largest category containing over 600 natural versions in humans. RING E3 ligases are unique because they contain two zinc ions coordinated together by histidine and cysteine amino acid residues. The transfer of ubiquitin comes directly from the E2 protein to the substrate protein without the involvement of an intermediate. HECT E3s are a much smaller group only having 28 unique natural structures and are composed of an amide terminal substrate binding to the HECT domain resulting in an indirect ubiquitin transfer involving an intermediate (Buetow & Huang, 2016). The third and final class of E3 ligases, RBR (RING-between-RING), contains characteristics of both RING and HECT ligases. RBR E3 ligases are the smallest group, only having 14 different varieties naturally found, and like the HECT ligases, also transport ubiquitin using an intermediate (Walden & Rittinger, 2018). The PROTAC warhead ligands target over 400 individual proteins, over 80% of which are involved in a multitude of cancers, which all have unique structures making it impossible to categorize like the E3 ligases and linkers. PROTAC linkers can be easily categorized, as they are organic chains with much less complexity than proteins but are often not the focus of PROTAC studies. The two most common structures found in linkers are polyethylene glycol, oxygen atoms present in chains of carbon, or alkyl chains, chains of carbon atoms. 54% of PROTAC linkers include polyethylene glycol and 31% contain alkyl chains with 65% of linkers containing both structures (Troup et al., 2020). The linkers, even without binding to a protein, are essential as they keep the other two ligands close together so when both bind to their respective proteins, the proteasome can bind to the protein of interest and degrade it.

PROTACs are unique in that instead of attacking tumors directly, they indirectly flag cancer-causing proteins for proteasome degradation using E3 ubiquitin protein ligase.

Being a general template for anticancer drugs, PROTACs are versatile because they can target many proteins for degradation, even those previously impervious to previous drugs. While a specific protein involved in a particular cancer must be targeted by one specific PROTAC drug, all PROTACs alter proteins in the exact same way: by attaching ubiquitin from an E3 ubiquitin ligase to the protein. This allows for numerous PROTAC drugs to target numerous different proteins. The target protein, regardless of which protein it is, is still linked to the E3 ubiquitin protein ligase by the linker (Qi et al., 2021). PROTACs are effective at

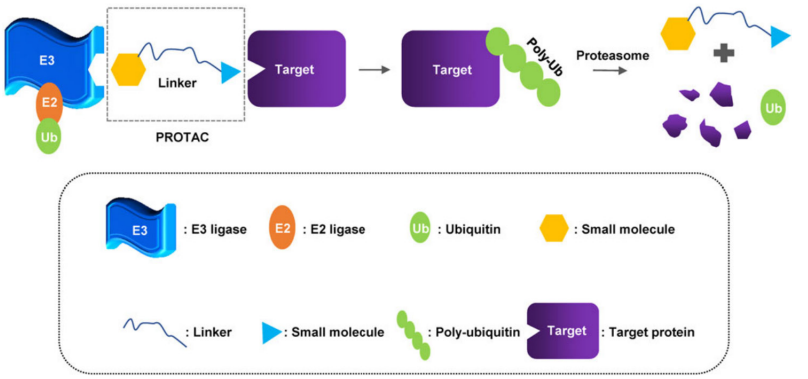

Figure 2. Diagram demonstrating how small molecule PROTAC works in degrading a target protein by linking the protein to Ubiquitin.

targeting nuclear receptors, protein kinases, regulatory proteins, cellular metabolic enzymes, and any other protein. Nuclear receptors successfully targeted to date include androgen receptors responsible for the prostate cancer cell lines VCaP, LNCaP, 22Rv1, and the breast cancer cell line T47D as well as the estrogen receptors in the breast cancer cell line MCF-7 (Zou et al., 2019). In addition to breast and prostate cancers, PROTACs have been specifically designed to attack proteins such as epidermal growth factor receptor L858R responsible for some lung cancers, the Ikaros gene which could play a significant role in lymphatic cancers, and the BRD9 gene carrying protein which is present in some lung cancers and other synovial sarcoma cancers (Garber, 2022). Each one of the listed proteins will be targeted by proteasomes in its own cell, resulting in a natural degradation preventing further spread of cancer cells and possibly shrinkage of said cancer.

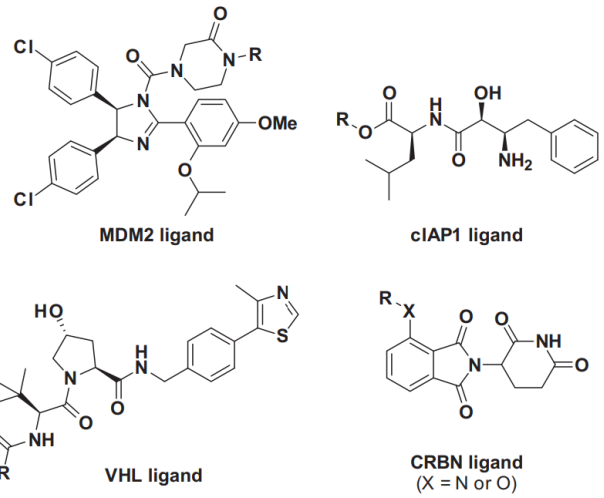

Figure 3. Examples of different E3 ubiquitin protein ligases binding ligands.

PROTAC, despite being a novel drug development, has already shown great progress as a viable treatment for multiple types of cancer. The two large factors preventing its rise to pharmaceutical stardom are problems that plague all new drugs: identifying optimal synthesis conditions and adverse side effects. Since PROTAC drugs are still in phase II clinical trials, the side effects of such drugs are still being discovered, especially with the potential of significant toxic effects from degrading a protein instead of inhibiting it (Garber, 2022). PROTAC synthesis is not yet optimized, with studies showing that PROTAC synthesis reactions have a very large range for the yield, between 32% and 85% with byproduct yields between 62% and 89% (Qiu et al., 2019). PROTAC drug development is still in the early stages, resulting in its vast potential being currently largely untapped --only one "undruggable" target protein is currently being treated by PROTACs, and a very small percentage of the 642 E3 ubiquitin ligases found in the human body are being utilized (Gao et al., 2020). Even more in-depth PROTAC synthesis studies recognize the difficulties of utilizing the flexibility of PROTACS by any singular syntheses process (Lohbeck & Miller, 2016).

The PROTAC warhead ligands target over 400 individual proteins, over 80% of which are involved in a multitude of cancers...

The flaws in PROTAC synthesis are not likely to bar PROTAC drugs from widespread use because scientists recognize that much of the potential is still unknown and the research on PROTAC synthesis and application is still in its infancy. The rate of research suggests that scientists may soon realize the potential of PROTACs in the widespread treatment of cancers and other serious diseases when more combination ligases and linkers are studied.

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Placed by Helen Griffith

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IMAGE REFERENCES

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Preventing a stroke and examining its aftermath

LAURA PAULE
Staff Writer

Stroke is the 5th cause of death and the leading cause of disability in the United States (American Stroke Association, 2015). More than 795,000 people in the United States have a stroke each year (Virani et al., 2020). A stroke occurs when a blood vessel that usually carries oxygen and nutrients to the brain is blocked or ruptured. Blockage by a blood clot is referred to as an ischemic stroke, which makes up 87% of all stroke cases. Rupturing of a blood vessel is known as hemorrhagic stroke (MedicalNewsToday, n.d.). When the brain is unable to receive the blood and oxygen it needs, brain cells die. Numerous studies have documented the extensive consequences following a stroke. These consequences can be physical and psychosocial, significantly impairing long-term functioning and quality of life. However, preventable measures and effective treatment routes can greatly reduce the consequences of the incident, significantly improving the lives of patients.

The aftermath of a stroke can range from mild consequences to severe impacts on lives of the affected patients. Several risk factors, such as age, family history, and lifestyle, are associated with strokes. Age is noteworthy: In 2009, 66% of the people hospitalized for a stroke were older than 65 years old (Hall, Levant, and DeFrances, 2012). Patients with a family history of stroke are also more likely to suffer from this condition. Pre-existing health conditions such as diabetes, hypertension, hyperlipidemia, and cardiac problems can place individuals at a higher risk of developing a stroke. Whether the stroke is mild or severe, the best approach is to take the necessary precautions to prevent it from happening altogether. Although age and family history are immutable, many of the risk factors can be reduced, perhaps eliminated, if patients become aware of them and take appropriate steps. "If there's one good thing that can be said of strokes, it's this: The vast majority of them don't need to happen" (American Stroke Association, 2015).

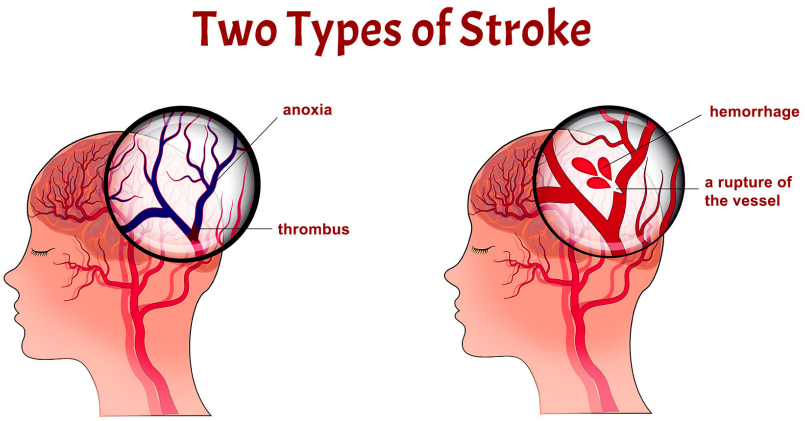

Figure 1. Differences between Ischemic Strokes and Hemorrhagic Strokes. Image on the left shows a thrombus/blood clot impeding blood flow within the vascular system. Image on the right shows the rupture of a blood vessel, with blood from the artery bleeding into the brain.

These consequences can be physical and psychosocial, significantly impairing long-term functioning and quality of life.

Stroke prevention strategies rely mainly on diet and exercise. A low-fat, high-fiber diet is recommended, including plenty of fruits, vegetables, whole grains, and fish. Foods with a high salt content should not be consumed in excess, and the intake of salt should be limited to no more than 0.2 oz a day. Exercise is equally important to maintain low cholesterol and stable blood pressure. Experts recommend at least 150 minutes of moderate-intensity aerobic activity weekly, which include activities such as cycling and fast walking ("Stroke - Prevention - NHS," n.d.). Practical measures to attain this goal include walks around the neighborhood, taking the stairs instead of the elevator, starting a fitness club with friends, and exercising to the point of hard breathing but still being able to talk (Harvard Health Publishing, n.d.). Moderating alcohol consumption is another prevention strategy high-

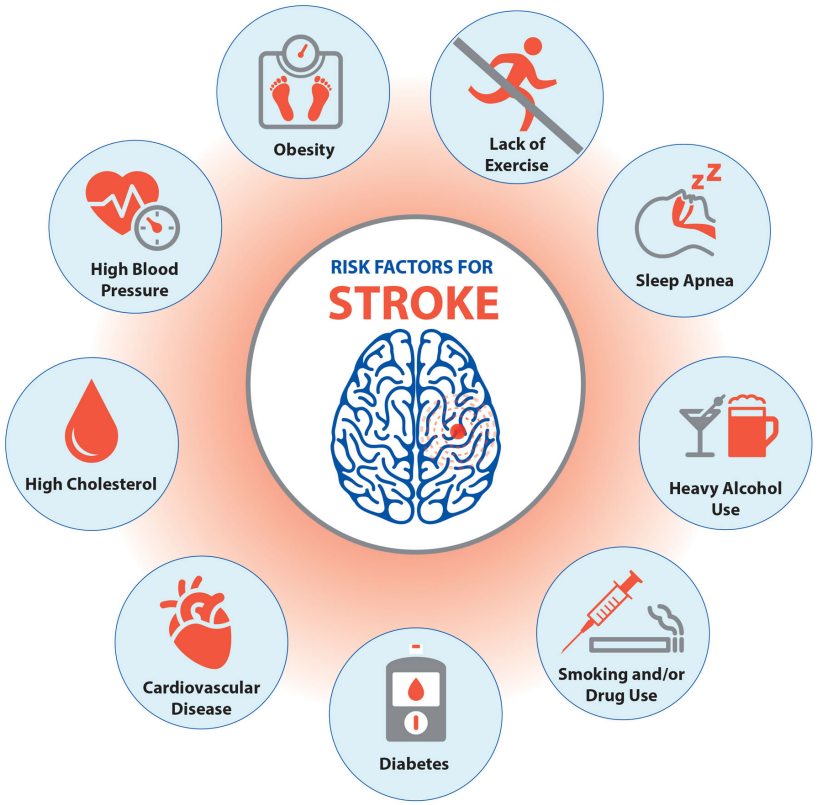

Figure 2. Risk factors for having a stroke include alcohol and tobacco use, lack of exercise and pre-existing conditions such as obesity, diabetes, sleep apnea, and cardiovascular disease.

ly recommended by physicians. Excessive alcohol consumption can lead to atrial fibrillation, or an irregular heartbeat, which further increases the risk of having a stroke. Having one drink of alcohol per day is not significantly linked to an increased risk for stroke, but more than two drinks per day increases the risk of stroke by a factor of 3. When drinking, a top choice is red wine because it contains resveratrol, an organic chemical (polyphenol) that is thought to protect the heart and brain (Harvard Health Publishing, n.d.).

Preventing a stroke is not limited to the behavior of the patient. Scientists and healthcare professionals have developed strategies to minimize the risk of stroke and still continue to explore more efficient treatment options. Long-term oral anticoagulation has been the mainstay of medical stroke prevention therapy (Henninger, 2019). However, many recurrences of stroke are not prevented, and the use of anticoagulants carries the risk of bleeding complications. Hence, scientists have worked to develop antithrombotic regimens that can be regulated to prevent excessive bleeding. A remarkable example is the REG1 aptamer-antidote system. Aptamers are nucleic acid molecules that fold into complex 3D shapes to bind specific targets. Under the REG1 system, an active anticoagulant is neutralized by an antidote, acting as a molecular on-off switch that regulates anticoagulation, especially when the risk of bleeding is elevated (Henninger & Mayasi, 2019).

Although genetic predispositions to stroke are more complex to address, nucleic acid-based therapies have proven potentially useful. Individuals born with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) tend to develop migraine with aura, and 2/3 of symptomatic subjects have a stroke/transient ischemic attack. CADASIL is caused by mutations in the NOTCH3 gene on chromosome 19, which can lead to cell surface aggregates, complications in autoregulation of small vessels in the central nervous system and ultimately stroke (Tikka, 2012). In a study in which CADASIL patients were treated with antisense oligonucleotides to alter pre-mRNA splicing, the resulting notch-3 protein was functional and did not form surface aggregates. Although these results need yet to be verified in-vitro, they reveal potential prevention of genetically induced stroke (Rutten, 2016).

Despite clinical preventive therapies, and although 80% of strokes appear preventable through healthy lifestyle and risk factors regulation, on average, someone in the United States has a stroke every 40 seconds (Williamson, 2021;Virani et al., 2020). Following a stroke, a patient may present with a wide variety of symptoms that could significantly affect their quality of life.

In 2009, 66% of the people hospitalized for a stroke were older than 65 years old.

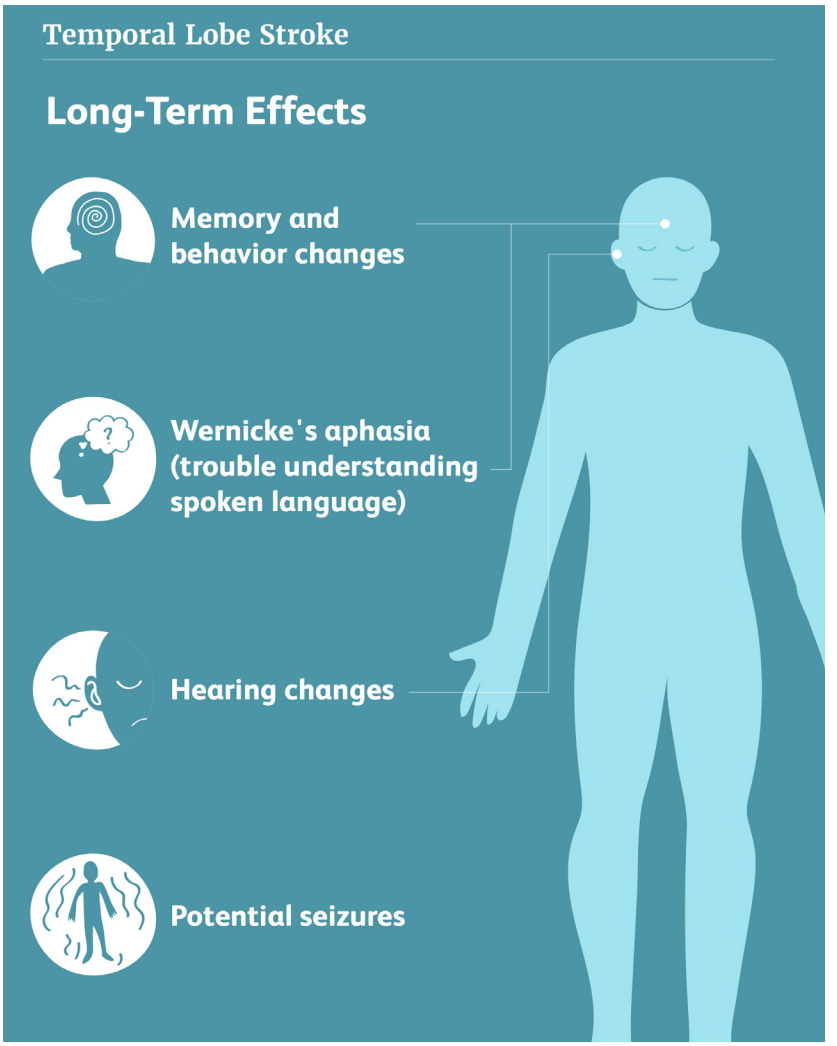

Figure 3. Long-term effects following a stroke include behavioral changes, speech disorders, hearing problems and potential seizures.

Some of the most common physical symptoms include weakness, paralysis, problems with balance or coordination, numbness, tingling sensations, and fatigue. These symptoms usually improve with time and rehabilitation (UPMC, n.d.). Patients may also develop difficulty in communication because of significant damage to their speech, language, and cognitive-linguistic skills. For example, stroke patients may present with apraxia of speech, a condition in which the brain is unable to provide normal sensory and motor control of the jaw, lips, tongue, soft palate, and vocal cords. They may also suffer from aphasia, which affects the patient's ability to understand spoken and written words, to recall phrases and to formulate sentences. These symptoms are so alien to the patient that they can simply be described as "trying to learn and use a foreign language when living in a foreign country" (UPMC, n.d.). Other changes in cognitive-linguistic abilities can include difficulties in attention and impaired memory.

Patients who have had a stroke may also experience psychosocial consequences that affect not only themselves but also their family members or caregivers. Emotional changes can occur as a result of a stroke, including feelings of anxiety, helplessness, and frustration (Kindred, n.d.). When these symptoms are severe, they may affect patients' ability to socialize with others, enjoy living, and complete common, daily life activities such as showering, cooking, and driving. Caregivers may also suffer from depression by observing the slow deterioration of the patient, especially when the patient is a beloved family member.

Following a stroke, patients can be supported through a variety of therapies that seek to relieve their symptoms and improve their quality of life. Stroke rehabilitation is a multidisciplinary process that enables patients to regain bodily functions and live a meaningful life. Rehabilitation also helps patients adapt to their environment and limitations in case total recovery does not occur. Successful recovery from a stroke will often involve speech therapy. Treatment sessions are tailored to each patient according to their medical condition. Patients with aphasia would participate in therapy involving language stimulation to formulate sentences and verbally express their thoughts. Augmentative Alternative Communica-

Emotional changes can occur as a result of a stroke, including feelings of anxiety, helplessness, and frustration (Kindred, n.d.).

tion (AAC) is used to maximize all forms of communication by using pictures and gestures. Occasionally, therapy may include treatments to improve reading and writing skills. For apraxia, speech therapy would typically include exercises to improve mouth coordination and muscle strength (Vital, n.d.).

Occupational therapists provide another integral part of the rehabilitation process. Occupational therapy starts with a review of a patient's individual set of symptoms and functional difficulties resulting from the stroke; this review may include the impact on function or occupation, the level of personal support, and the needs of the caregivers and family members. The inclusion of friends and family in treatments is seen as a useful method to empower them to feel part of the process and acquire useful skills for the ongoing care of stroke patients (Govender & Kalra, 2007).

Suffering from a stroke is a life-changing event that affects the physical and psychosocial abilities of patients. However, with the right lifestyle and preventive clinical therapies, many of these strokes can be avoided. When a stroke does occur, it represents a challenge to the individual and the family, who are often unprepared to deal with the consequences of a stroke. The inability to no longer communicate easily, together with concomitant feelings of depression and anxiety, often requires patients to undergo months of rehabilitation. The assistance and support of loved ones are essential for stroke patients to successfully adapt to the changing environment or regain a more normal quality of life. ❧

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Predicting eating disorders: Genetic linkages as risk factors

JOSIE CHEN
Secretary

It is estimated that approximately 28.8 million people within the United States will suffer from an eating disorder in their lifetime, and this number rises to 70 million people globally. Among adolescent females in the United States, eating disorders are the third most common chronic illness (Kalisvaart & Hergenroeder, 2007). Researchers have yet to identify one singular reason why females are more vulnerable to developing eating disorders, but current evidence points to a combination of developmental, social, and biological factors (Figure 1). Western beauty standards, profit-driven diet, and fitness industries, as well as the widespread use of social media, have been linked to an increase in the prevalence of eating disorders. However, documented cases of anorexia nervosa from 1689 in England provide evidence that eating disorders are not a unique contemporary occurrence (Muhlheim, 2020). Researchers are currently conducting studies to explore the development of eating disorders such as anorexia nervosa, binge-eating disorder, and bulimia nervosa, and the potential role of genetics in predisposing individuals to such a phenomenon–otherwise known as having a "biological vulnerability" (Berrettini, 2004).

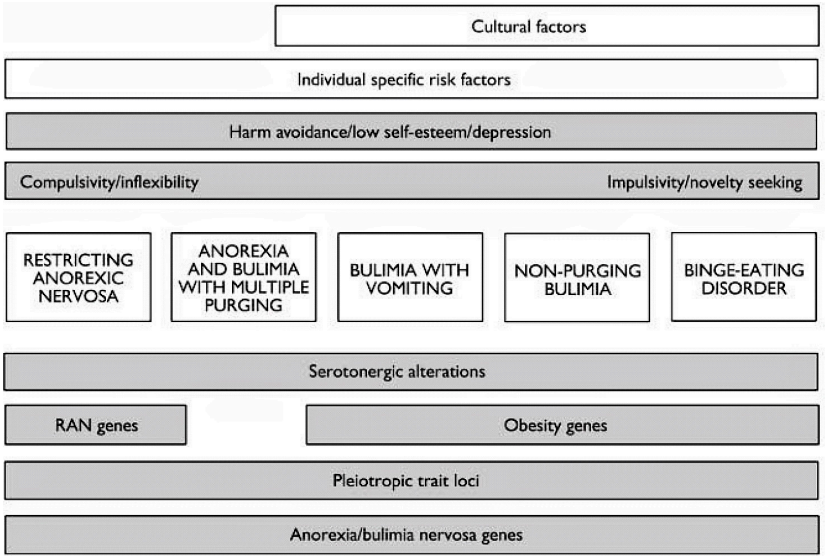

Figure 1: This empirical structure of eating disorders depicts a hierarchical relationship between the various factors that may contribute to its development.

To clarify the connection between genetics and eating disorder development, a foundational research approach includes using family and twin studies. These studies provide data about genetic influences on certain characteristics through observing clusters of biologically related individuals. These studies assess degrees of resemblance through correlation coefficients and differentiate genetic influences from environmental effects through a comparison of identical, or monozygotic (MZ) and fraternal, or dizygotic (DZ) twins. Family studies often involve probands, the first individual in a family affected by a genetic condition, or the first person to be tested for and receive genetic counseling for a particular condition. Through identifying probands to establish genetic relationships with other family members, data shows an increased prevalence among anorexia nervosa and bulimia nervosa relatives, with findings from the largest systematic studies (Strober et al., 2000) depicting a seven to twelve-fold increase in eating-disordered probands' relatives (Lilenfeld et al., 1998).

Researchers are currently conducting studies to explore the development of eating disorders...to such a phenomenon–otherwise known as having a "biological vulnerability"

The methodology of twin studies to explore the link between genetics and eating disorder development relies on the concept that monozygotic twins have an identical set of genes since they come from the same egg and sperm, while dizygotic twins have half of the same genes since they developed from two separate zygotes. Thus, when controlling for environments, MZ twin correlations based on identical genomes that are twice as large as DZ twin correlations generally point to

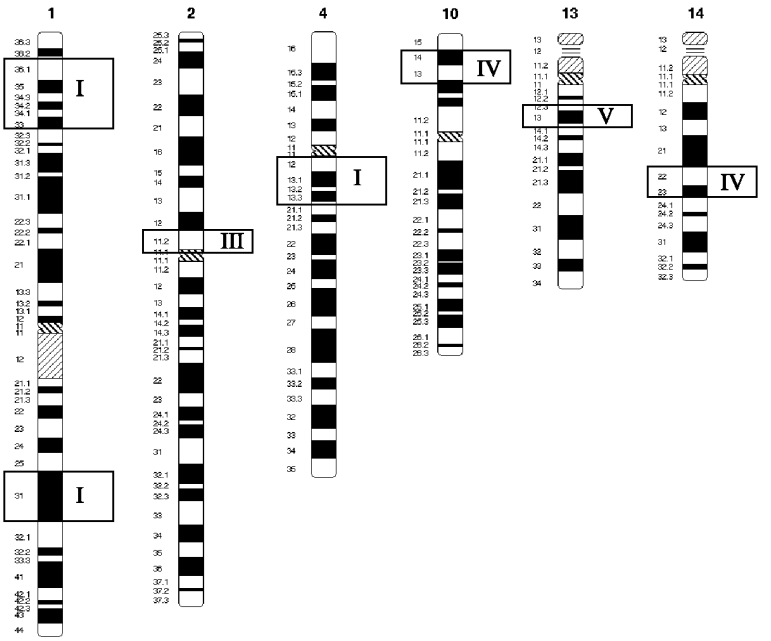

Figure 2: Linkage studies play a critical role in identifying genetic components that may place individuals at greater risk of eating disorders.

genetic effects. In a crossover study, Klump and their colleagues had a sample consisting of 672 female 17-year-old twins and used biometric model-fitting analyses in comparison with predetermined values and models. They saw that genetic factors, indicated by the significant difference between monozygotic and dizygotic twin concordance of anorexia nervosa syndrome, accounted for 74% of the variance in individuals with anorexia nervosa (Klump et al., 2001). In another twin study with a population-based sample of 2,163 female twins, anorexia nervosa was estimated to have a heritability of 58%, accounting for shared environment effects (Wade et al., 2000). As for bulimia nervosa and binge-eating disorder, Bulik and their colleagues utilized a structural equation model based on a liability-threshold model that partitioned variation in liability into three sources: additive genetic, familial or common environmental, and individual-specific environmental effects (1997). The study of 1897 female twins incorporated diagnostic information and measurement error, and researchers estimated heritability probabilities of 83% and 82% for bulimia nervosa and binge-eating disorder, respectively. Taken together, the consistent data suggest a moderate level of heritability for certain traits in anorexia nervosa and bulimia nervosa. While there is still some unexplained variance, it likely stems from an intricate relationship between environmental factors unique to siblings compared to common factors shared between other family members (Berrettini 2004). Even so, repeated studies on family and twin populations support a significant role of genes in the heritability of eating disorders.

...repeated studies on family and twin populations support a significant role of genes in the heritability of eating disorders.

Another method of identifying genetic components involved in the diagnosis and progression of eating disorders is to use linkage studies. Linkage studies utilize genetic markers across the human genome to identify regions of the chromosome that contain genes that can contribute to the penetrance of these disorders (Figure 2). To assess eating disorders in linkage analyses, researchers identified attributes such as obsession with order, symmetry and exactness, perfectionism, anxiety, and emotional and behavioral overcontrol. These psychological markers correlate with the fact that eating disorders are considered to be mental illnesses that stem from more than just a desire to look a certain way; external factors such as stressors influence mental states and emotions, leading to effects on disordered behavior. Specifically, the drive for thinness and obsessionality is critical in typifying anorexia nervosa. Through the study of anorexia nervosa proband and genotyping by examining DNA sequences with biological assays, Devlin and colleagues found near genome-wide significance linkages with chromosomes 1, 2, and 13 (2002). Short tandem repeats, the markers used in this particular genotyping, resulted in high power, or high statistical validity, and discrimination. Furthermore, Bacanu and their colleagues used covariate-based linkage analysis to measure six traits: obsessionality, age at menarche, levels of anxiety, lifetime minimum body mass

index, concern over mistakes, and food-related obsessions and found large linkage signals for bulimia nervosa. Specifically, the behavior of self-induced vomiting was associated with a marker found on chromosome 10 (Bacanu et al., 2008). Interestingly, chromosome 10 is also a known locus for obesity, a trait commonly observed in the family history of those suffering from bulimia nervosa (Collier and Treasure, 2004). However, many of these findings are limited due to low power, meaning that there is an increased likelihood of statistically significant findings representing a false positive. To combat this, more widespread research on an international level is necessary to accurately detect genes involved in eating disorder development (Grave 2011).

Association studies serve as another type of molecular genetic research, where knowledge of a disorder's pathophysiology points toward candidate genes, and consequently, genetic connections. Thus far, no relevant susceptibility genes have been identified to have a considerable effect on AN and BD, but it is understood that genes with a crucial role in regulating eating behaviors and body weight are important influences on the etiology of eating disorders (Berrettini 2004). Previous studies demonstrate that brain-derived neurotrophic factor (BDNF) is involved in the food intake and body weight of rodents through hypothalamic activity, such as regulating serotonin levels. A similar pattern is also seen in humans, where serotonin acts as a natural appetite suppressant through increased gut motility during the post-feeding nutrient storage phase. In a case-control study of 1,142 patients with eating disorders, Ribasés and his colleagues found that the Met66 chromosomal variant has a strong association with both anorexia nervosa and bulimia nervosa and that the BDNF gene has been implicated as a susceptibility gene for AN. These two variants are the first to be associated with the pathophysiology of eating disorders and provide evidence for the role of BDNF in increased susceptibility to abnormal eating patterns (2004). Similar to linkage studies, association studies face various challenges that hinder the effectiveness of their results. Larger-scale studies are necessary to provide information about which genes have the greatest influence on eating disorder development.

Concerning the prevalence of eating disorders, it is worth investigating comorbidities to further demonstrate familial linkages, such as the co-transmission of familial personality or other mental illnesses. Just as twin and family studies are used to distinguish genetic and environmental effects of eating disorders, they also play an important role in exploring heritable characteristics that are often comorbid with anorexia nervosa and bulimia nervosa. Generally, eating disorders tend to display comorbidity with other diagnoses such as anxiety and depression, and those with anorexia nervosa and bulimia nervosa commonly demonstrate affective and anxiety disorders (Bulik et al., 2000).

To assess eating disorders in linkage analyses, researchers identified attributes such as obsession with order, symmetry and exactness, perfectionism, anxiety, and emotional and behavioral overcontrol.

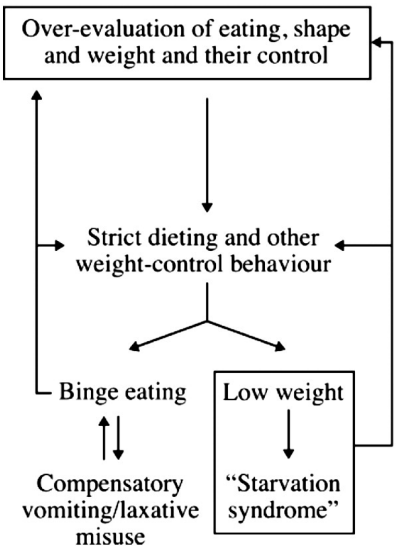

Figure 3: The transdiagnostic cognitive behavioral theory points to the over-evaluation of eating, shape, and weight, and their control as a cornerstone of developing eating disorders.

It is this frequent co-occurrence with other mental illnesses that makes the diagnosis of eating disorders complicated, especially after accounting for environmental influences, which can be difficult to measure. It is important to note that diagnostic measures for eating disorders are not without error and that there are notable implications such as stigmatization. Currently, the most influential psychological theory for producing evidence-based treatments is cognitive behavioral therapy, which identifies the over-evaluation of eating, shape, weight, and individual control as foundational to the eating disorder. Secondary aspects such as compensatory

vomiting, low weight, and strict dieting either directly or indirectly stem from this core psychopathology to then maintain it (Fairburn et al., 2003) (Figure 3).

The development of eating disorders is highly complex and multifactorial, thus posing a difficult challenge for researchers trying to discern their root causes. However, twin and family studies, along with linkage and association studies, can provide important genetic insights into the future of diagnosis and treatments for patients with eating disorders. Currently, much of the genetic research is in its early stages and largely focused on female participants. Larger-scale studies that include greater sample sizes and stricter phenotype classifications are necessary to provide clarity around the development and management of eating disorders. Eating disorders are dangerously prevalent in modern-day society, but genetic research may provide invaluable insights for more effective prevention and treatment of individuals who live with eating disorders through the detection of individual risk factors. ❧

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The promising potential of psychedelic therapy

ANUSHA TANNERU
Staff Writer

The United States has a mental health problem. This issue has spanned decades, leading medical professionals and researchers to find and utilize new treatments to treat the unique issues these patients present. In recent years, many clinical professionals have begun to consider psychedelics as a viable treatment for psychiatric disorders. These drugs may invoke images of the 1960s counterculture or transformative spiritual experiences, but they have a deep medical history related to mental health. Psychedelics carry a certain perception bolstered by previous public disapproval, yet they have also been used for millennia in numerous cultural and medical contexts. Not to mention, it is estimated that more than 30 million people have used psychedelics in the United States. Despite their illegal status, psychedelics have been looked at by some researchers as a potential treatment for mental illness. The efficacy of psychedelic therapy must be understood to best benefit potential patients.

Psychedelics have been used medically throughout human history. For example, psychedelics have been used for thousands of years in holistic healing by various cultures (Carhart-Harris & Goodwin, 2017). Despite this extensive history, psychedelics did not emerge as a potential treatment in Western medicine until the mid-20th century. With a promising future as a treatment for mood disorders and addiction to alcohol, psychedelics are starting to gain traction in the medical and scientific world as legitimate treatments.

The efficacy of psychedelic therapy must be understood to best benefit potential patients.

This manifested as increased research into psychedelics from the 1950s to the 1970s. A recent systematic review of all these studies suggests that a majority of patients with mood disorders showed improvement in attitude and behavior after psychedelic treatment (Rucker et al., 2016). Furthermore, an analysis of studies conducted in the 1950s on lysergic acid diethylamide (LSD) supports its potential for treating alcoholism,

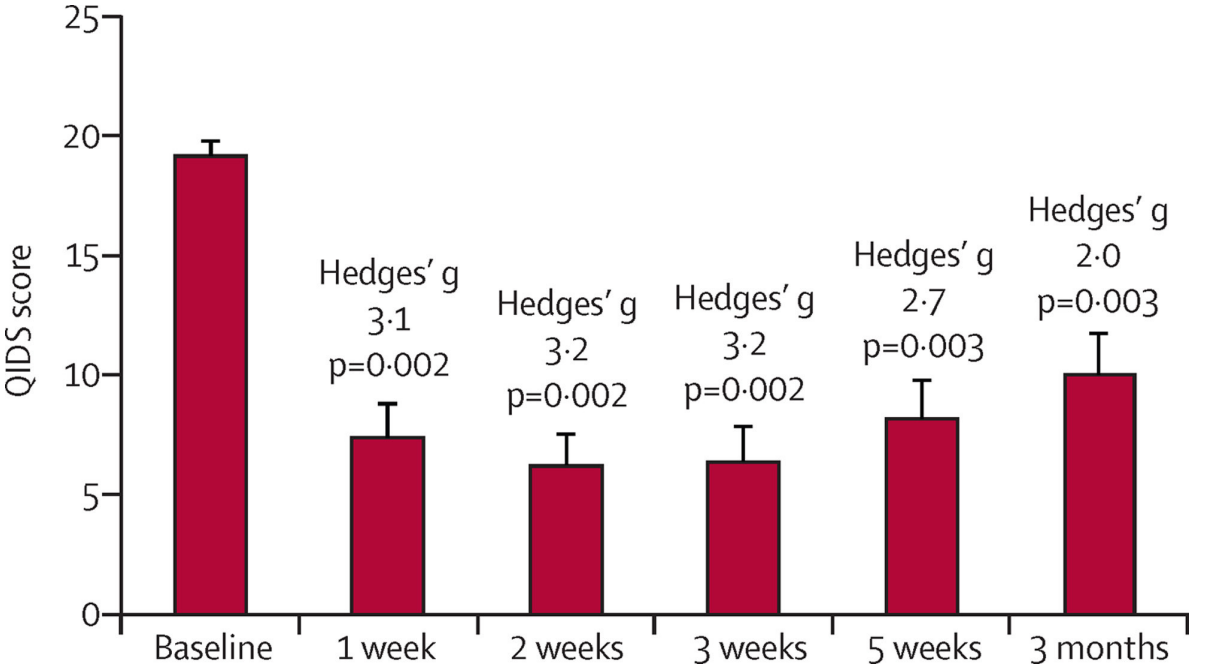

Figure 1. Psilocybin-assisted psychotherapy has reduced depression severity significantly and over a long period of time.

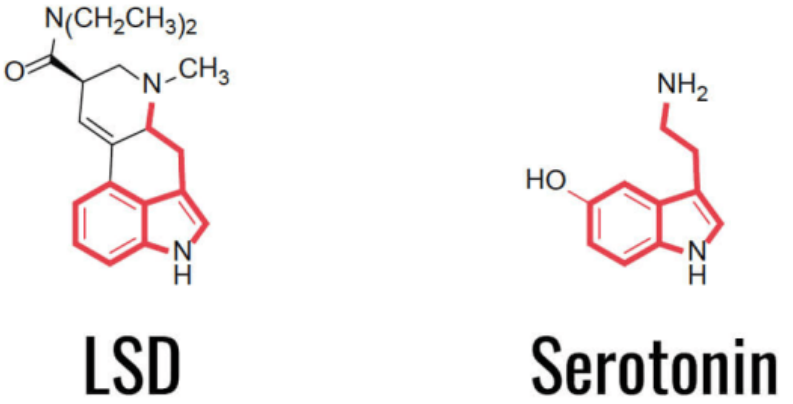

Figure 2. The chemical structures of LSD and serotonin and their illustrated similarities as a suggestion for LSD's potential efficacy in therapeutic treatment.

though the authors admit that further analyses are required in the future (Krebs & Johansen, 2012). Other researchers, including Davis and colleagues, reported that another prominent psychedelic, psilocybin, exhibited powerful antidepressant effects in patients with major depressive disorder (Figure 1) (2021). In general, scientific evidence has suggested some potential for psychedelics as clinical treatments.

However, anti-psychedelic political forces from the 1960s and 1970s, manifesting most prominently in the Nixon administration, refuted pro-psychedelic progress (Schlag et al., 2022). This massive backlash came with reports of visual hallucinations and flashbacks that persisted long after psychedelics like LSD had left the body. This, coupled with the increasing unethical and covert use of psychedelics, as well as the general shift in socio-political attitudes against drugs, led to widespread public disapproval (Rucker et al., 2018). The public had begun to view psychedelics as fueling the delinquency of young adults. This socio-political shift was also accompanied by the War on Drugs, a war that has been cited as perpetuating racial stereotypes surrounding drugs and using societal racism to make several classes of drugs feared, including psychedelics (Provine, 2011). Nonetheless, Congress swiftly passed legislation such as the Controlled Substances Act of 1970, and psychedelics were classified as Schedule 1 drugs, the most restrictive category, making them near impossible to study clinically for more than 30 years (Nichols, 2016).

As with most, if not all, healthcare treatments, psychedelic therapy is already encumbered by pre-existing health disparities.

It is important to understand these drugs outside of the fervor surrounding them. So-called classic psychedelics, such as LSD and psilocybin, are known as "serotonergic hallucinogens," meaning they affect the human mind by binding to specific receptors for serotonin and causing a certain physiological response (Nichols, 2016). Serotonin itself is important in regulating processes like mood and behavior (Mohammad-Zadeh et al., 2008). Because previous research into psychedelics yielded promising results, it is important to continue this research so as to further scientific understanding of the clinical use of psychedelics.

Like previous research on the subject, contemporary research investigates the use of psychedelics as a treatment for mood and substance abuse disorders (Nichols, 2016). For LSD, the drug can potentially help treat substance abuse by acting as a serotonin agonist (Winkelman, 2015). This means that LSD can activate certain serotonin receptors and produce similar effects to those of serotonin, which is crucial, as serotonin is critical to the function of psychedelics. For example, addict populations, such as those with alcohol dependency, tend to exhibit lower serotonin levels, which indicates serotonin's role in substance abuse (Winkelman, 2015). The structural similarities between LSD and serotonin could explain why LSD can work as a treatment for substance abuse (Figure 2). Gasser and colleagues found that LSD can reduce symptoms of anxiety disorders when administered in medically supervised settings (2014).

Contemporary research also supports the previous notion that psilocybin can be used with psychotherapy to effectively treat major depressive disorders and that this psychotherapy can also be extended to treatment-resistant depression (Davis et al., 2021). These observations also suggest psilocybin as a treatment for tobacco and alcohol

addiction (Johnson et al., 2018). In regard to efficacy, however, laboratory research has suggested that through small, increasing dosages, psilocybin can provide and maintain long-term benefits to patients (Garcia-Romeu & Richards, 2018). More generally, there is already preliminary support for psychedelic-assisted psychotherapy and its positive impact on suicidal tendencies (Zeifman et al., 2022). However, there are caveats. For example, Zeifman and his colleagues mention that their analysis of psychedelic-assisted therapy and suicidality could be hindered by the fact that they could only analyze seven relevant trials (2022). These limitations are also present for LSD, where researchers have had similar issues in designing their clinical trials, which has led to a call for more studies to investigate the therapeutic potential of LSD (Fuentes et al., 2020). More research is needed to examine the exact benefits and costs of these psychedelics. Unfortunately, there is still a massive barrier to further progress.

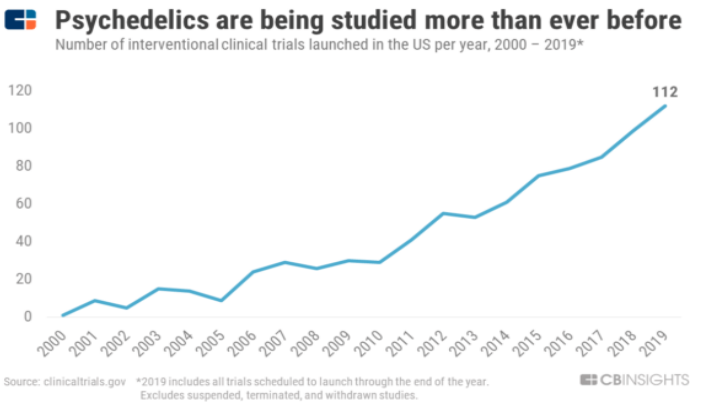

Figure 3. There has been a significant rise in interventional clinical trials of psychedelics over the past two decades.

Perhaps psychedelic therapy has a role in the future of medicine, but it must not be a resource that is out of reach for those whom it was meant to help from the start.

The aforementioned psychedelics are still currently labeled as Schedule I drugs, meaning that they are designated as having no clinical use. However, this contradicts current evidence from numerous studies rejecting psilocybin as harmful or addictive and thus should be scheduled as a Schedule IV drug (Johnson et al., 2018). For LSD, prior to its ban in 1970, the National Institutes of Health (NIH) funded studies to explore its clinical use (Nutt et al., 2020). However, since the ban, the NIH has provided no funding to similar studies. These restrictions have generally impeded research (Garcia-Romeu & Richards, 2018).

However, as decades have progressed, restrictions have loosened to allow new federal research. In the late 1990s, the DEA allowed some research with limited psychedelics, leading to some FDA-regulated trials on psilocybin as a treatment for treatment-resistant depression (Marks & Cohen, 2021). Since then, research has been steadily increasing, as shown in Figure 3, to 112 interventional clinical trials as of 2019. However, the general lack of federal funding has led to private companies funding most research (King & Hammond, 2021). If these companies are allowed to proceed without federal oversight, there is a chance that marginalized communities could be left out of the research (Marks and Cohen, 2021).

This is not a problem exclusive to psychedelic therapy. A recent National Cancer Institute study found that fewer than two percent of 10,000 cancer clinical trials targeted racial or ethnic minorities (Chen et al., 2014). This is despite a law passed in 1993 that mandated the inclusion of minorities in all NIH-funded research as appropriate (Chen et al., 2014). In order to progress, the FDA must perform unbiased reviews of psychedelics and ensure that more inclusive clinical trials take place (Marks & Cohen, 2021). Additionally, if there is to be any progress in the therapeutic application of psychedelics, the government must consider rescheduling psychedelics as Schedule IV drugs, particularly those that are already supported as being clinically useful (Nutt et al., 2020).

As with most, if not all,

healthcare treatments, psychedelic therapy is already encumbered by pre-existing health disparities. One "solution" to this problem is the removal of barriers to psychedelic research using legislation and research. These barriers include a general lack of education about psychedelics, as well as a lack of personnel who can administer psychedelic treatments if needed (King & Hammond, 2021). Oregon has taken steps to address this issue by training facilitators to administer psilocybin regardless of medical diagnosis (Marks & Cohen, 2021). While no such measures have been taken for LSD, Denver and Oakland have decriminalized compounds containing psilocybin (Holoyda, 2020). Furthermore, the American Psychiatric Association stated that psychedelics should be studied further in relation to mental disorders (Holoyda, 2020).

Oftentimes, psychedelic therapy is marred by more questions than answers and more worry than hope. Nonetheless, regulatory barriers should not hinder the progress of biomedical research. If psychedelics can alleviate human suffering, then researchers must investigate that potential in safe and regulated conditions. However, none of this can be done if the federal government does not commit to seeking out the best and safest answers to its citizens' problems. Perhaps psychedelic therapy has a role in the future of medicine, but it must not be a resource that is out of reach for those whom it was meant to help from the start. ❧

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Antisense oligonucleotides: Breakthroughs in brain disease therapies

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For decades, scientists have devoted their lives to understanding the genetic causes of neurodegenerative diseases, such as Huntington's disease (HD), Alzheimer's, and Parkinson's in order to formulate treatments for their aggressive symptoms. Effective therapies for these diseases, however, continue to elude researchers due to the complex mechanisms and etiologies. Most neurodegenerative diseases currently lack a permanent solution to stop their progression, leading to the inevitable relapse of symptoms after diagnosis. However, a new class of drugs, called antisense oligonucleotides (ASOs), are providing researchers and patients newfound optimism for possible remission and successful treatment. ASOs, made up of short strings of RNA or DNA, are designed to target the sequences of disease-causing proteins by base-pairing with protein-producing messenger RNA (mRNA). They work by either silencing faulty genes or replacing missing proteins needed to regain normal function, featuring high specificity to targets and low toxicity which make these drugs ideal for addressing neurodegenerative diseases (Rinaldi & Wood 2017). Since the US Food and Drug Administration's approval of the first ASO in 2016, research in this field has skyrocketed in the last few years.

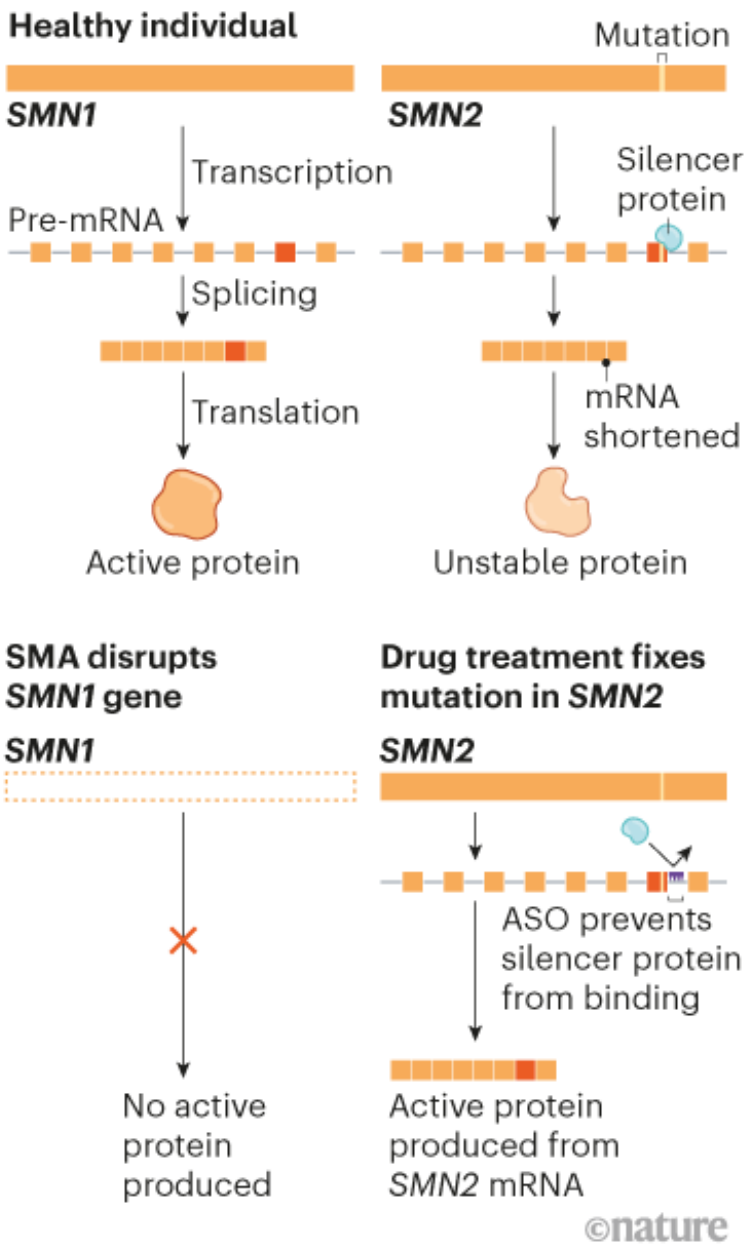

Figure 1. Healthy individuals have a functional SMN1 gene but a silenced SMN2 gene. In patients with spinal muscle atrophy (SMA) with a disrupted SMN1 gene, SMN protein cannot be produced naturally.

ASOs have shown promise for spinal muscle atrophy (SMA), a neurodegenerative disease that results from a mutation in a gene called SMN1. SMN1 produces a protein called survival motor neuron (SMN); not enough SMN is produced when SMN1 is mutated. This mutation leads to the manifestation of SMA1, the most severe and common form of SMA. Insufficient levels of SMN protein prevent the brain from effectively communicating with itself and

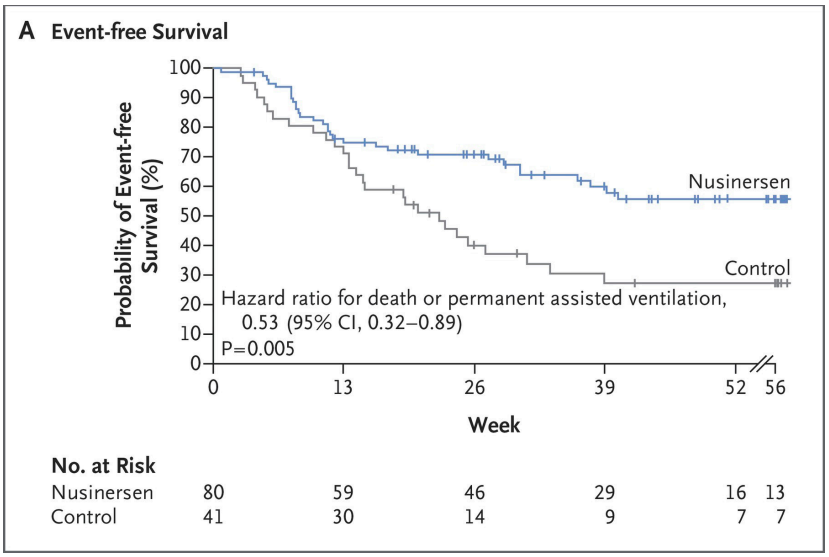

Figure 2. Survival rates of infants with spinal muscle atrophy in the nursinersen group and the control group. Event-free survival is the proportion of infants who were alive wihtout the use of permanent assisted ventilation.

contribute to the onset of symptoms like feeding and breathing problems, muscle weakness, and hypotonia, or poor muscle tone, before 6 months of age. Most affected children do not survive past 2 years of age due to respiratory failure (U.S. Department of Health and Human Services n.d). SMN2 is another gene that, in healthy individuals, contains a mutation that corresponds to an error in mRNA splicing, a process where pre-messenger RNA is transformed into protein-making instructional units, as shown in Figure 1. As a result, SMN2 typically produces less viable SMN protein than its counterpart, SMN1, in healthy individuals, but scientists reasoned that if SMN2 somehow produced more protein, it could make up for a mutated SMN1 gene in people with SMA1 (Kwon 2021).

Clinical trials utilizing ASOs for children born with SMA have shown great promise for reversing some of the severe effects of the disorder; nusinersen is one ASO that modifies pre-messenger RNA splicing of the SMN2 gene and thus promotes increased production of functional SMN protein. Researchers tested the efficacy of nusinersen in 121 infants diagnosed with SMA by randomly assigning the infants to either the nusinersen group, where infants were administered nusinersen via lumbar-puncture injection, or the control group, where infants were administered a sham procedure via a small needle prick to the skin over the lumbar spine to imitate a lumbar-puncture injection (Finkel et al. 2017). At various time points, the motor-milestone response of the infants was measured using the Hammersmith Infant Neurological Examination (HINE), which evaluates the categories of voluntary grasp, kicking, head control, rolling, sitting, crawling, standing, and walking (Finkel et al. 2017). The researchers considered infants to have a motor-milestone response if they showed improvement in at least one category and had more categories with improvement than categories with worsening. In an interim analysis, they found that 41% of infants in the nusinersen group had a motor-milestone response, a significantly higher percentage compared to the 0% of infants in the control group with a motor-milestone response (Finkel et al. 2017). The likelihood of event-free survival, defined as the time either to death or the use of permanent assisted ventilation, was also significantly higher in the nusinersen group than in the control group, as shown in Figure 2; overall, the risk of death or the use of permanent assisted ventilation was 47% lower in the nusinersen group than in the control group (Finkel et al. 2017). The clinical trials were terminated early because of the significance of the results in the interim analysis, as well as ethical consideration for the infants in the control group, and played a major role in the FDA's approval of nusinersen for the treatment of SMA in pediatric and adult patients (U.S. Department of Health and Human Services n.d).

...a new class of drugs, called antisense oligonucleotides (ASOs), are providing researchers and patients newfound optimism for possible remission and successful treatment.

ASOs also display great potential for replacing lost neurons in patients with Parkinson's disease. Parkinson's disease is

a neurological disorder caused by the impairment or death of dopaminergic nerve cells in the basal ganglia, the area of the brain that controls movement (U.S. Department of Health and Human Services). A loss of dopaminergic neurons, which are the main source of dopamine in the nervous system, and the consequent lack of dopamine lead to the characteristic symptoms of Parkinson's disease, including tremors of the hands, arms, legs, jaw, head, slowness of movement, and impaired balance and coordination. Alongside colleagues at UCSD, Xiang-Dong Fu utilizes preclinical mouse models of Parkinson's disease by injecting an ASO that depletes the RNA-binding protein PTB into areas of the brain where neurons are lost due to Parkinson's (Kwon 2021). He and his colleagues found that the depletion of PTB in mice successfully converts astrocytes, which are non-neuronal brain cells, into dopaminergic neurons, repairing damaged neuronal circuits and reversing motor deficits (Qian et al. 2020). Yet, since this study is still in its early stages, Fu advises that the treatment be tested in non-human primates first before moving on to human patients diagnosed with Parkinson's.

Clinical trials utilizing ASOs for children born with SMA have shown great promise for reversing some of the severe effects of the disorder...

However, scientists face disappointing drawbacks with ASO research, as not all treatments end up being effective therapies. Researchers are working towards a treatment for Huntington's disease, an inherited genetic disorder that causes a wide variety of motor, cognitive and psychiatric symptoms (Mayo Foundation for Medical Education and Research n.d). Huntington's disease impacts a gene called HTT that codes for the protein huntingtin by creating a faulty version that repeats a piece of its sequence too often. An ASO called tominersen works by tagging repeats on the RNA strand that are later destroyed by an enzyme called RNase H1; a phase I/II clinical trial revealed that tominersen successfully lowered concentrations of the mutant version of huntingtin in the cerebrospinal fluid without causing any serious side effects (Tabrizi et al. 2019). However, in early 2021, a phase III trial of tominersen that involved 791 participants from 18 countries was terminated early because the drug's potential benefits failed to outweigh its risks (Roche 2021). While the basis for this recommendation was not disclosed, Roche noted that no new or emerging safety concerns were identified in this review. Currently, the company continues to follow the study participants without any further dosing of the investigational therapy or a placebo (Figueiredo 2021).

Although there have been significant breakthroughs in research using ASOs, the field is still expanding, and much remains to be discovered about the efficacy of using ASOs to treat neurodegenerative diseases. One barrier researchers still face is the fact that not all neurodegenerative diseases clearly associate with specific genes; for example, Parkinson's disease is believed to manifest from a combination of genetic and environmental factors (U.S. Department of Health and Human Services n.d). More research must be done to fully grasp the effects of ASOs on aggressive neurodegenerative diseases, but the potential growth in this field of research is very promising for the communities affected by these disorders. ❧

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Small proteins, big effects

CLAIRE QU
Staff Writer

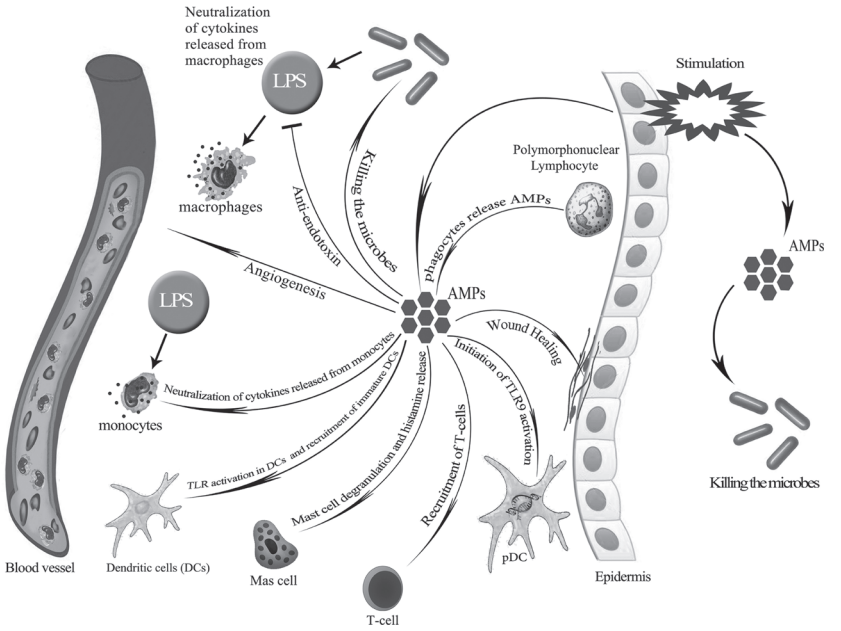

Figure 1: Some uses for antimicrobial peptides (AMPs) and their interaction with the body.

Over 7000 naturally occurring peptides (short amino acid chains) have been identified in the human body (Fosgerau and Hoffman, 2014). Each peptide has a specific physiological function as a hormone, neurotransmitter, ion-channel ligand, or anti-infective. Since the introduction of insulin, a peptide regulator of glucose, to the medical industry a century ago, peptide therapeutics have garnered commercial interest due to their potency, low toxicity, and selectivity. However, because proteins are degraded by enzymes in the body that are essential to digestion, peptide-based drugs have limitations such as low oral bioavailability, short circulation time, and low plasma stability (Muttenthaler et. al., 2021). Nevertheless, peptide drugs are used for some diseases like diabetes and specific types of cancers. Anti-infective peptides have also garnered interest as a promising way to make anti-microbial, anti-viral, and antifungal drugs during the post-antibiotics era. Recently, due to developments in protein technology, the FDA has approved an increasing number of novel peptide-based drugs, with many of those being used in the aesthetic industry (Muttenthaler et. al., 2021). With the advent of social media, however, there has been a surge in mass marketing of cosmetic products that claim to include scientifically backed peptide ingredients. The claims made by the aesthetics industry about peptide supplements are largely unfounded, using biased scientific evidence, and based on exaggerated claims for marketing purposes.

...the aesthetics and supplement industries provide most of the research funding on cosmetic supplements, hence encouraging favorable results for these industries.

For decades, doctors have prescribed peptide-based hormone drugs like insulin, oxytocin, and DDSs (peptide-conjugated drug delivery systems). These drugs have life-saving impacts; insulin therapy alone is taken by more than 200 million diabetic people worldwide to control diabetes (Garg et. al., 2018). Additional hormonal peptide diabetes treatments like glucagon-like peptide 1 injections are also popular clinical treatments. Moreover, Gynecological peptide drugs like oxytocin have largely changed the way modern medicine deals with delivering babies (Carter et. al., 2020). Mothers who take oxytocin report improved contractions and decreased bleeding during childbirth. This is due to the positive feedback loops associated with the hormone (Hidalgo-Lopezosa et.al., 2016). Most of these drugs, including insulin and oxytocin, are injected into the bloodstream, but there are other types of delivery methods like intratumoral injections in the case of cancer drugs like gonadotropin-releasing hormone derivatives (Ghaly and Varamini, 2021). Delivery methods of these drugs are essential for increased bioavailability, or the proportion of the peptides that are taken up by the body and are used

actively. Oral or topical peptide delivery methods are prone to degradation and limited absorption in the gastrointestinal tract and through the epidermis to reach the internal environment of the body (Bruno, 2013; Mathur, 2018). Thus, peptide drugs are limited to clinical delivery since proteins are unstable in reducing, low pH environments like the stomach.

Due to the soaring usage of antibiotic-resistant bacteria, there has been a newfound push in finding innovative methods of treating bacterial infections (CDC, 2021). A large sum of investment chases research looking to find ways to treat infections, especially healthcare-associated infections. Fortunately, peptide and immunology research has heavily emphasized the clinical use of antimicrobial peptide (AMPs) derivatives to fight infections. These molecules have several antimicrobial mechanisms, and induction of drug resistance has been deemed unlikely (Zhu et. al., 2022). Thus, antimicrobial peptides have great potential to be the next generation of antibiotics in a post-antibiotic era (Mahlapuu et. al., 2016). In vitro studies have favored the use of AMPs, because AMPs have evolved in the body to become direct, rapid, and effective countermeasures to numerous infections (Mahlapuu et. al., 2016). Most AMPs are highly selective and attack the fundamental differences between bacterial and mammalian phospholipid cell membranes. Mammalian cell membranes are saturated with cholesterol, which reduces the activity of AMPs. This allows for the positively charged AMPs to effectively attack the negatively charged protrusions in both gram-negative and gram-positive bacterial cell membranes. Nevertheless, in vivo studies are less promising. Like insulin and oxytocin, AMPs are difficult to deliver with high bioavailability, circulation time, and plasma stability, making it a challenge to maximize the benefits of the medication. AMPs are highly susceptible to environmental stresses like pH changes and enzyme degradation. Furthermore, the clinically delivered AMPs that have survived the bio-environment have resulted in functioning as immunomodulating signals rather than antimicrobials (Mahlapuu et. al., 2016). This may result in inflammation. Therefore, the development of AMPs for clinical applications is challenging.

In vitro studies have favored the use of AMPs, because AMPs have evolved in the body to become direct, rapid, and effective countermeasures to numerous infections.

With the pervasive presence of social media marketing, natural health remedies that emphasize methods of self-care, supplements, and herbal medicine for aesthetic purposes have become mainstream (Albornoz et.al., 2020). Over the last five years, many beauty companies that manufacture skincare goods have succumbed to these tactics by making, marketing, and selling creams/oral products with "infused" collagen. Collagen is a naturally occurring peptide that is found in several types of connective tissues that make up parts of the skin, joints, and hair ("Collagen", 2021). Due to the unique left-handed helical structure of the protein, collagen is responsible for the elasticity and "bounciness" of collagen connective tissue. Consequently, utilizing collagen as a treatment for cutaneous rejuvenation has become widespread (Wang et. al., 2020). Over-the-counter peptide beauty supplements are purported to be the "fountain of youth" by reducing wrinkles, adding elasticity to the skin, as well as forming thicker hair and nails. However, almost all these products are applied to the skin or ingested via pills and powder. As stated above, these avenues of peptide delivery have incredibly low bioavailability (Wang et. al., 2020). Although some research supports the advertising claims, the aesthetics and supplement industries provide most of the research funding on cosmetic supplements, hence encouraging favorable results for these industries. Consequently, it is difficult to determine if these papers are truly scientifically accurate ("Collagen", 2021). There are limited unbiased, non-industry funded studies but most of them contend that the ingestion of collagen supplements leads to statistically insignificant results in skin moisture and elasticity (Wang et. al., 2020).

Peptide drugs are short polypeptide chains that are usually derived from naturally occurring hormonal, antimicrobial, or signaling peptides found in the human body. As five percent of the larger global pharmaceutical market, peptide-based medica-

tions have treated people with chronic diseases like diabetes and cancer as well as helped in hormonal clinical therapies. They are also potential candidates to replace antibiotics. Nevertheless, oral and topical delivery of peptides has been found to be ineffective in reaching the desired effects. Thus, ingestible and cream beauty supplements that contain the peptide collagen are marketed with false claims. To make peptide drugs more effective in everyday applications, more peer-reviewed research must still be conducted. ❧

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Implementing euthanasia: The nuances of physician-assisted suicide

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Figure 1. Active euthanasia occurs when a physician injects a patient with a lethal drug.

Euthanasia, translating to "good death" in Greek, is the intentional termination of a patient's life. Physician-assisted suicide (PAS), another emerging method of euthanasia, occurs when the patient self-administers a lethal substance prescribed by the physician (Pereira, 2011). These practices are highly controversial and illegal in many countries due to numerous ethical implications; for instance, the Hippocratic Oath, patient autonomy, considerations for patient dignity, and the slippery slope effect all throw ethical wrenches in the works of euthanasia.

There are several different types of euthanasia, including active, passive, and indirect. Active euthanasia involves ending a patient's life by active means, such as injecting a patient with a lethal drug [Figure 1]. Passive euthanasia, alternatively, may involve withdrawing or withholding life support or life-sustaining devices. Finally, indirect euthanasia refers to palliative treatment that can inadvertently increase the speed of death despite a physician's intention of using the treatment as a method for alleviating suffering (Abohaimed, 2019).

Active euthanasia involves ending a patient's life by active means, such as injecting a patient with a lethal drug.

Historically, there have been contrasting views on the legalization of euthanasia and PAS. Early Roman and Greek civilizations held a more liberal attitude and believed that a patient experiencing severe suffering related to an untreatable disease had a right to request an assisted death. Meanwhile, Judeo-Christians believed that God inflicted pain and suffering on individuals for specific reasons, and thus we should not interfere with the natural process of death (Brigham and Pfeifer, 1996). On December 10, 1828, the first law forbidding PAS was enacted in New York. In 1905, the Ohio legislature rejected a bill to legalize euthanasia. A few years later, however, in 1915, a physician named Dr. Haiselden allowed a physically impaired baby boy to die instead of performing life-saving surgery. In the context of treating disabled children, some supported infanticide rather than raising a disabled child who may face severe challenges in the future. Additionally, due to the Great Depression and the difficult economic times, the public gradually began to support Dr. Haisdelden's belief, and support for suicide and controlled death grew. By 1974, the Society for the Right to Die was founded with the mission to legalize active euthanasia ("Historical Timeline", 2022). Oregon became the first state to legalize PAS through the Death with Dignity Act in 1974. As shown in Figure 2, PAS is currently legal in nine states and decriminalized in Montana, however, at the federal level, euthanasia is still illegal (Hetzler et al., 2019). Both euthanasia and PAS are legal in the Netherlands and Luxembourg, as the Dutch law believes in the "right to die with dignity" (Pereira, 2011).

Today, there are many supporters of euthanasia and PAS. For example, as seen in Figure 3, a recent Gallup poll revealed that 67% of Americans support the legalization of euthanasia and PAS (Hetzler, 2019). Based on deontological ethics (which uses rules to distinguish right from wrong), many people believe that every individual should have the right

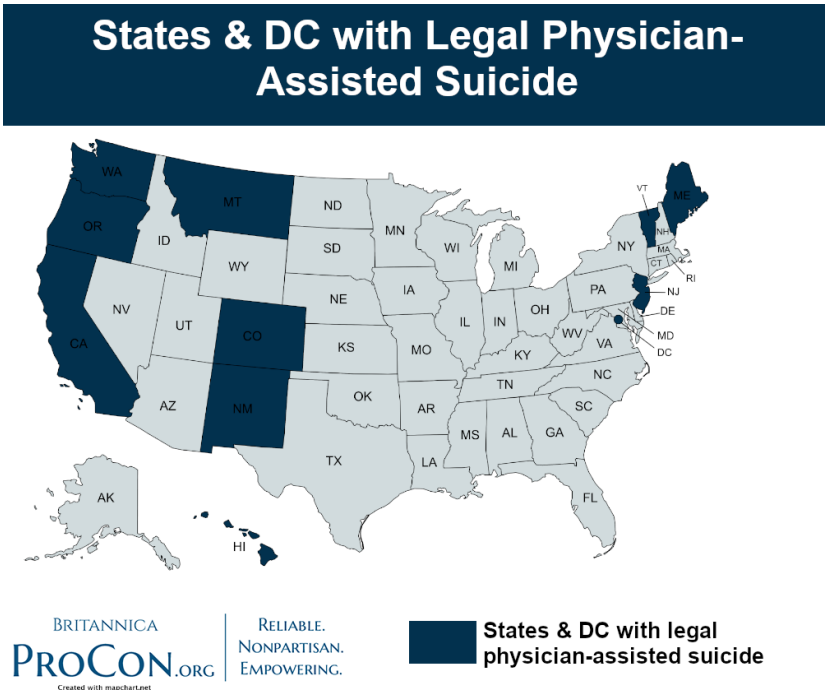

Figure 2. 9 states (CA, CO, HI, ME, NJ, NM, OR, VT, and WA) and DC have legalized physician-assisted suicide.

to exercise their autonomy with respect to their right to die. Thus, 'right to die' supporters believe that patients who are claimed terminally ill should be allowed to die with dignity rather than wait out their deaths in a hospital. In this case, dignity is described as people dying with respect to their last wishes and comfort. Many patients do not want to be a burden on their families and to be continuously cared for, knowing that they will eventually die. Thus, they prefer to die through a process of euthanasia or PAS to spare themselves and their family extensive pain and suffering (Math and Chaturvedi, 2012). However, what is the moral difference between participating in physician-assisted suicide and allowing a patient to die on their own through indirect means or withdrawal of care? Supporters of PAS believe that people may commit suicide in a dangerous way if they are refused physician assistance, so legalizing euthanasia through PAS may make this process easier and less dangerous for the patient. Additionally, from a utilitarian perspective, this could reduce healthcare costs and enable the use of medical resources and equipment for other patients who desire to live (Kalal, 2018). In today's world of ICU bed shortages and limited hospital staffing, the opportunity to save resources and funds could be viewed as helpful in these settings. Euthanasia and PAS also increase opportunities for organ transplantation, as patients who want to die can advocate for organ donation and help save another person's life who is awaiting transplantation (Math and Chaturvedi, 2012). The relevance of these factors raises the question: should terminally ill patients have the right to die and be given the autonomy to choose when and how to die? Should physicians be allowed to help? Recently, there has been increasing support for an individual's right to die amongst the general public.

However, what is the moral difference between participating in physician-assisted suicide and allowing a patient to die on their own through indirect means or withdrawal of care?

At the same time, there are many individuals who oppose the legalization of euthanasia and PAS. Before a physician can begin working, they must swear by an oath, known as the Hippocratic Oath, to uphold ethical standards. The oath states "I will neither give a deadly drug to anybody who asked for it, nor will I make a suggestion to this effect" (Antoniou et al., 2010). This emphasizes the value placed on human life and reminds the physician to do no harm to the patient, even if they are asked to do so. The oath obliges the physician to practice beneficence, maximizing the benefit to the patient based on their best clinical judgment, and minimizing harm. However, is refusing PAS for a patient who wishes to die in alignment with beneficence or non-maleficence? Alternatively, is engaging in PAS harming or helping a patient? Thus we revisit the question, is it morally right to assist in ending a person's life who is undergoing severe pain and suffering? For many who view human life as a sacred gift given by God, allowing euthana-

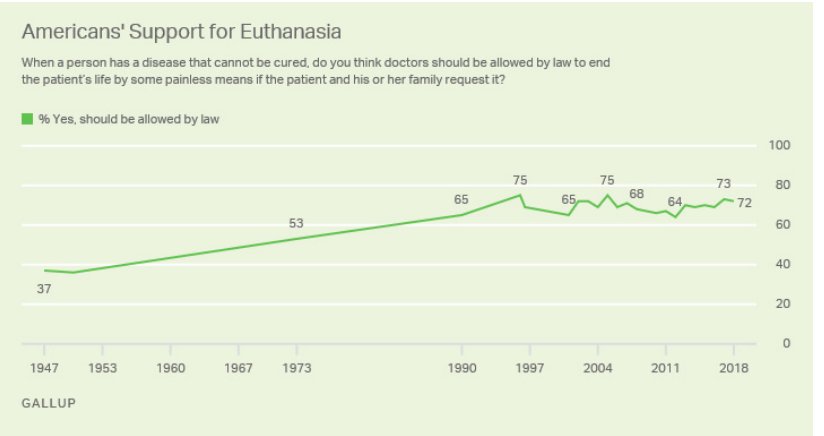

Figure 3. Americans' support for the practice of euthanasia has been increasing in recent years, according to a 2018 Gallup poll.

sia and PAS, the value of life is demeaned. If a doctor abruptly ends a patient's life, the slight possibility of a patient recovering from their disease and having a second chance at life is instantly ruined. If the evidence does not support the terminal nature of the illness or the unrecoverable nature of symptoms, doctors may be making a haste judgment. It can, thus, be argued that doctors have too much power in this process and that they may be, instead, intervening in the role of fate. Further, many people are afraid that the legalization of euthanasia may lead society down a slippery slope. The argument here suggests that an exception to one law is followed by more exceptions until a point is reached allowing morally unacceptable actions (Benatar, 2011). In this case, the legalization of one type of PAS may lead to the acceptance of other, more dangerous types of euthanasia. Eventually, euthanasia may even become a premature first choice in some situations, rather than the absolute last resort (Pereira, 2011). Additionally, patients suffering from mental illnesses, such as depression, schizophrenia, and substance use are more likely to consider suicide or ask for assisted death (Math and Chaturvedi, 2012). Thus, many people are hesitant to support euthanasia for patients who may not be deemed mentally competent to make such decisions. Overall, ethical concerns related to the Hippocratic Oath, slippery slope, the possibility of miracle recoveries, and debilitating mental illnesses are the primary reasons why many people oppose euthanasia and PAS.

There are also several alternatives to PAS that can alleviate patients' pain and suffering. The most common is palliative care, which allows for compassionate care with the aim of increasing comfort to ease patients' suffering at end of life (Math and Chaturvedi, 2012). Patients may also be administered pain medications and sedative drugs to relieve their symptoms and possibly extend their life expectancy (Erdek, 2015). These interventions allow patients to continue living without pain and suffering and possibly allow them to spend more time with their loved ones.

The utilization of euthanasia and PAS are heavily debated to this day. While many prioritize the importance of human life and ethical principles of a physician's role, others are strong supporters of the "right to die" movement and believe in honoring the individual's autonomy and minimizing harm for all. Regardless of these considerations, questions and deliberations regarding whether or not euthanasia and PAS are justifiable remain persistent in society today. ❧

AUTHOR BIO

Aastha is a second year majoring in Neuroscience Behavior and Biology. Her interests are in neurodegenerative diseases, vaccine hesitancy, and healthcare access.

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Chimeras: Their formation and ethicality

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Staff Writer

Chimeras are organisms formed from the cells of two separate organisms, each with its own genetic code. Chimeras can occur naturally, sometimes between two fraternal twins who fuse in the womb or through biological engineering, like the mouse-rat chimera. While chimera formation in the womb is natural from two zygotes fusing into one, artificial chimeras are much harder to make. They must be created in a lab using gene editing. Stem cells from Organism A are removed and put into the developing embryo of Organism B. Then, the embryo can grow with the combined genetic material from A and B. The organism born from this combination is an artificial chimera and will have cells with both the DNA of A and the DNA of B at different amounts throughout its body. Some examples of artificial chimeras that are a result of bioengineering include pig-monkey chimeras and mouse-rat chimeras. Recently, scientists are using technology to create human-animal chimeras. This development has opened up a new field of research and has many potential applications for human health, but it raises ethical concerns among scientists and activists and questions about the definition of being "human."

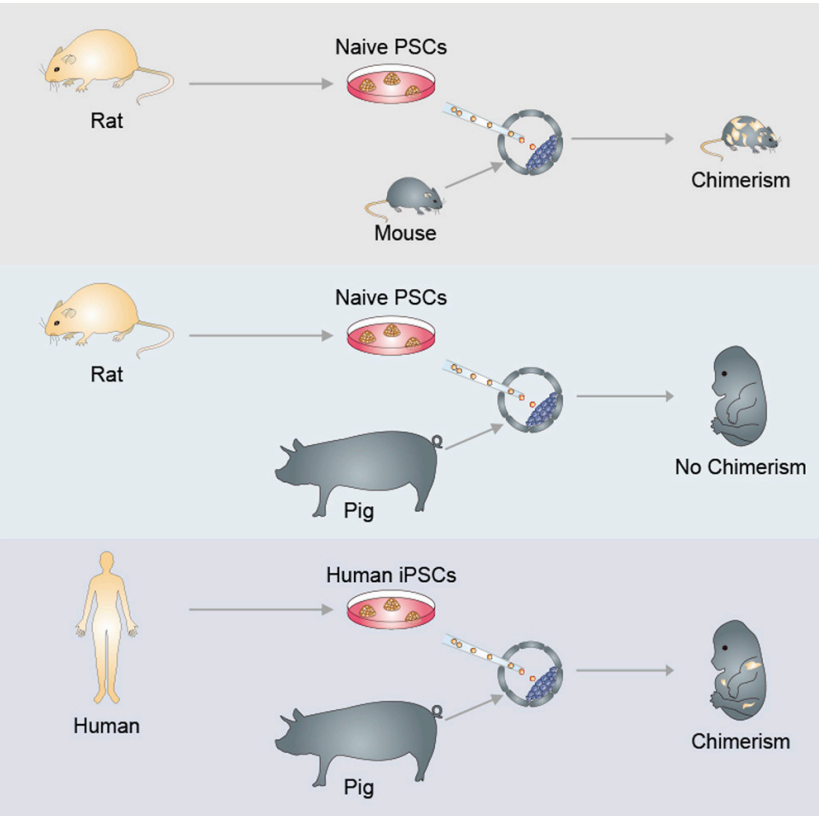

Figure 1. Pluripotent stem cells are combined with the embryonic cells of another organism to create a chimera.

...is it right to create an entire organism for the purpose of growing one organ for someone else?

Human-animal chimeras are created by taking human-induced pluripotent stem cells (iPSC) and implanting them into an animal blastocyst (refer to the figure below). They are then allowed to develop into an organism, which, when born, will contain both some human cells and some animal cells at different concentrations.

However, the process of creating chimeras is very difficult to perform successfully. For example, Tang Hai's team in China created pig-monkey chimeras by implanting 4,000 sows. Ten piglets were born but only two were chimeras, with monkey cells in them at all (Page, 2019). It is also hard to predict whether both species' cells will end up in the offspring and where the cells will end up in the body. In both cases, the amount of monkey cells present was between 1:1,000 and 1:10,000 (Page, 2019). This low number of monkey cells in the chimera shows how chimeras with high concentrations of cells from the second organism are to create, which is important to know when attempting to make an entire organ of human cells in human-pig chimeras. On top of the fact that it is incredibly difficult to create chimeras, very few cells from the organism whose pluripotent stem cells are used are put into the chimeric offspring. This is one reason why using organs from human-animal

chimeras can be risky; it is hard to create organs, or even tissues, that are made solely of human cells. Oftentimes, these organs will be made up of a combination of animal and human cells, which could have unknown and potentially dangerous effects on the human recipient.

Human-animal chimeras have been made with a variety of animals including monkeys, cows, rabbits, and rats. However, most experiments use pigs to create chimeras since they are good model organisms for human physiology and genetics (Bendixen, 2010). Pigs and humans share important similarities in their anatomy and genetic composition like metabolic rates and similar organ sizes, making them ideal candidates for the creation of human-animal chimeras (Bourret, 2016).

In September 2021, Dr. Jayme Locke's team at the University of Alabama at Birmingham was able to transplant pig kidneys into a brain-dead human patient. Though this patient was on life support, the doctors were able to mimic normal body conditions. The pig kidneys functioned well as they were able to maintain blood flow and produce urine, suggesting that this could be a possible avenue for organ transplant (Thompson, 2022).

...if humans are defined by their brains and their ability to have rational thoughts, could chimeras be considered human?

In 2022, doctors also successfully transplanted a genetically modified pig's heart into a live patient because this patient's conditions did not make them a good candidate for a human heart transplant (Metcalfe, 2022). However, the surgery was successful and the patient is still alive. This has major impact when considering using human-pig chimeras for organ donations for humans.

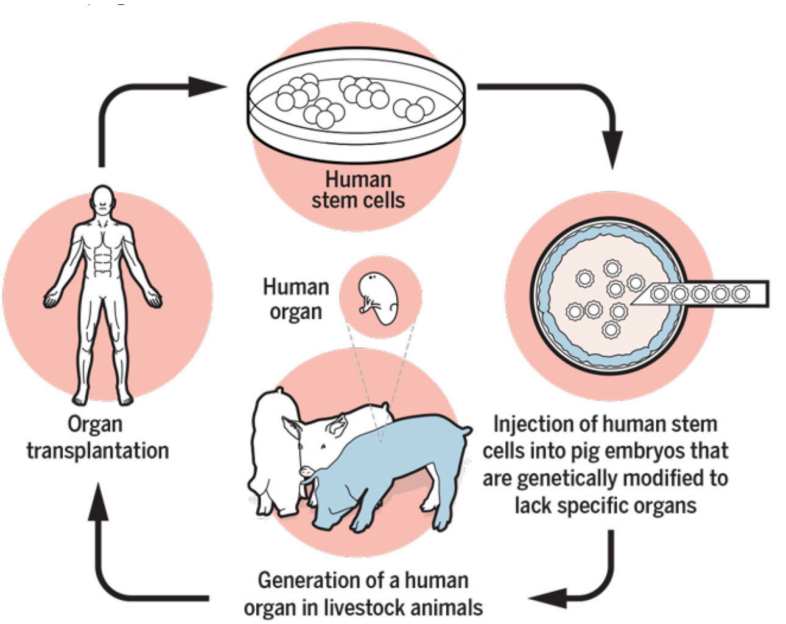

Figure 2. Simplified version of the process used to create human-pig chimeras.

There are many ethical implications to consider when creating human-pig or human-animal chimeras for organ transplants: while human-animal chimeras may provide patient-specific organs that can save thousands of lives a year, is it justified to raise an animal only to kill it to harvest one organ? In other words, is it right to create an entire organism for the purpose of growing one organ for someone else?

Another danger with using organs from human-pig chimeras is the lack of understanding of pig-specific diseases. For example, it may be possible for human recipients to become sick with a disease that usually affects pigs, thus creating another avenue for the start of a zoonotic pandemic. It is also unknown how these diseases could affect humans. This is one of the main reasons why pig organs are not directly transplanted into human patients unless there is an emergency. Another reason why pig organs are not put directly into human patients is due to hyperacute rejection, whereby the body recognizes the transplanted organ as foreign and begins aggressively attacking it (Thompson, 2022). This often can kill patients within a few days after the organ transplant.

Perhaps the most important ethical question with human-animal chimeras is what is considered "human." Roman philosopher Boethius once said that to be human is to have "individual substance of a rational nature" (Teichman 1985). Boethius postulated that to be human, one would have to be able to consider complex actions and reason through their actions and opinions. Modern philosophers

have a more refined view on the definition of humanity - having traits like emotions, creativity, and self-reflection. One of the key traits contemporary researchers attribute solely to humans is our brains (Goldenring 1985). The human brain is where the personality is housed, where the instructions for the body originate from, and the essential organ that marks a human as alive or dead.

Defining what we consider to be truly human is important when working with human-pig chimeras. When creating these chimeras, it is impossible with contemporary technology to control where the human cells end up in the pig's body. There is a high likelihood that if a human-pig chimera were created, at least a few of the chimera's brain cells would be human. If enough human cells end up in the human-pig chimera's brain, would it be able to have rational thought? Moreover, if humans are defined by their brains and their ability to have rational thoughts, could chimeras be considered human? Would chimeras develop a distinct personality and experience human-like emotions? At what point would these human-pig chimeras be considered a pig or thought of as a human, or will they spend their lives belonging to neither? From a legal perspective, would this chimera need to be treated in accordance with human or pig health standards? These are all issues that researchers need to clearly define before going deeper into this field. Without concrete precedent to these questions, researchers will be in uncharted territory, lacking real solutions to ethical conundrums when creating human-animal chimeras.

Though these organs would save the lives of many humans, there are other options besides harvesting organs from chimeras – like organoids. Organoids are organs grown in vitro to study how individual organs in the body behave. However, organoids can be grown in the lab setting using a patient's pluripotent stem cells (PSC). These organs are primarily used in vitro to study the specific organ they form, however, there are instances where they have worked in vivo. iPSC retinal cells were transplanted into humans with macular degeneration (Reza 2021). There have also been recent studies showing that liver organoids can work as functional organs in mice (Reza, 2021).

Human-animal chimeras have the potential to change the field of healthcare in many ways, but it also comes with a multitude of dangers and moral considerations.

Human-animal chimeras have the potential to change the field of healthcare in many ways, but it also comes with a multitude of dangers and moral considerations. Though this field offers the opportunity to make human-animal hybrids–which could save lives through organ donations and serve as research models–it also has drawbacks, such as the morality of creating an organism to kill it for one organ or the unknown nature of pig diseases. While much progress is being made in the field, there is still much to discover before the use of human-animal chimeras becomes widespread. ❧

AUTHOR BIO

Uma is a second year majoring in Biology. Her interests are in cell-cell interactions and their impact on overall body function. She hopes to use her knowledge to help people feel better and to ease their pain.

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Placed by Richard Lee

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Aging as a disease?

YUNA LEE
Staff Writer

If youth knew; if age could. — Sigmund Freud.

As we grow older, we become wiser and more experienced—simultaneously, our bodies grow weaker and slower. In the US, the top two leading causes of death are heart disease and cancer (CDC, 2022). Adults 65 and older are more likely than younger adults and children to suffer from heart disease, as is the same with most types of cancer and chronic diseases (U.S., 2018). As we age, the breakdown of the human body is expressed as conditions or diseases. While efforts have been to treat these diseases, there seems to be another potential approach—targeting aging itself.

Figure 1. Diagram depicting the 9 hallmarks of aging.

Aging is a broad term encompassing numerous processes. It is an oversimplification to name aging simply as a disease and to assign it a cause and effect relationship with age-related diseases. However, a new generation of researchers in the field of longevity has identified key hallmarks of aging that can be targeted to slow down the pace of aging, as well as actions we can take ourselves to possibly even reverse aging.

...a new generation of researchers in the field of longevity has identified key hallmarks of aging that can be targeted to slow down the pace of aging...

In the field of longevity research, there have been some studies that suggest that age-related damage is reversible by removing or reprogramming any cells that are problematic, or by blocking the activity of proteins made by these cells. In fact, DNA methylation—a frequently-used biomarker of biological age—is not just marking time in our bodies, but is "actually controlling time within cells," according to David Sinclair, an expert on aging at Harvard Medical School (Pesheva, 2018). This finding emerged from a study he published in Nature where researchers demonstrated, for the first time, that the pattern of DNA methylation in the genome can be reset in a safe way to a younger age. This is exciting news because the study shows that there are steps we can take to influence how we age, rather than our biological age being solely determined by genetics and time. In fact, Dr. Sinclair states that 80% of what contributes to your longevity is your lifestyle (Pesheva, 2018). Epigenetics, the study of how your behavior and environment change the way your genes work, influences the majority of your longevity.

One major influence on the epigenome that is within our control is our diet. The questions of what represents a macro nutritionally balanced diet and how this maintains health and longevity have long been debated. In a

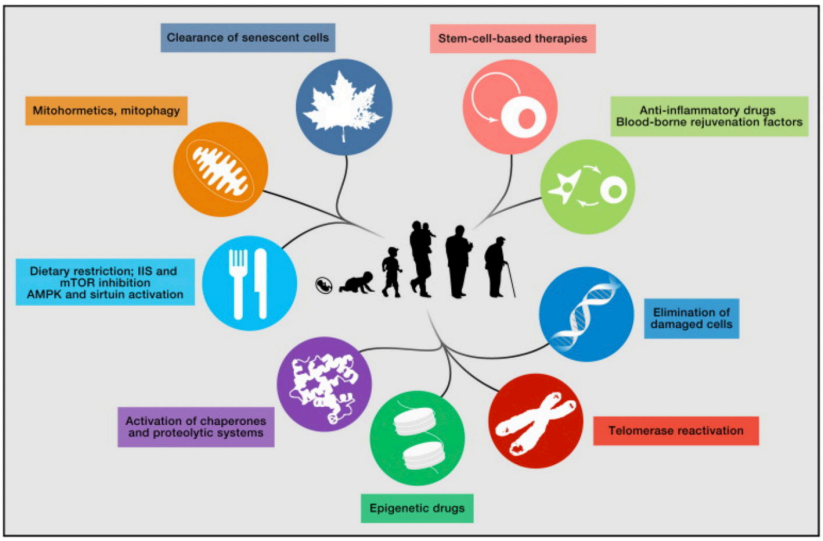

Figure 2. The active site of PylRS. (Wan et al., 2014) Image from Wan et al. 2014.

study exploring the relationship between longevity and different ratios of protein and carbohydrate content, it was found that longevity and health were optimized when protein intake is suppressed and then displaced with carbohydrates (Solon-Biet, 2014). Fasting also seems to be a major player in how one can extend their longevity. According to a study that explored the relationship between intermittent and periodic fasting with longevity and disease, intermittent and periodic fasting are known as safe strategies that positively affect longevity and healthspan by impacting cellular aging and disease risk factors without causing major side effects (Longo, 2021). More specifically, fasting from 12 to 48 hours and repeated every 1 to 7 days, and periodic fasting lasting 2 to 7 days and repeated once per month or less have the potential to prevent and treat disease, but their effect on cellular aging and the molecular mechanisms involved are only beginning to be explored (Longo, 2021).

Another interesting study focuses on chaperone-mediated autophagy (CMA), a type of autophagy that plays an important role in eliminating damaged and altered proteins (Juste, 2019). Autophagy describes the body's process of cleaning out damaged cells in order to regenerate new cells. CMA regulates the degradation of key cellular proteins that participate in processes such as lipid and glucose metabolism, the cell cycle, DNA repair, and cellular reprogramming (Juste, 2019). CMA becomes dysfunctional with age and has now been described in a growing list of human pathologies such as metabolic disorders, neurodegeneration, cancer, immunodeficiency, and diabetes (Juste, 2019).

Dr. Sinclair states that 80% of what contributes to your longevity is your lifestyle.

Exercise, a long-known must for health, also contributes its fair share to maintaining longevity. Along with a healthy diet and psychosocial well-being, the benefits of regular exercise on mortality are well established. Exercise can partially reverse the effects of the aging process on physiological functions and preserve functional reserve in the elderly (Gremeaux, 2012). Many studies have shown that maintaining a minimum quantity and quality of exercise decreases the risk of death, prevents the development of certain cancers, lowers the risk of osteoporosis, and increases longevity (Gremeaux, 2012).

Another interesting factor one might not expect to have an impact on longevity is body temperature. Temperature is an essential property of biological systems and many studies of various species associate temperature with aging and longevity. Early studies focused on animals that rely on external sources of heat (ectotherms) and maintain highly variable internal temperatures that are affected by environmental conditions (poikilothermy) (Keil, 2012). A century ago, Loeb and Northrop showed that lifespan correlates negatively with temperature in fruit flies, Drosophila melanogaster (Loeb, 1916). Another early study to observe the effects of temperature on longevity was in the cladoceran crustacean, Daphnia magna (MacArthur, 1929). Later studies in other poikilotherms— particularly fishes—demonstrated that even mild changes in temperature over long periods of time can influence lifespan (Walford, 1965).

In addition to behaviors we can adopt to live longer, we can also use supplements to boost chemical and biological processes that promote longevity. Nic-

otinamide adenine dinucleotide (NAD+) is an essential cofactor in all living cells that is involved in fundamental biological processes (Aman, 2018). Evidence from recent studies reveals numerous roles of NAD+ metabolism on aging and longevity (Aman, 2018). In particular, an age-dependent decline in NAD+ levels has been reported, possibly because of an imbalance in the synthesis and consumption of NAD+ (Aman, 2018). Decreased levels of NAD+ are also associated with the hallmarks of aging as well as several age-related diseases, such as metabolic disorders, cancer, and neurodegenerative diseases (Aman, 2018). Replenishment of NAD+ levels has been demonstrated to display beneficial effects against aging and age-related diseases. Importantly, boosting NAD+ levels has been shown to extend the lifespan of various laboratory animal models including worms, flies, and rodents (Aman, 2018).

CMA regulates the degradation of key cellular proteins that participate in processes such as lipid and glucose metabolism, the cell cycle, DNA repair, and cellular reprogramming.

In the study of longevity, there is much we still do not know about, with thousands of research studies only scratching the surface of what there is to discover. However, with the information at hand, we have the freedom and knowledge to apply what we learned to our own lives, with the potential of not only becoming healthier individuals but younger ones too. ❧

AUTHOR BIO

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Is segregation good for your health?

MURIEL STATMAN
Staff Writer

Research on the social determinants of health often suggests that residential segregation is a key determinant of health disparities, yet the truth about the relationship between residence, health, and race may be even more complex. The group density effect is a perplexing phenomenon in which members of low-status minority groups tend to have better health outcomes when living in communities with a larger proportion of their own group (Pickett & Wilkinson, 2008). Studies supporting the group density effect are often surprising given that minority-group members living in a community with a lower proportion of minority residents are often accompanied by an increase in material assets and access to resources (Pickett & Wilkinson, 2008). Even though members of minority groups who reside in white-majority communities are likely to be better off materially, the group density effect suggests that psychosocial pathways may offset this expected advantage. The group density effect sheds light on the power of status and social ties as determinants of health, and understanding its complexities may play a pivotal role in minimizing health disparities in the future.

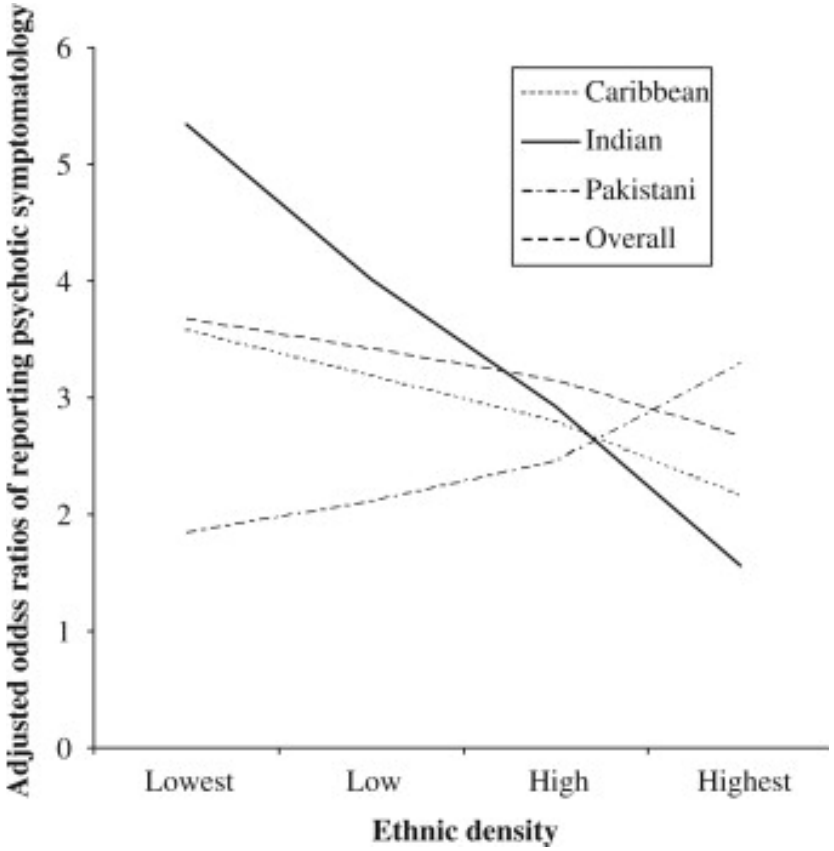

Figure 1. Graph relating ethnic density and adjusted oddss ratios of reporting psychotic symptomatology.

The group density effect has most commonly been studied with regard to mental health. In their review of research related to ethnic density effects on health, Jane Pickett and Richard Wilkinson characterize the group density effect as "status inconsistency" and demonstrate that this is correlated with higher stress and worse psychological health (2008). Numerous research studies have tracked psychiatric hospital admissions as they pertain to ethnic density and have found evidence in support of the group density effect. For example, studies in Chicago comparing predominantly black and white communities, in Canada comparing English and French-speakers, and in Boston with Italian and non-Italian communities have all suggested that "areal ethnic-specific psychiatric admission rates show a highly significant negative correlation with the numerical strength of that group in the area" (Halpern, 1993). Other variables, such as suicide and self-harm, have also been researched. A study in London found that Afro-Caribbeans

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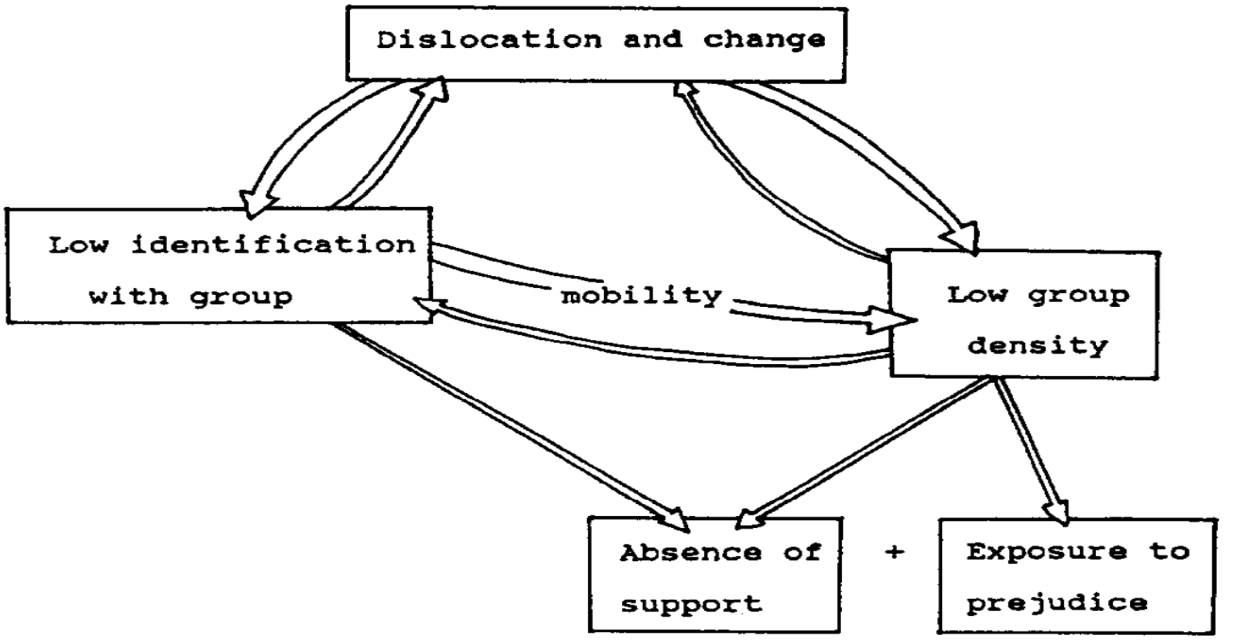

Figure 2. A model of the relationship between dislocation, identity, and the group density effect.

and Asians had lower self-harm rates when living in areas with a higher percentage of their own group (Neelemen et. al, 2001). The abundance of research investigating the relationship between ethnic density and mental health suggests that social ties and community involvement are key to overall well-being and happiness.

While it is understandable and expected that group density is correlated with mental health, it may be surprising that the phenomenon is associated with physical health as well. There is significantly less research on the association between ethnic density and physical health outcomes, but several key studies illuminate how physical health relates to the group density effect. In New York City, "elderly blacks living in black areas, despite their less favorable socioeconomic status, had lower mortality rates for all-cause, total cardiovascular disease, and coronary heart disease, than did those living in white areas, even after adjusting for available socioeconomic variables" (Fang et al., 1998). A 2003 study in Texas found that while Blacks and Hispanics had higher rates of mortality due to heart disease than whites, rates were lower when they lived in communities with a higher proportion of their own race (Franzini & Spears, 2003). Black mothers in Chicago were found to have a higher risk of giving low birth weight newborns than white mothers, yet their risk decreased when living in neighborhoods with a greater proportion of other black people (Collins et al., 1997). Similar results regarding birthweight and preterm weight were found for Hispanic mothers in the U.S. (Masi et al., 2007). Such findings suggest that material wealth and residential opportunity as determinants of health may be an oversimplification; community identity and social connections may be protective against deleterious health outcomes as well.

...material wealth and residential opportunity as determinants of health may be an oversimplification; community identity and social connections may be protective against deleterious health outcomes as well.

Ample research supports the crucial role that social ties play in supporting positive health outcomes, a potential explanation for the mental and physical health findings associated with the group density effect. Factors such as being married, having friends, and belonging to religious communities all improve health outcomes (Stansfeld, 2006). One study even found that married couples' wounds healed faster after "social support interactions" compared to

"hostile interactions" with their partner (Kiecolt-Glaser et al., 2005). There remains a lack of consensus about the various explanations for these findings, but the impact of social ties likely involves a combination of behavioral, psychosocial, and physiological mechanisms (Montez & Umberson, 2010).

As explained in the book Stress and Resilience: The Social Context of Reproduction in Central Harlem, black people were "willing to live under conditions of systemic neglect of community and higher levels of violence in exchange for the protective features offered by living in a black community, including the feelings of community, access to cultural resources, and a more limited exposure to everyday acts of racism in their neighborhoods" (Mullings and Wali, 2001). Studies have shown significant associations between prejudice and discrimination and poor health outcomes. Black individuals living in majority-white neighborhoods are also likely to experience more interpersonal and institutional discrimination than those living in black communities (Davis, 2020). Davis posits that the major pathways through which discrimination impacts health include psychosocial stress, access to community resources, and violence and bodily harm (Davis, 2020).

David Halpern similarly explores how discrimination impacts health in his article "Minorities and Mental Health." Halpern characterizes the psychological effects of low ethnic density as "the experience of prejudice", "dislocation and change", "cultural isolation and the absence of social support", and "the localization of identity" (Halpern, 1993). These categories illuminate the importance of community, acceptance, and cultural resources for minority groups. Additional studies have shown that upward social mobility, often accompanied by living in a majority-white community for minorities, is associated with poor health outcomes because people may "feel their class of origin disqualifies them from full acceptance or membership in their achieved social status" (Pickett & Wilkinson, 2008). It is important to note that the pathways between ethnic density and health are not mutually exclusive; they all likely intersect with one another to explain the group density effect on mental and physical health.

While it may seem as though the solution to ethnic density findings is support for racial/ethnic separatism, this approach fails to acknowledge the root of the problem or the broader political and socio-economic consequences of segregation...

Studies investigating the group density effect offer insight into how it can impact public health policy. The ability for psychosocial pathways to "override material advantage may have implications for our understanding of how low social status affects health more generally" (Pickett &Wilkinson, 2008). While it may seem as though the solution to ethnic density findings is support for racial/ethnic separatism, this approach fails to acknowledge the root of the problem or the broader political and socio-economic consequences of segregation: "We know that in the short term, separatism may reduce the stresses of direct prejudice, yet we also know to actually reduce such prejudice, equal status contact between groups is essential" (Halpern, 2000). Halpern emphasizes the importance of making fundamental changes to ethno-racial relations in the United States in order to alleviate the group density effect. Urban planners can also play a role in addressing the group density effect, with some proposing "the meshing of contrasting groups on a macro-scale, while still allowing for clustering to occur on the finer, microscale" (Halpern, 2000). Ultimately, the lessons learned through research on the group density effect suggest that integration rather than assimilation must be prioritized in modern ethno-racial relations to reduce health disparities. ❧

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The misnomer of the medical world: Pediatric palliative care

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Palliative Care is a subspecialty of medicine that focuses on assisting with medical decision-making and alleviating symptoms of serious illnesses (Rome, 2011). The goal of Palliative care is to provide support for the patient and their family rather than diagnosing and curing the patients of their illnesses. Palliative care and hospice have many areas of philosophical overlap but palliative care does not depend on the prognosis of the patient to dictate its use or its specific approach (Rome, 2011).

Pediatric palliative care (PPC), a relatively new specialization of palliative care, provides support for young patients with serious or terminal illnesses. Approximately 177,360 children engaged with palliative care in 2016 (Feudtner 2016). Since these patients are children, the support systems place greater emphasis on family involvement. PPC can provide numerous benefits for children, especially due to the difficulty patients can face in trying to understand the implications of their illness. PPC can help ease the symptoms, discomfort, and stress that may come with illness by augmenting a treatment-oriented approach with a comfort-oriented one (Palliative Care for Children, 2015). PPC clinicians work with fellow pediatricians to create a feasible plan of treatment, supporting individual healthcare goals outside the medical condition while also facilitating open discussion regarding care (Palliative Care for Children, 2015).

...there is an additional layer of complexity in PPC due to the age of the patients and their cognitive development.

While mortality rates have improved over the past 20 years, there has been a surge in chronic conditions among the youth, causing a growing demand for

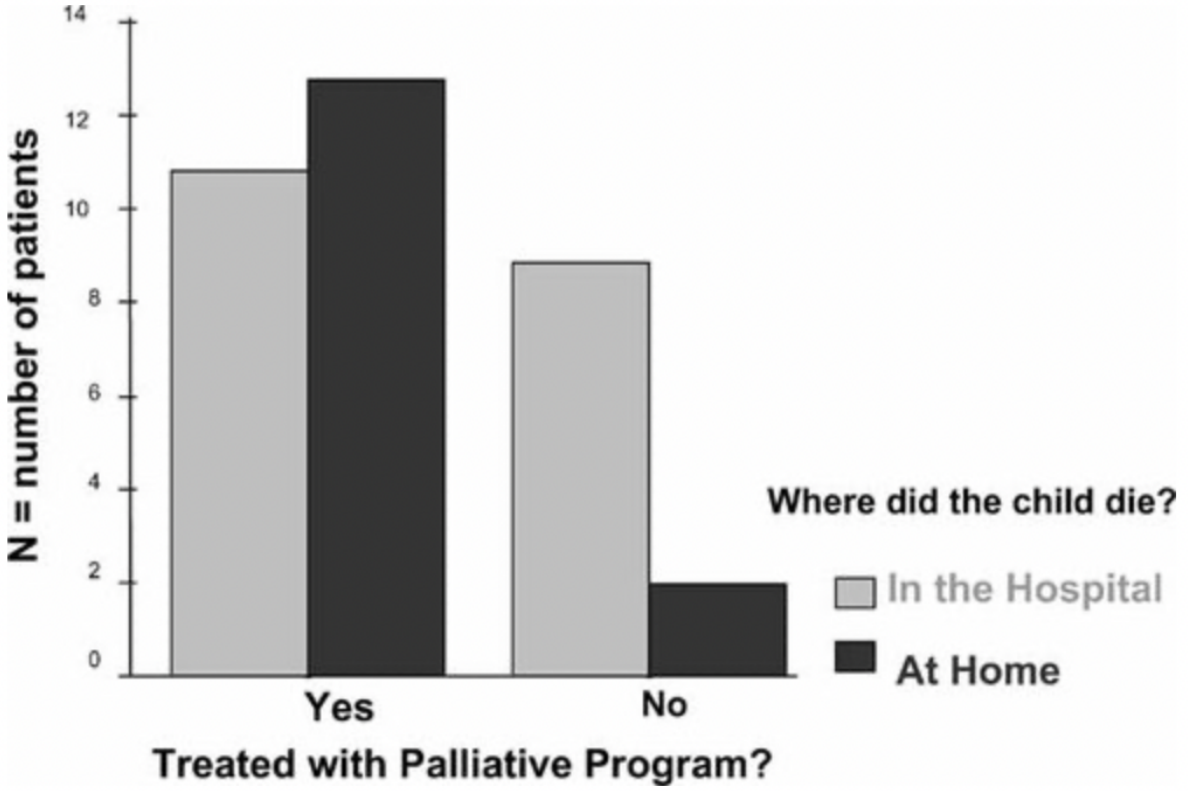

Figure 1. Frequency of Inpatient Pediatric Deaths has Decreased with the Increase in Palliative Care Program Development

Figure 2. Trajectory of Patient Care after a diagnosis of serious illness. Palliative Care eventually transitions into Hospice after all Life-Prolonging Therapies have been tried.

PPC Programs to treat these patients ("Children: Improving survival and well-being", 2020). As the demand for PPC grows, clinicians increasingly face regulations, setbacks, and ethical concerns they need to address in treating patients.

In order for a facility to be recognized as providing palliative care services, they are required to have a range of services—from nursing and physician services to psychological and spiritual counseling—in order to comply with federal regulations (Feudtner et al., 2013). The complexity of the physical symptoms and factors that affect decision-making necessitate the presence of a large interdisciplinary team that includes social workers, home health aides, chaplains, volunteers, and many more (Feudtner et al., 2013).

Unfortunately, despite this increasing need, pediatric palliative services still remain largely inaccessible (Feudtner et al., 2013). This is primarily due to the reduced capacity of medical facilities to cater to pediatric patients on top of the lack of insurance coverage to support these needs (Feudtner et al., 2013). The lack of financial consideration given to terminally ill children is a pervasive issue and is a key factor contributing to the lack of access to care. The Patient Protection and Affordable Care Act of 2010 limits the financial coverage given to terminal pediatric beneficiaries, with children who receive treatment in Medicare hospice being excluded and not mandating that hospice benefits should be covered under Medicaid, leaving the insurance policies largely up to state legislation (Lindley, 2011). Additionally, hospice eligibility is limited to children whose prognosis is under 6 months, leading to a large number of pediatric patients who are underserved (Lindley, 2011).

The lack of financial consideration given to terminally ill children is a pervasive issue and is a key factor contributing to the lack of access to care.

There are different challenges and laws that palliative care facilities are forced to abide by. Chris Feudtner and his colleagues, provide twelve recommendations to ensure that PPC (Pediatric palliative care) is administered successfully. Their study states that it is essential to monitor the composition of the team and the overall number of health care providers in order to ensure holistic care. The guidelines emphasize it is essential to provide the family with a realistic prognosis and plan for future complications. Team members should be responsive and frequently re-evaluate treatment plans to match the goals of care set by the patient and guardians as the clinical situation changes. (Feudtner, 2013). It can be hard to standardize rules and regulations of PPC due to the dynamic nature of the specialty and national policies are essential to set these standards of care. Oregon has been a trailblazer over the past decade, passing legislation to establish a task force to facilitate statewide inter-organizational cooperation. The task force has helped ensure that patient treatment directives are honored, regardless of the facility in which they are treated (Field, 2003).

Within this specialty, there are numerous parties that have a vested interest— healthcare providers, family members, and patients. In contrast to adult palliative care, there is an additional layer of complexity in PPC due to the age of the patients and their cognitive development. Because the decision-making power lies with the legal guardians, the degree to which the patient's opinion is factored in can vary. (Field, 2003). This can cause enormous emotional strain on guardians as well as the healthcare team. While not legally required, ethicists and clinicians alike recommend sharing age/development-appropriate information with the patients in order to maintain a "therapeutic alliance" – a healthy relationship

between healthcare providers and patients working towards a shared goal (Burns and Truog, 1997, p. 73; Field, 2003; Wissow et al., 2010).

There is much disagreement regarding the 'right' course of action for most PPC cases. When health care providers were presented with a clinical scenario and asked if palliative care should be initiated, opinions varied. 78% of physicians felt referral was indicated but only 57% of nurses shared the same opinion (Field, 2003). It is no wonder that healthcare providers are often placed in ethical dilemmas to find a balance between the principles of "autonomy" and "fidelity." Fidelity emphasizes that "health care professionals place the interest of their patients first" (Feudtner, 2014) while autonomy allows "patients to make their own decisions about which health care interventions they will or will not receive" (Entwistle, 2010). This can be especially hard for pediatric physicians as their patients may be able to express their wishes but are not legally able to make treatment decisions. As a result physicians in pediatric specialties often grapple with moral distress, "distress that occurs when constraints make it nearly impossible to pursue the right course of action" (Trotochaud et al., 2015). These feelings are best summed up by Kantian ethics which states that "ought implies can." Professionals are forced to combat moral distress when being bound by medicine's capacity to heal as well as the patient's wishes that might not align with the physician's recommendations. The bereavement that accompanies pediatric cases is incontestable, often causing long-term distress to families, siblings, and communities (Entwistle, 2010). This grief can cause treatment obstacles that are not seen in other specialties. For example, schools often refuse to honor do-not-resuscitate orders so as not to cause emotional distress to other students and staff members (Evans A, 2020).

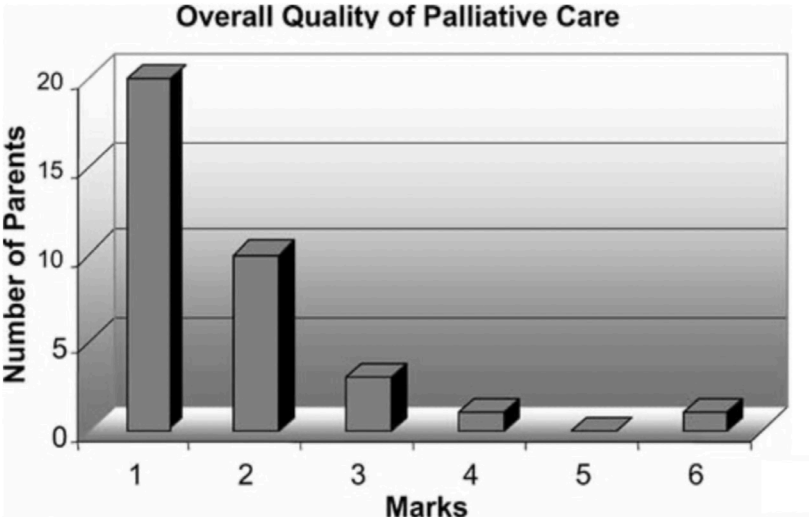

Figure 3. Parents of deceased children were asked to evaluate their experience with Pediatric Care Programs on a scale of 1 to 6, with 1 being the best possible score.

Only 10 percent of pediatric oncologists reported taking a formal course in end-of-life care and only two percent of these individuals completed a rotation in a palliative care or hospice service.

As the field of PPC grows, healthcare professionals should work toward addressing some of the problems facing the field. Only 10 percent of Pediatric Oncologists reported taking a formal course in end-of-life care and only two percent of these individuals completed a rotation in a palliative care or hospice service (Field and Berman, 2003). This lack of knowledge puts vulnerable patients and families in the dark (Field and Berman, 2003). To meet this discrepancy, recommendations are being made to develop undergraduate curricula about palliative care, end-of-life, and bereavement care for pediatric patients and institute residency program requirements for pediatric specialists in palliative care (Field and Berman, 2003). In addition, there is not enough synthesis of evidence generated from research on palliative care priorities, let alone specifically PPC (Hansson, 2020). A systemic review of journal databases for articles that focused on Palliative Care found that there was little representation of patient and caregiver-driven agendas (Hansson, 2020). Care-provider voices dominate the conversation of PPC, calling for more inclusivity for the patients and their families (Hansson, 2020). From a more service-based perspective, many hospitals have underfunded PPC Day services, which provide

patients with a range of services and their families with a source of respite (Hansson, 2021). By diverting funding to PPC Day services, both patients and their families can get the support they need.

A once-unfamiliar field, pediatric palliative care is carving a place for itself in the medical community. However, there are still many hindrances that delay the field from being able to help some of the most vulnerable people in society. As the medical community progresses, these issues deserve to be highlighted and fixed so that patients and their families are well taken care of. ❧

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A plant-based remedy: Cannabidiol as a treatment for rare forms of epilepsy

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The recent surge in the recreational use and legalization of marijuana is paralleled only by the influx of research into its medical potential. Over the last thirty years, the booming debate over the legalization of marijuana in multiple states and subsequent controversy surrounding recreational use has fueled researchers to consider the medical uses of marijuana. While cannabis may seem like a novelty in the medical world, its use as a treatment for epilepsy dates back to ancient China (Ben-Zeev, 2020). The two most commonly used compounds found in the marijuana plant are tetrahydrocannabinol (THC) and cannabidiol (CBD). In medical settings, only CBD is used because it does not cause a "high," unlike its psychoactive counterpart, THC (Ben-Zeev, 2020). The anticonvulsant properties of CBD oil offer immense benefits to patients suffering from epilepsy, most notably a significant reduction in seizure frequency. However, for some, the short-term and long-term side effects of CBD are a reason for concern. When evaluating the effectiveness of CBD treatments for epilepsy, it is crucial to examine the benefits CBD offers patients, how it interacts with the human brain, and most importantly, the safety of the drug.

The brain communicates through a complex network of electrical currents and chemical signals between neurons.

The brain communicates through a complex network of electrical currents and chemical signals between neurons. A seizure occurs when there are abnormal surges in the electrical currents propagated along these neurons (Fisher et al., 2014). Neurons can play a variety of different roles in the brain, and can be categorized as inhibitory or excitatory. Inhibitory neurons, such as GABAeric interneurons, prevent overexcitation by limiting electrical signals. Excitatory neurons with AMPA receptors, by contrast, promote the transmission of neural impulses. Both of these subsets of neurons play a role in seizures when their function is impaired or altered.

One rare form of epilepsy called Dravet syndrome has been linked to a mutation in the SCN1A gene, which codes for a sodium channel on GABA receptors. Mutations in the sodium channels lead to excessive sodium currents because the neuron is unable to inhibit hyper-excitation (Conolly, 2016). In Dravet syndrome, patients may experience chronic febrile seizures,

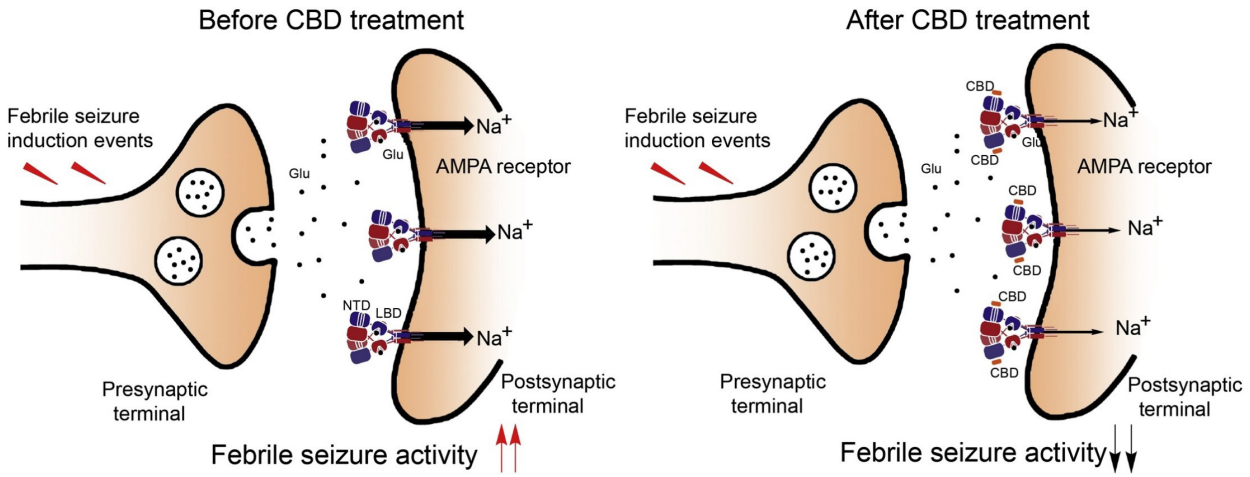

Figure 1. Diagram of CBD's interactions with neural receptors which decrease convulsant activity..

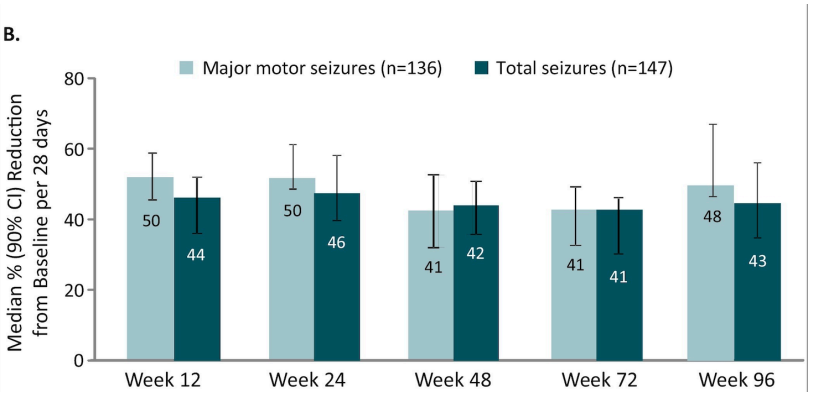

Figure 2. Results from IAT test. Slower response times define greater implicit racial bias.

which are triggered by changes in temperature (NIH, 2021). The frequency of these seizures typically increases with age, which is why early treatment is imperative (NIH, 2021). Dravet syndrome has an extremely high morbidity rate, and because the seizures present in early childhood, the disease often leads to severe neurological impairment, which develops with age (Conolly, 2016). Such severe symptoms indicate the critical demand for an effective remedy, and the effectiveness of CBD treatment is immensely promising for alleviating seizures.

By binding to these receptors, CBD reduces seizure frequency and severity, making it an effective treatment for epilepsy.

The anticonvulsant properties of cannabidiol make it a highly effective treatment for patients suffering from chronic seizures. Anticonvulsants prevent seizures by blocking surges of neural electrical impulses and preventing hyperexcitability.

Given the complex nature of epilepsy, the effect of CBD in the brain is multifaceted and involves a variety of neurons and receptors. One study using mice models found that CBD interacts with AMPA receptors to reduce seizure symptoms. Glutamate (Glu) is one of the primary excitatory neurotransmitters in the brain (Zhou et al., 1996). At the onset of a seizure, neurons release glutamate into the synapses, which then binds to AMPA receptors, causing excitatory responses. CBD reduces this response by acting as an antagonist, binding to AMPA receptors, and inhibiting the effect of glutamate. Lessening the effect of glutamate reduces the magnitude of the sodium current that it precipitates (Figure 1). Additionally, CBD mitigates seizures by interacting with GABA receptors (Ben-Zeev, 2020). CBD activates non-permeable ion channel receptors to inhibit integral membrane receptors found in the prefrontal cortex and basal ganglia (Pretzch et al., 2019). By binding to these receptors, CBD reduces seizure frequency and severity, making it an effective treatment for epilepsy. Furthermore, the FDA recently approved the clinical usage of Epidiolex, which contains purified CBD, to treat epilepsy. The approval of Epidiolex is a step towards providing patients with access to a safe and pure form of CBD for medical treatment.

The long-term effectiveness of CBD treatment is extremely promising. In one clinical

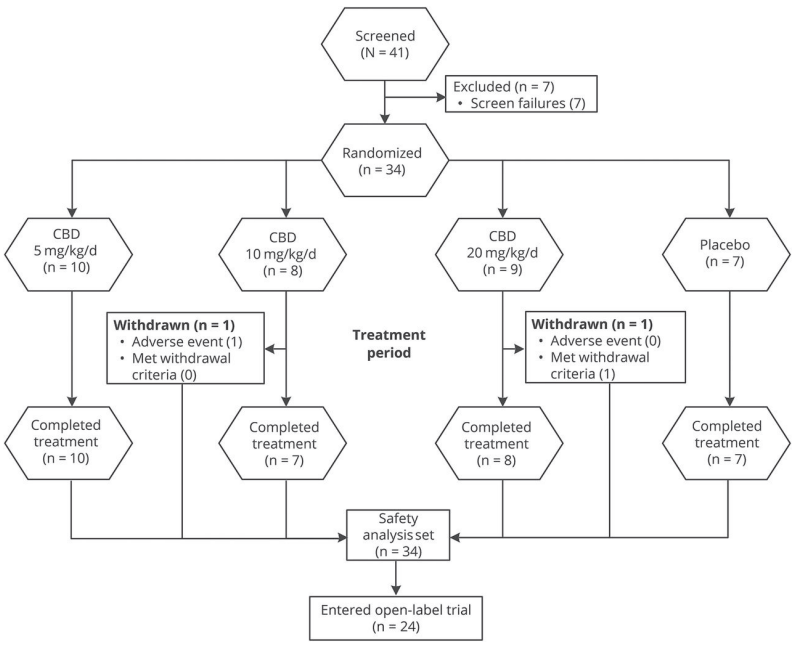

Figure 3. Methods of Devinskey's 2014 study in which patients with Dravet Syndrome ages 4-10 were randomly assigned to one of four treatment groups, each prescribed a certain dosage of CBD.

study, 607 epileptic patients with either Dravet Syndrome or Lennox-Gastaut Syndrome received 25-50mg of CBD branded as Epidiolex per day for 96 weeks (Laux et al., 2019). During the study, seizure frequency experienced by individual patients was evaluated at various time points. By 12 weeks, patients were experiencing a 50% reduction in median monthly seizures and total seizures, on average. The study reported similar results at 96 weeks. CBD treatment also appears to be well received from the perspective of patients and their families. In a retrospective study of 75 epileptic children treated with CBD, 35% of parents reported a 50% reduction in their children's seizure frequency (Ben-Zeev, 2020). Furthermore, in a long-term clinical trial, Szaflarski found that patients using isolated CBD (5 mg/kg/day incremental doses of 5 mg/day, with some patients reaching 2,000 mg/day) as an adjunct to anti-epileptic drugs had a sustained reduction in seizure frequency at 24 months. Overall, there was a 63.6% decrease in seizure frequency at 12 weeks, and this reduction remained consistent at both 24 and 48 weeks (Szaflarski et al. 2018). Furthermore, this reduction in seizure frequency corresponded with a sustained decrease in the adverse events profile. This data indicates that cannabidiol, even in pediatric cases, can be a safe and effective treatment for epilepsy. More broadly, in a 2021 clinical study at a Canadian cannabis clinic, patients reported that medical cannabis significantly improved their seizure symptoms, as well as additional medical conditions including PTSD, arthritis, and sleep disorders (Cahill et al., 2021). This study suggests that CBD not only has a high success rate in seizure alleviation, it also appears to improve other medical conditions as well.

Figure 4. CBD oil has a minimal effect on neurological pathways. Blue and green squares indicate downregulated and unchanged protein profiles, respectively, at 24 hours post-treatment with CBD oil V1 at 100 µg/mL final CBD concentration. Squares in other colors indicate proteins that are not applicable to the given pathways.

While clinical evidence suggests that CBD treatment does not lead to serious negative reactions, it is not free of side effects. In 2018, a group of researchers studied the effect of various dosages of CBD treatment in a sample of pediatric patients with Dravet Syndrome (Devinsky et al., 2018). Safety analyses were conducted on each group via laboratory and vital assessments, and the study concluded that even though there were more adverse events (decreased appetite, vomiting, sedation) in treatment groups than in the placebo group, CBD treatment was generally well tolerated. However, many non-CBD anti-seizure drugs (ASDs) have been reported to cause severe side effects (Szaflarski et al. 2018). Another clinical study assessed how prescribing CBD to a in conjunction with other ASDs affected the severity and frequency of adverse events. The study found that incorporating CBD into an existing ASD regimen resulted in a statistically significant decrease in patient-reported side effects, as well as the adverse events profile (Szaflarski et al. 2018). Therefore, even though CBD does produce mild side effects, it appears to alleviate the more severe adverse events and side effects caused by other anti-seizure drugs.

While clinical evidence suggests that CBD treatment does not lead to serious negative reactions, it is not free of side effects.

Despite its demonstrated seizure alleviation benefits, CBD is not without its controversies. A danger of using CBD is the potential contamination with the psychoactive component of the cannabis plant, THC. THC is linked to short-term memory loss, impaired motor skills, and cognitive impairment (Bridgeman et al., 2017). CBD alone does not cause these effects, unless contaminated by THC (Lachenmeier et al., 2019). Though not as severe as THC, CBD has the potential to induce moderate side-effects such as "CBD-induced drug-drug interactions, hepatic abnormali-

ties, diarrhea, fatigue, vomiting, and somnolence" (Huestis et al., 2019). In animals, CBD's adverse effects include developmental toxicity, CNS inhibition, and neurotoxicity. Although this study does not mention CBD contamination, this evidence could still suggest the possibility that CBD could cause adverse effects not previously known (Huestis et al., 2019). While the potential safety hazards and side effects might dissuade its recreational use, patients with severe epileptic conditions may find weighing the benefits and hazards of CBD treatment to be a daunting task.

Though still widely debated, CBD treatment for epilepsy offers massive benefits to patients suffering from life-altering conditions. However, because of the potential dangers of THC contamination, it is critical that patients have access to well-regulated and purified CBD through legalized channels. Various states in the U.S continue to regulate access to medical CBD, which puts pressure on patients and families who lack other treatment options. Ultimately, it can be argued that patients and their families, not the state, should decide between the possible drawbacks and benefits of using CBD oil. While the vast scope of applications of CBD have yet to be explored, it is clear that in the coming years, CBD holds significant potential in the medical world.

AUTHOR BIO

Claire is a first year majoring in Neuroscience and Behavioral Biology and minoring in Spanish. Her intersts are in gene therapy and immunotherapy, especially pertaining to food allergies and cancer research.

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Edited by Edward Xue, Niki Patel, and Dr. Arri Eisen

Placed by Jay Patel

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ADVISORY BOARD

MICHAEL CRUTCHER Ph.D.

Senior Lecturer and Director of Undergraduate Studies at Emory University

EUMR's main advisor is Dr. Michael Crutcher, one of the many distinguished faculty members in Emory's Neuroscience and Behavioral Biology Department. Having received his PhD in Physiology from Johns Hopkins University, he joined the Department of Neurology and of the Neuroscience Ph.D. program at Emory in 1991. His research is primarily focused on the neural mechanisms of visually guided reaching movements in monkeys.

Dr. Crutcher has taught many NBB courses over the years such as: freshman seminar courses (NBB 190) on Brain Enhancement, Curiosities of Neurology and Neuroscience, and Neuroethics as well as Perspectives in Neuroscience and Behavioral Biology (NBB 401 SWR), Biology of Movement Control (NBB 370), Neuroscience Research Methods (NBB 221), Functional Neuroanatomy (NBB 470), and Topics in Neuroscience and Behavioral Biology (NBB 270).

Emory Undergraduate Medical Review articles are peer-reviewed by medical professionals from more than a dozen leading academic institutions. The Emory Undergradute Medical Review would like to extend its thanks to the following advisors.

MUHAMMAD AZEEM

Medical doctorate in Child Psychiatry at Yale University

Dr. Azeem's primary clinical and research interests include Autism Spectrum Disorders, ADHD, child and adolescent psychiatry training, global mental health, and looking into innovative ways in reducing seclusions and restraints in inpatient child and adolescent settings.

TYLER CYMET

Medical doctorate from Nova Southeastern University College of Osteopathic Medicine

Dr. Cymet is an internist with research interests in joints and the musculoskeletal system. He discovered a new syndrome in 2006 which was named for him called the Erondu-Cymet syndrome. He now serves as the chief of clinical education for the American Association of Colleges of Osteopathic Medicine.

ARRI EISEN

Doctorate in Biochemistry from the University of Washington

Dr. Eisen is a professor of pedagogy at the Center for Ethics at Emory University. He aims to engage undergraduate students in the exploration of science and its applications in broad contexts. He has led the Emory-Tibet Science Initiative since 2005 and continues to be involved in many projects at Emory.

LAWRENCE MARKS

Doctorate from Harvard University

Dr. Marks is professor emeritus of epidemiology and public health at Yale. His research interests center around sensory disorders and perceptual experiences such as synesthesia. Though retired, he is active in writing and collaborates with other researchers in his areas of interest.

ADVISORY BOARD

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Dr. Li is a hospice and palliative care physician who is active in both clinical and educational work. His primary site of service is the VA hospital where he engages in medical counseling and education for learners of all levels. He is a member of the Emory Palliative Care Center.

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Dr. Caston is an assistant professor in the Division of Physical Therapy in the Department of Rehabilitation Medicine. Her areas of clinical expertise are in the fields of geriatric and neurologic rehabilitation, while her scholarly interests focus on humanities and ethics in rehabilitation, healthcare graduate student well-being, and the stories and lived experiences of individuals living with disability. Dr. Caston is also on the Editorial Board for the Journal of Humanities in Rehabilitation.

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Doctorate from Harvard University, NAS

Dr. Houk is a Distinguished Research Professor at the University of California, Los Angeles (UCLA). He is an expert on the computational investigation of chemical and biological reactions and has developed models to understand reactivity, selectivity, and catalysis.

Executive Board

ANJANAY NANGIA

Editor in Chief - Copy

Anjanay is a third year majoring in Chemistry and co-majoring in Quantitative Sciences. He originally joined EUMR as a first-year liaison and organized the first Data Science Symposium with the School of Nursing. As Editor in Chief for copy, he spearheads the editorial process and communicating with the Advisory Board. He has survived the pandemic by learning how to cook and catching up on his favorite movies and shows.

RICHARD LEE

Editor in Chief - Layout

Richard is a third year majoring in Biology and minoring in English. He joined EUMR as a contributing writer and became involved with the Events team in his last two years. As Editor in Chief for layout, he leads the creation of the semesterly journal along with the layout editors. Outside of the organization, Richard conducts research at Winship Cancer Institute, swims for Emory Club Swimming, and enjoys playing both classical and acoustic guitar.

GANESH CHILUKURI

Treasurer

Ganesh is a third year majoring in Neuroscience and Behavioral Biology with a minor in South Asian Studies. He began EUMR as a contributing writer and now has served as treasurer for two years, working on budgeting for all operations and the club's dealings with SGS. Outside of EUMR, he is also involved in Emory Synapse and works as a student ambassador for prospective/incoming students. In his free time, Ganesh loves listening to music of all genres and later composing them into pop sonnets.

JOSIE CHEN

Secretary

Josie is a second year majoring in Human Health. She first joined EUMR as a contributing writer for Open Access and now as secretary, is involved in facilitating communication across EUMR, planning events, and leading social media initiatives to further the organization's presence across campus. Outside of EUMR, she's also involved in Emory Planned Parenthood and Emory Red Light. In her free time, she enjoys spending quality time with friends and family, visiting the beach, and getting creative with art, baking, and yoga.

NATHAN JACOB

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Nathan is a fourth year majoring in Biology with a minor in Philosophy. He began as first-year liaison, went on to serve as the club secretary, and as editor in chief - copy last year. Outside of EUMR, he is also involved in organizations such as club tennis and is a pre-health peer mentor. Nathan was an extra in Spider-Man Homecoming and you can actually see a blurry image of him during the first ten minutes of the movie!

DAISY LI

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Daisy is a fourth year majoring in Anthropology & Human Biology and co-majoring in Integrated Visual Arts. She originally joined EUMR as a first-year liaison and organized the first Suture Lab with the Emory School of Medicine, eventually going on to serve as editor-in-chief for two years. Daisy's main goal is to continue expanding EUMR's presence and reach across campus. That aside, there is nothing she loves more than a day with no agenda spent on all sorts of creative endeavors.

Editorial Board

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Anu is a fourth year majoring in Neuroscience and Behavioral Biology and Creative Writing. She loves helping writers grow by integrating her scientific knowledge.

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Bushra is a fourth year double majoring in Anthropology and Spanish & Portuguese. Her favorite part of EUMR is collaborating with the staff.

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Daphne is a second year double majoring in Neuroscience and Behavioral Biology and minoring in Political Science. She enjoys the interdisciplinarity in EUMR.

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Edward is a third year double majoring in Psychology and Chemistry. His favorite part of EUMR is the semesterly events.

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Luisa is a third year majoring in Biology and Philosophy. Her favorite part of EUMR is reading the variety of articles.

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Sarah is a fourth year majoring in Chemistry and Psychology. She especially enjoys the full topic selection, outline, and full drafting process in EUMR.

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Siya is a second year majoring in Biology. She loves EUMR for the emphasis on creativity, perspective, and innovation in the medical field.

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Editorial Board

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Helen is a third year majoring in Neuroscience and Behavioral Biology and minoring in Spanish. She especially enjoys seeing the journal come together in EUMR.

CARISSA WU

Carissa is a third year majoring in Biology and Spanish. She loves reading the articles that her peers write in EUMR.

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Shreya is a fourth year majoring in Neuroscience & Behavioral Biology and minoring in Computer Informatics.

HENRY MANGALAPALLI

Henry is a fourth year double majoring in Biology and African American Studies. He loves seeing all the different article topics as he places their final drafts.

JOCELYN CHOW

Jocelyn is a fourth year majoring in Neuroscience and Behavioral Biology and minoring in Music. Her favorite part of EUMR is planning exciting events like the Suture Lab.


EUMR

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