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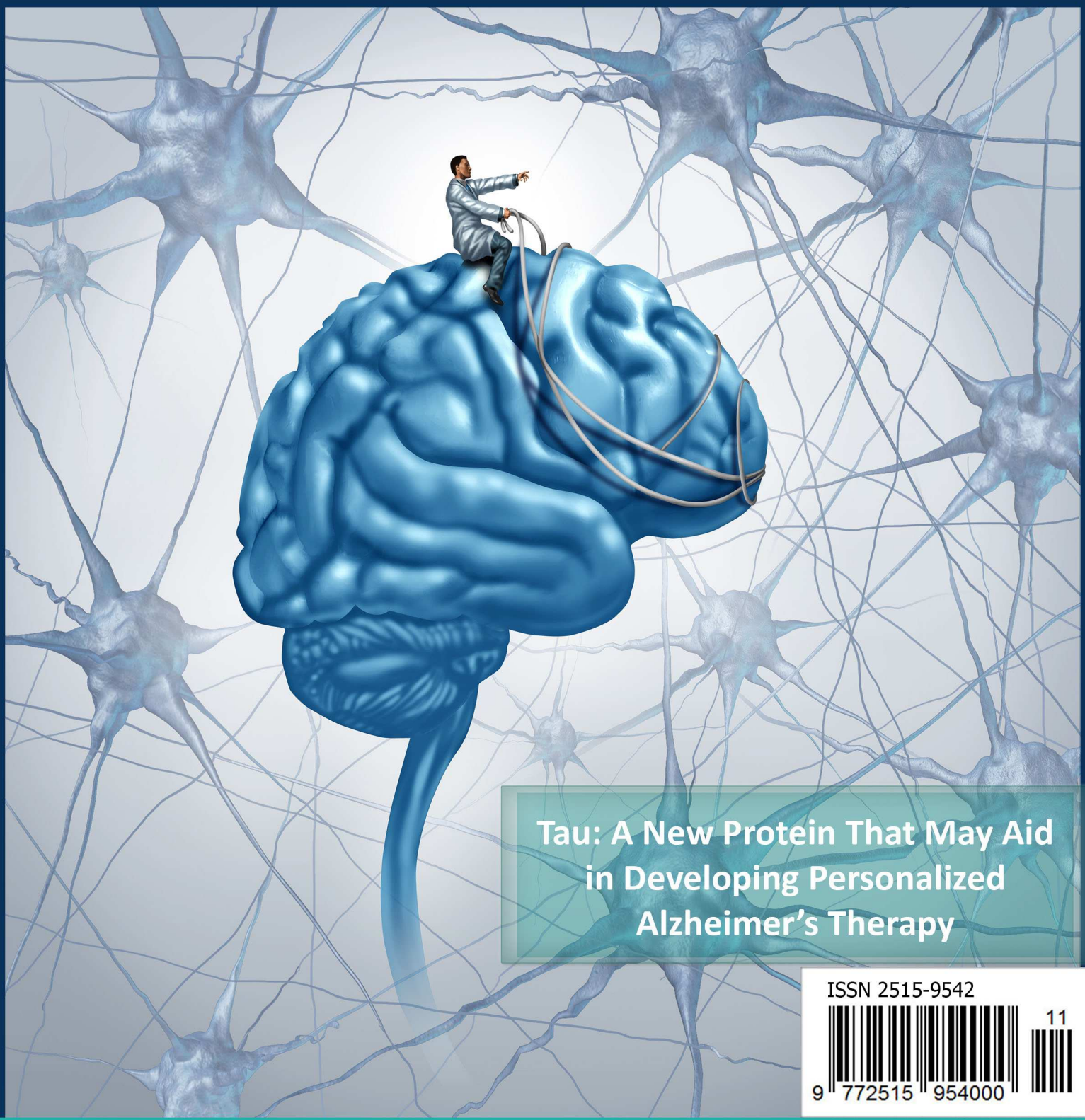

Tau: A New Protein That May Aid in Developing Personalized Alzheimer's Therapy

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Contents

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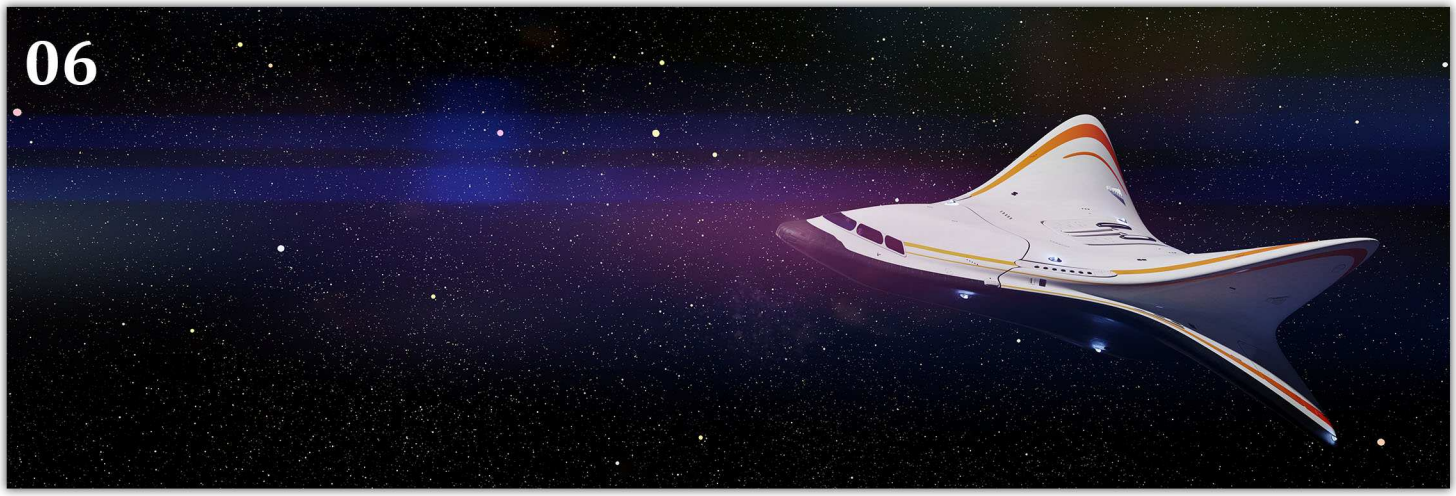


06 'Ionic Wind' Powered Airplane: A Plane That Has No Moving Part

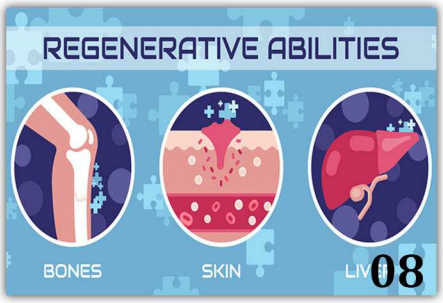
Airplane has been designed which won't be dependent on fossil fuels or battery as it won't have any moving part

07 DNA Origami Nanostructures for Treatment of Acute Kidney Failure

A novel study based on nanotechnology generates hope for treating acute kidney injury and failure.

08 'Adult Frog Regrows Amputated Legs': An Advance in Organ Regeneration Research

Adult frogs have been shown for the first time to regrow amputated legs marking it as a breakthrough for organ regeneration.



09 A New Easy Treatment for Peanut Allergy

A promising new treatment using immunotherapy to treat peanut allergy by building tolerance over time.

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EDITOR-IN-CHIEF: *Umesh Prasad*
ADVISOR: *Syed Munir Hoda*
ADVISOR: *Rajeev Soni*
ASSOCIATE EDITOR: *Jasmita Gill*
CREATIVE & DIGITAL: *Carl Saunders*

NOTE FROM EDITOR-IN-CHIEF

We are thrilled to bring to you nine articles on latest scientific advancements which are bound to make an impact on our daily lives including a new treatment for peanut allergy, neurotechnology to treat paralysis, treatment for acute kidney injuries, advancement in organ regeneration and many more.

Hope you enjoy them!

Umesh Prasad

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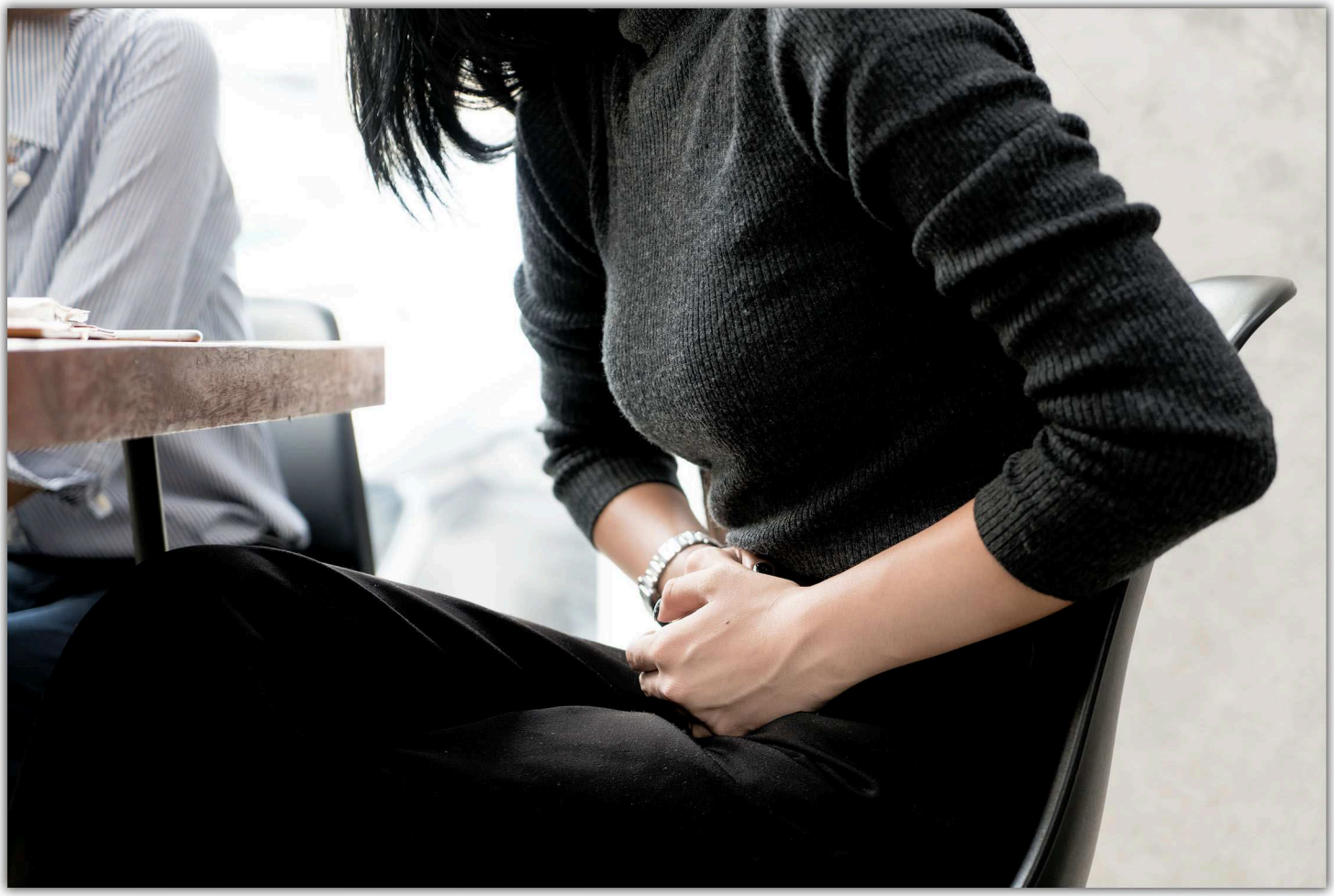
Cefiderocol: A New *Antibiotic for Treating Complex and Advanced* Urinary Tract Infections

A newly discovered antibiotic follows a unique mechanism in fighting drug-resistant bacteria responsible for UTIs.

Antibiotic resistance is no doubt a major global threat to healthcare. Antibiotic resistance occurs when bacteria modify themselves in some manner which then either reduces or completely removes the effectiveness of an antibiotic drug which were originally developed and designed to prevent or cure infections caused by this bacterium. The 'changed' bacteria survive and continue to grow/multiply and the same drugs now become ineffective on them. Therefore, many existing antibiotics are no longer able to combat most bacterial infections after developing high resistance against them. With time many different strains of bacteria have become or are becoming resistant to antibiotics. Misuse and uncontrolled overuse of antibiotics had further compounded this problem. The few new antibiotics which have been made available in the last several years or the ones which are currently undergoing trials rely on existing mechanisms of killing bacteria which clearly indicating that most bacteria might already be resistant to them. There is an urgent need for new strategies and novel antibiotics which will have unique modes of action. World Health Organisation (WHO) has labelled gram-negative bacteria like Pseudomonas aeruginosa, Acinetobacter baumannii and Enterobacteriaceae – carbapenem-resistant strains- as responsible for difficult-to-treat infections in clinical care and they are in the highest resistance category and are hardest to treat. For such bacterial strains no alternative antibiotics are available and the ones available have serious and drastic side effects. We are in urgent need of novel antibiotics.



A novel antibiotic

A new antibiotic has been discovered which is very effective in treating complex and advanced urinary tract infections (UTIs) that are caused by many gram-negative bacteria which are resistant to multiple drugs. This study, a phase II randomized clinical trial, has been led by researchers at a pharmaceutical company Shionogi Inc in Japan and has been published in *The Lancet Infectious Diseases*. The antibiotic drug called cefiderocol is a siderophore-based drug which can eradicate higher levels of 'stubborn' bacteria (pathogen) and is seen to be not only very similar to standard antibiotics clinically used called imipenem-cilastatin but the new drug outperforms its effects.

The trial was conducted with 448 adults who were hospitalized due to a complicated UTI infection or kidney inflammation due to a severe bacterial infection. Majority of the patients were infected with bacteria E. coli, klebsiella and other gram-negative group bacteria which are strongly resistant to many standard antibiotic drugs. 300 adults received three daily doses of cefiderocol and 148 adults received standard treatment of imipenem-cilastatin for a total of 14 days. This new drug is very unique in its approach to combat antibiotic resistance used by gram-negative bacteria in comparison to all therapies known so far.It targets main three mechanisms (or barriers) which are used by

bacteria to cause strong resistance to antibiotics in the first place. This drug succeeds in bypassing all defence mechanisms of the bacteria. The barriers are firstly, the two outer membranes of the bacteria which create difficulty for antibiotics to infiltrate the bacterial cell. Secondly, the porin channels which readily acclimatize blocking entry of antibiotics and thirdly, the efflux pump of the bacteria which expels the antibiotic out of the bacterial cell rendering the antibiotic drug ineffective.

A smart mechanism

When a bacterial infection happens in our body, our immune system responds by creating a low-iron environment which can then hamper bacteria's ability to grow. The bacteria are also smart, for example E Coli. bacteria respond by gathering up as much iron as they can. Interestingly, this newly discovered antibiotic drug uses a unique mechanism to enter the bacteria by exploiting this very own mechanism of bacteria trying to gain iron in order to survive. Firstly, the drug binds to iron and gets intelligently transported through the outer membrane of the bacteria's own iron-transport channels into the cells where it can then disrupt and destroy the bacterium. These iron-transport channels also enable the drug to bypass porin channels of the bacteria countering bacteria's second barrier mechanism. This scenario also helps the drug to gain repeated access even in the presence of efflux pumps.

The adverse effects of this new drug cefiderocol were similar to earlier therapies and most common symptoms were nausea, diarrhoea, constipation and abdominal pain. The drug was found to be effective, safe and well tolerated especially in older patients who were multi-drug resistant with had serious urinary tract or kidney infections. It was clear that cefiderocol was as effective as the standard antibiotic but whilst showing a sustained and superior antibacterial activity. When approved, drug cefiderocol is being labelled as a new important option for treating highly resistance gram-negative bacteria but more studies are required before it can be universally accepted. Further clinical trials are ongoing to evaluate this new drug in patients suffering from hospital-acquired pneumonia and ventilator-associated pneumonia which is a common infection problem in healthcare settings. Authors stated that patients with carbapenem-resistant infections were not included in the current study because carbapenem was a comparator and this is being considered as one critical limitation of the study. Nevertheless, this study has brought immense hope in fighting drug resistance and is seen as an initial first important step towards creating novel antibiotics.

Source

Simon Portsmouth et al. 2018, 'Cefiderocol versus imipenem-cilastatin for the treatment of complicated urinary tract infections caused by Gram-negative uropathogens: a phase 2, randomised, double-blind, non-inferiority trial', *The Lancet Infectious Diseases*, DOI: https://doi.org/10.1016/S1473-3099(18)30554-1 ■

Nanorobots That Deliver Drugs Directly into The Eyes

For the first time nanorobots have been designed which can deliver drugs directly into the eyes without causing damage.

Nanorobot technology is a recent technique at the centre of focus of scientists for treating multiple diseases. Nanorobots (also called nanobots) are tiny devices made from nanoscale components and are of size 0.1-10 micrometres. Nanorobots have the potential of delivering drugs into the human body in a very targeted and precise manner. Nanorobots are designed or engineered in such a way that they are 'attracted' to diseased cells only and thus they can make a targeted or direct treatment in those cells without causing any damage to healthy cells. Generally, for most diseases such a targeted drug delivery may not be essentially required, however for complicated illnesses such as diabetes or cancer it can be very beneficial.

Retinal diseases of the eye

The treatment of eye diseases is generally geared towards reducing inflammation in the eye, repair traumatic injuries and protecting or improving eyesight. A healthy retina – the thin layer of tissue at back of the eye - is critical for good vision. Our retina consists of millions of light-sensitive cells (called rods and cones) and nerve fibres/cells which allow light that enters the eye to be converted into electrical impulses to reach the brain. This is how visual information is received and processed by our eye and sent to the brain through the optic nerve. The whole process enables vision and controls how we see images. Retinal diseases of the eye affect any part of retina. Few forms of treatment are available for some retinal diseases, but they are quite complex. The aim of any treatment is

to completely halt or slow the eye disease and to protect vision (preserve, improve or restore it). It is crucial to detect retinal problems early because the damage is irreversible. If left untreated, some retinal diseases can cause vision loss or blindness.

It is extremely difficult to treat diseases affecting retina because it is very challenging to deliver targeted drugs through the dense biological tissue present in eye. Though eye tissues are mostly composed of water but they consist of viscous eye ball and a dense network of molecules (hyaluronan and collagen) which cannot be penetrated easily by particles as these both are very strong barriers. A great deal of precision is required to make a targeted drug delivery to the eye. This is the reason that traditional methods which have been used to deliver drugs to eyes have mainly relied on random and passive diffusion of molecules and these methods are not suited for delivering medicines to the posterior of the eye.

Key points

- Nanorobots are designed or engineered in such a way that they can make a targeted or direct treatment in diseased cells without causing any damage to healthy cells.
- Scientists have developed nanorobots which can for the very first time go through the dense eye tissue.
- Such nanorobots can be loaded with appropriate therapeutics and they can reach retina and other soft dense tissues in unreachable parts of the human body.

Nanorobots to treat retinal diseases

Researchers at Max Planck Institute for Intelligent Systems in Stuttgart along with a team have developed nanorobots ('vehicles') which can for the very first time go through the dense eye tissue. These nanorobots were made using a vacuum-based technique in which silica-based nanoparticles were patterned on a wafer which were then placed inside a vacuum chamber at a particular angle while depositing silica material like iron or nickel. The shadowing caused by a shallow angle makes sure the material only deposits on nanoparticles which then assume helical propeller structure. These nanorobots are about 500nm wide and 2 μm in length, magnetic in nature and shaped like micro propellers. This size is about 200 times smaller than the diameter of a single strand of human hair. The nanorobots are then coated with a non-stick bio liquid layer on the outside to prevent any adherence between the nanorobot and biological protein network in the eye tissue when nanorobots are navigating through it. The optimal size of nanorobots makes sure that they slip through the mesh of biological polymeric network without damaging the sensitive eye tissue. These amazing nanorobots can be loaded with drugs or medicines and can be navigated cm by cm and targeted to a particular area in the eye by use of magnetic fields in real time.

Scientists injected thousands of nanorobots into a pig eye using a needle and applied magnetic field just aptly to stir the nanorobots towards the retina of the eye in a total duration of 30 minutes starting from injection. They constantly monitored the path taken by the nanorobot using an imaging technique which is commonly used in diagnosing eye diseases. This technique is unique and minimally invasive. Though it has been shown so far only in

model systems or fluids. Scientists hope that in the near future this technique will be used to load nanorobots with appropriate therapeutics and they will reach other soft dense tissues in unreachable parts of the human body. The field of nanomedicine - use of nanorobots for therapy – has been gaining a lot of attention in the past several years and many different types of nanorobots are being developed, some using 3D manufacturing process. Interestingly, almost a billion nanorobots can be developed in a few hours by vaporizing silicon dioxide and other materials like iron onto a silico wafer under high vacuum conditions.

Source

Zhiguang, Wu et al. 2018, 'A swarm of slippery micropropellers penetrates the vitreous body of the eye', *Science Advances*, Vol. 4, no. 11, DOI: https://doi.org/10.1126/sciadv.aat4388 ■

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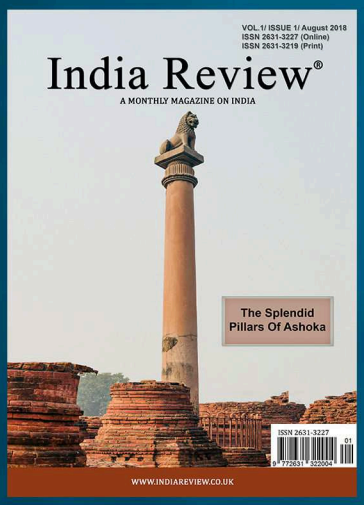

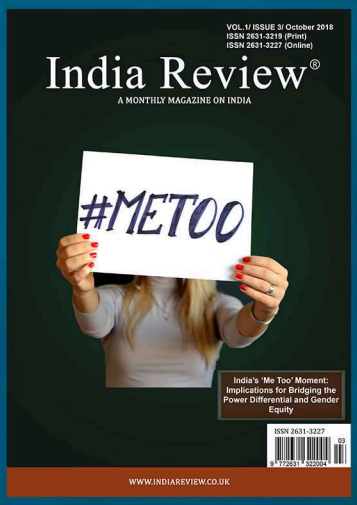

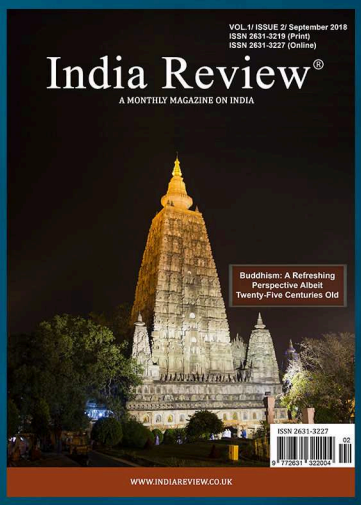

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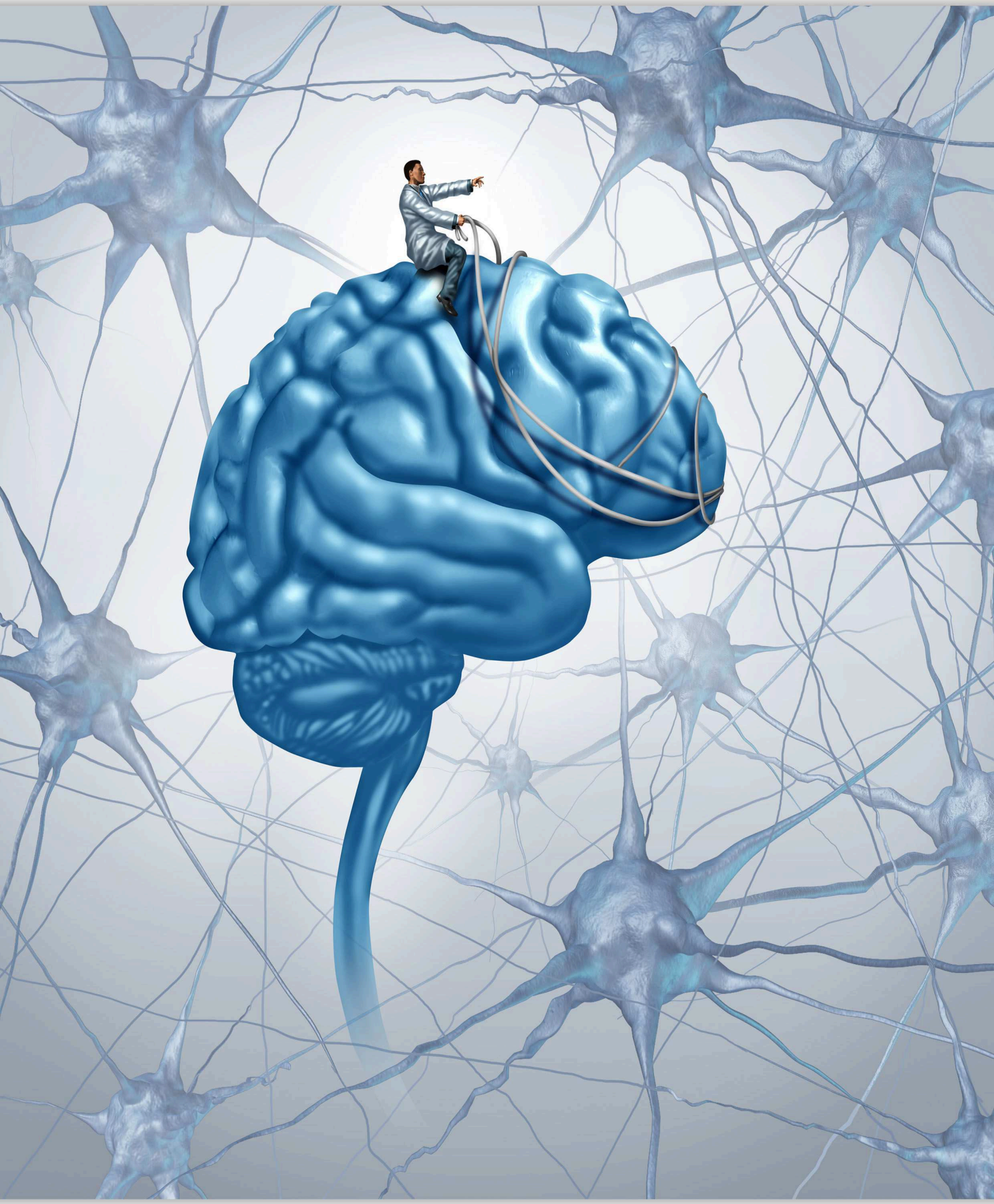
Tau: A New Protein That *May Aid in Developing* Personalized Alzheimer's Therapy

Research has shown that another protein called tau is responsible for early symptoms of Alzheimer's disease and this information may aid in developing therapies.

Alzheimer's Disease (AD) or simply Alzheimer's has no cure and it also cannot be prevented. Deferring the onset of symptoms of Alzheimer's for up to 10-15 years can certainly impact the lives of patients, their families and healthcare givers. Currently, only a late diagnosis of AD can be made and by that time function of the brain is largely weakened. Key characteristics of Alzheimer's is build-up of plaque and defective proteins around neurons inside the brain which are responsible for advancement of the disease. Multiple research shows that higher levels of protein amyloid in the brain are the very early indicators of developing AD. Most of the research on Alzheimer's disease has been focused on understanding how this protein amyloid beta accumulates in the brain. Positron Emission Tomography (PET) imaging technique has been used to visualize deposits of amyloid in Alzheimer's patients. These images and analysis of brain tissue has shown that people with Alzheimer's definitely have higher accumulation of amyloid protein in their brains compared to healthy people.

Is there another protein responsible?

Though it is seen that even after amyloid beta gets accumulated and Alzheimer's disease is at its earliest stage, many patients still have their cognitive processes – both memory and thought – very much intact. This is indicative of a scenario in which amyloid protein must be changing first and then there must be some other factor responsible which researchers predicted could be a second



protein present inside brain cells called tau. It could even be a combination of both because of which a patient may show mild cognitive impairment. Interestingly, even people who have no signs of Alzheimer's have sometimes amyloid proteins accumulated in their brains. Recent studies have generated interest in tau protein which though has been associated with the disease but hasn't been the focus of much research. One obstacle in pursuing study on tau protein has been that a non-invasive way to get an image of this protein inside a living person's brain has been only lately achieved. Researchers at Washington University School of Medicine, St. Louis have used a previously unknown imaging agent which binds to the tau protein (without causing side effects) making it visible in PET scans. In their study they aimed to understand the significance of tau as a marker of cognitive decline – a critical characteristic of Alzheimer's. Their study is published in *Science Translational Medicine.*

In the study, 46 participants - 36 healthy adults and 10 patients with mild AD - underwent brain imaging which used the new PET imaging agent. Their brain images were then compared to understand decline in cognitive abilities due to AD. The extent of cognitive impairment was evaluated using cerebrospinal fluid measures, clinical dementia rating and paper tests for memory and other brain functions. The severity of cognitive dysfunction was analysed along with images. Results seen in 10 patients (with mild AD) in PET scans clearly showed that tau is a better predictor of symptoms of cognitive decline compared to amyloid. And tau protein might be more closely linked to symptoms like memory loss. This new tau protein (called T807) is seen to be critical in firstly understanding progression of Alzheimer's and secondly to gather information about which portions of the brain are affected and involved in disease progression. Though increased tau protein is already an established marker of Alzheimer's but for the first-time regions in the brain which accumulate these abnormal proteins have been pinpointed. As long as tau is deposited in the hippocampus of the brain, its well tolerated. Its spread to other areas like temporal lobe (which is associated with memory processing) can be damaging which is reflected in memory and attention tests. This allows potential use of tau as a diagnostic tool. Such a situation was not applicable to amyloid protein and this confirmed that tau protein can predict more accurately when a person is transitioning from an early stage – with no symptoms – to mild Alzheimer's disease. A combination of both amyloid and tau could also be responsible. The study does have some limitations because the images are basically 'one snapshot' of the brain at one point of time and they cannot wholly depict association of tau and mental deterioration.

Since imaging agents are now available for both amyloid beta and tau, the debate of which one is more crucial can continue but necessary tools can be used to study effect of experimental therapies targeting both these proteins. The new imaging agent for tau is already approved for clinical trials and can be used in brain imaging for various disorders which involve elevated tau protein – example brain injury or trauma. There is immense hope that an earlier diagnosis of Alzheimer's disease could help to design drugs for build-up of amyloid and tau proteins. Researchers optimistically propose a personalized Alzheimer's therapy in the future which would be based upon the exact scenario in a patient's brain.

Source

Brier, MR. 2018, 'Tau and Ab imaging, CSF measures, and Cognition in Alzheimer's disease', *Science Translational Medicine*, Vol. 8, no. 338, DOI: https://doi.org/10.1126/scitranslmed.aaf2362

■

Treatment of Paralysis Using a Novel Method of Neurotechnology

Study had shown recovery from paralysis using a novel method of neurotechnology

The vertebrae in our body are bones which make up the spine. Our spine contains several nerves which extend from our brain down till the lower back. Our spinal cord is a group of nerves and related tissue which this vertebra of the spine consists of and provides protection to. The spinal cord is responsible for transmitting messages (signals) from brain to different parts of our body and vice versa. Because of this transmission we are able to feel pain or move our hands and legs. A spinal cord injury is an extremely severe physical trauma when damage is caused to the spinal cord. When the spinal cord sustains an injury, some of the impulses from our brain "fail" to get delivered to different parts of the body. This results in complete loss of sensation, strength and mobility anywhere below the injury location. And if the injury occurs close to the neck, this results in paralysis throughout large part of the body. Injury of the spinal cord is very traumatic and has a significant impact on the sufferer's daily life inflecting lasting physical, mental and emotional effects.

New promising study

Currently there is no cure to repair damage caused by a spinal injury as it is irreversible. Some forms of treatment and rehabilitation help patients to lead fruitful and independent lives. Lot of research is ongoing with the hope that someday it would be possible to completely

treat spinal cord injuries. In a breakthrough study a team of scientists from Ecole Polytechnique Fédérale de Lausanne and Lausanne University Hospital in Switzerland, have designed a novel therapy to advance recovery from spinal cord injury. This study called as STIMO (STImulation Movement Overground) has been published in *Nature*[1] and *Nature Neuroscience*[2]. Scientists state that their findings are based upon the understanding they have gained in analysing animal models through years of research.

Scientists aimed to mimic real time behaviour of brain and spinal cord. The participants in this study were three paraplegics who had suffered cervical spinal cord injuries and had been

paralysed since many years (minimum four). All had undergone different rehabilitations and though there were neural connections at the injury site, they did not gain movement. After undergoing the new rehabilitation protocol described in the current study, they were able to walk just within a week's time with the help of crutches or walker showing that they recovered voluntary control of leg muscles which were paralysed after they sustained injury.

Researches achieved this by 'targeted electrical stimulation of nerve cells' in lumber spinal cord along with weight-assisted therapy. The electrical stimulation of the spinal cord was done with very high levels of precision and this made this study unique. The stimulation was like short electric jolts which would amplify signals and help the brain and legs of paralyzed participants communicate better. For this purpose, implants - array of electrodes (16 electrodes onto a pulse generator)- were placed on the spinal cord allowing researchers to target distinct individual muscles in participant's legs. This implant, a machine of size of a matchbox had been originally designed for muscular pain management. It was technologically challenging to be able to surgically implant this device at specific regions in the spinal cord. Different configurations of these electrodes in the implants activated targeted regions of the spinal cord and mimicked signals/messages which needed to be delivered to the brain to be able to walk. Alongside electrical stimulation, patients also had to on their own 'think' about moving their legs so as to awaken any dormant neuron connections.

Key points

- When the spinal cord sustains an injury, some of the impulses from our brain "fail" to get delivered to different parts of the body resulting in complete loss of sensation, strength and mobility.
- Researchers designed a novel therapy to advance recovery from spinal cord injury by 'targeted electrical stimulation of nerve cells' in lumber spinal cord along with weight-assisted therapy.
- There is hope that patients who have sustained different types of chronic spinal cord injuries can recover with the right training.

Training

It was important for the participants to have a precise time and location of the electrical stimulation so as to produce a particular movement. Targeted pulses of electricity were delivered by a wireless control system. It was challenging for the participants to adapt and finetune the coordination between their own brain's 'intention' to walk and the external electrical stimulation. The experiment led to better neurological function and allowed the participants to naturally train overground walking abilities in the laboratory for an extended period of time. After a week, all three participants were able to walk hands-free with help of targeted electrical stimulation and some body-weight support system for over one kilometre. They didn't experience leg-muscle fatigue and their stepping quality was consistent so they were comfortably able to participate in lengthy training sessions.

After five months of training, voluntary muscle control of all participants significantly improved. Such a long and high-intensity training session was seen to be very good for maintaining plasticity by utilizing our nervous system's inherent ability to 'reorganize' nerve fibres and growth of new nerve connections. Longer training led to improved and consistent motor function even after external electrical stimulations were turned off.

Previous studies which used empirical approaches have been successful in which few paraplegics were able to take few steps over a short distance with help of walking aids as long as electrical stimulations were provided. When stimulations were

turned off their previous state returned where patients could not activate any leg movements and this is because the patients were not 'trained enough'. A unique aspect of the current study is that neurological functions was seen to persist even after training ended and electrical stimulation was turned off though participants walked much better when stimulations were on. This training treatment might have helped to rebuild and strengthen neural connections between brain and spinal cord which had become non-functional as a result of injury. Scientists were delighted at the unexpected response of human nervous system to their experiment.

This is a breakthrough research for patients who have sustained different types of chronic spinal cord injuries and a hope has been generated that with the right training they can recover. Start-up company called GTX medical cofounded by the authors of this study is looking to design and develop tailored neurotechnology which can be used to provide rehabilitation within the healthcare system. Such a technology shall also be tested much earlier, i.e. immediately post-injury when the recovery potential is much higher as body's neuromuscular system has not experienced complete atrophy associated with chronic paralysis.

Source

1. Fabien B. Wagner et al., 2018, 'Targeted neurotechnology restores walking in humans with spinal cord injury', *Nature*, Vol. 563, no. 7729: 65, DOI: https://-doi.org/10.1038/s41586-018-0649-2

2. Leonie Asboth et al. 2018, 'Cortico–reticulo–spinal circuit reorganization enables functional recovery after severe spinal cord contusion', *Nature Neuroscience*, Vol. 21, no. 4, DOI: https://doi.org/10.1038/s41593-018-0093-5 ■

Omega-3 Supplements May Not Offer Benefit to The Heart

An elaborate comprehensive study shows Omega-3 supplements may not offer benefit to the heart

It is believed that small portions of omega-3 – a type of fat - can be good for one's health. Alphalinolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) are the three main types of omega-3 fatty acids. These can be naturally found in foods which we eat daily example plant foods like nuts and seeds contain ALA and fatty fish like salmon or tuna and fish oils contain EPA and DHA. It is a widely accepted and popular belief or rather a 'fact' based upon some early clinical trials in 1980s and 1990s that consuming omega-3 fats can provide protection against heart related diseases like heart attack, stroke or death by lowering blood pressure or reducing cholesterol levels. Omega-3 supplements in the form of capsules are available over-the-counter and are consumed by many on

a daily basis with or without a doctor's prescription.

Meta-analysis – a combination of many trials

A recent Cochrane systematic review shows that omega-3 supplements have very slight or no effect on one's risk of heart diseases based upon a comprehensive review of evidence. Cochrane organisation is a global network of experts dedicated to informing health policy. For this study, a total of 79 randomized trials were conducted with 112,059 people to evaluate the effects of taking omega-3 fat on heart circulation and diseases. 25 studies were designed and conducted and participants were from North America, Australia, Europe and Asia. Both men and women either healthy or having minor or major illnesses were included as participants. Randomly chosen, each participant had to either maintain their diet or along with diet take omega-3 fat supplement in the form of a daily capsule for one year. The meta-analysis assessed daily intake of omega-3 fat and few studies assessed intake of oily fish like salmon and tuna or ALA-rich foods while other participants were asked to maintain usual intake of food.

Omega-3 supplements have no considerable effect

Researchers concluded after evaluating the outcomes that there was evidence of high certainty that omega-3 had slight or no impact on a person's risk of heart attacks, strokes or heart irregularities. Also, omega-3 has 'no considerable effect' on risk of death as it was calculated at 8.8% for participants who took supplements, while 9% for controlled group who took normal food and did not take supplements. Omega 3 supplements had no effect on risk of cardiovascular events like stroke etc. EPA and DHA- the long chain omega-3 fatty acids - reduced some blood fat, triglycerides (which could be indicative of protection from heart diseases) and HDL cholesterol but then reducing HDL had an opposite effect.

There was 'moderate evidence' that consuming more ALA from supplemented walnuts may have small benefit on risk of main cardiovascular events or body weight seeing that risk of irregularities in the heart was reduced from 3.3 to 2.6 %. Consumption of canola oil and nuts was seen of a small benefit especially in preventing heart arrhythmias. No evidence was collected on benefits of eating more oily fish and not much information could be collected on adverse scenarios like bleeding or blood clots from ALA. From extensive information collected from the 25 studies, no clear-cut protective effects of omega-3 were seen. The overall chance of receiving any benefits from omega-3 supplements was stated as one in 1,000.

Healthy diet is more important

The popular and widely accepted belief that EPA and DHA omega-3 supplements protect the heart has been cited as controversial and is still debatable. Many experts believe that it is anyway very unlikely that one particular element of diet could be alone responsible for reducing risk of heart diseases. The financial aspect of consuming supplements is also side-lined and it would rather be recommended to have an overall healthy diet and stop unnecessary use of over-the-counter supplements. However, if omega-3 supplements have been advised by the doctor for some specific reason then one must continue their intake. Otherwise the best recommendation to get omega-3 through natural foods rather than supplements.

This meta-analysis is seen as a dependable

comprehensive systematic review which has collected information spanned over long time durations from large groups of people providing strong evidences and has concluded that increasing intake of omega-3 fats may not be protective of our hearts. Only ALA which is actually an essential fatty acid, is said to be an important part of a balanced diet and its increased intake can be somewhat useful for preventing and maybe treating cardiovascular events. This review conducted by Cochrane organisation was requested by World Health Organization who are in the process of updating their guidelines on polyunsaturated fats.

Source

Asmaa S Abdelhamid et al. 2018, 'Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease', *Cochrane Database of Systematic Reviews*, DOI: https://doi.org/10.1002/14651858.CD003177.pub3 ■

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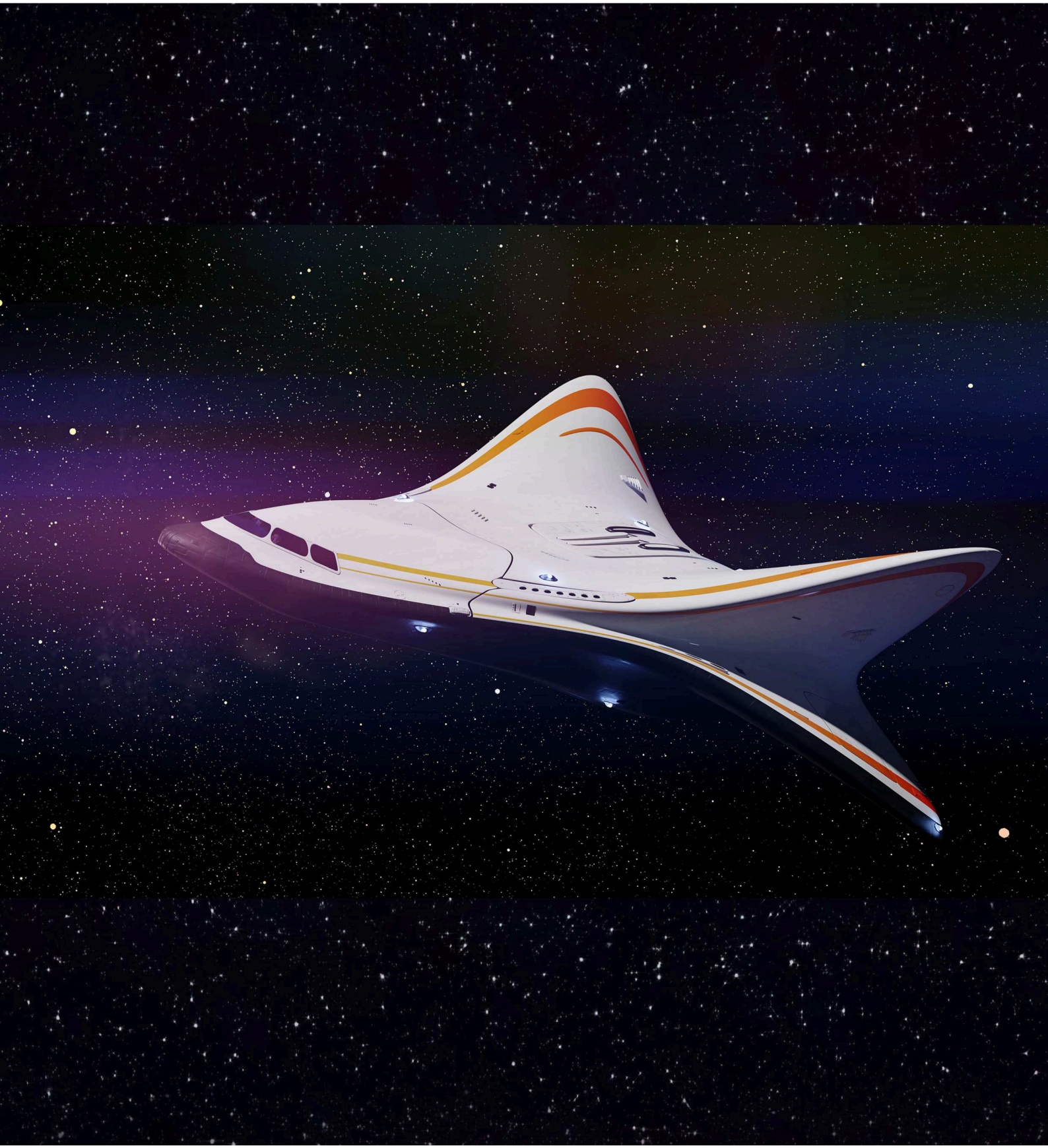
Airplane has been designed which won’t be dependent on fossil fuels or battery as it won’t have any moving part

Ever since the discovery of airplane more than 100 years ago, every flying machine or aircraft in the sky flies uses moving parts like propellers, jet engine, blades of a turbine, fans etc which obtain power from either fossil fuel combustion or by using battery which can produce a similar effect.

After almost a decade long research, aeronautic scientists at MIT have built and flown for the first time a plane which has no moving parts. The method of propulsion used in this airplane is based on the principal of electroaerodynamic thrust and is called ‘ion wind’ or ion propulsion. So, in place of propellers or turbines or jet engines used in conventional airplanes, this unique and light machine is powered by ‘ionic wind’. The ‘wind’ can be produced by passing strong electric current between a thin and a thick electrode (powered by lithium ion batteries) which results in ionizing of gas thereby producing fast-moving charged particles called ions. The ionic wind or flow of ions smash into air molecules and push them backwards, giving airplane the thrust to move forward. The direction of the wind depends upon the arrangement of electrodes.

Ion propulsion technology is already used by NASA in outer space for satellites and spacecrafts. In this scenario since space is vacuum, there is no friction and thus its quite simple to drive a spacecraft to move forward and its speed also gradually builds up. But in the case of aircrafts on Earth it is understood that our planet’s atmosphere is very dense to get ions to drive an aircraft above the ground. This is first time ion technology has been tried to fly airplanes on our planet. It was challenging firstly because just enough thrust is needed to keep the machine flying and secondly the airplane will have to overcome the drag from resistance to air. The air is sent backward which then pushes the airplane forward. The crucial difference with using the same ion technology in



space is that a gas needs to be carried by the spacecraft which will be ionized because space is vacuum while an aircraft in Earth's atmosphere ionizes nitrogen from atmospheric air.

The team performed multiple simulations and then successfully designed an aircraft having five-meter wing span and weight of 2.45 kilograms. For generating electric field, set of electrodes were affixed underneath the plane's wings. These consisted of positively charged stainless steel wires in front of a negatively charged slice of foam covered in aluminium. These highly charged electrodes can be switched off by remote control for safety.

The airplane was tested inside a gymnasium by launching it using a bungee. After many failed attempts this airplane could propel itself to remain airborne. During 10 test flights, airplane was able fly up to a height of 60 meters minus any weight of a human pilot. Authors are looking to increase the efficiency of their design and produce more ionic wind while using less voltage. The success of such a design needs to be tested by scaling up the technology and that may be an uphill task. The biggest challenge would be if the size and weight of the plane increases and covers bigger area than its wings, the plane would require higher and stronger thrust to stay afloat. Different technologies can be explored example making batteries more efficient or maybe using solar panels i.e. finding new ways of generating the ions. This airplane does use the conventional design for aircrafts but it may be possible to try another design in which electrodes could shape the ionizing direction. Any other novel design could be conceptualized.

The technology described in the current study could be perfect for silent drones or simple airplanes because drones currently used are a big source of noise pollution. In this new technology, silent flow generates ample thrust in the propulsion system which can propel the plane over a well-sustained flight. This is unique! Such a plane will not require fossil fuels to fly and thus would not have any direct polluting emissions. Also, when compared to flying machines which use propellers etc this is silent. The novel discovery is published in *Nature*.

Source

Xu H et al. 2018, 'Flight of an aeroplane with solid-state propulsion', *Nature*, Vol. 563, no. 7732,
DOI: https://-doi.org/10.1038/s41586-018-0707-9 ■

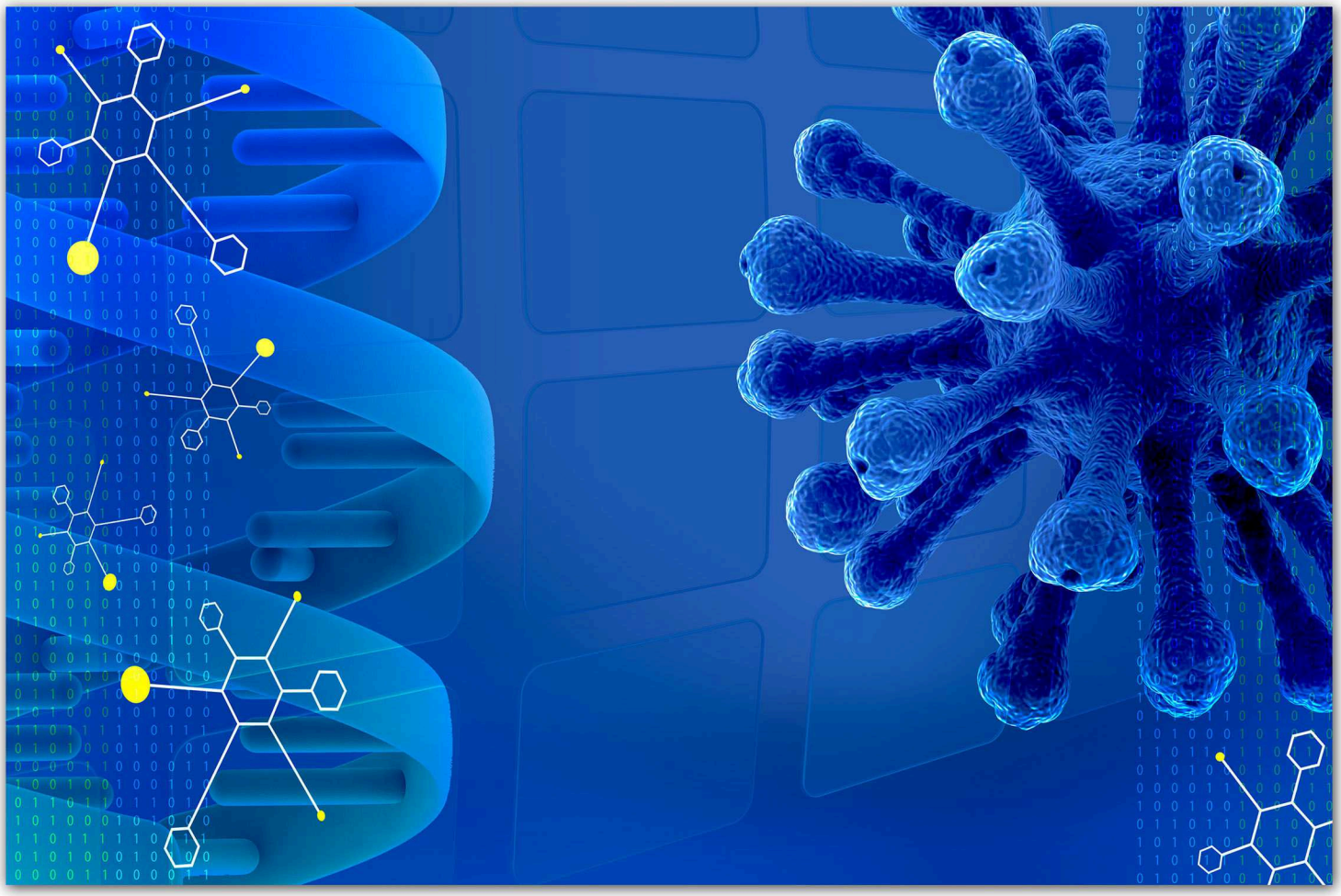
DNA Origami Nanostructures for Treatment of Acute Kidney Failure

A novel study based on nanotechnology generates hope for treating acute kidney injury and failure.

Kidney is an essential vital organ which performs critical functions in the body. It removes wastes and extra water from our blood stream to produce urine which then flows from kidneys to the balder through the ureters. These wastes which are produced in our body from normal breakdown of muscle and foods must be discarded and excreted efficiently.

In acute kidney failure, now called Acute Kidney Injury (AKI) nitrogenous wastes rapidly build up and urine output decreases i.e. the body struggles to produce urine. This happens within a short span of time (days or even hours) of the onset of the ailment causing causes serious complications. The leading cause of AKI is oxidative stress which occurs due to disturbed balance between free radicals and anti-oxidant defences resulting from increase in oxygen-containing waste products thus causing damage to lipids, proteins and DNA. This scenario causes inflammation and advances the kidney disease. That is why anti-oxidants rich foods and supplements are known to protect from harmful effects of oxygen-containing waste products. Also, there are then high chances of developing cardiovascular diseases and cancer. When severity of kidney disease advances, support therapies like rehydration and dialysis are needed and even kidney transplant can be required. There is no cure available for AKI making it responsible for millions of deaths every year.

Protecting and treating injured kidneys remains an



Key points

- There is no cure available for acute injuries to kidney, an important vital organ.
- A new preventive method has been designed for stopping AKI (Acute Kidney Injury) by treating it using nanotechnology involving tiny self-assembling forms called DNA origami nanostructures.
- These structures coat around the kidney and can provide localized protection to kidneys from AKI.

enormous challenge in medicine. An anti-oxidant drug NAC (N-acetylcysteine) considered the gold standard is generally used to protect kidneys from toxicity during procedures but this drug has poor bioavailability and thus has limited effectiveness.

Nanotechnology approach for therapy

Application of nanotechnology in biomedical methods including therapy has picked up pace in the recent decades. But such applications have shown limitation in treating kidney diseases. In a new study, scientists from USA and China have described a new preventive method for stopping AKI and treating it by using nanotechnology involving tiny self-assembling forms which measure just billionth of a meter in diameter. These shapes were designed and developed using the nanotechnology method called 'DNA origami' in which base pairing of four DNA nucleotides is

used to engineer and fabricate what is called DNA origami nanostructures (DONs). These nanostructures – either triangular, tubular or rectangular in shape –can be then used for performing various tasks inside the body. The architecture of such nanostructures is ideally suited for living systems because they are stable and they have low toxicity and immunogenicity.

DNA origami nanostructures self-assemble and latch onto different parts of the kidneys and form a protective layer around them. This has been seen when assessing their physiological distribution using quantitative imaging by positron emission tomography (PET). Their study is published in Nature Biomedical Engineering. The group prepared various DNA origami structures and also used radio labelling to study their behaviour in mouse kidney while analysing them using PET imaging. These were seen to accumulate in kidneys of healthy mice as well those who had AKI.

The study showed how DNA origami nanostructures act as a fast (within only 2 hours) and very active kidney protectant and was also therapeutic in relieving symptoms of AKI. Upon examination of their real-time distribution using PET scan it was see that rectangular nanostructures particularly were most successful in protecting the kidneys in the same manner as a standard drug would. These structures track down oxygen-containing waste products and insulate the cells from damage due to oxidative stress. They help maintain balance of free radicals and anti-oxidant defences in and around the kidney and thus reduce and alleviate oxidative stress which is the leading source and symptom of AKI. The measures taken by DONs stop the kidney disease to progress. DONs were tested both on living mice kidney and human embryonic kidney cells. And clearly, these structures acted as a protective guard and improved kidney function in AKI as effectively as traditional drug therapies particularly NAC drug for AKI.

The DNA origami structures were persistently present in kidneys which authors suggest is owing to several factors including resistance of DONs to digestive enzymes and their avoidance of immune system surveillance. Physiologically, improvement in kidney function was assessed by noting levels of serum creatinine and blood urea nitrogen and it was clear that there was significant improvement in kidney excretory function comparable to standard drug therapy.

This multidisciplinary study combines expertise of nanomedicine and in-vivo imaging and is the first ever to investigate distribution of DNA nanostructures in a living system by live tracking their behaviour. DONs have low toxicity in main organs of the body making them ideally suited for clinical use in humans. This modern technology is a strong foundation which can provide localized protection to kidneys from AKI and also can be used to design novel therapeutic approaches for treating AKI and other kidney diseases. Immense hope has been generated that a solution for kidney diseases can be a reality for patients suffering from acute kidney injury. A very exciting study indeed, it adds to the potential of therapeutic programmable nanostructures which can be used for targeted drug delivery and organ and tissue repair in the body.

Source

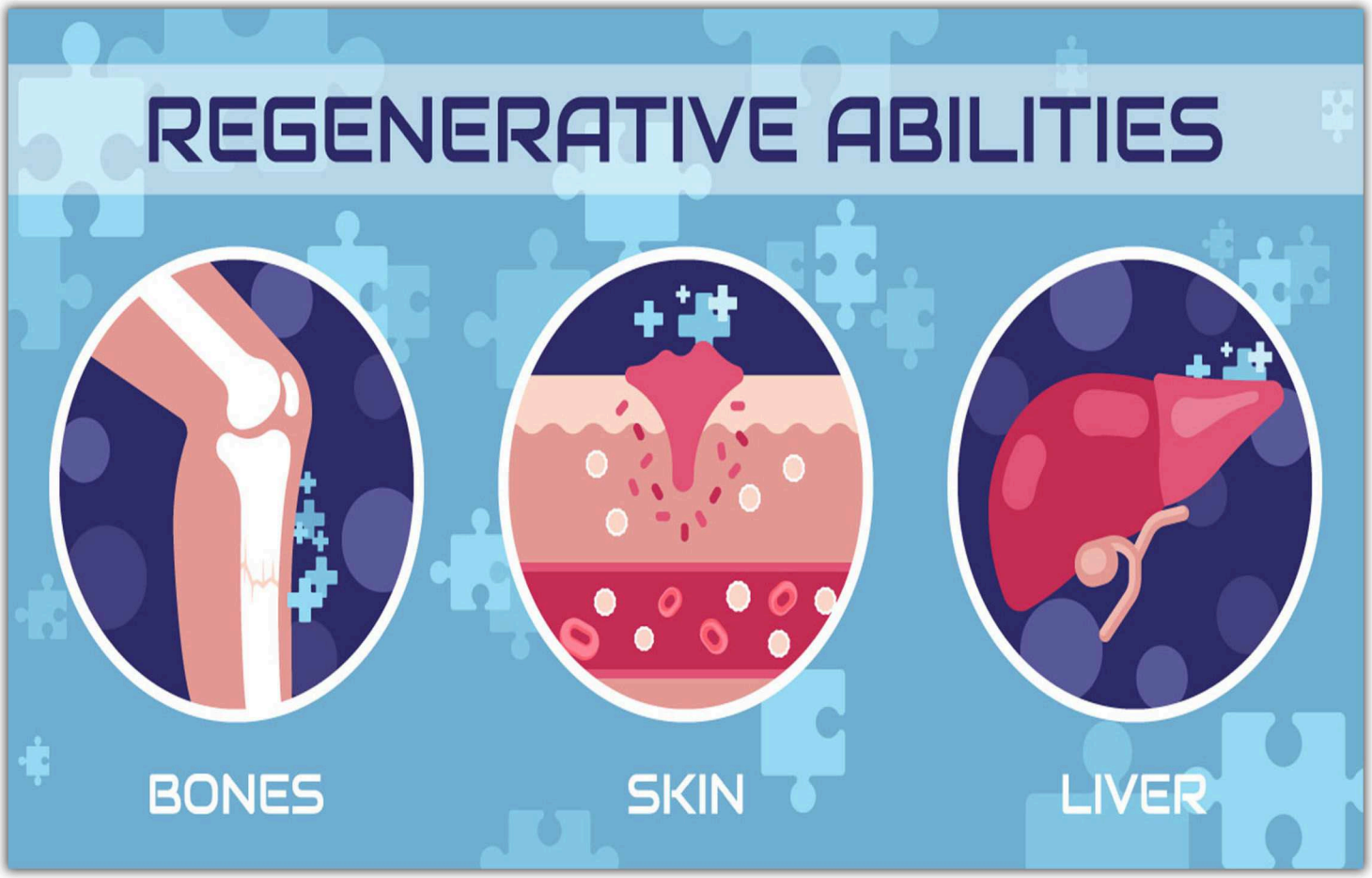
Dawei Jiang et al. 2018, 'DNA origami nanostructures can exhibit preferential renal uptake and alleviate acute kidney injury', *Nature Biomedical Engineering*, Vol. 2, no.11,
DOI: https://doi.org/10.1038/s41551-018-0317-8

'Adult Frog Regrows Amputated Legs': *An Advance in Organ Regeneration Research*

Adult frogs have been shown for the first time to regrow amputated legs marking it as a breakthrough for organ regeneration.

Regeneration means re-growing a damaged or missing part of an organ from residual tissue. Adult humans can successfully regenerate some organs like liver and especially skin which is regularly renewed and repaired but unfortunately human tissues of most organs do not have the ability to regenerate. The field of regenerative medicine aims to find ways to retrigger regeneration of tissue in our body. The ideal solution would be to set in motion important pathways which can restore a tissue, example a limb, from its own cells, however, it is not such a straightforward case as scientists are still trying to understand the nuances of tissue regeneration.

In a breakthrough study published in *Cell Reports*, scientists from Tuft University USA aimed to understand tissue regeneration capacity and how cells cooperate and form a three-dimensional organ. They chose to reproduce tissue growth in an animal which normally does not regenerate and they chose an amphibian - adult aquatic African clawed frog (Xenopus laevis) - a commonly used laboratory animal in research. Amphibians have very limited tissue renewal capacity similar to humans. Scientists successfully designed a device which retriggers tissue generation at the amputation site and enables to partially regenerate a hindlimb in adult Xenopus frog.



Re-growing amputated limbs

First, a wearable bioreactor was printed in 3D in silicon and it was filled with hydrogel. Next, hydrating silk proteins were placed on this hydrogel polymer which are known to promote healing and regeneration. The hormone progesterone - a neurosteroid - was added which is generally known to be involved in menstruation, pregnancy and breastfeeding. Progesterone is also involved in promoting repair of nerve blood vessel and other tissue. The frogs were divided into experimental, control and sham groups. In control and sham groups, the bioreactor device was sutured into the frogs instantly following the limb amputation. In experimental group progesterone was released by the bioreactor onto the amputation site. The devices were removed after 24 hours. The frogs were then routinely observed for several months. Frogs in control and sham groups developed a thin, cartilaginous spike at the amputation site which is normal when tissue regeneration progresses unaided. It was seen only in frogs of experimental group that bioreactor device triggered bigger limb regeneration and frogs regrew a more structured paddle-shaped appendage close to an almost fully formed limb. This was indicative of an aided tissue regeneration. The visible difference was noticeable within few weeks itself suggesting that the bioreactor device created a support environment around the wound to enable tissue to grow – similar to how tissues would grow in an embryo inside the uterus. It is very interesting that just a brief delivery of progesterone from the bioreactor (placed only for 24 hours) had triggered growth of soft tissue and bone over course of several months. Upon histology analysis and molecular inspection of the regenerated structures it was revealed that these limbs were thicker and had more developed bones, innervation and vascularization. The animals treated with progesterone were also more

active than the control and sham groups.

The growth of limbs stopped after about six months but it did lead to under typical growth of fingers and toes. Interestingly the regrown limbs had good bone volume and density, main blood vessels, well-set nerves and these frogs could even swim similar to how normal unamputated frogs would using their native limbs. RNA sequencing and transcriptome analysis showed that gene expression in the cells at the amputation site was modified by the bioreactor. So, genes related to oxidative stress and white blood cells activity were active (upregulated) and some others were downregulated. The scarring and immune response was also reduced thus allowing for regeneration to proceed by weakening the body's natural response to injury which would have otherwise hampered the regeneration process.

Future

This study is very encouraging because it is based upon the logic of defining a kickstart or trigger program which would lead way to a long-term growth. It can be called as a new model of cell-stimulation. Earlier studies have shown that mice can partially regenerate amputated fingertips under normal circumstances but because they are not aquatic and there is no water to protect them, so unlike amphibians the process in mice was not efficient because sensitive regenerated cells were subjected to hard surfaces again and again. Authors of this study are hopeful that this regeneration approach in a vertebrate animal should be applicable to mammals and to human body and maybe very soon in the future we can regenerate complex organs which could be used for organ transplant or any kinds of injuries maybe even cancer.

Source

Celia Herrera-Rincon et al. 2018, 'Brief Local Application of Progesterone via a Wearable Bioreactor Induces Long-Term Regenerative Response in Adult Xenopus Hindlimb', *Cell Reports*, Vol. 25, No 6, DOI: https://doi.org/10.1016/j.celrep.2018.10.010

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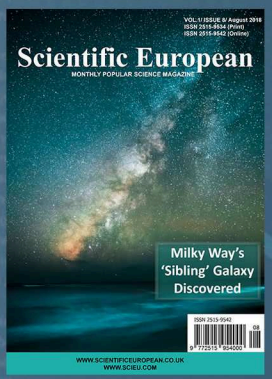

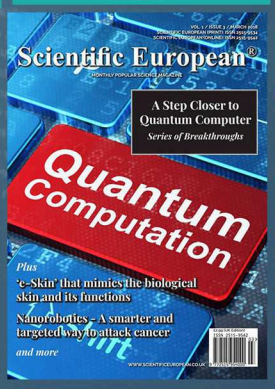

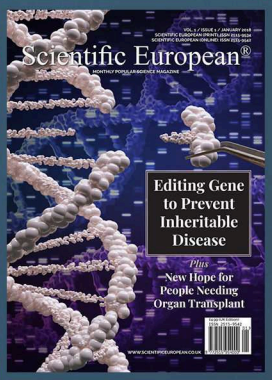

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A New Easy Treatment *for Peanut Allergy*

A promising new treatment using immunotherapy to treat peanut allergy by building tolerance over time.

Key points

- People who have peanut allergy, one of the most common type of food allergies, need to remain vigilant throughout their lives otherwise severe, life threatening reaction can occur.
- Research shows that peanut allergy could be treated by building up one's tolerance level to peanut via a controlled incremental exposure to the allergic substance.
- This type of oral immunotherapy treatment could work for some if not all people who have peanut allergy.

Peanut allergy, one of the most common food allergies, is when our immune system identifies peanut protein to be harmful. Peanut allergy is most common in children in industrialized countries. Even slight off chance exposure to trace amounts of peanuts in confectionaries or other food items can cause allergic reaction and even sometimes hospitalization. In more than 30 percent cases severe allergic reaction occurs such as anaphylaxis. There is no cure for peanut allergy and also no treatment options have been approved till date. If at all any treatment for peanut allergy is approved, it is to be only prescribed to the patient by a doctor and the patient will need to continue to use the treatment to be able to stay protected from any accidental consumption of peanut at any given time in their life. Such a treatment is also no longer effective once the prescription is stopped. People who have peanut allergy need to remain vigilant throughout their lives and this is very difficult to cope with especially for children.

Building tolerance to allergen peanut

A study has shown for the first time that it may be possible for persons with peanut allergy to get protection from unintentional intake of peanut by desensitizing themselves to the allergy gradually over time. This is done by building up one's tolerance level to peanut via a controlled incremental exposure to the allergic substance which otherwise can cause a serious reaction. The method is based upon the principle of immunotherapy and aims to build one's immune system's tolerance to an allergen, in this case peanut. The systematic study published in *New England Journal of Medicine* was conducted on 551 participants of 4 to 55 years age group who had peanut allergy and they were given the experimental drug for a year. This drug called AR101 is a


ALLERGY

protein powder derived from peanut and is developed by Aimmune Therapeutics Inc. USA. The total number of participants in this study were high and also additional detailed data analysis has been done compared to all prior studies combined. One third participants were given a placebo (i.e. no peanut at all) and others were given peanut protein powder (from peanut flour) slowly in incremental manner until a dose (equivalent of one peanut daily) was reached which was then maintained till the end of the study. Almost 80 percent participants reached this 'maintenance' dose, which was then given up till six months. The peanut protein was part of the 'oral food challenge' considered the gold standard in testing for food allergy. Any participant in this challenge is given some amount of food from mouth supervised by a certified allergist to tackle any severe reaction.

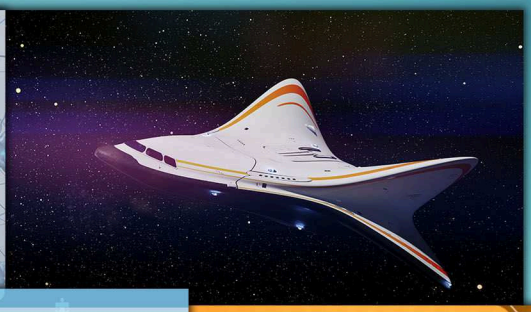
At the end of the study, participants were able to tolerate 100-fold higher dosage of peanut compared to when they started. During the study, the symptoms were also seen to be mild even for higher dosage compared to symptoms for a lower dosage at the start of the study. Two-thirds of participants could now tolerate an equivalent of daily two peanuts and after 9-12 months the tolerance level of half of the participants went up to equivalent of four peanuts daily. Best results were seen in the age group of 4-17 years i.e. children and adolescents. Only a meagre 6 percent dropped out due to gastrointestinal / skin / respiratory etc side effects and one-third patients had very mild negligible side effects. All 372 children did suffer allergic reaction, though only less than five percent were severe. Severe reaction effects were seen in 14 percent of children which would require the drug epinephrine – a powerful hormone - to control.

Authors do state that this is not the 'ultimate' solution or 'complete cure' of peanut allergy and they do not advocate 'anytime anywhere' consumption of peanut. This type of oral immunotherapy treatment may not work for everyone who has peanut allergy and a major drawback of the study which authors point out is that it may be difficult to predict who can or who cannot use this treatment. Nevertheless, this study suggests that a robust treatment can be available in the near future where people who have peanut allergy and who can tolerate this treatment (i.e. tolerate one peanut a day) may be able to tolerate two peanuts and thus could get protection from accidental consumption which leads to life-threatening reactions. The regime from this study has to be followed only under expert supervision and the goal is not for everyone to consume large quantities but rather be able to tolerate small amounts of peanut which can improve their quality of life.

Peanut allergy is a serious problem especially among children and adolescents and this group can be protected from accidental or unintentional consumption of food containing peanut. The drug AR101 looks promising to reduce frequency and severity of allergic reactions to peanut and thus appears beneficial. Understanding food allergy is key to designing strategies for prevention of severe allergic reactions and also for correct application of oral immunotherapy approach. If this meets success, similar approach can be used for other common allergies example from egg.

Source

The PALISADE group of Clinical Investigators 2018, 'AR101 Oral Immunotherapy for Peanut Allergy', *New England Journal of Medicine*, Vol. 379, DOI: https://doi.org/NEJMoa1812856 ■




REGENERATIVE ABILITIES
BONES
SKIN
LIVER


HOIL
BEST
OMEGA-3
DHA
EPA


ALLERGY