CUSJ

Columbia Scientist

Edition 5, Fall 2026



Cover Art
Deekshitha Ravipati
Kognovate Education and Research
Hyderabad, India

CUSJ
COLUMBIA UNDERGRADUATE SCIENCE JOURNAL

ABOUT THE JOURNAL

AIM AND SCOPE

The Columbia Undergraduate Science Journal (CUSJ) was founded in 2006 by students who were passionate about showcasing undergraduate excellence in scientific research. Since then, CUSJ has remained Columbia's premier publication for original scientific research and scholarly reviews and is managed by an editorial board of undergraduates with a vast scope of interests across all disciplines. The editorial board also manages the Columbia Junior Science Journal (CJSJ), a publication designed to introduce high school students to research, and Columbia Scientist, a publication aimed at increasing scientific engagement and thought at all academic levels. In addition to our publications, the CUSJ team is dedicated to nurturing the scientific community, both within Columbia and in the surrounding Morningside Heights and Harlem communities. To this end, the board frequently plans outreach and networking events relevant to young and early career scientists, including an annual Research Symposium poster session each spring.

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LETTER FROM CO-EDITOR-IN-CHIEF

Dear Readers,

We are delighted to introduce the fifth edition of The Columbia Scientist, our Fall 2026 issue.

The Columbia Scientist was founded in 2022 to spotlight student work that breaks from the conventions of traditional scientific writing. Its goal was to give student writers a space to bring creativity, curiosity, and their own perspectives to science, while making scientific writing easier for a wider audience to approach. Over the years, the magazine has grown, and we now receive submissions from students across the globe. Their pieces show how many forms science can take, from pioneering medical advances to the ethical questions raised by emerging technologies. Today, we remain committed to amplifying a range of voices and expanding what scientific writing can look like.

This edition reflects the efforts of our writers and editors over the past year, and it would not exist without the commitment of the entire Columbia Scientist team. We are grateful to our former Editor-in-Chief, Jenny Deng, who guided the editorial process for the last issue and helped set us up for this one. We also thank our President, Param Sampat, and our past presidents, Cindy Lu and Kayla Pham. Finally, we thank our devoted editorial staff and every student who shared their work with us.

This issue is a tribute to the hard work of our student writers and editors. As you read, we hope you sense the passion and effort behind each piece.

Best,
Ahmed Hamdan ’28
Co-Editor-in-Chief, Columbia Scientist

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LETTER FROM CO-EDITOR-IN-CHIEF

Dear Readers,

It is with great honor that we present the fifth edition, the Fall 2026 issue, of The Columbia Scientist. First established in 2022, The Columbia Scientist was created to highlight student findings and editorials that defy the conventions of traditional scientific writing. It was meant to provide a platform for student writers to express their creativity, curiosity, and unique perspectives in science, while making scientific literature more accessible to its readers.

Since its founding, our publication has grown, receiving submissions from students around the world. These works showcase the many forms science can take, from cutting-edge medicinal experimentation to the ethical implications of AI. Today, The Columbia Scientist continues to serve as a platform that highlights diverse perspectives from New York City and beyond while further pushing the boundaries of what scientific literature can be.

The Fall 2026 edition represents the culmination of hard work put in by both the writers and editors this past year. It would not have been possible without the dedication of the entire Columbia Scientist team and editorial staff. Thank you to the previous Editor-in-Chief Jenny Deng, who spent the previous year leading the editing process and putting together the pieces in this publication. Special thanks as well to Managing Editor Andrew Chen and previous president Cindy Lu. Additionally, thank you to our dedicated editorial team and the students who submitted their work to Columbia Scientist. Most of all, thank you to my Co-Editor-in-Chief Ahmed Hamdan, whose efforts have considerably expedited the editing and refined the publication of our journal, and to Param Sampat, the President of CUSJ and the person who has overseen the entire editorial process.

This publication stands as a testament to the dedication of our student writers and editors. As you read through these articles, we hope you carry with you the passion and work that went into every piece.

With my best regards,
Gautam Ray ’28
Co-Editor in Chief, Columbia Scientist

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LETTER FROM CUSJ PRESIDENT

Dear Readers,

Thank you for picking up the fifth edition of The Columbia Scientist, our Fall 2026 issue.

Every issue of this magazine rests on a simple belief: that students have something worth saying about science, and that they can say it in a way any curious reader can follow. The pieces in this edition make that case better than I could. Inside, you will find an argument that the biomarkers used to choose patients for cancer immunotherapy behave more like a lottery than a test, a look at why artificial intelligence misreads depression in the brain's electrical signals, a tour of organs grown on chips no bigger than a USB drive, and a case for teaching film through neuroscience. Alongside them are two works of scientific art and a podcast you can play by scanning the code on its page. Our contributors this year wrote to us from schools across the United States and from as far away as Hyderabad, India.

This year also changed how we share student work. The Columbia Scientist now has a home online at columbiascientist.org, where readers can browse our editions and find each article on its own page, ready to be read, shared, and cited. CUSJ also continued its Summer Publishing Program, a month-long program in which students take a piece of science writing from first draft to publication with mentorship from our editors, and some of the work in these pages began there.

None of this would be possible without our Co-Editors-in-Chief, Ahmed Hamdan and Gautam Ray, who brought this edition to print with remarkable care. I am grateful to Jenny Deng, our former Editor-in-Chief, who led the editing of these pieces over the past year, and to our previous president, Cindy Lu, for the foundation this year was built on. Thank you to our editors for reading every draft closely and patiently, to our Faculty Advisory Board for their continued guidance, and to every student who trusted us with their work.

Finally, thank you for reading. We hope these pages leave you more curious than when you started, and we hope some of you will send us your own work for the next edition.

Cordially,
Param Sampat '28
President, Columbia Undergraduate Science Journal

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MASTHEAD

LEADERSHIP

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BIOETHICS

Triumphs and Ethical Concerns of Animal De-Extinction

Alex Zhong

Columbia University

On October 1st, 2024, Colossal Laboratories & Biosciences (CLB) accomplished what was once thought of as impossible: they brought back the *Aenocyon dirus*, colloquially known as the dire wolf, from extinction (Arif, 2025). But the reality behind this "de-extinction" headline reveals a deeper ethical dilemma pervading academia: the pursuit for engaging, sensational titles may be obscuring and muddling the real and interesting science behind these breakthrough discoveries.

The exact method behind this process of de-extinction is CRISPR-Cas9. A single guide RNA (sgRNA) directs the Cas9 protein to a specific genomic locus, and precise cuts are then made to the DNA sequence to perform specific insertions or deletions. Other methods of resurrection do exist: for example, Dolly the sheep—the first mammal to ever be cloned—was cloned using Somatic Cell Nuclear transfer (SCNT), a process in which the nucleus of an egg cell is replaced by any mature body cell that is not the sperm or egg. However, SCNT specifically requires an intact, living somatic cell to replace the egg cell's nucleus, and so only in rare cases can SCNT be utilized for the task of animal de-extinction. In contrast to CRISPR-Cas9, the procedure used to resurrect the dire wolves was more akin to creating a genetic chimera/proxy rather than a clone and exact replica of the species. Scientists modified specific genetic traits of a gray wolf to produce a wolf with extremely similar, albeit not identical, traits to the original dire wolf species. The dire wolves produced by CLB also differ from the original species in that they do not share the same learned behaviors and ecological context.

There is no denying that the CLB dire wolf project is a momentous step forward for the field of genetic engineering, but as with any groundbreaking discovery, the ethics and implications that ensue are just as important to consider. According to the National Society of Professional Engineers (NSPE), "Engineers shall issue public statements only in an objective and truthful manner" (NSPE, n.d.). The claim that CLB makes about "de-extinction" is indubitably a misrepresentation of the actual scientific achievement, and even though few individuals may be directly impacted by these misleading claims, dubbing the project de-extinction is definitely ethically ambiguous. Additionally, the NSPE proclaims that "Engineers shall hold paramount the safety, health, and welfare of the public" (NSPE, n.d.). As a consequence of the irreversible ecological and environmental harm that humans have caused, one key consideration for the future of CRISPR-Cas9 technology is to "right the wrongs" of the deterioration and degradation of Earth's ecosystems and biodiversity. The movement to potentially de-extinct the Thylacine (Tasmanian tiger) and reintroduce them to the Australian wilderness is a great step in this direction. As the keystone species balancing the ecological web of the Australian mainland and the islands of Tasmania and New Guinea, the complete extinction of the species nearly 90 years ago has caused almost irreversible damage to those areas. With no predator to keep them in check, the populations of wallabies and kangaroos have skyrocketed, leading to overgrazing and immense reduction in shrubbery, which in turn disrupts the nesting habits of local bird populations. Scientists hope to restabilize the ecological balance through the reintroduction of Thylacines, as even after almost one hundred years of extinction, the Tasmanian tigers could still potentially curb the wallaby and kangaroo population size and return the ecosystem to equilibrium (Abram, 2025).

> *Scientists modified specific genetic traits of a gray wolf to produce a wolf with extremely similar, albeit not identical, traits to the original dire wolf species.*

Equally as significant as bringing species back from extinction is the possibility of preventing species from going extinct in the first place. By editing key genes in critically endangered species, CRISPR-Cas9 can help adapt core species to environmental or genetic stressors—coral can gain heat and acid resistance, genetic rescue can be performed on inbred populations like cheetahs and Tasmanian devils, and disease and fungal resistance can be engineered into vital crops and vegetation.

As technology and science become ever more sophisticated and powerful, it becomes all the more important to critically consider the ethical reverberations of scientific revelations. To truly benefit society, scientific endeavors must harmonize technical achievement with rigorous ethical standards, ensuring that human interventions in the natural world are directed towards long-term prosperity rather than short-sighted and temporary novelty or profit.

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NEUROSCIENCE

Depression Between the Electrodes: Why AI Misreads the Brain's Broken Network

Jacob Crainic

Nova High School

"Fine."

It's the most common lie told in a psychiatrist's office and the reason half of all depression cases walk out undiagnosed (Mitchell et al., 2009). A psychiatrist sits across a patient and asks how they've been sleeping. The patient likely responds with "not well", "fine", or shrugs. The conversation that follows is watered down through a structured questionnaire and whatever the clinician's training and intuition can extract from it. From this, a diagnosis either emerges or doesn't. Catching it takes time: six to twelve months on average for formal diagnosis (Ghio et al., 2014). First-line antidepressants, typically SSRIs such as sertraline or fluoxetine, work for barely a third of the people who take them (Rush et al., 2006); the other two out of three are, pharmacologically speaking, guessing.

A better signal has been available the whole time. For decades, electroencephalography (EEG) has been placing electrodes across the scalp and recording the brain's electrical activity in real time, a standard tool for diagnosing epilepsy and studying sleep for nearly a century. Unlike brain imaging machines that cost millions of dollars and fill entire rooms, an EEG system costs only a few thousand dollars and is portable and fast enough to deploy in a primary care office. Buried in those recordings are patterns, from frontal asymmetries to breakdowns in how brain networks communicate, that decades of EEG studies have linked to depression, sitting undetected in that conversation. Artificial intelligence (AI) designed to read those signals should have changed everything, but it hasn't because it's been looking at the brain the wrong way.

Start with the earliest finding: a simple imbalance. In the late 1990s, researchers using EEG noticed that in depressed patients, the left side of the brain's frontal region was quieter than the right. This is the area of the brain that drives motivation and engagement with the world, and it looked as though someone had reached in and turned it down at the source. The finding survived decades of replication, and raw EEG could reveal it without sophisticated processing (Thibodeau et al., 2006). For a field that in over a century of clinical psychiatry never had an objective diagnostic marker, this felt like the breakthrough. Then a second pattern complicated the picture. Excessive slow-wave activity showed up in the brain's frontal regions, meaning that the mind would be suspended in a feedback loop, replaying the same regret, rehearsing the same dread like a broken record (Pizzagalli et al., 2003). Now there were two biomarkers instead of one, and both showed up at individual electrode sites, which made detection look like a matter of better engineering, or so the field thought.

Then, researchers changed the question. Instead of asking which region was malfunctioning, they began asking how those regions communicate. They stopped looking at individual regions and started listening to the conversations between them, and what they heard back changed what depression was. The brain runs a default mode network, the system responsible for self-reflection and inward thought, the one that switches on when you stare out a window and replay a conversation from six years ago. Normally a second system, the salience network, acts as its emergency brake, pulling attention outward and overriding the loop before rumination takes hold. In depressed patients, that balance collapses. The default mode network runs hyperconnected, rumination looping with no off switch, while the salience brake stays disconnected from the wheels and

never engages. Kaiser et al. (2015) mapped these disruptions across both the default mode and salience networks, showing that the problem wasn't any single region but the collapse of communication between them (Kaiser et al., 2015; Fingelkurts, 2007). Fingelkurts (2007) traced the same failure in the brain's electrical rhythms: the alpha and theta waves, the slow oscillations that normally keep the front and back of the brain in sync, had fallen out of step. Depression had never been a region producing the wrong signal, but a conversation between regions breaking down. Reading that conversation was like diagnosing a failing phone network by checking whether each tower's light was on without ever testing whether the towers could talk to each other.

Convolutional neural networks (CNNs) are the dominant AI used for reading EEG, and they were built for exactly the framework that neuroscience had just overturned. A CNN works like a technician inspecting a phone network one tower at a time, confirming that each tower has power and a blinking light but never asking whether the towers can reach each other. Each electrode channel is the equivalent of one tower, scanned on its own, its patterns learned in isolation. How those signals relate to one another never enters the picture (Schirrmeister et al., 2017). The model confirms that every tower is lit but never tests the lines between them. Most of the time, checking the towers alone is enough to get the answer right.

Recent studies report that these models correctly classify patients 85 to 89 percent of the time (Ay et al., 2019; Saeedi et al., 2020), but those numbers carry a caveat. Most EEG depression datasets contain fewer than 100 subjects, and some fewer than 40. High accuracy on small samples is notoriously inflated by the model memorizing specific patients rather than learning the disease itself, where the model essentially learns to recognize a specific patient's brain rather than depression's brain. Inflated or not, that success may have been the worst thing to happen to the field. 89 percent are seductive. High enough to publish, all the while being too high to question. So researchers kept optimizing the approach instead of asking whether it could see the disease at all.

Depression had never been a region producing the wrong signal, but a conversation between regions breaking down.

So what happens when the model built to find the connections can't actually see them? Graph-based models were supposed to be the answer. They treat electrodes like stations on a transit map, connected by tracks representing their relationships. As a framework, this was a genuine conceptual advance. It acknowledged what neuroscience had been saying, that the brain is a network and the disease lives in that network's wiring. Before the model ever sees a patient's data, researchers have to decide which electrodes are connected to which. They measure how correlated the activity between each pair of electrodes is and draw a line between the pairs that pass a threshold. Pairs that don't pass get no line and become invisible to the model (Li et al., 2022). If a connection between two regions falls just below the threshold, the model will never know it existed. Even if that connection is exactly where the disease lives. That same pesky blind spot kept moving.

Consider what changes when the model turns into a cartographer and draws its own map. In 2020, Song's team did what the depression field had not, they built a model that learns the brain's connections during training (Song et al., 2018). The model figures out which electrodes matter to each other by listening to the data itself. Say a study builds its map from 60 healthy controls and 60 depressed patients. That map is an average. Patient 61 walks in with a connectivity disruption that the average model never saw, in a connection the group data said didn't matter. When the model learns its own connections from each individual recording, the map changes with the patient. Every connection in that map carries a weight, a number representing how much it mattered to the classification. A clinician can open it up and ask: which connections drove this diagnosis? Do they line up with what we know about the disease? That's the difference between a tool that hands an answer and a tool that shows how it got there.

Catching on has been slow, held back by scarce training data and by methods that have worked well enough for long enough to discourage change. No published study as of 2026 has applied fully adaptive graph learning to depression EEG classification on a clinical-scale dataset. Only in preprints have the first attempts begun to surface (Wang et al., 2024). Half a decade of models published, optimized, and celebrated, without ever being asked to see the disease the way neuroscience describes it.

Electrodes were never the bottleneck, and neither were the biomarkers. Neuroscience had identified the network disruptions underlying depression years ago; what lagged behind was the model reading the signal. Even when the model gets it right, catching the disease is only half the answer. Depression is not one uniform disease. A patient trapped in the same spiral of self-critical thought may respond to cognitive behavioral therapy. Someone whose attention-control system has weakened may need an entirely different intervention. Drysdale et al. (2017) took connectivity data from over 1,000 patients, all diagnosed with depression, and found that those patients sorted into four distinct subtypes. Patients in two of the four subtypes responded to transcranial magnetic stimulation at roughly three times the rate of patients in the other two (Drysdale et al., 2017). Same diagnosis on paper. Wildly different brains underneath. Anyone building the next model needs to answer a harder question: where in the brain to look, and once you've found something, what it actually tells you about which treatment might work.

The psychiatrist is still asking. The patient is still answering. The brain is generating a signal the entire time. The question is whether the tools we build will be designed to see it, or whether we'll keep optimizing the ones that can't.

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The Immunotherapy Lottery

Kundana Kommini

Wiregrass Ranch High School

Imagine you walk into a casino. The house tells you roughly one in three players walk out with their lives. The rest go home empty. Now imagine this happens in real life, except in an oncologist's office, and the chips on the table are years. That, stripped of its clinical veneer, is the current reality of cancer immunotherapy. In theory, it's an elegant premise. Instead of poisoning the body with traditional chemotherapy, these drugs "unmask" the disease, training the patient's own killer T-cells to recognize and destroy the tumor. But in practice, this cellular battle rarely goes as planned. When clinicians talk about a successful response, they mean significant, measurable tumor shrinkage or long-term durable survival. Responses have been detected in only twenty to forty percent of patients across most cancer types[1], and in some settings, the effective response rate sits even lower [2]. We have spent the better part of a decade celebrating immunotherapy as a triumph in modern medicine, and it mostly is. But a treatment that fails for 60 percent of those who receive it is, by any standard, a coin flip in a lab coat.

The core issue is prediction. Specifically, we are not good at it. PD-L1, a protein that cancer cells use to hide from the immune system, has historically been the default marker doctors use to decide who gets immunotherapy. It works, kind of, sometimes, more in some tumors than others. The problem is that PD-L1 is highly dynamic and wildly inconsistent. A single needle biopsy captures only a frozen snapshot of a tumor; it can vary dramatically between the primary site and a metastasis, or change entirely after a round of radiation. More fundamentally, looking for PD-L1 expression only tells you if the tumor is actively trying to suppress an immune attack. If the tumor is "immunologically cold" (meaning killer T-cells never managed to infiltrate the tissue in the first place), blocking PD-L1 does absolutely nothing. You are releasing the brake on an engine that isn't even running. Tumor mutational burden (TMB), a measure of how many genetic errors have accumulated in a tumor, got FDA approval as a selection tool for one major immunotherapy drug back in 2020. But the more carefully researchers look, the clearer it becomes that neither marker is sufficient on its own, relying on one instead of the other simply trades one blind spot for another[2]. TMB indicates how genetically unstable a tumor is. The theory is intuitive: the more mutations a tumor has, the weirder its cells will look to the body, making it easier for T-cells to spot them as foreign threats. TMB does not tell you whether the immune system in and around that tumor is actually capable of mounting a response, which turns out to be important. If the local tumor microenvironment is fiercely immunosuppressive, teeming with cells designed to shut down inflammation, even the most conspicuous, highly mutated tumor will stay unbothered.

Fumet and colleagues put it clearly in a 2020 review: TMB has biological plausibility as an immunotherapy marker, but the clinical evidence is messier than the theory would predict [3]. Tumors with high TMB do not reliably respond better. The cutoffs are arbitrary. The assays vary between labs. It is not that TMB is useless; it is that it is being asked to carry more predictive weight than the underlying biology actually supports.

Jardim and colleagues traced a lot of this back to a more fundamental problem: TMB was developed under a specific set of assumptions about how the immune system recognizes cancer cells, and those assumptions hold true in some contexts and not at all in others [4]. Prior treatment history, tumor type, and other biological factors all interact with TMB in ways that make a universal cutoff essentially meaningless. Wang and colleagues extended this analysis in 2024, showing the prediction problem is even worse when applied across different cancer types [8]. They demonstrated that a "one-size-fits-all" TMB threshold is effectively a statistical mirage. Because every organ has a different biological baseline for mutation, driven by cell turnover rates, exposure to environmental carcinogens, and intrinsic DNA repair efficiencies, a TMB value considered "high" in lung

cancer might be indistinguishable from a "low" score in a sarcoma. By forcing a universal number onto radically different biological landscapes, we aren't just missing the mark but instead trying to measure temperature with a ruler. We keep reaching for simple molecular proxies for a biological problem that is not simple.

The Real Culprits Are Harder to Measure

What both PD-L1 and TMB miss is the actual immune landscape inside the tumor. Not just whether the immune system has something to recognize, but whether the immune cells that are supposed to do the killing are present, functional, and not actively being shut down. That shutting down is the part we have been underweighting, and it is carried out by specific cell populations that standard tests do not even look at.

> *By forcing a universal number onto radically different biological landscapes, we aren't just missing the mark but instead trying to measure temperature with a ruler.*

Regulatory T cells are the most well-characterized of these cell populations. Think of them as the immune system's peacekeepers, cells whose normal job is to prevent the immune system from attacking healthy tissue. In a tumor, they do that same job at exactly the wrong time, suppressing the killer cells that immunotherapy is trying to activate. Togashi and colleagues found in 2019 that high levels of regulatory T cells inside a tumor correlate with worse outcomes across multiple cancer types [(5)].

Tumor-associated macrophages add another layer. Macrophages are immune cells that patrol the body and flag threats. Inside a tumor, a subset of them gets reprogrammed into something closer to the tumor's bodyguards, secreting chemicals that suppress immune activity and actively remodel the environment around the tumor to protect it. Mantovani and colleagues laid this out in a 2022 review [(6)]. These cells are not passive bystanders. They are working against the treatment. Myeloid-derived suppressor cells, another population of immune cells that tumors recruit to block attacks against them, pile on top of that. Veglia and colleagues described in 2021 how these cells disable killer T cells through multiple overlapping mechanisms [(7)]. They don't just hit a single off-switch; they wage a multi-front war. MDSCs mass-produce enzymes that starve T-cells of critical amino acids like L-arginine, rendering them too weak to divide. Simultaneously, they flood the local tissue with reactive oxygen species that chemically warp T-Cell receptors, effectively blinding the immune cells right as they arrive. To seal the perimeter, they secrete suppressive cytokines that recruit even more regulatory T-cells to the frontline. This creates a total systemic shutdown.

None of these populations show up in standard tumor tests. A tumor can have high mutational burden, strong expression of the PD-L1 protein, and still be sitting in an immune environment so thoroughly suppressed that no immunotherapy drug is going to matter. And we will not know that until after the patient does not respond.

The Tools Problem

Part of why we are still here, still debating the same markers a decade after they were proposed, is that mapping the immune environment inside a tumor at the resolution needed to actually understand it is hard. Single-cell RNA sequencing, a technology that can read the activity of tens of thousands of individual cells at once, is powerful, but standard analysis pipelines treat each cell as an isolated data point. They do not model how cells talk to each other. They do not account for where cells sit physically inside the tissue. And they have a well-documented tendency to lose rare cell populations entirely because those populations get statistically absorbed into larger groups during analysis.

The immunosuppressive cells we actually need to measure are often present at very low frequencies below the threshold where standard methods reliably detect them. This means we are building response prediction models on a picture of the tumor immune environment that systematically leaves out the cells most likely to explain why treatment failed. Newer approaches using graph-based deep learning, which model cells as a connected network rather than isolated points and can factor in where cells are physically located relative to each other, are starting to recover what conventional methods have missed. The clinical application

of these approaches is still early, but the direction is the right one.

What Actually Needs to Change

The biomarker conversation in immunotherapy has been stuck in a loop. A new marker gets proposed, shows promise in early studies, gets approved or widely adopted, and then real-world use reveals it is not as predictive as hoped [1, 3, 4, 8]. The cycle keeps repeating because the underlying problem has not changed: we are measuring features of the tumor itself when the relevant biology is in the immune cells surrounding it.

That is a harder measurement problem. The immune environment inside a tumor is dynamic, varies across different regions of the same tumor, and involves rare cell populations that current standard tests do not capture. Solving the prediction problem in immunotherapy is not going to come from a better version of TMB or a more sensitive PD-L1 test. It is going to require mapping the immune environment comprehensively enough to detect the suppressive networks that immunotherapy is trying to overcome, at a resolution that can actually guide clinical decisions.

The sixty percent of patients who do not respond are not failing because of bad luck. They are failing because of biology we currently do not have reliable ways to measure, suppressive networks operating below the threshold of every test we have standardized, in cell populations we have spent a decade not looking at. The biomarker we need already exists inside the tumor. We haven't built the tools yet to find it.

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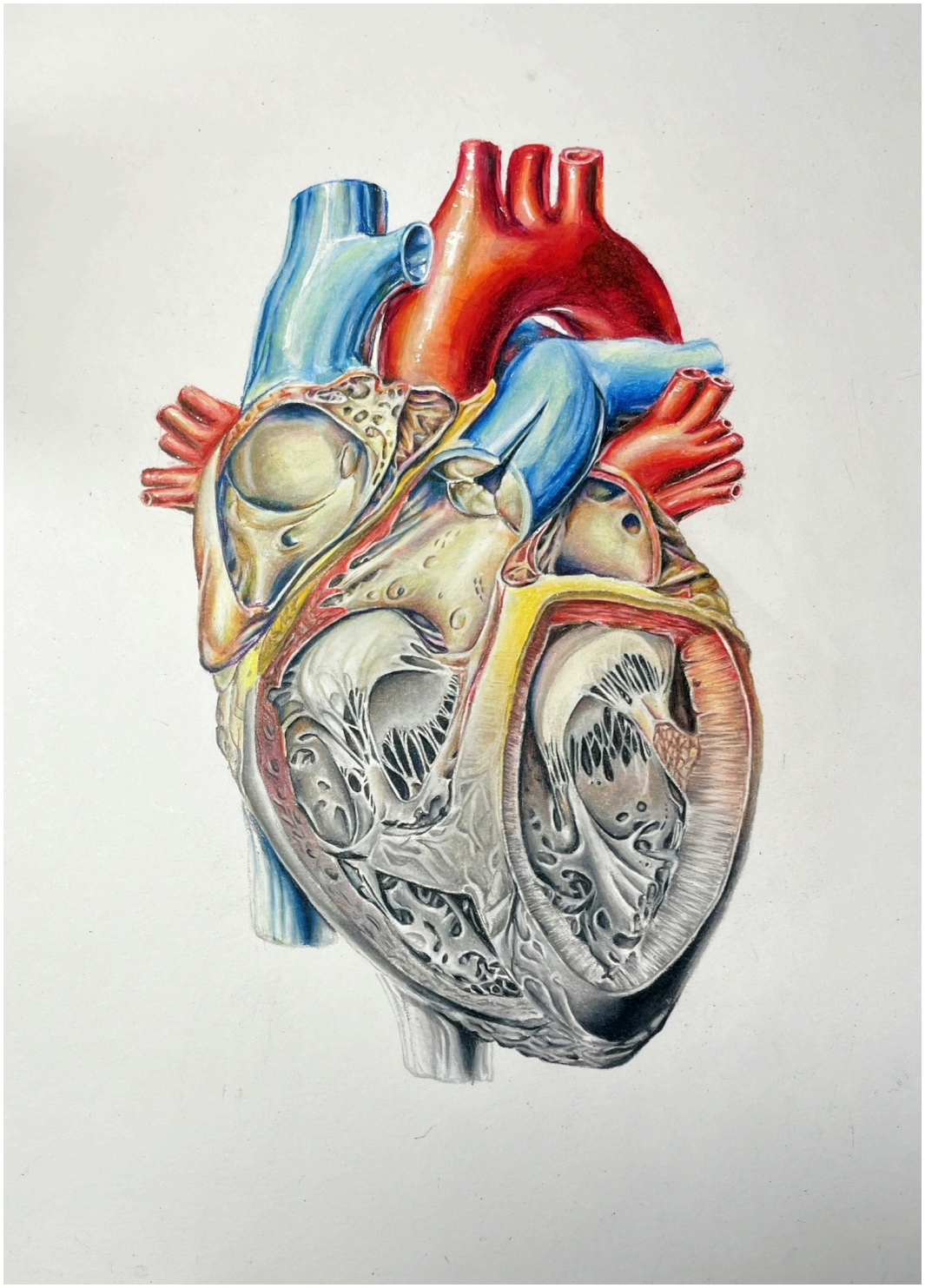
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CARDIOVASCULAR

The Human Heart

Leslie Gao
Queen's University



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Organ-on-a-Chip: No, it's Not a Snack

Bernardo Carlos Navarro

Columbia University

If you were presented with a drug and tasked with determining whether it could be therapeutic or safe for humans, what would you do? Would you give it to your next-door neighbor and record whether they go limp? Of course not! Well, hopefully not.

Naturally, safety should be your first concern, and the thought of jumping straight into human experimentation should seem reckless. However, prior to the mid-twentieth century, there were few regulations to ensure drug safety, often leading to devastating consequences. In the late 1950s, Thalidomide was widely prescribed to pregnant women as a safe way to treat nausea, but due to lax testing, over 10,000 children were born with phocomelia, a severe limb malformation disorder (Kim and Scialli, 2011). Cases like this highlight the dangers of haphazardly introducing foreign substances into the human body and justify the reality of current pharmaceutical testing. The rigorous modern drug development process begins with an array of chemical analyses, followed by progressively demanding stages of animal testing, and ultimately culminates in multiphase human clinical trials. The clinical trials are separated into four phases spanning from initially testing basic safety and dosage to eventually evaluating efficacy and side effects in increasingly larger and diverse populations, with each phase taking years to design, conduct, and analyze (U.S. Food and Drug Administration, 2018). Even at this final stage, nearly 90% of drug candidates still fail (Sun et al., 2022). As a result, the average production cycle for a single drug takes more than a decade and costs upwards of a billion dollars (Patheon, 2023). With this in mind, it's no wonder that researchers are searching for methods to expedite the process by incorporating human biology into earlier stages of testing.

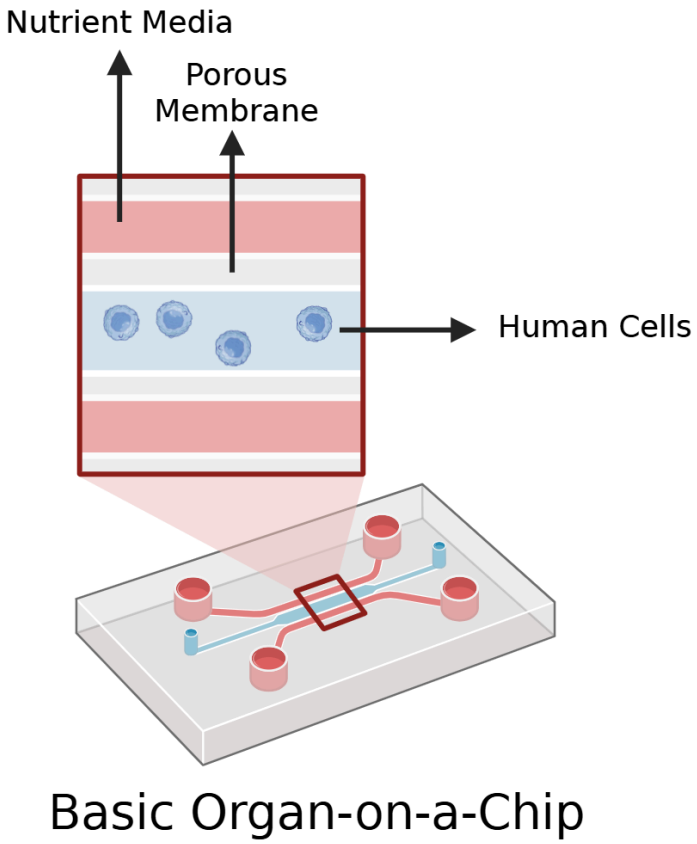


Fig. 1. General structure of OoC showing how nutrient fluid and human cells interact

Enter Organ-on-a-Chip (OoC) Technology—a remarkable innovation that merges biology and engineering to simulate the functions, structure, and biochemical environment of human organs on a miniature scale and completely separate from the body. First introduced in the early 2010s with the pioneering work by the Wyss Institute on a lung-on-a-chip, this technology is rapidly evolving as a promising tool for drug modeling (Huh et al., 2010). Often no bigger than a USB drive, OoCs contain a network of precise channels that work with fluids as small as one trillionth of a liter and a chamber lined with human cells sourced from either tissue donations or differentiated stem cells, as seen in Figure 1 (Leung et al., 2022). Like tiny blood vessels, these channels provide a continuous flow of nutrient-rich fluid over the cells so that they can function. At the same time, they also give scientists unique access and customizability over what is introduced to the cells, allowing them to systematically vary nutrients or drugs and directly observe cellular response in real time, enabling controlled analysis of drug effects without risking a human life.

As their name suggests, each chip is designed to emulate a specific organ. This is achieved not only by incorporating organ-specific cells and carefully controlled fluid environments that replicate nutrient delivery, but also mechanically. Modern chips have engineered features to replicate the defining characteristics of their organ, providing more realistic modeling. For example, a lung-on-a-chip provides a cyclic stretching motion on the cell tissue to mimic what occurs during breathing; a heart-on-a-chip uses a rhythmic pulse and electrical stimulation on the cells similar to how a heart beats; a gut-on-a-chip uses a controlled flow of nutrients to model the gut's interaction with food (Wyss 2010 & Singh et al., 2022).

> *Often no bigger than a USB drive, OoCs contain a network of precise channels that work with fluids as small as one trillionth of a liter*

Together, these features mean that OoC technology occupies a sort of limbo territory within drug modeling—they are more complex than traditional 2D tissue engineering typically done on petri dishes, which lack layered cells, realistic cell-on-cell interactions, and fluid flow, but are not nearly as biologically complete as living organisms or even organs themselves (Leung et al., 2022). While this position comes with limitations in replicating realistic organ responses, what OoC technology sacrifices in physiological relevance, it makes up for in improved investigation. Because OoC systems isolate specific tissues and function under a controlled setting, researchers do not have to account for the myriad of interacting biological systems in human patients that can introduce noise and variability. Factors such as metabolism, immune responses, and the interaction between organs can all obscure the effects of what researchers want to study. Instead, scientists are able to precisely vary variables such as oxygen levels or pH to test them one at a time, leading to more reproducible and clear experiments that make it easier to identify how a drug, toxin, or disease affects a specific biological process. Beyond merely controlling what is introduced into the cells, researchers also have the ability to swap out the cells themselves (Leung et al., 2022). As previously mentioned, the cells can come directly from a person's organ, meaning that researchers can better test sub-populations or unique patient profiles that might otherwise go unnoticed until the final phases of clinical trials. For example, cells derived from patients suffering from cystic fibrosis (an autosomal recessive disease) were used on OoC models to better study the effects of different therapies and pave the way towards more personalized medicine (Ogden et al., 2021).

For now, this marks just the beginning of OoC technology. The drug research field has yet to standardize its chip design, and some engineering challenges—such as material choices causing uncontrolled evaporation and leakage—are still being addressed and optimized. The Food and Drug Administration (FDA) has recently begun to show growing interest and engagement through its acceptance of its first OoC technology (a liver-on-a-chip) into the Innovative Science and Technology Approaches for New Drugs (ISTAND) Pilot Program (U.S. Food and Drug Administration, 2024). Here, the chip will be assessed for its efficacy and performance as a predictive tool for drug-induced liver toxicity, and if the results are positive, it could mark an important step toward formal integration and widespread approval for the technology. As expected, OoCs have already begun to evolve, with current designs linking different types of organ cells to create a "Body-on-a-Chip" (Singh et al., 2022). These advances not only hold promise in improving how we study drugs by introducing a safer and accessible alternative for observing human biological reactions, but also build on technology's core strengths in experimental control, reproducibility, and patient-specific customization. As researchers refine their designs and aim towards more ambitious modeling, OoC technology edges closer to a more efficient future where testing drugs might not require a patient at all—just a chip that mimics one.

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NEUROSCIENCE

Why Our Picture of Parkinson's Is Wrong

Maliha Rahman

Bronx High School of Science

When people think of Parkinson's disease, they often envision an older man with a shaking hand. A stereotype so ingrained, it shapes diagnoses, care, and even self-perception. This narrow image ignores the full reality of the disease and actively hurts people. Women get dismissed. Younger folks get laughed off. Non-motor symptoms get ignored for years. This stereotype has ultimately become a barrier to care as this disease doesn't just affect old men.

Parkinson's is a neurodegenerative disease that leads to a significant reduction in dopamine, a chemical that regulates movement; this causes symptoms such as tremors, stiffness, and slow movement (What Is Parkinson's?, n.d.). But these are only the motor symptoms-- the symptoms that everyone sees and thinks of when they hear about Parkinson's. Non-motor symptoms of Parkinson's include sleep problems, constipation, anxiety, depression, and even losing your sense of smell, all of these showing up 5-20 years before any shaking (Goldman & Postuma, 2014). Yet our cultural picture of Parkinson's is stuck on visible shaking in older men, which hides the people who do not fit that frame: women, younger adults, and people whose first symptoms are invisible.

> *A working mom's exhaustion just looks like burnout even though her brain's neurons and movement capabilities are slowly being destroyed.*

Women Pay the Price

Men get diagnosed twice as often, but women suffer longer with worse symptoms and less support (Cerri et al., 2019; Miller & Cronin-Golomb, 2010). Dropping estrogen levels after menopause accelerate brain cell loss and inflammation, unlike the protective effects estrogen provides earlier in life (Cerri et al., 2019). Women lose their biological protection from Parkinson's after hitting menopause, making them suffer more with faster disease progression compared to men. Despite this, men end up having better treatment simply because they get diagnosed more frequently.

Even though women suffer more, The Parkinson's Outcomes Project found that 20% of women have no regular caregiver, and those who are caregivers report less strain compared to men (Parkinson's Foundation, 2017). Women are often juggling kids or caring for anyone but themselves. A working mom's exhaustion just looks like burnout even though her brain's neurons and movement capabilities are slowly being destroyed.

When the default mental picture of Parkinson's is a retired grandfather, it becomes much harder for a mother, nurse, or teacher to be seen as a possible patient.

Young People Don't Fit Either

Parkinson's patients who are under 50 face brutal stigma, leading some to be "afraid to see how people look at [them]" (Crooks et al., 2025). Friends think it's attention-seeking, family thinks they're faking, and even doctors say it's psych issues first because no one expects Parkinson's before retirement age. This fear can keep patients hidden, delaying diagnosis by years while non-motor symptoms, such as violent dream enactment, deteriorate their sleep and work life. Non-motor symptoms strike first in young-onset cases, with REM sleep behavior disorder where patients physically act out violent dreams affects up to 50% of early PD cases, before tremors appear (Radad et al., 2023). By the time that tremors come along, years of possible treatment are lost.

Even though the younger population is very online, the media doesn't help either. Most fundraising ads for Parkinson's Disease depict the cane-shuffling grandpa, but never the 40-year-old fighting brain fog at work. The "old white

man" image becomes self-fulfilling: if you don't see yourself there, you don't seek care.

Time to Polish the Picture

Fixing how we see Parkinson's has to include fixing how we talk about stigma in the clinic, not just in public campaigns and advertisements (McDaniels et al., 2023). Even the best medications and surgeries don't fully work if doctors ignore how stigma drives social rejection, isolation, and "self-stigma", the case in which patients start believing they are a burden and avoid going out or asking for help. In other words, polishing the picture of Parkinson's is not just about changing stock photos: it's about training neurologists and primary care doctors to routinely ask about shame, loneliness, and fear of being seen, then offering counseling, support groups, and honest education to counter the false assumptions that keep people, especially younger patients, hidden.

We can change the picture, starting with what people see. Swap endless images of cane-shuffling grandfathers for the full reality: mid-career women powering through fatigue, young men dealing with a slipping balance, Asian elders sharing years of sleep troubles, not just close-ups of tremors. Foundations reflecting on Parkinson's should audit every brochure, website, and billboard until they reflect Parkinson's true face.

Representation, training, and education. Each rewrites the story so no one slips through the cracks of an outdated, biased image.

No More Excuses

We can't afford to keep this image of Parkinson's. Parkinson's hits diverse people with messy, early symptoms. Society must match that reality. For every mom mislabeled "tired," every young worker gaslit, every elder dismissed, updating the image isn't unnecessary. It's lifesaving.

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BIOETHICS

Brains in a Dish: The Looming Concerns of Brain Organoids

Chloe Hu

Jericho High School

A few years ago, journalists would have described brain organoids as just brain blobs in a dish. But in just the last year, brain organoid research has made tremendous advancements. At Johns Hopkins University, for example, researchers recently developed an organoid with tissues from each region of the brain, opening opportunities to explore treatments for neurological diseases that affect the entire brain, such as schizophrenia, autism, and Alzheimer's disease (Johns Hopkins University, 2025). Meanwhile, in Japan, researchers have recreated human neural circuits using assembloids, a combination of multiple organoids, to reveal the role of the thalamus in neural networks (Nagoya University, 2026). Similarly, Stanford neuroscientists have produced four neural organoids from different parts of the brain and spinal cord to form a linked sensory pathway, capable of detecting stimuli and transmitting information (Kim et al., 2025). Without doubt, brain organoids are a pioneering form of biotechnology in the expanding field of neuroscience. However, regardless of biomedical potential, is society capable of regulating such rapid and complex development? These recent advances highlight that brain organoids are progressing faster than society can ethically manage, leaving ambiguities as to what to do next.

Brain organoids are small, three-dimensional models of the human brain grown in the lab from human pluripotent stem cells. These unique cells can develop into other cell or tissue types, allowing researchers to mimic early brain development outside the human body. Organoids have gained attention for holding a notable advantage over animal models and 2D cells due to their complex cortical layers that host various neuronal populations and supporting cells that reflect human biology (Sun & Pan, 2025; Chen et al., 2022). Furthermore, organoids can serve as tools to study diseases and neurological development, offering novel insight into creating new treatments (Wang et al., 2025). However, the ethical question remains. With such fast progression of the field, it is questionable if advancements are truly advancements or rather exaggerations of technological potential that require further planning. The debate continues on the need for clear regulatory boundaries on experimentation and how far brain organoid development should be allowed to proceed.

> *Nowadays, news coverage has thrown around the term "mini-brains," riling up public concern about organoids' ability to develop consciousness and even feel pain*

Nowadays, news coverage has thrown around the term "mini-brains," riling up public concern about organoids' ability to develop consciousness and even feel pain (Hamilton, 2026; Hartung et al., 2024). Such uncertainty raises discussion on whether stem cell donors should be required to give informed consent or whether experimentation on conscious organoids would be to disregard their existence, violating ethical principles (Kataoka et al., 2024). However, brain organoids currently lack consciousness and are likely to stay that way in the near future, as various restrictions, such as anatomical resemblance and the absence of experience, still hinder further complexity and maturity (Kosik, 2024, Hamilton, 2026).

Taking a step further, scientists have considered implanting organoids into other species, which public attitudes reject, citing animal welfare, species identity, and ethical frame-

works of experiments. A key concern is how a human brain organoid would affect the animal's consciousness (Leslie, 2025). Previously, other Stanford neuroscientists demonstrated that human stem cell-derived organoids could be transplanted into rats during early development and integrated into sensory circuits to successfully produce sensory responses (Revah et al., 2022). With further technological development, there are growing concerns about the effects brain organoids could have on other animal species. One such development is organoid intelligence, the merging of brain organoids with artificial intelligence (Hartung et al., 2024). Whether by enforcing donor privacy or consent, it remains essential to hold research practices to ethical standards.

While it is true that brain organoids offer groundbreaking insights into a new era of neuroscience and technology, the field is simply moving too fast. If stakeholders do not hold necessary ethical conversations now, regulation will begin to trail behind as rapid development opens the door to unsafe or immoral experimentation that puts animal welfare or patient privacy at risk. Socioeconomically, claims that overestimate the potential of biotechnology can lead researchers to adopt experimental methods before they have been validated, potentially promoting misleading conclusions and resource depletion (Nature Reviews Bioengineering, 2024; Jarrell, 2019). It is not clear what the next step in organoid advancement will be, and whether that step is feasible and ethical. The scientific community should work with policymakers to formulate flexible guidelines for brain organoid research, considering ethical perspectives and public concern (Lavazza, 2023). Policymakers should invest in research cautiously and instead focus on reviewing ethics. Taking a slower step in advancing brain organoids will enable society to understand the true potential of brain organoids and their implications on entire communities.

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LFP batteries: The Chemistry That Waited for the Right Time

Satvik Chenna

Kognovate Education and Research, Bionest, Avishkaran (NIPER), Hyderabad, India



This podcast explores how Lithium Iron Phosphate (LFP) batteries, considered one of the most reliable batteries globally, rose to prominence. Lithium Iron Phosphate batteries were plagued with conductivity issues and less energy density as compared to other lithium-ion batteries. However, material innovations, patent battles, and manufacturing momentum altered their course. This podcast discusses how safety, costs, cycle life, and manufacturing scalability made LFP batteries the leaders in electric cars, public transit, and power storage. A science-based story of invention, where innovation is more about timing, practicality, and real-world adoption.

Scan to listen
Episode length 6:15
Below is the full script.

Opening Hook

To understand why LFP batteries matter today, it helps to think about time, not simply as dates on a timeline, but as the slow force that determines which technologies survive and which quietly disappear.

Section 1: The Battery History Lens

The history of batteries is full of technologies that initially appeared promising but eventually faded away. What makes LFP interesting is that it did the opposite. It waited.

The story begins in 1996 at the University of Texas at Austin, where John Goodenough identified lithium iron phosphate as a potential new cathode material. Goodenough would later receive the Nobel Prize for his contributions to the development of lithium-ion batteries.

At the time, most lithium-ion batteries relied on cobalt-based chemistries. Cobalt was expensive, difficult to source, and concentrated in only a few regions around the world. LFP offered an alternative. It used iron instead, a material that was inexpensive, abundant, and non-toxic. From a materials perspective, it almost seemed too good to be true.

Section 2: The Early Failure

That early promise quickly faded. The first LFP batteries suffered from extremely poor electrical conductivity. Electrons could not move efficiently through the material, which severely limited the amount of power the batteries could deliver.

In practice, this made the early LFP cells weak and inefficient. Most engineers concluded that LFP was scientifically interesting but commercially impractical.

As a result, the wider battery industry shifted its attention toward other chemistries.

Section 3: Patents, Power, and the Legal Wall

Instead of being aggressively developed within the United States, the patents were licensed out. They eventually became part of Hydro-Québec, which helped establish an international consortium to control the intellectual property.

The consortium adopted an extremely defensive legal strategy. Any Western company attempting to manufacture LFP batteries risked paying massive royalties or becoming trapped in lengthy and expensive lawsuits.

That legal uncertainty created a major problem. Battery production requires enormous upfront investment, and few companies were willing to build billion-dollar factories around a chemistry they could not fully control.

Section 4: A123 Systems and a Breakthrough

One company still attempted to move forward. A123 Systems, an MIT spin-off led by Yet-Ming Chiang, developed a solution to the conductivity problem using carbon coatings and nanotechnology.

This marked a genuine breakthrough. For the first time, LFP batteries could operate at high power.

However, A123 outsourced manufacturing to China in order to reduce costs and remain competitive. Lawsuits from the patent consortium soon followed. Although a settlement was eventually reached in 2011, the damage had already been done.

Years of legal conflict drained investor confidence and pushed A123 into bankruptcy. In 2012, the company's manufacturing expertise was ultimately acquired by China's Wanxiang Group.

Section 5: The China Split

Around this time, something important changed. The patent holders realized that enforcing their intellectual property rights within China was becoming extremely difficult.

Rather than continuing the legal battle, they reached a compromise with a group of manufacturers known as the China Alliance. Under this agreement, Chinese companies could produce LFP batteries without paying royalties, as long as the batteries were sold and used within China.

> *These policies guaranteed demand. Guaranteed demand enabled scale. And scale changed everything.*

That single decision created a sharp global divide. Outside China, LFP remained legally risky and expensive. Inside China, it became affordable, accessible, and increasingly attractive.

This is where time began to play its most important role.

Section 6: Scale as the Real Innovation

Throughout the 2010s, Chinese manufacturers continued producing LFP batteries at massive scale. Companies such as CATL and BYD did not treat LFP as a temporary solution. They treated it as infrastructure.

Their focus was not on dramatic scientific breakthroughs, but on refining manufacturing processes, improving consistency, and lowering costs year after year. Chinese government policy strengthened this strategy.

Domestic suppliers received battery subsidies, while major government programs excluded many foreign manufacturers. At the same time, China required a large share of its electric buses to use LFP batteries because of their safety and thermal stability.

These policies guaranteed demand. Guaranteed demand enabled scale. And scale changed everything.

As production volumes increased, costs fell dramatically. Manufacturing errors declined. Supply chains matured. Engineers gained experience.

None of this required a revolutionary scientific discovery. It required repetition.

Section 7: Why LFP Wins

While Western companies pursued higher-energy-density chemistries such as nickel manganese cobalt, Chinese manufacturers made a different bet: a battery that was cheaper, safer, and longer lasting.

This became the true innovation behind LFP. It was never the most impressive battery on a specification sheet, nor did it lead in energy density. Compared to many cobalt-based batteries, LFP stores less energy per kilogram.

For a long time, that made it appear inferior.

But batteries are not chosen in isolation. They are chosen based on their applications.

In electric buses, delivery trucks, taxis, and grid storage systems, energy density matters less than safety, lifespan, and cost.

LFP batteries can endure significantly more charge cycles. They are far less likely to catch fire. They tolerate abuse and extreme temperatures more effectively. And when manufactured at scale, they become dramatically cheaper.

Closing: The Context Changed

By the end of the 2010s, the consequences of this strategy could no longer be ignored. LFP batteries had become so inexpensive that they fundamentally changed global expectations around battery pricing.

Projects once considered financially unrealistic suddenly became possible.

At the same time, attitudes in the West began to shift. Consumers proved willing to trade maximum driving range for lower prices and greater safety.

LFP itself had not radically changed. What changed was the world around it.

As major patents began expiring globally, some as late as 2022, China had already built control over most of the LFP supply chain, from raw material processing to cathode manufacturing and final cell production. Even today, the vast majority of LFP cathode material is produced in China.

Thank you!

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EPIDEMIOLOGY

The Infrastructure of Survival: Integrating High-Performance Computing and SIR Frameworks into Global Health Policy

Why Are We Still Gambling with Lives When the Odds Are Not Good?

Domenica Pineda

Columbia University

In March 2020, predictive mathematical modeling done by the team at Imperial College London produced a forecast that, for better or for worse, was going to fundamentally change the planet's trajectory: 2.2 million. The models showed that without NPI, lethality as a result of COVID-19 in the United States alone would reach this threshold by the end of the month. Within forty-eight hours the forecasts were presented to global leaders, and borders across the world were closed, lockdowns were instituted, and one-third of the world's population was confined to their homes. The death toll would continue to be horrific, but mathematical modeling provided—rather literally, as we will see in the next paragraphs—the forecast we needed in order to survive.

And yet despite the IMF's forecasts that the overall impact to the global economy will exceed $12.5 trillion in cumulative losses by 2024, the technical tools that saved us are sorely underfunded. A future pandemic is inevitable—it's simply a question of when, and (probably) where, it will manifest. Climate-induced habitat shifting, massive deforestation, and rapid urbanization mean that we're seeing zoonotic spillover events occurring with ominous strength and frequency.

Even if we postulate the existence of specific and focused data "hubs," government funding for predictive infrastructure remains woefully outmatched against even the smallest existential threats. By continuing to bolster outdated IT infrastructure with "national intelligence" gathered from disparate datasets and human reporting—by collectively walking into the next modern epidemiological crisis with a 1980s-era IT medium—we condemn ourselves to reactive, rather than proactive, remediation.

The Utility of Predictive Analytics: From Theory to Intervention

Mathematical modelling is often mischaracterised as solely academic; when put to use, it is a powerful tool of public health intervention. The 2009 H1N1 influenza pandemic makes for a clear cut case study in such utility. Germann et al. (2006) showed models suggesting that with vaccinations prioritised in children, transmission could be curtailed and death rates reduced. Likewise, in January 2020 while fewer than 300 COVID-19 cases were reported officially, the Imperial College London model suggested that a couple of thousand in Wuhan may already have been infected. This pointed to the evidence the world would follow in turn.

> *A future pandemic is inevitable—it's simply a question of when, and (probably) where, it will manifest.*

At the heart of this prediction lies the **SIR model**, developed by Kermack and McKendrick in 1927. A population (N) is split between three dynamic groups: **Susceptible** *(S)*, **Infected** *(I)* and **Recovered** *(R)*. The course of any outbreak is characterised by an ordinary differential equations:

$$dS/dt = -\beta SI/N$$

$$dI/dt = \beta SI/N - \gamma I$$

$$dR/dt = \gamma I$$

These equations quantify fundamental biological interactions. The "generation" of new infections is determined by

the **transmission rate** (β) and the density of close contacts between susceptible and infected individuals (SI/N). Conversely, the transition from infected to recovered is dictated by the recovery rate (γ), a parameter largely dependent on the natural history of the specific pathogen. When simulated across large populations over time, these dynamics produce the "epidemic curves" that become a staple of public discourse during COVID-19 pandemic.

The Threshold of interventions: Mathematics Foundations

The SIR modelling paradigm is conceptually elegant, because it packages complex epidemic dynamics into a handful of governing parameters of interest. Most critical amongst those is the basic reproduction number (R_0), a dimensionless ratio defined by:

$$R_0 = \beta / \gamma$$

This dimensionless ratio represents on average the number of secondary infections generated by a primary case in a wholly susceptible population. If $R_0 > 1$, the pathogen is theoretically capable of continuous exponential growth and the aim of public health intervention is to introduce measures (vaccination, social distancing) that reduce the effective reproduction number to below 1 to drive the epidemic to extinction.

The friction of Application: Bridging Math and Reality

However, the mathematical beauty of the SIR abstraction is often dulled by the friction of its implementation in the real world. R_0 has a precise mathematical meaning, but in a crisis it only has operational meaning in proportion to how fast and honestly its data can be supplied to it. The bottleneck in the predictive power of modeling during COVID-19 pandemic became the infrastructure, the seamless system that allows surveillance, computing, and communication to combine in a consistent, just-in-time manner.

Systemic Gaps in Global Forecasting

Even with this power, the justification for modelling misfires globally was the "reactive response of systems" for three main reasons:

- **Data Availability and Latency Constraints:** Predictive models require access to real-time, high-fidelity data to remain relevant, yet many local health departments continue to rely on antiquated manual reporting methods. This "garbage in, garbage out" situation compels modelling teams to first clean these disparate records rather than produce a stockpile of real-time insights destined for action by legislators.
- **Computing Infrastructure and Scaling:** High-resolution simulations of urban density and demographic movement are computationally demanding. While the CDC Forecast Hub was a major leap forward toward ensemble modelling, it did not have the kind of sustained investment necessary to be run as a "high-performance national system."
- **The Human Capital Gap:** There aren't enough interdisciplinary experts who have feet in both worlds of "the rigorous maths of disease modelling plus the politics, bureaucracy and ambiguity of public health policymakers. Analysts have been forced to hack together dodgy technical workarounds.

Strategic Recommendations for Global Preparedness

Creating an effective global pandemic modelling system is projected to require $10 billion and $20 billion annually, following the "One Health" framework estimates by World Bank and WHO which estimate annual costs at $10.3 to $11.5 billion. Against cumulative $12.5 trillion COVID economic losses, this represents an important insurance policy against further catastrophe. This investment needs to be targeted on three pillars:

- **Mandate Real Time, Electronic Case Reporting:** We need to automate data reporting to all jurisdictions so that modelers can access epidemiological information quickly.
- **Scale Up High Performance Computing networks:** We need computational networks capable of running complex, multi-variable outbreak simulations in hours rather than days.
- **Professionalise the Policy and Modelling Interface**: Modelers of disease must be recruited, trained, paid, and embedded in public health agencies to

ensure that mathematical forecasts are turned into real-time actionables and informed political deliberation.

Stacking the Deck

Reducing the next pandemic's punch by 10% would yield economic savings that would far exceed that investment while saving lives. The need for this is not about economics; it is our obligation to defend those we love. We have seen these cards before. Will global leadership continue to be blind to how they are dealt—or will it back commitment to the technical and financial infrastructure to stack them in our favor?

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NEUROSCIENCE

From Scene to Synapse: Rethinking Film Education with Neurocinematics

Dylan Rateshwar

Jericho High School

Why does one scene grip an audience while another falls flat? In the discussion of pacing and payoff, film students tend to rely on intuition. They analyze cut sequences with fellow students, incorporate feedback, and have a shared vocabulary regarding tension, release, and character development. What neurocinematics offers is a fresh paradigm for film education. Through quantifiable neurological and biological indicators, it examines how narrative material shapes audience attention and emotion over time. It is imperative that such a paradigm be incorporated into film education, providing objective findings regarding how narrative affects the audience with each successive moment of the story.

The first question that neurocinematics asked was: "Do the brains of several individuals watching the same film behave in a similar pattern?" Researchers scanned the brains of volunteers and showed them edited scenes of commercial movies. The machine, called functional magnetic resonance imaging (fMRI), measured the flow of blood in the brain, which correlates with activity level. Hasson et al. (2008) found that for well-directed scenes, the activity levels of many areas of the brain increased and decreased in very similar ways for different individuals. They termed this "inter-subject correlation," which measured the strength of the synchronization of the viewers' brain activity. For scrambled versions of the same scenes, or scenes that lacked any kind of structure, the synchronization was reduced. Decisions about editing and audio influence the synchronization of activity across many brains, and this synchronization can be measured rather than simply hypothesized.

Although few film classrooms will ever have access to fMRI machines, the insights they provide can still shape the way film is taught. The key takeaway for a film education program is the recognition that collective response can serve as a substitute for collective engagement. Scientists have already found a way to express this concept using simpler variables. For instance, Maffei and Angrilli (2019) focused on the rate of blinking during the viewing of emotional video clips. Because blink rate decreases during periods of intense attention, it serves as a useful, low-cost index of engagement. The rate of blinking was found to be low during some points, such as the experience of awe or romantic feelings, but increased during the less engaging parts of the video (Maffei & Angrilli, 2019). For an editor, this would correlate to questions such as which images the eyes linger on, at which points the mind pauses, and the relationship between this data and the length of the shot or the use of camera movement.

> *"The movie was the same, but the focus in the brain was different.*

Other experiments demonstrate that movies engage attention in different ways depending on which aspects of the story resonate most strongly with a particular audience. Ou et al. (2022) applied the method of movie-watching fMRI to compare autistic and non-autistic individuals. They identified different "events" in the movie, where something important happened, and then analyzed the strength of the synchrony between brain activity in such events. In the parts of the movie where the audience's attention was focused on the feelings and social interactions of the characters, the synchrony between the autistic and the non-autistic viewers, as well as between the autistic viewers themselves, was lower in the parts of the brain responsible for social and emotional processing (Ou et al., 2022). However, in the parts where the audience's attention was focused on the objects and the physical space, the attention networks became more synchronized in the autistic viewers. The

movie was the same, but the focus in the brain was different. The role of neurocinematics here is to reveal which parts of the movie lead to joint social attention and which parts tend to be more spatial or object-related.

These insights extend beyond attention and social processing to show how stories can engage viewers differently depending on age and cognitive ability. Research by Niu et al. (2022) and Jangraw et al. (2023) extends these findings even further. Niu et al. (2022) concentrated on the thalamus, a relay station that forwards sensory input, and its connection with the larger cortical networks on the surface of the brain during the viewing of a story film by adults of varying ages. The strength of this thalamo-cortical connection varied according to age and was associated with fluid intelligence, the type of flexible problem-solving that underlies learning (Niu et al., 2022). In the second study, Jangraw et al. (2023) asked adolescents and young adults with varying reading competence to listen to long stories and measured the similarity of their individual brain activity patterns with those of all the others, and found that the activity patterns of the competent readers were highly similar across a broad network of regions (Jangraw et al., 2023). These two studies demonstrate that the same story can produce varying levels of synchronized neural activity depending on the viewer.

Individually, these results all point in the same direction. When movies and stories are shown in the same way they are actually experienced, continuously, emotionally, and in time, they leave behind identifiable patterns of shared attention, shared emotion, and shared meaning in the brain (Hasson et al., 2008; Jangraw et al., 2023; Maffei & Angrilli, 2019; Niu et al., 2022; Ou et al., 2022). These patterns do not measure the quality of movies or what constitutes good storytelling. They show where meaning is constructed within story structure: to bind the audience to the emotions of a character, focus attention on a detail, or alienate the audience. This kind of specificity is what film programs aim for in their discussion of beats, reversals, and the form of a scene. Neurocinematics provides an additional level of feedback for such discussions.

Film has always been defined by the shared experience of a roomful of strangers watching the same story unfold at the same time. Neurocinematics does not quantify that experience. Rather, it offers educators and students a new way to understand the way a series of cuts and sounds and story moments moves across a roomful of brains. Applying this way of thinking to film education would bring the way stories work on the brain into alignment with the way stories are currently taught.

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MEDICINE

Neuronanomedicine and the Future of Central Nervous System-Related Disorders

Aryan Nadimpalli

Kognovate Education and Research, Bionest, Avishkaran (NIPER), Hyderabad, India

Disorders of the brain and central nervous system (CNS) are quietly becoming one of the greatest health challenges of the twenty-first century. Alzheimer's disease, Parkinson's disease, epilepsy, stroke, multiple sclerosis, depression, brain tumors, chronic pain, and many other conditions now affect hundreds of millions of people worldwide. These illnesses not only affect health but also significantly diminish quality of life. They steal memory, movement, mood, independence, and often dignity. And yet, despite enormous scientific progress, meaningful breakthroughs in treating many brain disorders have been unfortunately slow. Consequently, healthcare systems strain under growing demand. The brain is protected by a powerful biological barrier that carefully controls what enters its delicate tissue. This barrier is called the blood-brain barrier (BBB) and is essential for survival, as it shields us from toxins, infections, and harmful substances circulating in the blood. But it also blocks most therapeutic drugs (Tang et al., 2024). Many medicines that look promising in laboratory tests aren't successful in real patients because they simply cannot pass this invisible barrier. Other drugs must be administered in high doses to ensure that a small amount reaches the brain, often flooding the rest of the body in the process. The result is a well-recognized pattern of limited benefits, repeated dose adjustments, and unwanted side effects. For decades, the main response to this problem has been to design stronger drugs. But no matter how advanced a medicine becomes, it remains limited if it cannot effectively reach its destination (Nance et al., 2022). This delivery problem has quietly become one of the biggest hidden barriers in modern neurology. **We are searching for cures for neurological disorders, yet we are sending them on a journey they are not equipped to complete.**

Neuronanomedicine offers a way out of this long-standing impasse. It uses extremely tiny carriers (sizes range smaller than 300 nm) to transport medicines through the bloodstream and guide them more effectively into the brain. These microscopic carriers help drugs overcome biological barriers such as the BBB, improve their circulation time, and increase the likelihood that they will reach the tissues they are meant to treat. Instead of administering medicines and hoping for the best, neuronanomedicine introduces direction, precision, and control (Teleanu et al., 2019). These nanoscale carriers can be engineered to interact with specific receptors on the BBB, enabling them to cross into brain tissue through mechanisms such as receptor-mediated transport or transcytosis. Once inside, they release therapeutic agents in a controlled manner at the target site (**Figure 1**).

> *After all, a powerful drug that cannot reach the brain is like a life-saving package that never arrives at its address.*

Consider epilepsy, where unpredictable seizures can disrupt education, employment, and social life. More consistent delivery of medication to the brain could mean fewer seizures and greater independence. In Parkinson's disease, where motor symptoms can vary significantly between medication doses, improved delivery could lead to steadier control of symptoms (Li et al., 2024). In depression and anxiety disorders, where finding the right medication can take months or years, better targeting could improve the reliability of treatment response. In Alzheimer's disease, where even small delays matter, more effective delivery could preserve memory and daily functioning for longer. This means patients have more time spent living rather than managing illness. It also means fewer hospital visits, less disruption to family life, and greater ability to plan for the future (Nagri et al., 2023). The benefits also extend beyond individual

patients. Better delivery means lower doses and fewer side effects, which can reduce long-term damage to organs such as the liver, kidneys, and heart. This can result in fewer hospital visits and lower overall healthcare costs. Neuronanomedicine is not just a theoretical concept. Early examples already exist. It has shown improved safety and fewer side effects compared with older versions of the same medicines. These early successes are modest, but they carry an important message: **the brain is not unreachable; it has simply been undeliverable with the tools we have traditionally used** (Waqar et al., 2025).

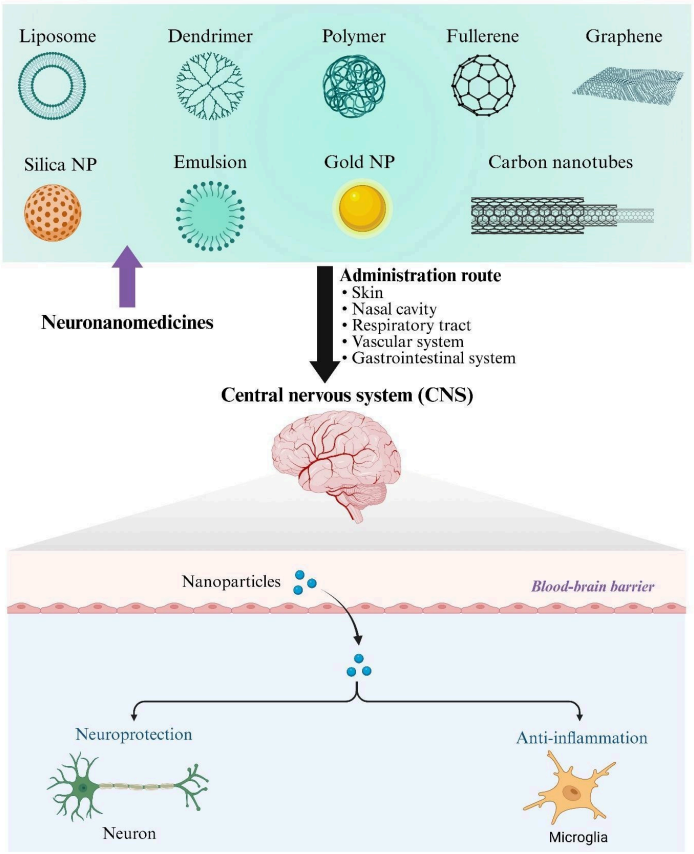


Figure 1. Conceptual framework of neuronanomedicine for CNS therapy.

Despite this promise, progress in brain drug delivery has been slow. One reason lies in how research priorities are set. Public attention, funding, and media coverage often focus on discovering new miracle drugs. Delivery science rarely receives the same recognition, even though it can determine whether a promising medicine succeeds or fails. After all, a powerful drug that cannot reach the brain is like a life-saving package that never arrives at its address. There is also a cultural aspect to consider. For years, medicine has been guided by the principle that stronger drugs and higher doses will solve difficult diseases. This approach has saved lives, but it has also reached its limits, especially in brain disorders (Gao et al., 2024; Deng et al., 2025). More force does not always mean better results. Often, it simply means more side effects and more suffering.

Neuronanomedicine represents a different philosophy. It values precision over pressure, guidance over flooding, and long-term quality of life over short-term intensity. It recognizes that effective treatment must also be humane treatment. As populations age worldwide, the urgency of shifting toward more precise and effective drug delivery approaches, such as neuronanomedicine, is growing. The number of people living with CNS-related disorders is rising faster than almost any other category of illness. These disorders shape not only individual lives but entire communities. For neuronanomedicine to fulfill its promise, coordinated action is needed. Governments must invest more in delivery-focused research. Further, regulatory bodies like the Food and Drug Administration (FDA) must modernize evaluation pathways to better accommodate the complexity of advanced delivery systems, enabling more efficient translation of safe and effective neuronanomedicines into clinical practice without compromising safety (Boyton et al., 2024; Sagar et al., 2025). Healthcare providers must be prepared to adopt new treatment platforms and integrate them into routine care.

The future of CNS care will not be shaped by a single miracle cure. It will be shaped by smarter systems such as neuronanomedicines that guide medicine to the places it is needed most. It has the potential to turn decades of laboratory discoveries into real-world applications and healing, to reduce suffering, and to give people more control over their lives (Yang, 2025). Neuronanomedicine is beginning to change that, and in doing so, it may redefine what modern medicine can finally achieve.

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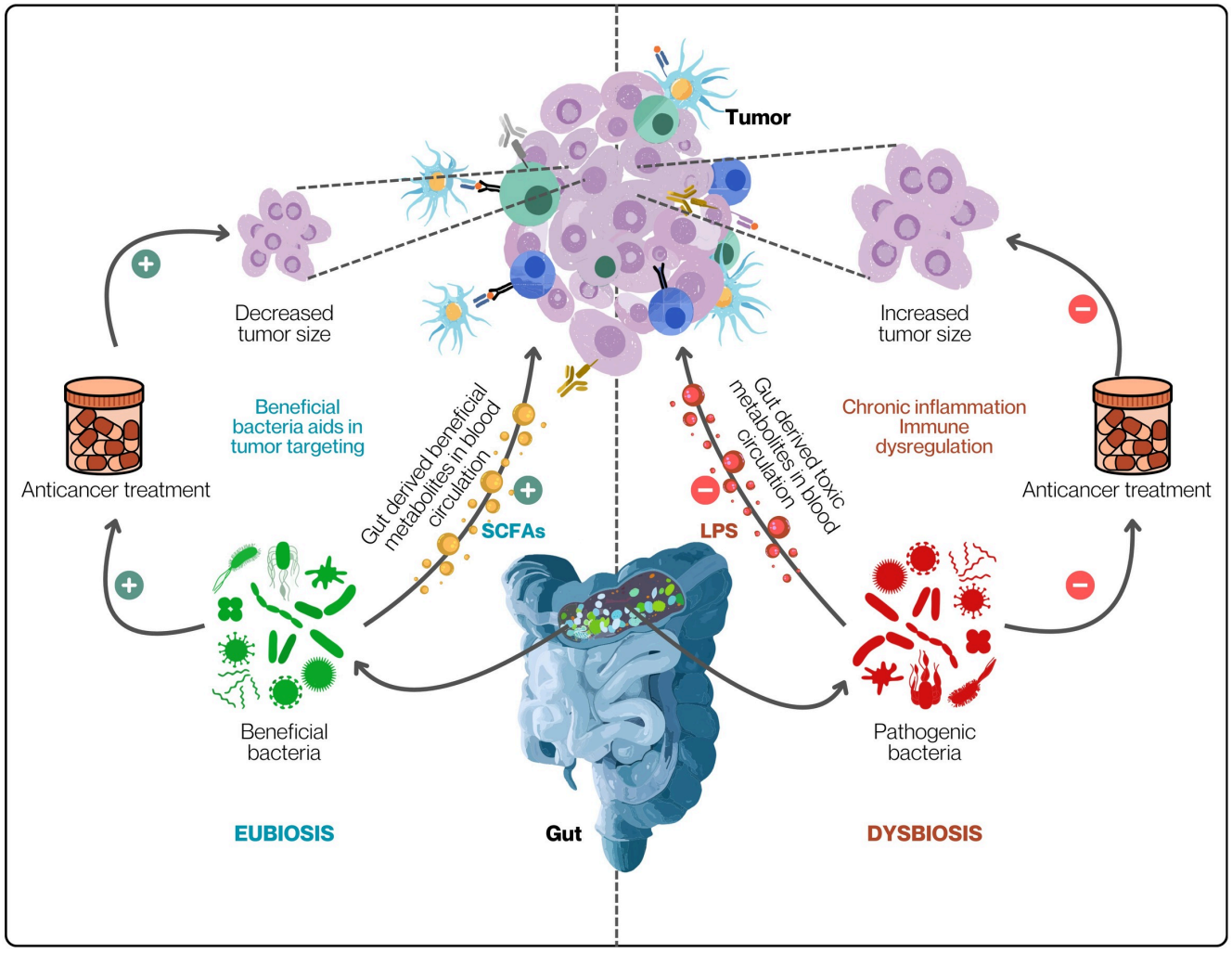
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Same Drug, Different Outcome

How Your Gut Microbiome Shapes Response to Cancer Therapy

Akshay Sandhyala
Kognovate Education and Research, Bionest, Avishkaran (NIPER), Hyderabad, India

This illustration shows how differences in the gut microbiome may influence patients' responses differently to the same anticancer drug. In patients with eubiosis, beneficial bacteria produce metabolites such as short-chain fatty acids (SCFAs) which help maintain the gut barrier integrity, reduce systemic inflammation, and enhance antitumor immunity through dendritic cell priming and $CD8^+$ T-cell function. This creates an immune-responsive tumor environment, improving treatment effectiveness and promoting tumor shrinkage. In patients with dysbiosis, pathogenic microbes increase inflammatory signals like Lipopolysaccharides (LPS) which can activate TLR4-NF-κB signalling and drive chronic inflammation, immune dysfunction, and therapy resistance, allowing tumors to persist or grow despite therapy.



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Microglia: Weaving the Link Between Hypertension and Alzheimer's

Sameera Rampertab

Sacred Heart Academy

Introduction

Is Alzheimer's just a brain disease? The simple answer is no. The complex answer takes us to the immune system, the unlikely force linking Alzheimer's to another life-threatening disease, hypertension. Alzheimer's is a neurodegenerative disorder that leads to memory loss and cognitive decline, eventually hindering the ability to conduct daily activities. Hypertension, commonly known as high blood pressure, is a condition noted for an excessive blood pressure against the artery walls and may maintain hidden roles in Alzheimer's (Carnevale et al., 2012). Traditionally, this link has been marked by considering interactions between the nervous and cardiovascular systems. But, what if the immune system harnesses the power to accelerate the link between hypertension and Alzheimer's? The catalyst facilitating the link between these deleterious conditions is none other than the brain's resident immune cells, the microglia.

Microglial-Induced Inflammation: A Double-Edged Sword

Inflammation is scientifically regarded as the body's natural defense mechanism against injury, infection, and toxins. When scraping your arm or fighting a cold, inflammation is the primary step on the road to recovery. Nonetheless, the inflammatory response is a double-edged sword: it protects during times of stress, but its perpetual presence provokes the transition to a harmful state, chronic inflammation. When such toxic conditions envelop the body, inflammatory signals are overstimulated, leading to chronic inflammation. Specifically, one type of immune cell in the brain, the microglia, clear toxins and damaged cells and refine neural connections imperative for learning and memory.

One of the major components triggering Alzheimer's is none other than the deleterious tau protein. The tau protein aids in forming insoluble neurofibrillary tangles, disrupting communication between neurons and impairing memory. Alzheimer's is triggered by the aggregation of amyloid-beta proteins (Aβ plaques) and neuron tangles, which disturb cell communication, induce cell death, and cause inflammation. The subsequent damage promotes cognitive decline. During the early stages of Alzheimer's, microglia attempt to engulf and destroy Aβ plaques and dead neurons during a resting state (Figure 1). As an integral component of the immune system, they release growth factors and anti-inflammatory signals to protect neurons (Miao et al., 2023). However, throughout the disease's progression, the microglia succumb to chronic activation via plaque, and the protective mechanisms it once possessed degrade. Although seemingly covert, these activated microglia trigger neuroinflammation in the release of pro-inflammatory proteins called cytokines (Miao et al., 2023). Over time, as the microglia remain activated, they lose their ability to clear plaque and the tau protein, leading to a buildup of plaque (Figure 1). **This emerging research on microglial function suggests that Alzheimer's disease is not only a neurological disorder but also an inflammatory one** (Miao et al., 2023).

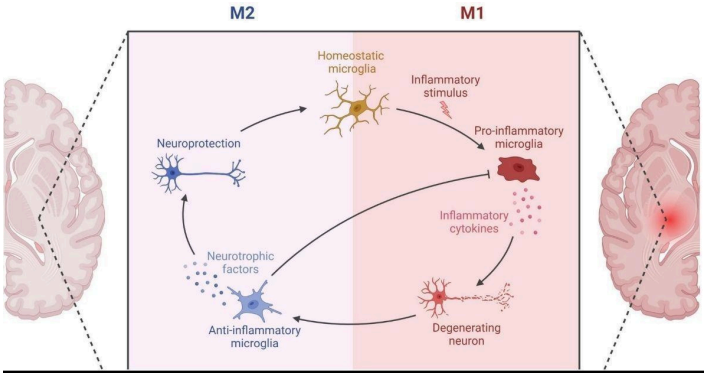


Figure 1: Microglia Transforming from Protective to Harmful in Alzheimer's (Miao et al., 2023)

Furthermore, microglia exert a virulent role in the context of hypertension, significantly exacerbating the risk for Alzheimer's. In paraventricular nucleus (PVN) neurons, a group of nerve cells that control hormones and homeostasis, microglia become activated when they detect excess ATP during hypertensive episodes (Figure 2). These activated microglia secrete pro-inflammatory signals, enhancing the body's "fight or flight" response (Rao and Peng, 2024). During this response, the nervous system prepares the body to fight or escape from danger, increasing heart rate and cortisol, the stress hormone. This chain reaction further elevates blood pressure, the genesis of a vicious cycle.

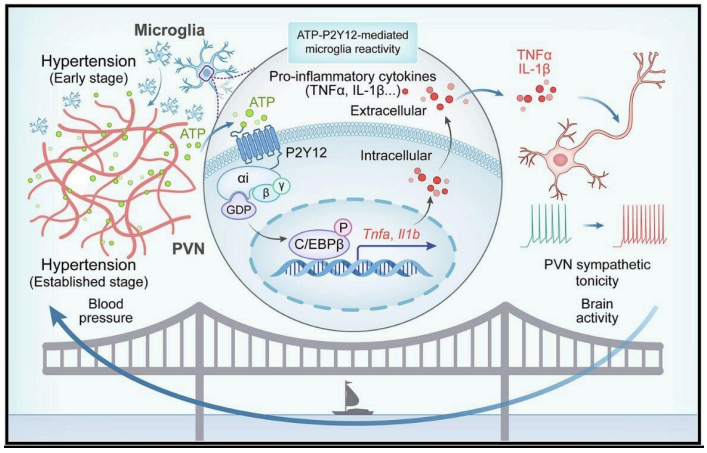


Figure 2: Microglia Responding to ATP During Hypertension (Rao and Peng, 2024)

Assessing the Link Between Alzheimer's and Hypertension: A Chain Reaction

Neuroinflammation has become the deleterious link between Alzheimer's and hypertension, endangering the body's homeostasis. Hypertension diminishes the brain's ability to clear Aβ plaques and can even increase their production, heightening neurotoxic conditions. Damaged blood vessels attributed to hypertension increase the permeability of the blood-brain barrier (BBB), a semipermeable membrane controlling what substances pass from the bloodstream to the brain (Santisteban et al., 2023). In turn, this allows the excessive penetration of pro-inflammatory proteins and microglia, stimulating chronic inflammation. Additionally, narrow blood vessels harm brain tissue and reduce blood flow, creating limited oxygen conditions that induce microglial activation (Mogi et al., 2025). These simultaneous effects — inflammation, neuronal death, vascular damage, protein accumulation — lead to cognitive decline, inducing memory loss, the primary symptom of Alzheimer's.

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Limitations and Implications: Are Pharmaceutical Strategies Enough for Modulation?

If hypertension is the catalyst expediting the onset of Alzheimer's, then harnessing the power to target microglia is indispensable to remediating this global health concern.

Several pharmaceutical methods have been administered to reduce hypertension and target microglia: ACEs, ARBs, and clopidogrel. Angiotensin-converting enzyme inhibitors (ACEs) and angiotensin II receptor blockers (ARBs), generally used separately, are both antihypertensives that aid in relaxing blood vessels and managing fluid balance. Both drugs widen blood vessels by blocking the hormone angiotensin II, combating Alzheimer's by decreasing inflammation and increasing blood flow to the brain (Lee et al., 2023). Additionally, clopidogrel, a blood thinner, inhibits a microglial receptor P2Y12, significantly reducing blood pressure spikes, while reducing Aβ plaque accumulation and the release of inflammatory markers (Maeda et al., 2021). Antihypertensives and clopidogrel are often used together to collectively control the inflammatory response.

However, studies have reported mixed results regarding the performance of these pharmaceutical drugs alone in mitigating Alzheimer's and microglial activity (Yasmin et al., 2025). While some studies report ARBs having a higher likelihood of decreasing Alzheimer's, others provide evidence that ACE inhibitors may lead to an increased dementia risk (Yasmin et al., 2025). Therefore, research has concluded that combining pharmaceutical interventions with lifestyle modifications would be the most effective treatment in combating the disease (Yang et al., 2022). Such lifestyle modifications, including avoiding pro-inflammatory foods, exercising consistently, managing stress, and

maintaining good sleep hygiene, reduce microglial activation and neuroinflammation and contribute to better heart health (Yang et al., 2022). This novel combinatory approach leverages the role of immune cells in Alzheimer's development to restore neurological function. By preventing microglial activation, we can strengthen the path to explore new treatment options for alleviating Alzheimer's and hypertension. It's time to revitalize our perception of Alzheimer's, a disease not limited to the brain but that impacts the whole body.

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From Ayurveda to Instagram: The Hype and Hope of Ashwagandha

Kylie Castillo

Columbia University

Let's be honest: if your health advice is coming from someone who also just posted a dance challenge or a "What I Eat in a Day" video, it's fair to ask some questions. In the last few years, the dietary supplement market has reached over sixty-nine billion dollars, with 5.2% growth in health supplements marketed through social media (Moloughney). Of these supplements, one that has risen to the top of the market is ashwagandha. Sold as a powder, softgel, pill, and even gummy bear, this supplement generated over an estimated 721.5 million USD in 2024 and is projected to reach 1.5 billion USD by 2033 (Grand View Research). With such massive popularity, the question remains—is ashwagandha yet another cash crop for alternative medicine or does it truly possess qualities that make it preferable to conventional medicine?

Ashwagandha, or *Withania somnifera*, isn't exactly new. A staple in Ayurvedic medicine, a traditional Indian system of medicine practiced for over 3,000 years, Ashwagandha has been historically used to help manage heightened emotions such as stress and sleep deprivation. Specifically, it is categorized as an "adaptogen," a type of substance thought to help the body handle stress more effectively. According to research from the NIH Office of Dietary Supplements, ashwagandha extracts have the possibility of reducing anxiety and improving sleep quality for certain people, which are appealing benefits in today's high-stress world (NIH Office of Dietary Supplements).

Compared to modern medicine, the contrast is striking. Drugs like benzodiazepines and SSRIs are made to directly influence brain chemistry. Benzodiazepines boost the effects of GABA, a neurotransmitter that helps quiet the nervous system and ease anxiety. SSRIs help balance serotonin levels, which can stabilize mood and reduce symptoms of depression. These medicines are powerful and well-tested, but they're not without drawbacks, ranging from drowsiness and weight gain to dependency or brain fog (Anxiety Association of America).

> *Many supplements thrive online by capitalizing on society's relentless pursuit of instant solutions.*

Ashwagandha takes a different approach. Rather than directly impacting neurotransmitter activity, it releases withanolides, a group of naturally occurring steroids which are believed to gently reduce cortisol levels and help balance other systems in the body. In a 60-day randomized, double-blind, placebo controlled study, 60 stressed but otherwise healthy adults were randomly allocated to take either a placebo or a standardized ashwagandha extract once daily. Those in the treatment group showed statistically significant reductions in morning cortisol levels, as well as improvements in anxiety scores, as measured by the Hamilton Anxiety Rating Scale (Lopresti et al.). Unlike benzodiazepines that directly influence GABA receptors, ashwagandha shows to be more supportive of our body's regulatory systems rather than overriding them.

So how does Ashwagandha truly stack up against modern medications like SSRIs and benzodiazepines? Clinical trials cited by the NIH suggest modest but promising effects. For instance, participants consuming ashwagandha in capsule form at daily doses ranging from 240 to 600 mg showed noticeable improvements in stress and sleep within several weeks. However, while promising, the NIH emphasizes that "study results are mixed, and more high-quality research is needed to confirm these findings" (Lopresti et al.). Thus, Ashwagandha should maintain a broader wellness ap-

proach, not act as a replacement for modern medicine. While modern medicine offers precise results, backed by years of testing, regulation, and clear guidelines, ashwagandha doesn't work as quickly or as predictably, but it takes a different path. Instead of targeting one detailed issue, it supports overall balance. For those dealing with everyday stress or trouble sleeping, it may offer relief without the stronger side effects that often come with pharmaceuticals.

It would be helpful for future research to compare how withanolides in ashwagandha differ from the mechanisms of modern medications, such as those that enhance GABA activity. Clarifying whether ashwagandha supports GABA function or primarily reduces stress hormones like cortisol could help define its proper use. Until then, its role should be seen as complementary to modern medicine, not a replacement.

It is difficult to say whether ashwagandha truly lives up to its social media hype. Many supplements thrive online by capitalizing on society's relentless pursuit of instant solutions. Though ashwagandha may not be a "magic bullet," its presence is beneficial as it challenges long-standing alternatives that have allowed large pharmaceutical companies to dominate the medicinal industry. Encouraging dialogue around supplements like ashwagandha challenges conventional medicine, promoting broader health perspectives and giving people more control over their health and well-being.

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