The Lord is like a strong tower, where the righteous can go and be safe.
Proverbs 18:10

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Be alert, stand firm in the faith, be brave, be strong.
1 Corinthians 16:13

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NCR, Calabarzon have most cases of 2 COVID-19 variants in PH — DOH

Metro Manila and Calabarzon (Cavite, Laguna, Batangas, Rizal, and Quezon) have the highest number of cases of B.1.1.7 and B.1.351 variants of the SARS-CoV-2 virus in the country, the Department of Health (DOH) said last May 5.


VERGEIRE

Health Undersecretary Maria Rosario Vergeire said Metro Manila has a total of 358 cases of the B.1.1.7 variant that was first detected in the United Kingdom, 602 cases of the B.1.351 first detected in South Africa, and 39 cases of the P.3 variant that was first reported in the Philippines.

Meanwhile, in Calabarzon, there are a total of 145 cases of the B.1.1.7, 121 cases of the B.1.351, and six cases of the P.3 variant.

"In NCR (National Capital Region) and Region 4A, nandito 'yung bulk of cases for both South African and UK variants," Vergeire said in an online press briefing.

But despite the increasing number of variant cases, Vergeire said the World Health Organization (WHO) still has yet to determine if there is already community transmission for these variants.

"We are only doing sampling. Ang sampling natin purposeful 'yan. Ibig sabihin we get samples from areas with clustering of infection, with linkages to specific individuals who turned positive

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DILG won't extend distribution of 'ECQ aid' in NCR Plus

The Department of the Interior and Local Government (DILG) will no longer extend the distribution of cash aid to residents affected by the strict community quarantines in the so-called National Capital Region (NCR) Plus.


MALAYA

DILG Undersecretary and spokesman Jonathan Malaya said they have given local government units (LGUs) in Metro Manila the giving of financial help came after the national government's declaration of enhanced community quarantine (ECQ) in the capital region as well as nearby provinces Bulacan, Rizal, Laguna, and Cavite from March 29 to April 12.

"We have not received any request for extension and according to [DILG] Secretary [Eduardo] Año, we will not grant any further extension because we have given them more than ample time to complete the distribution," Malaya said.

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Process for eliminating unneeded cells may also protect against cancer

For all animals, eliminating some cells is a necessary part of embryonic development. Living cells are also naturally sloughed off in mature tissues; for example, the lining of the intestine turns over every few days.

One way that organisms get rid of unneeded cells is through a process called extrusion, which allows cells to be squeezed out of a layer of tissue without disrupting the layer of cells left behind. MIT biologists have now discovered that this process is triggered when cells are unable to replicate their DNA during cell division.

The researchers discovered this mechanism in the worm C. elegans, and they showed that the same process can be driven by mammalian cells; they believe extrusion may serve as a way for the body to eliminate cancerous or precancerous cells.

"Cell extrusion is a mechanism of cell elimination used by organisms as diverse as sponges, insects, and humans," says H. Robert Horvitz, the David H. Koch Professor of Biology at MIT, a member of the McGovern Institute for Brain Research and the Koch Institute for Integrative Cancer Research, a Howard Hughes Medical Institute investigator, and the senior author of the study. "The discovery that extrusion is driven by a failure in DNA replication was unexpected and offers a new way to think about and possibly intervene in certain diseases, particularly cancer."

MIT postdoc Vivek Dwivedi is the lead author of the paper, which appears today in Nature. Other authors of the paper are King's College London research fellow Carlos Pardo-Pastor, MIT research specialist Rita Droste, MIT postdoc Ji Na Kong, MIT graduate student Nolan Tucker, Novartis scientist and former MIT postdoc Daniel Denning, and King's College London professor of biology Jody Rosenblatt.

In the 1980s, Horvitz was one of the first scientists to analyze a type of programmed cell suicide called apoptosis, which organisms use to eliminate cells that are no longer needed. He made his discoveries using C. elegans, a tiny nematode that contains exactly 959 cells. The developmental lineage of each cell is known, and embryonic development follows the same pattern every time. Throughout this developmental process, 1,090 cells are generated, and 131 cells undergo programmed cell suicide by apoptosis.

(NCR... from page 1)

for these variants," said Vergeire.

"WHO, until now, cannot give that classification yet because they need further studies so that we can be able to determine if there is community transmission already for these variants," she added.

The three variants of concern, such as the B.1.1.7, B.1.351, and the P.1 variant have been associated with higher transmissibility of the virus while initial studies also showed that the B.1.351 variant may have a potential impact on vaccine efficacy.

(DILG... from page 1)

According to him, the distribution of cash aid in Metro Manila was 75 percent done, which means over P8.4 billion of the assistance fund were already given to more than 8.4 million beneficiaries.

Malaya said that among LGUs in NCR, Caloocan City was leading in the cash aid distribution with 96.31 percent accomplishment, trailed by Quezon City with 94.96 percent, Mandaluyong City with 92.51 percent, and Navotas City with 90.68 percent.

Laguna, he also said, has already completed cash aid distributions to 81.29 percent of its total beneficiaries while Bulacan, Rizal, and Cavite have handed out the financial assistance to 67.22 percent, 64.61 percent, 57.82 percent of recipients, respectively.

EXTRA-JUDICIAL SETTLEMENT OF ESTATE OF THE DECEASED ANDRES FUSTER NIETO With WAIVER OF RIGHTS AND DONATION

NOTICE is hereby given that the estate of the late **ANDRES FUSTER NIETO** who died intestate on October 19, 1993 at Sydney, Australia, consisting of a 1/2 conjugal share over a certain parcel of land without improvement located at Barrio Molino, Municipality of Bacoor, Province of Cavite, covered by Transfer Certificate of Title Nos. T-70419 and T-70420, containing areas of TWO HUNDRED FORTY (240) SQUARE METERS and TWO HUNDRED FORTY (240) SQUARE METERS, respectively, has been adjudicated and extra-judicially settled by and among his heirs pro indiviso with waiver of rights, interest and participation in share/portion in the above-mentioned parcel of lands and donation in favor of Danilo Romero Nieto, Joyce Romero Nieto and Ismael Romero Nieto, their heirs, assignees and successors-in-interest on March 28, 2017 at City of Dasmariñas, Cavite, Philippines before Notary Public Atty. Candido P. Villanueva and entered in his Notarial Register as Doc. No. 294; Book No. 59; Page No. III; Series of 2017.

(Sgd.) **Servicing Spouse-Heir and Cheryl V. Torres as Attorney-in-fact of Danilo Romero Nieto, Joyce Romero Nieto and Ismael Romero Nieto**

Publication : DIYARYO KABITENYO
Dates : April 26, May 3 & 10, 2021

Republic of the Philippines
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MUNICIPALITY OF TANZA
Province of Cavite

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R.A. 10172

NOTICE TO THE PUBLIC

CCE-0013-2021 Date: April 30, 2021

In compliance with the publication requirement and pursuant to OCRG Memorandum Circular No. 2013-1 Guidelines in the Implementation of the Administrative Order No. 1, Series of 2012 (IRR on R.A. 10172), Notice is hereby served to the public that **HEIDI T. CENIZAL** has filed with this Office, a petition for CORRECTION OF ENTRY IN CHILD'S SEX from "**MALE**" to "**FEMALE**", in the Certificate of Live Birth of one HEIDI TOLEDO CENIZAL, who was born on January 26, 1985 at Tanza, Cavite of parents Edilberto Esguerra Cenizal & Amelia Esteban Toledo.

Any person adversely affected by said petition may file his/her written opposition with this Office not later than **May 17, 2021**.

(Sgd.) **MA. THERESA J. CESA**
Municipal Civil Registrar

DIYARYO KABITENYO - May 3 & 10, 2021

No guy has a magic.
Magic is in the heart of the girl loving the guy who can send her whole being up in 'Cloud Nine' even with the mere touch on her fingertips.
- Arnold Barco

EXTRAJUDICIAL SETTLEMENT OF ESTATE

NOTICE is hereby given that the estate of the late **IRENE Y. JAMERA** who died intestate on February 2, 2021, consisting of a certain sum of money deposited at the Bank of Philippine Island (BPI), located at 0743 Eastwood City, Libis, Quezon City under Savings Account No. 007431-0234-41 has been adjudicated and extrajudicially settled by and among her heirs on March 22, 2021 at Bacoor City, Cavite, Philippines before Notary Public Atty. Vivien Lucido Noble and entered in her Notarial Register as Doc. No. 101; Page No. 22; Book No. 4; Series of 2021.

(Sgd.) **All Heirs**

Publication : DIYARYO KABITENYO
Dates : May 3, 10 & 17, 2021

EXTRA JUDICIAL PARTITION OF ESTATE WITH WAIVER OF RIGHTS

NOTICE is hereby given that the estate of the late **RONALD B. LOBATON** who died intestate on April 6, 2021 in Cavite City, Philippines, consisting of Savings Account No. 2428100333012 maintained with the Philippine National Bank (PNB), Cavite City Branch has been adjudicated and extra-judicially settled by and among his heirs with waiver of rights in favor of ROMER S. LOBATON and ROMELYN S. LOBATON on April 27, 2021 in the City of Cavite, Philippines before Notary Public Atty. Antonia B. Cabuco and entered in her Notarial Register as Doc. No. 520; Page No. 105; Book No. LXV; Series of 2021.

(Sgd.) **All Heirs**

Publication : DIYARYO KABITENYO
Dates : May 3, 10 & 17, 2021

Stem cells create early human embryo structure in advance for fertility research

Exeter scientists have discovered a simple, efficient way to recreate the early structure of the human embryo from stem cells in the laboratory. The new approach unlocks news ways of studying human fertility and reproduction.

Stem cells have the ability to turn into different types of cell. Now, in research published in Cell Stem Cell and funded by the Medical Research Council, scientists at the University of Exeter's Living Systems Institute, working with colleagues from the University of Cambridge, have developed a method to organise lab-grown stem cells into an accurate model of the first stage of human embryo development.

Republic of the Philippines
MUNICIPAL CIVIL REGISTRY OFFICE
MUNICIPALITY OF TANZA
Province of Cavite

Publication Notice
R.A. 10172

NOTICE TO THE PUBLIC

Date: May 07, 2021

CCE-0015-2021

In compliance with the publication requirement and pursuant to OCRG Memorandum Circular No. 2013-1 Guidelines in the Implementation of the Administrative Order No. 1, Series of 2012 (IRR on R.A. 10172), Notice is hereby served to the public that **CJ A. DEL ROSARIO** has filed with this Office, a petition for CORRECTION OF ENTRY IN CHILD'S SEX from "MALE" to "FEMALE", in the Certificate of Live Birth of one CJ ARCON DEL ROSARIO, who was born on December 03, 1998 at Biga, Tanza, Cavite of parents Dionisio A. Del Rosario & Soledad P. Arcon.

Any person adversely affected by said petition may file his/her written opposition with this Office not later than **May 24, 2021**.

(Sgd.) **MA. THERESA J. CESA**
Municipal Civil Registrar

DIYARYO KABITENYO - May 10 & 17, 2021

EXTRAJUDICIAL SETTLEMENT OF ESTATE OF SPOUSES EPIMACO A. VELASCO and YOLANDA YMSON

NOTICE is hereby given that the estate of the late **Spouses EPIMACO A. VELASCO and YOLANDA YMSON** who both died intestate on January 27, 2014 and on March 10, 2014, respectively, both residents of Tanza, Cavite until the time of their death, consisting of a parcel of land without improvement erected thereon, identified as Lot No. 1088, located in Barangay Santol, Tanza, Cavite, covered by Transfer Certificate of Title No. T-64368, of the Registry of Deeds of Cavite, with a total area of FORTY FIVE THOUSAND EIGHT HUNDRED FIFTY FIVE SQUARE METERS (45,855), more or less, has been adjudicated and extrajudicially settled by and among their heirs on December 7, 2020 in Tanza, Cavite, Philippines before Notary Public Atty. Julius B. Arca and entered in his Notarial Register as Doc. No. 485; Page No. 97; Book No. XXXIX; Series of 2020.

(Sgd.) **EILEEN YVONNE VELASCO-SANTOS**
(for herself and as Attorney-in-fact of her siblings namely: Eric Y. Velasco, Maria Therese Yasmin Velasco-Bunez and Erlissa Yvette Velasco-Foster) and MARIA ASUNCION R. FORTIT (Attorney-in-fact of Erwina Velasco-Javier)

Publication : DIYARYO KABITENYO
Dates : May 10, 17 & 24, 2021

Targeted methods to control SARS-CoV-2 spread

At the beginning of the COVID-19 pandemic, intense social distancing and lockdown measures were the primary weapon in the fight against the spread of SARS-CoV-2, but they came with a monumental societal burden. New research from the Center for the Ecology of Infectious Diseases and the College of Public Health at the University of Georgia explores if there could have been a better way.

Published in the journal Proceedings of the Royal Society B, the research analyzes more palatable alternatives to the kind of social distancing mandates that threw a wrench at how businesses, schools and even family gatherings work. The alternatives -- widespread testing, contact tracing, quarantines, certification for non-infected people and other public health policy measures -- can slow the spread when combined together, but only with significant investments and broad public compliance.

"I understand why government leaders quickly enacted strict social distancing mandates as the COVID-19 pandemic was rapidly spreading in 2020," said lead author John Drake, director of the Center for the Ecology of Infectious Diseases and Distinguished Research Professor in the Odum School of Ecology. "This was the best that we could do at the time. However, school and workplace closures, gathering limits and shelter-in-place orders have had extreme economic consequences. These are harsh, and we really need to find alternative solutions."

Drake worked with other researchers to develop two models. One targeted how to find infected people to limit transmission through active case finding (through testing of at-risk individuals), thorough contact tracing when cases arise, and quarantines for people infected and their traced contacts.

The second model focused on a strategy of limiting exposure by certifying healthy individuals.

"Each model was tested independently and in combination with general non-pharmaceutical interventions (NPIs)," said co-author Kyle Dahlin, a postdoctoral associate with the center.

For this study, those interventions were defined as behavioral or generalized interventions that can be broadly adopted, such as wearing a face mask, hand washing, enhanced sick leave, micro distancing and contactless transactions.

"When we run the model to evaluate the effectiveness of only using social distancing measures, like workplace closures, after the onset of the first wave, approximately half of the population eventually became infected," said study co-author Andreas Handel, associate professor of biostatistics and epidemiology in UGA's College of Public Health who helped design the models.

Focused ultrasound enables precise noninvasive therapy

Carnegie Mellon University's He Lab is focusing on noninvasive neuroengineering solutions that not only provide diagnostic techniques, but also innovative treatment options. Their latest research has demonstrated that noninvasive neuromodulation via low-intensity ultrasound can have cell-type selectivity in manipulating neurons.

Parkinson's Disease, epilepsy and insomnia are just a few of the neurological disorders that use neuromodulation treatment techniques today. Neuromodulation delivers controlled physical energy to the nervous system to treat and improve patients' quality of life. Current neuromodulation approaches, while effective, bring both drawbacks and limitations.

"Deep brain stimulation, which is highly successful, but an invasive form of electric stimulation through implanted electrodes, is one example of how neuromodulation is being used in a clinical setting today," explained Bin He, professor of biomedical engineering at Carnegie Mellon University. "Medical professionals have also used noninvasive transcranial magnetic stimulation and transcranial current stimulation, both of which lack the ability to specifically focus on the neuro-circuit level. My group is interested in helping to develop a more effective and completely noninvasive alternative."

Low-intensity transcranial focused ultrasound, or tFUS, is an emerging and fully reversable neuromodulation technology. It is noninvasive, precise, and it does not require surgery. During tFUS neuromodulation, pulsed mechanical energy is transmitted through the skull, with high spatial resolution and selectivity, at highly-targeted brain regions, which can be steered to elicit activation or inhibition through parameter tuning.

In work recently published in Nature Communications, He's group demonstrated, for the first time, that specific cell types can be targeted through tFUS neuromodulation. Their study found that excitatory neurons showed high sensitivity to ultrasound pulse repetition frequency, while inhibitory neurons did not.

This finding is significant, because it demonstrates the first capability for a noninvasive neuromodulation technique to modulate a selected cell subpopulation, using a technique that can be directly translated for human use. With the demonstrated capability of tFUS to activate excitatory or inhibitory neurons, future applications may lead to precise targeting of brain circuits using focused ultrasound energy, and activate or inhibit selected sub-populations of neurons by tuning ultrasound parameters.

"As a result of our research, we obtained direct evidence that different neuron populations unequally respond to ultrasound stimulation in the brain," said Kai Yu, co-first author of the paper and a research scientist in He's lab at Carnegie Mellon University. "We identified a critical stimulation parameter that is able to tune the balance between excitatory and inhibitory neuronal activities, and we conducted thorough control experiments to support these valuable neuroscience findings."

The application of this research has broad implications; it's not just limited to one disease. For many people suffering from pain, depression and addition, He believes non-invasive tFUS neuromodulation could be used to facilitate treatment.

"If we can localize and target areas of the brain using acoustic, ultrasound energy, I believe we can potentially treat a myriad of neurological and psychiatric diseases and conditions," said He. "This type of treatment option has great potential to shift what doctors study in medical school and go on to practice. Of course, a noninvasive, precise, reversive treatment option also presents endless benefits for patients. My dream would be to make everything noninvasive."

He's next goal is to further develop the tFUS neuromodulation technology with increased spatial resolution and focality, and directly test the applicability of tFUS to treat brain conditions in humans.

Restricting growth, spread of head and neck cancers

Researchers from the UCLA School of Dentistry have discovered a key molecule that allows cancer stem cells to bypass the body's natural immune defenses, spurring the growth and spread of head and neck squamous cell cancers. Their study, conducted in mice, also demonstrates that inhibiting this molecule derails cancer progression and helps eliminate these stem cells.

Published in the journal Cell Stem Cell, the findings could help pave the way for more effective targeted treatments for this highly invasive type of cancer, which is characterized by frequent resistance to therapies, rapid metastasis and a high mortality rate.

Cancer stem cells, also known as tumor-initiating cells, are considered to be the original source of cancerous tissues – the cells that give rise to all other cancer cells. Their ability to survive and proliferate in the early stages of cancer development, as well as during tumor growth and metastasis, suggests they have an intrinsic ability to evade detection by the body's immune surveillance system. The researchers set out to better understand how and why this happens.

When the immune system is functioning properly, the body's natural infection-fighting T cells help to identify and ward off carcinogenic cells, foreign viruses and other invaders. However, it is known that some cancer cells elude this immune response by means of protein molecules on their surface known as "checkpoints," which bind to similar molecules on the T cells, essentially nullifying the immune cells' cancer-killing capabilities.

To help rectify this, immunotherapy drugs called checkpoint inhibitors can be administered; these drugs turn off the cancer cells' checkpoint receptors, allowing T cells to perform their normal job. In several types of cancer, including melanoma and non-small cell lung cancer, this approach has proven effective, decreasing the size of tumors and slowing their spread. Yet results for head and neck squamous cell carcinomas have been mixed, indicating that something else may be occurring that mutes the immune system's response.

To begin the study, the researchers tested a common checkpoint inhibitor that uses anti-PD1 antibodies on a well-defined mouse model of head and neck squamous cell carcinoma. The drug, they found, did very little to slow the spread of the cancer.

At the same time, they discovered that cancer stem cells in head and neck tumors had a notably elevated expression of the gene CD276, which encodes a protein molecule on the cell surface. They also found that CD276 expression was highest along the outer layers of tumors, suggesting that the CD276 molecule functions as a checkpoint that shields both the stem cells and cells in the interior of the tumor from the body's T cell response to the cancer.

Similar to the use of checkpoint inhibitors, the researchers next administered anti-CD276 antibodies to a mouse model of the disease to see if this treatment could turn off the checkpoint and inhibit the growth and spread of the cancer. After a month, they witnessed a significant decrease in the number of cancerous lesions and cancer stem cells.

"Not only did we see a reduction in cancer stem cells and tumors in our model when we introduced the CD276 antibodies, but we also noticed that the total number of tumors that metastasized to the lymph nodes was significantly reduced," said Dr. Cun-Yu Wang, the study's corresponding author and a professor of oral biology and medicine. "We were able to show that by blocking the gene CD276, we could effectively stop the growth of tumors derived from cancer stem cells."

Dr. Paul Krebsbach, dean of the UCLA School of Dentistry and a study co-author said, "These findings suggest that by focusing our attention on the CD276 gene and the immune response process, there is the potential for promising preventive therapeutic approaches against head and neck squamous cell carcinoma."

The work was supported by grants from the National Institute of Dental and Craniofacial Research, part of the National Institutes of Health.

Our immune systems blanket the SARS-CoV-2 spike protein with antibodies

The most complete picture yet is coming into focus of how antibodies produced in people who effectively fight off SARS-CoV-2 work to neutralize the part of the virus responsible for causing infection. In the journal Science, researchers at The University of Texas at Austin describe the finding, which represents good news for designing the next generation of vaccines to protect against variants of the virus or future emerging coronaviruses.

Previous research focused on one group of antibodies that target the most obvious part of the coronavirus's spike protein, called the receptor-binding domain (RBD). Because the RBD is the part of the spike that attaches directly to human cells and enables the virus to infect them, it was rightly assumed to be a primary target of the immune system. But, testing blood plasma samples from four people who recovered from SARS-CoV-2 infections, the researchers found that most of the antibodies circulating in the blood -- on average, about 84% -- target areas of the viral spike protein outside the RBD -- and, apparently, for good reason.

"We found these antibodies are painting the entire spike, both the arc and the stalk of the spike protein, which looks a bit like an umbrella," said co-corresponding author Greg Ippolito, who is a research associate professor in UT Austin's Department of Molecular Biosciences and an assistant professor of oncology at the university's Dell Medical School. "The immune system sees the entire spike and tries to neutralize it."

Many of these non-RBD-directed antibodies the team identified act as a potent weapon against the virus by targeting a region in a part of the spike protein located in what would be the umbrella's canopy called the N-terminal domain (NTD). These antibodies neutralize the virus in cell cultures and were shown to prevent a lethal mouse-adapted version of the virus from infecting mice.

The NTD is also a part of the viral spike protein that mutates frequently, especially in several variants of concern. This suggests that one reason these variants are so effective at evading our immune systems is that they can mutate around one of the most common and potent types of antibody in our arsenals.

"There's an evolutionary arms race going on between the virus and our immune systems," said Jason Lavinder, research associate in the McKetta Department of Chemical Engineering and co-corresponding author of the new study. "We're all developing a standard immune response to this virus that includes targeting this one spot and that's exerting selective pressure on the virus. But then the virus is also exerting its evolutionary strength by trying to change around our selective immune pressures."

Despite these maneuvers by SARS-CoV-2, the researchers said about 40% of the circulating antibodies target the stalk of the spike protein, called the S2 subunit, which is also a part that the virus does not seem able to change easily.

"That's reassuring," Ippolito said. "That's an advantage our immune system has. It also means our current vaccines are eliciting antibodies targeting that S2 subunit, which are likely providing another layer of protection against the virus."

That's also good news for designing vaccine boosters or next-generation vaccines against variants of concern, and even for developing a vaccine that can protect against future pandemics from other strains of the coronavirus.

"It means we have a strong rationale for developing next-generation SARS-CoV-2 vaccines or even a pan-coronavirus vaccine that targets every strain," Ippolito said.

UT Austin researchers are among several in the world now aiming to develop a single coronavirus vaccine to fight infection from all coronaviruses, not just SARS-CoV-2.

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Novel CBD analog shows promising pain-halting effects in mice

For patients with chronic pain, ineffective treatments, lowered work productivity, and other factors often coalesce, fueling feelings of hopelessness and anxiety and setting the stage for even bigger problems, including substance use disorders. In 2017 alone, some 18 million Americans misused prescription pain relievers over the course of the previous year. In many of these instances, patients suffering from chronic pain became addicted to prescription opioids.

In addition to being highly addictive, many studies suggest that prescription opioids do not effectively control pain over the long term, and hence researchers have been exploring various alternatives, including cannabidiol (CBD). CBD is a non-psychoactive substance derived from the Cannabis plant.

Studies have shown that while CBD reduces pain sensation in animals, its ability to do so in humans is limited by low bioavailability, the extent to which the drug successfully reaches its site of action. Now, new work by scientists at the Lewis Katz School of Medicine at Temple University suggests this obstacle may be overcome by a novel CBD analog known as KLS-13019.

"In a mouse model of chemotherapy-induced peripheral neuropathy (CIPN), we've been able to show for the first time that KLS-13019 works as well as, if not better than, CBD in preventing the development of neuropathy and reversing pain sensitivity after pain has been established," said Sara Jane Ward, PhD, Assistant Professor of Pharmacology at the Katz School of Medicine and senior investigator on the new study. The findings were published online April 6 in the British Journal of Pharmacology.

Gene therapy in Alzheimer's disease mouse model preserves learning and memory

Researchers at University of California San Diego School of Medicine, with colleagues elsewhere, have used gene therapy to prevent learning and memory loss in a mouse model of Alzheimer's disease (AD), a key step toward eventually testing the approach in humans with the neurodegenerative disease.

The findings are published online in advance of the June 11, 2021 issue of Molecular Therapy-Methods & Clinical Development.

AD is characterized by the accumulation of clumps of misfolded proteins called amyloid plaques and neurofibrillary tau tangles, both of which impair cell signaling and promote neuronal death. Current AD treatments targeting plaques and tangles address only symptoms, which the study's authors say suggests a reversal and cure of AD will likely require a combination of interventional approaches that both decrease aggregating toxins and promote neuronal and synaptic plasticity.

Gene therapy is based on the premise that introducing a therapeutic compound to a precisely targeted region of the brain may restore or protect normal neural function and/or reverse neurodegenerative processes. In this case, researchers used a harmless adeno-associated viral vector to introduce synapsin-Caveolin-1 cDNA (AAV-Syn-Cav1) into the hippocampus region of three-month-old transgenic AD mice.

The mice had been genetically modified to exhibit learning and memory deficits at 9 and 11 months, respectively. These deficits are associated with decreased expression of Caveolin-1, a scaffolding protein that builds the membranes housing cellular signaling tools, such as neurotrophin receptors that receive the critical extracellular signals, which govern all cellular life and function. With decay and destruction of these membranes, cell dysfunction and neurodegeneration follow.

"Our goal was to test whether SynCav1 gene therapy in these AD mouse models might preserve neuronal and synaptic plasticity in targeted parts of the membrane, and improve higher brain function," said senior author Brian P. Head, PhD, adjunct professor in the Department of Anesthesiology at UC San Diego School of Medicine and research health scientist at the VA San Diego Healthcare System.