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

DIYARYO KABITENYO
Nagmamalasakit sa lalawigan

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

Vol. 22 No. 31 | September 23-29, 2019 | P 10.00

Open canals seeded with tadpoles in GenTri

GENERAL TRIAS CITY, Cavite — The city government has seeded open canals and estuaries with tadpoles to prevent the spread of dengue in the barangays.

Dr. Jonathan Luzco of the City Health Office was joined by village leaders, barangay health workers, and volunteers in tadpole seeding. These tadpoles feed on wriggliers of dengue-carrying mosquitoes.

The vector control method is part of the city's massive drive to combat dengue through the Department of Health (DOH) "Sabayang 4 O'clock Habit para Deng-Get

Turn to page 2

General Trias City Health Office personnel and volunteers embark on tadpoles "seeding" in open canals to prevent dengue in General Trias City. Trashes that clogged the waterways were also cleaned up.

Tagaytay bans flying gas balloons, sky lanterns

TAGAYTAY CITY, Cavite — This city has banned flying gas balloons and sky lanterns to keep it free and prevent environment and health problems.

The ban against was only one of the latest environmental measures that the local government has adopted.

The ban was contained in City Ordinance No. 322 Series of 2019 which Mayor Agnes Delgado Tolentino approved last August 13.

The city council unanimously passed the ordinance's provisions following a session deliberation that lasted for about a month.

Councilor Luis Andrea R. Pico, Sanggunang Kabataan Federation (SKF) president

Turn to page 2

DIYARYO KABITENYO
ISSN: 2651-8313

ARNULFO BARCO
Publisher / Editor

GENER BARCO
Operations Manager

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Papi
Publishers Association of the Philippines, Inc.

(TAGAYTAY... from page

and Committee on Environmental Protection and Sanitation chairperson, was the ordinance author.

Gas balloons and sky lanterns are used in festivities, promotional events, burial ceremonies, and similar outdoor activities.

"Releasing of flying gas balloons and lanterns outdoor causes littering; fur-thermore balloons are biodegradable wastes which takes years to break down; may release chemicals to the environment; while latex balloons primarily affect animals, and/or mylar/foil balloons can cause dangerous power outages and spark fires," the ordinance stated.

The City Environment and Natural Resources Office (CENRO) and Business Permit and Licensing Office (BPLO) will oversee the ordinance's implementation.

Fines for violators range from P300 to P1,000 and community service.

The owner or manager of establishments selling the balloons and lanterns faces fines of as much as P5,000 and closure of their business.

Antimicrobial resistance is drastically rising

The world is experiencing unprecedented economic growth in low- and middle-income countries. An increasing number of people in India, China, Latin America and Africa have become wealthier, and this is reflected in their consumption of meat and dairy products. In Africa, meat consumption has risen by more than half; in Asia and Latin America it is up by two-thirds.

To meet this growing demand, animal husbandry has been intensified, with among other things, an increased reliance on the use of antimicrobials. Farmers use antimicrobials to treat and prevent infections for animals raised in crowded conditions but these drugs are also used to increase weight gain, and thus improve profitability.

This excessive and indiscriminate use of antimicrobials has serious consequences: the proportion of bacteria resistant to antimicrobials is rapidly increasing around the world. Drugs are losing their efficacy, with important consequences for the health of animals but also potentially for humans.

Low- and middle income countries have limited surveillance capacities to track antimicrobial use and resistance on farms. Antimicrobial use is typically less regulated and documented there than in wealthy industrialized countries with established surveillance systems.

The team of researchers led by Thomas Van Boeckel, SNF Assistant Professor of Health Geography and Policy at ETH Zurich, has recently published a map of antimicrobial resistance in animals in low- and middle income countries in the journal Science.

The team assembled a large literature database and found out where, and in which animals species resistance occurred for the common foodborne bacteria Salmonella, E. coli, Campylobacter and Staphylococcus.

According to this study, the regions associated with high rates of antimicrobial resistance in animals are northeast China, northeast India, southern Brazil, Iran and Turkey. In these countries, the bacteria listed above are now resistant to a large number of drug that are used not only in animals but also in human medicine. An important finding of the study is that so far, few resistance hotspots have emerged in Africa with the exception of Nigeria and the surroundings of Johannesburg.

The highest resistance rates were associated with the antimicrobials most frequently used in animals: tetracyclines, sulphonamides, penicillins and quinolones. In certain regions, these compounds have almost completely lost their efficacy to treat infections.

The researchers introduced a new index to track the evolution of resistance to multiple drugs: the proportion of drugs tested in each region with resistance rates higher than 50%. Globally, this index has almost tripled for chicken and pigs over the last 20 years. Currently, one third of drugs fail 50% of the time in chicken and one quarter of drug fail in 50% of the time in pigs.

(OPEN... from page 1)

Out" campaign.

Aside from the seeding operation, local and national government agencies also conducted massive clean-up operations in open canals in Barangay Pasong Camachile.

The clean-up teams of volunteers removed trashes that clogged waterways, which are possible breeding sites of the dengue-carrying mosquitoes.

REPUBLIC OF THE PHILIPPINES
FOURTH JUDICIAL REGION
REGIONAL TRIAL COURT
BRANCH 23
TRECE MARTIRES CITY

BDO UNIBANK, INC.,
Mortgagee,

FORECLOSURE CASE NO. F-228-19

-versus-

ANNALYN A. MONTILDE,
Mortgagor.
x- -x

NOTICE OF EXTRA-JUDICIAL SALE

Upon Extra-Judicial Petition for Sale under Act 3135, as amended by Act 4118, filed by Mortgagee, **BDO UNIBANK, INC.**, with business address at BDO Corporate Center, 7899 Makati Avenue, Makati City against the Mortgagor, **ANNALYN A. MONTILDE represented herein by her Atty-in-Fact LEONIDA A. CONTE**, with residence and postal addresses at Blk. 4, Lot 1, Ph-4, Tierra Nevada, San Francisco, Gen. Trias, Cavite; and Blk. 8, Lot 11, Tierra Nevada 7, San Francisco, Gen. Trias, Cavite; and Blk. 30, Lot 8, Ph-1A, Tierra Nevada, San Francisco, Gen. Trias, Cavite, to satisfy the mortgage indebtedness which as of July 1, 2019 amounts to **ONE MILLION TWO HUNDRED NINE THOUSAND EIGHTY FOUR PESOS and 78/100 (P1,209,084.78)** Philippine Currency, including interest, penalties, and other charges as of said date but exclusive of all other expenses incidental to this foreclosure and sale, the undersigned Sheriff will sell at public auction on **October 16, 2019** at 10:00 o'clock in the morning at the main entrance of the Government Center Building, located at the Provincial Capitol Compound, Trece Martires City, to the highest bidder for **CASH** and in Philippine Currency, the following described property with all the improvements thereon, to wit:

TRANSFER CERTIFICATE OF TITLE No. 057-2016004122

A parcel of land (Lot 1 of the cons-subdivision plan, Pcs-04-026097, being a portion of Lots 1 to 20, Block 8, Pcs-04-021654, L.R.C. Rec. No. ___) situated in Barangay of San Francisco, Municipality of Gen. Trias, Province of Cavite, Island of Luzon. Bounded on the SW., along lines 1-2-3 by Road Lot 4, Pcs-04-021654; on the NW., along line 3-4 by Lot 10 of the cons-subd. Plan; on the NE., along 4-5 by Lot 29, along line 5-6 by Lot 28, both of Block 8, Pcs-04-021654; on the SE., along line 6-1 by Lot 12 of the cons-subdivision plan. Beginning at a point marked "1" on plan; x x x **containing an area of SEVENTY (70) SQUARE METERS.** x x x

All sealed bids must be submitted to the undersigned on the above stated time and date.

In the event the public auction should not take place on the said time and date, it shall be held on **October 23, 2019** without further notice.

Prospective bidders/buyers are hereby required to investigate for themselves the title to the said property and encumbrances thereon, if any there be.

Trece Martires City, **September 02, 2019**

(Sgd.) **LUCIO C. ALEJO III**
Sheriff IV

Copy Furnished:

BDO UNIBANK, INC.
RISK MANAGEMENT GROUP REMEDIAL MANAGEMENT UNIT
11th Floor, BDO South Tower, BDO Corporate Center
7899 Makati Ave., Makati City

MS. ANNALYN A. MONTILDE
MS. LEONIDA A. CONTE
Blk. 4, Lot 1, Ph-4, Tierra Nevada, San Francisco,
Gen. Trias, Cavite; and
Blk. 8 Lot 11, Tierra Nevada 7, San Francisco,
Gen. Trias, Cavite; and
Blk. 30, Lot 8, Ph-1A, Tierra Nevada, San Francisco,
Gen. Trias, Cavite

WARNING: It is absolutely prohibited to remove, deface or destroy this Notice of Extra-Judicial Sale on or before the date of sale.

Publication: DITARYO KABITENYO
Dates: September 9, 16 & 23, 2019

EXTRA-JUDICIAL SETTLEMENT OF ESTATE

NOTICE is hereby given that the estate of the deceased **PELAGIO V. SAPIN and LEONIDA BAUTISTA SAPIN** who both died intestate on May 08, 2012 and on March 11, 2015, both at State of California, respectively, consisting of one (1) parcel of land without improvements situated in the Mun. of [illegible], Prov. of Cavite, covered by Transfer Certificate of Title No. 057-2016001455, containing an area of **THREE THOUSAND SEVEN HUNDRED SIXTY TWO (3,762)** square meters, more or less, has been adjudicated and extra-judicially settled by and among their heirs on May 29, 2019 before Notary Public Atty. [illegible] and entered in his Notarial Register as Doc. No. 373; Page No. 75; Book No. [illegible]; Series of 2019.

(Sgd.) Heirs

Publication: DITARYO KABITENYO
Dates: September 9, 16 & 23, 2019

Researchers find way to kill pathogen resistant to antibiotics

Pseudomonas aeruginosa is a dangerous bacterium that causes infections in hospital settings and in people with weakened immune systems. It can cause blood infections and pneumonia, while severe infections can be deadly. Highly resistant to antibiotic treatment, P. aeruginosa is one of the most critical pathogens urgently requiring alternative treatment strategies according to the World Health Organization.

This bacterium is one of many that have evolved a system that allows them to acquire difficult-to-access iron from the human body. Iron is essential for bacterial growth and survival, but in humans, most of it is held up within the 'haem' complex of haemoglobin. To get hold of it, P. aeruginosa and other bacteria secrete a protein, called HasA, which latches onto haem in the blood. This complex is recognized by a membrane receptor on the bacterium called HasR, permitting haem entry into the bacterial cell, while HasA is recycled to pick up more haem.

Bioinorganic chemist Osami Shoji of Nagoya University and collaborators have found a way to hijack this haem acquisition system for drug delivery. They developed a powder formed of HasA and the pigment gallium phthalocyanine (GaPc), which, when applied to a culture of P. aeruginosa, was consumed by the bacteria.

"When the pigment is exposed to near-infrared light, harmful reactive oxygen species are generated inside the bacterial cells," explains Shoji. When tested, over 99.99% of the bacteria were killed following treatment with one micromolar of HasA with GaPc and ten minutes of irradiation.

The strategy also worked on other bacteria with the HasR receptor on their membranes, but not on ones without it.

The haem acquisition system is so essential to these bacteria's survival that it is not expected to change, making it unlikely the bacteria will develop resistance to this drug strategy, the researchers believe.

"Our findings support the use of artificial haem proteins as a Trojan horse to selectively deliver antimicrobials to target bacteria, enabling their specific and effective sterilization, irrespective of antibiotic resistance," the team reports in their study.

Republic of the Philippines
Regional Trial Court
Fourth Judicial Region
BRANCH 19
City of Bacoor

ARTURO ARROYO,
Plaintiff,

-versus- Civil Case No. BSC-2012-14

SPOUSES GERINO CABILIS and LOURDES F. PASCUAL,
Defendants.

x---x

NOTICE OF SHERIFF'S SALE ON EXECUTION OF REAL PROPERTY

WHEREAS, by virtue of the Writ of Execution dated 26 April 2018, issued by Atty. Misty C. Herrerares-Vista, Clerk of Court V, Branch 19, RTC, Bacoor, Cavite, in Civil Case No. BSC-2012-14, wherein **ARTURO ARROYO** is the plaintiff and **SPOUSES GERINO CABILIS and LOURDES F. PASCUAL** are the defendants for Judicial Foreclosure of Real Estate Mortgage in the amount of **P1,050,000.00** inclusive of interest as of June 2012 until the judgment is rendered, moral and exemplary damages of **P100,000.00**, and attorney's fees of **P20,000.00**, **LEVY** was made by the undersigned on 9 September 2019, upon the Register of Deeds, Trece Martires City, Province of Cavite, on the rights, interests and participation of the said defendants in the real property more particulary described as follows:

TRANSFER CERTIFICATE OF TITLE NO. T-124261

A parcel of land (Lot 1 868, C1-C, of the consolidation-subdivision plan Psu-04-000283, being a portion of the consolidated Lots A, B and C, Psd-13882, Lot 1-E, Psd-1510, Lots 1-A-4 and 1-A-5, Psd-19973, and Block C-4-C1 and C-12-C1, (LRC) Psd-217418, Rec. No. 41026 and 20873), situated in the Barrio of San Gabriel, Mun. of Carmona, Province of Cavite, containing an area of TWO HUNDRED (200) SQUARE METERS x x x

NOW THEREFORE, by virtue of the said Writ of Execution and in accordance with the Provisions of Sec. 16, Rule 39, of the Rules of Court of the Philippines, the undersigned Sheriff IV, will sell at public auction to the highest bidder, for **CASh and in Philippine Currency**, on **8 October 2019 at 10:00 o'clock in the morning** or soon thereafter, at the main entrance of the New Hall of Justice, City of Bacoor, Cavite, the rights, interests and participation of the defendants **SPOUSES GERINO CABILIS and LOURDES F. PASCUAL**, in the above described real property in order to satisfy the Writ of Execution, together with the sheriff's fees and expenses of sale.

In the event the public auction should not take place on the said date, it shall be held on **15 October 2019**, without further notice.

City of Bacoor, Cavite, 11 September 2019

(Sgd.) **ARTHUR T. SAN MIGUEL**
Sheriff IV

WARNING: It is absolutely prohibited to remove, deface or destroy this notice of sale on or before the date of sale, under the penalty of law.

Publication: DIYARYO KABITENYO
Date: September 19 & 23, 2019

Republic of the Philippines
OFFICE OF THE MUNICIPAL CIVIL REGISTRAR
Indang, Cavite

In the matter of Change of First Name in the Certificate of Live Birth (SECPA) of

MARIA ESPERANZA PELLOS
CEN-0813-2019

MA. ESPERANZA P. CRIZALDO
Petitioner

NOTICE OF PUBLICATION

There is a petition filed for the change of first name in Certificate of Live Birth (**SECPA**) of **MARIA ESPERANZA PELLOS** from "**MARIA ESPERANZA**" to "**MA. ESPERANZA**"

NOTICE IS HEREBY GIVEN that any interested person is asked to notify this office and show cause why the same should not be granted.

Let this NOTICE be published at least once a week for two (2) consecutive weeks in a newspaper of general circulation as required under Section 3 of Republic Act No. 9048.

(Sgd.) **MERCI A. CHAVEZ**
Municipal Civil Registrar

DIYARYO KABITENYO - September 16 & 23, 2019

Multicultural millennials respond positively to health 'edutainment'

Storytelling that educates and entertains – aka "edutainment" – is a powerful communications tool that can lead to positive health-related changes among multicultural millennials, according to a new marketing study from Baylor University.

Tyrha Lindsey-Warren, Ph.D., clinical assistant professor of marketing in Baylor University's Hankamer School of Business, led the study, "Making multicultural millennials healthy: The influence of health 'edutainment' and other drivers on health-oriented diet change," which is published in the Journal of Cultural Marketing Strategy. Charlene A. Dadzie, Ph.D., assistant professor of marketing at the University of South Alabama, coauthored the research.

The research sought to determine which health issues most concerned multicultural millennials and to gauge how effective media can be as a tool to address these issues and drive change.

"This study finds that by bolstering self-identity and employing health edutainment, it is possible to have a positive impact on the health intentions and behaviors of the millennial generation," the researchers wrote.

There are more than 92 million millennials (ages 20-34) in the United States today, the researchers asserted. More than 9 million of those are identified as being overweight.

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

NOTICE TO THE PUBLIC

CTN: 0000-2019
CCE-0083-2019 RA 10172

12 September 2019

In compliance with the publication requirement as pursuant to OCRG Memorandum Circular No. 2011-1 Guidelines in the Implementation of the Administrative Order No. 1, Series of 2012 (AO on R.A. 10172), Notice is hereby served to the public that **DAISY V. HAIBG**, has filed with this Office, a petition for **CHANGE OF FIRST NAME** from **"DAILSAY"** to **"DAISY"** and **CORRECTION OF ENTRY** in **CHILD'S DATE OF BIRTH** from **"31 03"** to **"JULY 03, 1963"** in the Certificate of Live Birth of DAL2019 A. VALDERAMA, who was born on July 31, 1963 at Tanza, Cavite and whose parents were Remigio A. Valderama & Petra S. Aguirre.

Any person adversely affected by said petition may do his/her written opposition with this Office not later than **September 30, 2019**.

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

DIYARYO KABITENYO - September 16 & 23, 2019

Republic of the Philippines
Province of Cavite
Municipality of Alfonso

OFFICE OF THE MUNICIPAL CIVIL REGISTRAR

NOTICE FOR PUBLICATION

In compliance with Section 3 of R.A. No. 9048, notice is hereby served the public that **ARIEL JOVENTINO M. MALIGAYA** has filed with this office a petition for change of first name from **ARIEL** to **ARIEL JOVENTINO** in the birth certificate of **ARIEL MARANIGAN MALIGAYA** who was born on **January 25, 1963** at **Lucsuhin, Alfonso, Cavite**, and whose parents are **Pedro Maligaya and Paz M. Maranigan.**

Any person adversely affected by said petition may file his written opposition with this Office not later than **October 7, 2019**.

(Sgd.) **TERESITA A. GALANG**
Civil Registrar

DIYARYO KABITENYO - September 23 & 30, 2019

Republic of the Philippines
Province of Cavite
Municipality of Alfonso

OFFICE OF THE MUNICIPAL CIVIL REGISTRAR

Publication Notice
R.A. 10172

NOTICE TO THE PUBLIC

Date: September 17, 2019

CCE-0009-2019 R.A. 10172

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 **RHODVILLE D. DIMAPILIS** has filed with this office, a petition for correction of entry in sex from **FEMALE** to **MALE** in the certificate of live birth of **RHODVILLE DELOS SANTOS DIMAPILIS** at Alfonso, Cavite and whose parents are **Vilbumar C. Dimapilis and Rodora F. delos Santos.**

Any person adversely affected by said petition may file his written opposition with this office not later than **October 7, 2019**.

(Sgd.) **TERESITA A. GALANG**
Civil Registrar

DIYARYO KABITENYO - September 23 & 30, 2019

DEED OF EXTRAJUDICIAL SETTLEMENT OF ESTATE WITH WAIVER OF RIGHTS

NOTICE is hereby given that the estate of the late spouses **PORFIRIO ENCARNACION and MARIA ROSA MANALO ENCARNACION** who both died intestate on February 12, 2004 and on September 18, 2013 in the Richmond, B.C., Canada and City of Manila, respectively, consisting of a 2 storey residential house [illegible] situated at Sta. Isabel, Kawit, Cavite, Philippines covered by Tax Declaration No. 11-0009-[illegible] has been adjudicated and extrajudicially settled by and among their heirs in equal shares with Waiver of Rights in favor of MARINA E. DELA CRUZ, married to [illegible] Dela Cruz and to ESTRELLA E. VIDA, married to [illegible] Vida, in which that the entirety of said estate now belongs exclusively to said MARINA E. DELA CRUZ and ESTRELLA E. VIDA on March 15, 2018 in Kawit, Cavite before Notary Public Atty. [illegible] E. [illegible] and entered in his Notarial Register as Doc. No. 227; Page No. 47; Book No. 48; Series of 2018.

(Sgd.) Heirs (With MARINA E. DELA CRUZ signing for herself and as Attorney-in-Fact of Estrella E. Vida, Nelia E. [illegible], [illegible] E. [illegible], Celia E. [illegible] and Samuel M. Encarnacion)

Publication: DIYARYO KABITENYO
Date: September 23, 30 and October 7, 2019

DEED OF EXTRAJUDICIAL SETTLEMENT OF ESTATE OF EMILIANO MANALO

NOTICE is hereby given that the estate of the late **EMILIANO MANALO** who died intestate on January 23, 1997 in Kawit, Cavite, consisting of the following properties:

• A one-fourth (1/4) undivided portion share and interest in a fishpond situated at Noveleta, Cavite, (which 1/4 share consists of 3,195 square meters after deducting from the total area stated in the certificate of title the [illegible] square meters portion sold to the Republic of the Philippines) covered by Transfer Certificate of Title No. T-42227 of the Registry of Deeds for the Province of Cavite.

• A parcel of land situated at Sta. Isabel, Kawit, Cavite identified as Lot No. D, containing an area of Five (5) square meters and covered by Transfer Certificate of Title No. T-118362 of the Registry of Deeds for the Province of Cavite.

has been adjudicated and extrajudicially settled by and among his sole and exclusive legal heirs as follows:

To MYRNA M. CHUMACERA, MARISSA M. VILLEGAS and ARSENIA M. QUEMUEL – one-third portion for each in the one-fourth (1/4) undivided portion share and interest in the fishpond situated at Noveleta, Cavite which 1/4 share consists of 3,195 square meters, covered by Transfer Certificate of Title No. T-42227 of the Registry of Deeds for the Province of Cavite.

To MYRNA M. CHUMACERA, MARISSA M. VILLEGAS and ARSENIA M. QUEMUEL – one third portion for each in that parcel of land situated at Sta. Isabel, Kawit, Cavite containing 5 square meters, covered by Transfer Certificate of Title No. T-118362 of the Registry of Deeds for the Province of Cavite.

on July 12, 2019 in Kawit, Cavite before Atty. [illegible] E. [illegible] and entered in his Notarial Register as Doc. No. 418; Page No. 84; Book No. 54; Series of 2019.

(Sgd.) Heirs

Publication: DIYARYO KABITENYO
Date: September 23, 30 and October 7, 2019

World's first gene therapy for glycogen storage disease produces remarkable results

At the Association for Glycogen Storage Disease's 41st Annual Conference, Dr. David Weinstein of UConn School of Medicine and Connecticut Children's presented his groundbreaking one-year clinical trial results for the novel gene therapy treatment for glycogen storage disease (GSD).

The rare and deadly genetic liver disorder, GSD type Ia, affects children from infancy through adulthood, causing dangerously low blood sugar levels and constant dependence on glucose consumption in the form of cornstarch every few hours for survival. If a cornstarch dose is missed, the disease can lead to seizures and even death.

Weinstein, whose team first administered the investigational gene therapy at UConn John Dempsey Hospital in Farmington, Connecticut, on July 24, 2018, calls the results "remarkable."

One year after patient Jerrod Watts first received the GSD vaccine during a 30-minute infusion, he is completely off of cornstarch. In addition to totally stopping daily cornstarch consumption, Watts has experienced normal regulation of his blood glucose levels, weight loss, increased muscle strength, and marked improvement in his energy.

"The clinical trial is going better than expected. The therapy is transforming patient lives," says Weinstein. "We have seen all of the patients wean their therapy with some already discontinuing treatment. Missed cornstarch doses no longer are resulting in hypoglycemia, which previously could have been life threatening."

Weinstein, the clinical trial's lead investigator, is pediatric endocrinologist-scientist who cares for more than 700 GSD patients from 51 countries as director of the Glycogen Storage Disease Program at Connecticut Children's and UConn Health – the largest center in the world for the care and treatment of this condition.

The clinical trial, conducted in conjunction with the biopharmaceutical company Ultragenyx, originally set out to simply test the safety and dosage of the gene therapy for three patients with GSD Type Ia.

The gene therapy works by delivering a new copy of a gene to the liver via a naturally occurring virus. Administered through the patient's bloodstream, the new copy replaces deficient sugar enzymes caused by the disease and jump starts the body's glucose control.

Both Weinstein and Watts were surprised by Watts' response to the gene therapy.

Transplanted brain stem cells survive without anti-rejection drugs in mice

In experiments in mice, Johns Hopkins Medicine researchers say they have developed a way to successfully transplant certain protective brain cells without the need for lifelong anti-rejection drugs.

A report on the research, published Sept. 16 in the journal Brain, details the new approach, which selectively circumvents the immune response against foreign cells, allowing transplanted cells to survive, thrive and protect brain tissue long after stopping immune-suppressing drugs.

The ability to successfully transplant healthy cells into the brain without the need for conventional anti-rejection drugs could advance the search for therapies that help children born with a rare but devastating class of genetic diseases in which myelin, the protective coating around neurons that helps them send messages, does not form normally. Approximately 1 of every 100,000 children born in the U.S. will have one of these diseases, such as Pelizaeus-Merzbacher disease. This disorder is characterized by infants missing developmental milestones such as sitting and walking, having involuntary muscle spasms, and potentially experiencing partial paralysis of the arms and legs, all caused by a genetic mutation in the genes that form myelin.

"Because these conditions are initiated by a mutation causing dysfunction in one type of cell, they present a good target for cell therapies, which involve transplanting healthy cells or cells engineered to not have a condition to take over for the diseased, damaged or missing cells," says Piotr Walczak, M.D., Ph.D., associate professor of radiology and radiological science at the Johns Hopkins University School of Medicine.

A major obstacle to our ability to replace these defective cells is the mammalian immune system. The immune system works by rapidly identifying "self" or "nonself" tissues, and mounting attacks to destroy non-self or "foreign" invaders. While beneficial when targeting bacteria or viruses, it is a major hurdle for transplanted organs, tissue or cells, which are also flagged for destruction. Traditional anti-rejection drugs that broadly and unspecifically tamp down the immune system altogether frequently work to fend off tissue rejection, but leave patients vulnerable to infection and other side effects. Patients need to remain on these drugs indefinitely.

In a bid to stop the immune response without the side effects, the Johns Hopkins Medicine team sought ways to manipulate T cells, the system's elite infection-fighting force that attacks foreign invaders.

Specifically, Walczak and his team focused on the series of so-called "costimulatory signals" that T cells must encounter in order to begin an attack.

"These signals are in place to help ensure these immune system cells do not go rogue, attacking the body's own healthy tissues," says Gerald Brandacher, M.D., professor of plastic and reconstructive surgery and scientific director of the Vascularized Composite Allotransplantation Research Laboratory at the Johns Hopkins University School of Medicine and co-author of this study.

The idea, he says, was to exploit the natural tendencies of these costimulatory signals as a means of training the immune system to eventually accept transplanted cells as "self" permanently.

To do that, the investigators used two antibodies, CTLA4-Ig and anti-CD154, which keep T cells from beginning an attack when encountering foreign particles by binding to the T cell surface, essentially blocking the go signal. This combination has previously been used successfully to block rejection of solid organ transplants in animals, but had not yet been tested for cell transplants to repair myelin in the brain, says Walczak.

In a key set of experiments, Walczak and his team injected mouse brains with the protective glial cells that produce the myelin sheath that surrounds neurons. These specific cells were genetically engineered to glow so the researchers could keep tabs on them.

The researchers then transplanted the glial cells into three types of mice: mice genetically engineered to not form the glial cells that create the myelin sheath, normal mice and mice bred to be unable to mount an immune response.

Then the researchers used the antibodies to block an immune response, stopping treatment after six days.

Long-acting injectable multi-drug implant shows promise for HIV prevention and treatment

A new study published September 20, 2019 in Nature Communications shows a promising alternative for those who have to take a daily pill regimen. Targeting HIV treatment and prevention, researchers across multiple departments at the University of North Carolina at Chapel Hill collaborated on a seven-year study in animals to make a better injectable drug implant that can combine multiple drugs and is ultra-long-acting, while also addressing many of the challenges faced with current HIV treatment and prevention methods.

"There is no FDA-approved or marketed technology for long-acting prevention of HIV, and we are the first to use this delivery method with multiple antiretroviral drugs," said Rahima Benhabbour, PhD, MSc, first author of the study and assistant professor in the UNC_NCSU Joint Department of Biomedical Engineering. "To have an HIV prevention treatment that consists of an injection once or twice a year would make an incredible impact for patients." She added, "This technology is not only promising for HIV, but for any kind of condition that requires a daily intake of medication. We're talking about a safe, removable, long-lasting injection that takes away the burden of adhering to a daily medication regimen."

Antiretroviral drugs are used in both prevention and treatment of HIV, and multiple types are used in combination to counteract resistance to any one antiretroviral drug. These drugs need to be taken consistently every day. There are many obstacles that stand in the way of adherence to these medication regimens. Benhabbour says this especially applies to otherwise healthy people trying to prevent infection.

"In sub-Saharan Africa where prevalence of HIV is highest, accessibility to these medications can be difficult, and there is much stigma associated with the virus," Benhabbour said. "It is a very big deal for someone who doesn't have HIV to go out of their way to not only access the drugs, but then associate themselves with HIV by taking a pill every day."

There's also the factor of human error. Anyone who strives to take a daily multivitamin can understand that some days the pill gets skipped, or gets taken at a different time of day. But such small deviations can make antiretroviral drugs less effective.

"Because one of the biggest difficulties associated with HIV prevention is lack of adherence to drug treatment, we wanted to create a drug delivery system that essentially solved this problem," said senior author J. Victor Garcia, PhD, professor of medicine at UNC School of Medicine, director of the International Center for the Advancement of Translational Science and member of the UNC Center for AIDS Research.

The injectable implant is comprised of three elements – an organic solvent, a polymer, and the drug or drugs that need to be delivered. The formulation results in a honey-like liquid that turns into a solid when injected under the skin. This phase inversion happens when the solvent diffuses into the body leaving behind the polymer and medication(s) – the combination of which determines over what time period the medication(s) will be released into the blood system.

In this study six antiretroviral drugs were tested, and all kept their physical and chemical properties within the formulation and upon release. All six were also released from the implant at effective levels for a sustained amount of time ranging from one month to a year.

The injectable drug implant created by UNC's research team is the first to address several drawbacks to the current method of long-acting drug delivery for HIV – namely the ability to remove it and quickly eliminate the presence of residual drug(s) in the system.

"If a patient needs to withdraw from the treatment because they've had a bad reaction to the drug(s), or maybe a woman has become pregnant, our implant can be easily surgically removed," said Martina Kovarova, PhD, contributing author to the study and associate professor of medicine at UNC SOM.

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Rethinking how cholesterol is integrated into cells

Most people have heard of "cholesterol levels" and the dangers of high blood cholesterol, which is one of the main causes of cardiovascular disease. But besides the harmful side effects of high cholesterol, cholesterol is an essential component of all cells and fundamental to a host of important functions of the body. Hormones like estrogen and testosterone are made from cholesterol, for example.

It has been known for a long time that cholesterol is transported around the body in the blood as small particles consisting of fat and protein. In the body's cells, these particles are broken down and cholesterol is released and integrated as part of the cell. Although this process is essential, not just for humans, but for all animals and plants, surprisingly little is known about how cholesterol is actually incorporated into the cells after the breakdown of these particles.

In recent years, interest in how cholesterol is integrated and incorporated — and not least how this process is regulated — has grown tremendously. This is partly due the huge pharmaceutical potential in regulating this process, as shown with blockbuster drugs such as Zetia, which regulate cholesterol uptake from food. In addition, it has been shown that many viruses, including Ebola, uses the same process to infect cells.

During the past five years, researchers from Aarhus University have collaborated with researchers from the University of Southern Denmark and the University of Leeds to investigate how cholesterol is incorporated into cells, using biophysical and structural biological methods. The results have led to a ground-breaking insight into the process and to a new model for how cholesterol is integrated and incorporated that fundamentally changes our prior understanding of the process.

Dengue virus becoming resistant to vaccines and therapeutics due to mutations in specific protein

Dengue virus (DENV) infects about 400 million people annually around the world, with a high prevalence in tropical and sub-tropical regions. The virus causes diseases ranging from mild dengue fever to severe dengue hemorrhagic fever and dengue shock syndrome.

DENV2 exists as smooth spherical surface particles while growing at the mosquito's physiological temperature (29 degrees Celsius), it then changes to bumps surfaced particles at human physiological temperature (37 degrees Celsius). This ability to morph helps the virus to evade the immune system of the human host, Hence, understanding the mechanism behind this is important for therapeutics and vaccine development.

"Together with Professor Pei-Yong Shi form UTMB, we found that in laboratory developed DENV2 strains, mutations in the virus' E protein causes its transformation into bumpy particles. These structural changes can cause vaccines and therapeutics to be ineffective against the virus.