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Disruption of Body Clock due to Irregular Insulin Secretion Associated with Untimely Eating IncreasesRisk of Chronic Diseases

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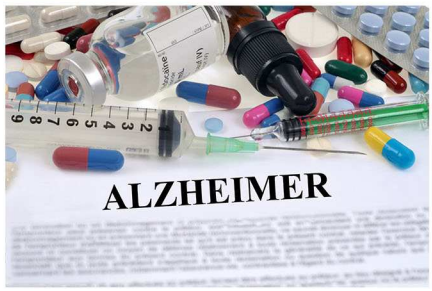

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NOTE FROM EDITOR-IN-CHIEF

We are delighted to bring to you thirteen articles on recent scientific advancements like measuring Vitamin D from hair, role of coconut oil in Alzheimer's, immortality, advances in treatment of HIV and many more.

Hope you enjoy reading them!

Umesh Prasad

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Coconut Oil in Food Reduces Skin Allergy

New study in mice shows effect of consuming dietary coconut oil in controlling allergic skin inflammation

Health benefit of a dietary oil is primarily determined by the composition of fatty acids – saturated and unsaturated fatty acids. These fatty acids play significant roles in the body including dealing with inflammation and allergy. Coconut oil, extracted from the edible meat of a mature coconut, constitutes mainly of absorbable medium chain saturated fatty acids which are considered healthy as they are easily metabolized by the liver. Coconut oil's unique combination of fatty acids is suggested to have a positive effect on one's health. Coconut oil is easily digestible, readily available and inexpensive. It is known that topical application of coconut oil reduces skin infections and inflammation, but the exact role of dietary coconut oil in reducing skin inflammation is unknown, until a new study.

A latest study published in *Allergy* researchers set out to elucidate the possible role of coconut oil as a dietary fat in skin inflammation. They conducted experiments using mice model of contact hypersensitivity (CHS). In CHS model a hypersensitivity reaction in induced in the skin by hapten 1-fluoro-2,4-dinitrobenzene (DNFB). In the condition - called allergic contact dermatitis - inflammation intensity is correlated with swelling in ear. The mice were given chow diets containing 4 percent coconut oil. Mice is the control group were given diet with 4 percent soybean oil. The mice were then treated with DNFB for eliciting hypersensitivity reaction. Subsequently their ear swelling was measured.

Results showed that mice who took and maintained a diet of coconut oil exhibited improvement in skin inflammation and signs like swelling in ear were correspondingly reduced. Further, mice on maintained diet of coconut oil showed substantially amplified levels of mead acid, a metabolite derived from oleic acid known to have anti-inflammatory properties. The increased levels of mead acid in mice on dietery

coconut oil was responsible for inhibiting CHS and reducing the number of neutrophils entering the skin. Neutrophils are known to play a critical role in inducing skin inflammation.

The current study shows a novel and promising anti-inflammatory role of dietary coconut oil and mead acid against skin inflammation in an animal model. Further studies on humans' allergic contact hypersenstivity model can elucidate role of coconut oil and mead acid in reducing skin inflammation in humans. The limited number of available medicines for skin inflammation like antihistamines, corticosteroids have several side effects e.g. stinging, burning etc. Mead acid is a safe and stable endogenously produced saturated fatty acid which could be a promising alternative for therapeutic approaches towards skin inflammation.

Source(s)
Tiwari P et al. 2019. Dietary coconut oil ameliorates skin contact hypersensitivity through mead acid production in mice. Allergy. DOI:10.1111/all.13762

■

Green Tea Vs Coffee: *The Former Seems* Healthier

According to a study conducted among elderly in Japan, consuming green tea may reduce risk of poor Oral Health Related Quality of Life

The tea and coffee are two most commonly used beverages in the world. The green tea is particularly popular in China and Japan.

Oral health or overall health and hygiene of mouth is an important aspect of general health and as such is a reflection of overall general health.

The general estimate of well being of individuals and societies is measured in terms of Quality of Life (QoL). It is about individual's perception of their position in life. Oral Health-Related Quality of Life (OHRQoL) is specifically about individual's oral health.

Consumption of both green tea and coffee is known to have positive health impact thus help improve quality of life. But how about their impact on oral health related QoL?

In a cross sectional study conducted among elderly people in Japan, the relationship between green tea and coffee consumption and oral health related QoL was studied by the researchers.

Upon suitable adjustments, the results showed increased consumption of green tea had positive effect on self reported oral health related quality of life. On the other hand, no significant association was observed in the case of increased consumption of coffee and oral health related QoL.

It was concluded that consumption of more than 3 cups of green tea per day may reduce the risk of poor oral health related quality of life especially in men.

This is significant because advanced age and compromising systemic conditions like

diabetes are known to have adverse impact on oral health. The green tea consumption may help improve oral health related QoL.

Source(s)

1. Nanri H. et al 2018. Consumption of green tea but not coffee is associated with the oral health-related quality of life among an older Japanese population: Kyoto-Kameoka cross-sectional study. Eur J Clin Nutr. DOI:10.1038/s41430-018-0186-y
2. Sischo L and Broder H.L 2011. Oral Health-related Quality of Life.What, Why, How, and Future Implications. J Dent Res. 90(11) DOI:10.1177/0022034511399918

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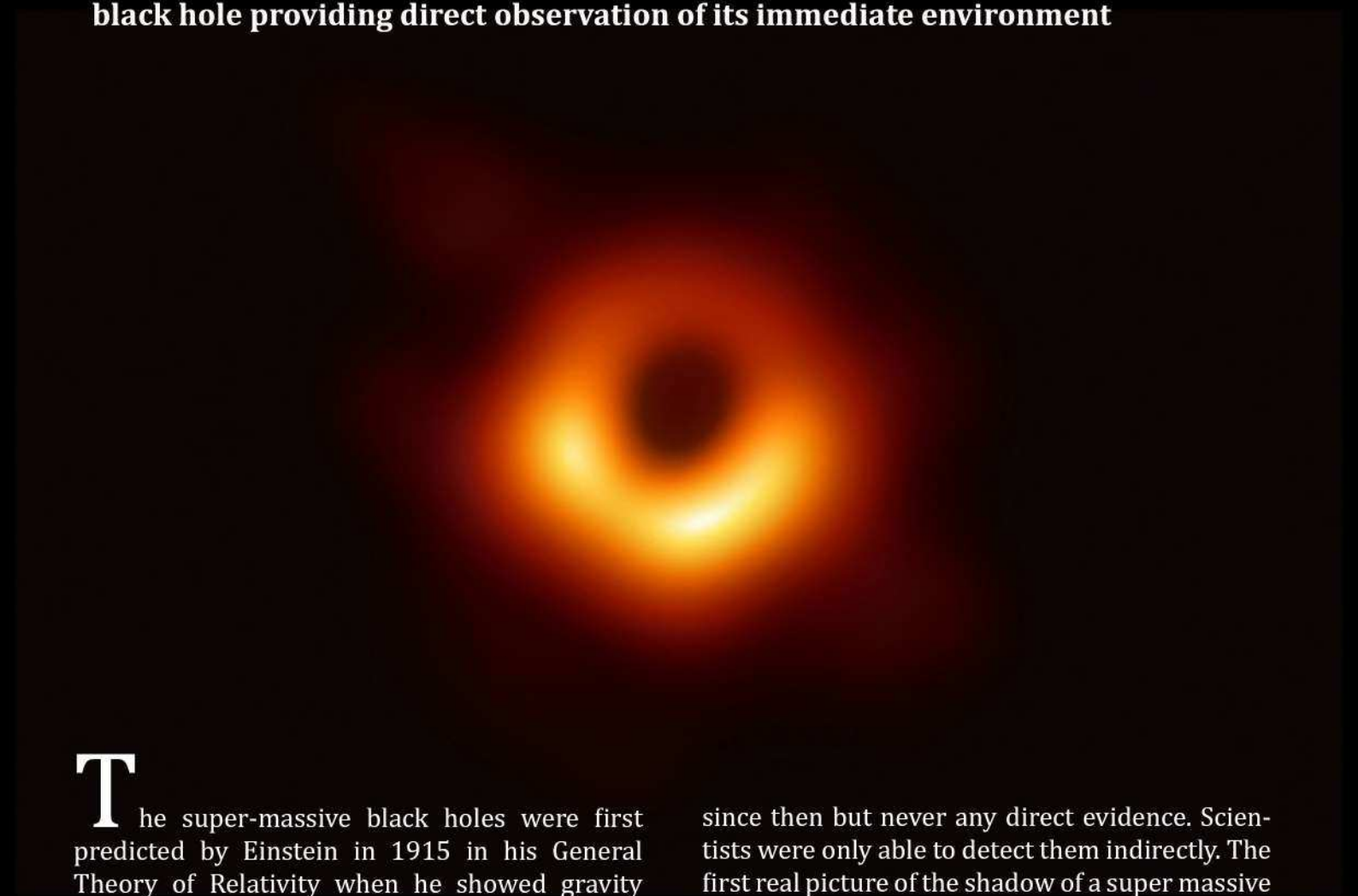
The First Ever Image *of The Shadow of a* Black Hole

Scientists have successfully taken first ever picture of the shadow of a black hole providing direct observation of its immediate environment



The super-massive black holes were first predicted by Einstein in 1915 in his General Theory of Relativity when he showed gravity bends light. There have been many developments since then but never any direct evidence. Scientists were only able to detect them indirectly. The first real picture of the shadow of a super massive black hole has now been captured providing first

direct evidence of their presence, thanks to "The Event Horizon Telescope Collaboration".

The black holes are extremely compressed mass in a very small region. Its gravity is so high that nothing at all escapes if gets too close to its boundary. The Event Horizon is the boundary around the black hole that marks what is inside and what is outside. Once anything crosses this boundary, it gets swallowed and can never come out. Black holes swallow all light therefore they are invisible and cannot be seen or pictured.

The intense gravity of black hole attracts and pulls interstellar gas onto itself faster and faster. This heats up the gas immensely and light radiation is emitted. These emissions are warped into a circular ring by the gravity of the black hole.

A black hole itself is invisible but its shadow against super-heated gas cloud around it could be pictured.

Black hole's presence couldn't be directly observed uptill now mainly due to the fact that black holes are extremely small targets for the available radio telescopes which were not capable enough to observe their event horizon. Observing black holes directly needed building an ingenious telescope virtually the size of Earth.

It took about a decade to organise a network of telescopes called the "Event Horizon Telescope" spanning the face of the Earth which combined eight separate telescopes in Mexico, Arizona, Hawaii, Chile and South Pole. All eight dishes of the telescope needed to be linked and pointed towards the black hole at exactly the same time. The signals received by the telescopes were combined by a correlator (a super computer) to give an image of the event horizon of the black hole.

The success of this experiment is a significant breakthrough in astronomy.

Source(s)

1. EHTC, Akiyama K et al 2019. First M87 Event Horizon Telescope Results. I. The Shadow of the Supermassive Black Hole'. The Astrophysical Journal Letters, 875(L1) DOI:10.3847/2041-8213/ab0ec7
2. Max Planck Institute for Radio Astronomy, 2019. First-ever picture of a black hole. Retrieved from https://www.mpg.de/13337404/first-ever-picture-of-black-hole
3. BlackHoleCam, 2019. IMAGING THE EVENT HORIZON OF BLACK HOLES, Retrieved from https://blackholecam.org/
4. European Commission - Press release, 2019. EU-funded scientists unveil first ever image of a black hole. Retrieved from http://europa.eu/rapid/press-release_IP-19-2053_en.htm

Cats Are *Aware of Their* Names

Study shows the ability of cats to discriminate spoken human words based on familiarity and phonetics

Dogs and cats are the two most common species which are domesticated by humans. It is estimated that worldwide more than 600 million cats live with humans. Though many studies are available on human-dog interaction, the interaction between domestic cats and humans is relatively unexplored. Studies on mammals including dogs, apes and even dolphins have shown that these animals understand some words spoken by humans. These mammals are considered naturally social and they have a higher inclination to interact and respond to humans. Some well-trained dogs can distinguish between 200-1000 words used by humans.

A new study published in *Nature Scientific Reports* provides first experimental evidence that pet cats can recognize their if they are familiar with it. This is the first study to analyse the ability of pet cats to understand and comprehend human voices. A previous study has shown that cats can distinguish between the voices of their owner and a stranger and cats may even change their behaviour depending upon their owner's facial expressions. Compared to dogs, cats are not naturally social and they are seen to interact with humans upon their own discretion.

"This may be a good time to tell you that I have decided to change my name."

In the current study conducted over a period of three years, six months to 17 years old cats of both genders and mixed breeds were chosen and divided into 4 groups to perform different experiments. All cats were spayed/neutered. Researchers tested a cat's name with other similar sounding nouns of same length and accent. The cats had heard their names before and were familiar with it, unlike the other words. Voice recordings were played containing five words spoken in a serial order, in which the fifth word was the cats' name. These recordings were made by researchers in their own voice and also in the voice of cat owners.

When cats heard their names, they responded by moving their ears or heads. This response is based upon both phonetic characteristics and familiarity with the name. On the other hand, cats remained still or ignorant when they heard other words. Similar results were seen for both the recordings made by cat owners and by researchers i.e. persons unfamiliar to the cats. The cats' response was though less enthusiastic and leaned towards more 'orientating behaviour' and less 'communicative behaviour' like moving their tails or using their own voice. This could be dependent on the nature of the situation in which their names are being called and some situations may elicit dynamic response.

Researchers state that if any cat did not respond, it is likely that the cat may still be able to recognize its name but chooses not to respond to it. Lack of response could be attributed to cats' low levels of motivation to interact with humans in general or their feelings at the time of the experiment. Further, cats cohabiting in an ordinary

home with 4 or more cats were able to distinguish between their name and the other cats' names. This was more likely to happen at a home rather than at a 'cat café' – a business place where people come and freely interact with the cats living there. Due to the difference in the social environment at a cat café, cats may not be able to clearly identify their names. Also, higher number of cats cohabiting at the café could have affected the results and that this experiment was conducted at only one café.

The current study shows that cats have the ability to discriminate words spoken by humans based on phonetic characteristics and their familiarity with the word. This discrimination is acquired naturally through daily normal communications between humans and cats and without any additional training. Such studies can help us understand social behaviour of cats around humans and tell us about cat's abilities in terms of human-cat communication. This analysis can enhance the relationship between humans and their pet cats thus benefitting both.

Source(s)

Saito A 2019. Domestic cats (Felis catus) discriminate their names from other words. *Scientific Reports*. 9 (1). DOI:10.1038/s41598-019-40616-4

■

Alzheimer's Disease: *Coconut Oil Decreases* Plaques in Brain *Cells*

Experiments on mice cells shows a new mechanism pointing towards potential benefits of coconut oil in managing Alzheimer's disease

Alzheimer's disease is a progressive brain disorder affecting 50 million people worldwide. No cure has been discovered yet for Alzheimer's; some forms of treatment available can only relieve symptoms associated with the disease. Alzheimer's disease is characterized by hard, insoluble plaque buildup (of amyloid beta proteins) between neurons in the brain. This leads to impaired transmission of impulses across neurons and causes symptoms of Alzheimer's disease - primarily deterioration of memory. Amyloid beta 40 and Amyloid beta 42 proteins are most abundantly present in the plaques. Amyloid beta proteins are dependent on expression of amyloid precursor protein (APP). Research has established the significance of amyloid precursor protein in Alzheimer's disease. Partial decrease of APP activity is seen as a therapy for Alzheimer's, though the exact mechanism explaining accumulation of amyloid beta proteins is not yet completely understood.

Multiple studies in the past have shown that virgin coconut oil possibly impacts several pathways which then contributes to progression of Alzheimer's disease. Coconut oil constitutes mainly of absorbable medium chain fatty acids metabolized easily by the liver. These fatty acids could also be converted to ketones - considered as an alternate

alternate source of energy for neurons. Coconut oil has been shown to have anti-oxidant effects in protecting neurons. These properties make coconut oil a unique dietary fat.

In a latest study published in *Brain Research*, researchers have investigated the potential effects of coconut oil on the expression of important amyloid precursor protein (APP) which is responsible for amyloid plaque formation. Researchers explored expression of amyloid precursor protein and secretion of amyloid peptides in mammalian cell line Neuro 2A (or N2a) cells which express APP gene. This neural cell line is routinely used to study neuronal differentiation, axonal growth and signaling pathways. In the current study, N2a cells underwent treatment with 0-5 percent concentrations of coconut oil and this led to reduced amyloid precursor protein expression in the cells and also decreased secretion of amyloid peptides 40 and 42. Additionally coconut oil also promoted N2a cells differentiation pointing out that coconut oil has a protecting effect on neuronal cells development.

Results indicated that ADP-Ribosylation Factor 1 (ARF1) – a protein important for secretory pathway - is likely contributing to the effects of coconut oil on both expression of APP and amyloid peptides secretion. It was clear that coconut oil achieved this through a likely interaction with ARF1. ARF1 is known to be responsible for sorting and transporting coat proteins in the cell. This is the first time an association between ARF1 and amyloid precursor protein (APP) processing is shown. This association is regulated through coconut oil treatment. Knocking out ARF1 reduced secretion of amyloid peptides establishing ARF1 protein's role in regulation of APP.

The study describes a previously unreported role of coconut oil in reducing amyloid precursor protein (APP) expression and secretion of amyloid peptides, the effect achieved due to down-regulation of ARF1. Thus, ARF1 is responsible for APP transportation inside neurons while coconut oil affects function and expression of APP. The study details a fresh perspective into intracellular trafficking of amyloid precursor protein and this is crucial to understand Alzheimer's disease.

Key points

- Alzheimer's disease is characterized by hard, insoluble plaque build-up (of amyloid beta proteins) between neurons in the brain.
- This leads to impaired transmission of impulses across neurons and causes symptoms of Alzheimer's disease - primarily deterioration of memory.
- The study describes a previously unreported role of coconut oil in reducing amyloid precursor protein (APP) expression and secretion of amyloid peptide.

This study suggests that using coconut oil in diet early in one's life, especially in people genetically predisposed towards Alzheimer's disease due to family history, can delay or even stop the onset of the disease. Current and past studies warrant additional investigations and human clinical trials to assess dosage and safety of coconut oil. Coconut oil is inexpensive, is readily available and could be easily incorporated into the diet of at-risk patients.

Source(s)

Bansal A et al 2019. Coconut oil decreases expression of amyloid precursor protein (APP) and secretion of amyloid peptides through inhibition of ADP-ribosylation factor 1 (ARF1). Brain Research.
DOI:10.1016/j.brainres.2018.10.001

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Diagnosing Vitamin D *Deficiency by Testing* Hair Sample Instead *of Blood Test*

Study shows first step towards developing a test for measuring Vitamin D status from hair samples

More than 1 billion people worldwide are deficient in Vitamin D. This deficiency affects primarily bone health and also increases one's risk of cardiovascular disease, diabetes, cancer etc. Due to this implication assessment of Vitamin D has gained interest. Vitamin D is measured via a blood test which measures the concentration of best biomarker of Vitamin D in blood called 25-hydroxyvitamin D (25(OH)D3). The blood sample needs to be collected in hygienic conditions under trained medical personnel. This test is an accurate estimate but its biggest limitation is that it reflects status of Vitamin D at a single time point and does not account for high variability of Vitamin D thus requires frequent sampling. A single value may not be an ideal representation as Vitamin D levels could differ in our body depending upon season or other factors. The test is expensive and a cost burden especially in low-and-middle-income countries. But, because high proportion of population is now deficient in Vitamin D this blood test is being increasingly requested.

A study published in *Nutrients* led by Trinity College, Dublin has shown for the first time that Vitamin D can be extracted and measured from human hair[1]. Authors themselves provided three hair samples for the study, two

harvested from crown area of the scalp and one from beard, which were cut into 1cm length, weighed, washed and dried. 25(OH)D3 was extracted from these samples using the same procedure used to extract steroid hormones from hair[2] in which a mathematical formula takes measured concentrations of the biomarker using Liquid chromatography-Mass Spectrometry (LC-MS) or Mass Spectrometry (MS) and provides an approximation of concentration in the hair. At the same time, blood from all tissue samples was also analyzed using MS. Quantifiable concentrations of 25(OH)D3 present in both hair and beard samples were measured validating feasibility of such a measurement.

Human hair grows approximately 1 cm every month and Vitamin D is deposited to the hair continuously. More Vitamin D is deposited to hair when levels of Vitamin D in the blood are high and less is deposited when they are low. A test which could measure vitamin levels from hair can tell us about Vitamin D status over a longer duration – several months at least taking into account seasonal differences. The longer one's hair, more accurately status of Vitamin D can be measured, example several months to years and this could be treated as a long-term record.

This is an inexpensive, non-invasive method to capture Vitamin D status and can help medical professionals to maintain levels of Vitamin D concentrations in a person over time. The exact association between Vitamin D in blood and in hair over a period of time needs further research as factors such as hair color, hair thickness and texture could affect Vitamin D in hair.

Source(s)

1. Zgaga L et al. 2019. 25-Hydroxyvitamin D Measurement in Human Hair: Results from a Proof-of-Concept study. *Nutrients*. . 11(2). DOI:10.3390/nu11020423
2. Gao W et al. 2016. LC-MS based analysis of endogenous steroid hormones in human hair. *J. Steroid Biochem. Mol. Biol*. 162. DOI:10.1016/j.-jsbmb.2015.12.022

■

Disruption of Body Clock due to Irregular *Insulin Secretion Associated* with Untimely Eating Increases Risk of *Chronic Diseases*

Feeding regulates level of Insulin and IGF-1. These hormones play key role in maintaining blood sugar level. This study proposes that these hormones also act as primary signals of feeding time to body clocks. They reset circadian clocks by induction of period proteins. Any irregular insulin signalling due to untimely eating disrupts circadian physiology and behaviour and clock gene expression. The disruption of body clock in turn is associated with increased incidence of chronic diseases.

Circadian rhythm or our 'body clock' is a 24-hour cycle which controls our daily physiological and mental changes including sleep. These body rhythms are responsive to primarily light and darkness in our immediate environment and to our eating time. Physiologically, humans are adapted to receive light and food during daytime. Our body clock is synched well with the external environment. This synchronization is important and that is why whenever there is a major change in our body

clock, it can have adverse effects on our health. Example of changes like when someone works night-shift or someone travels across time zones.

It is well known that irregular meal timings, especially eating late in the night may disrupt our body clock leading to poor health, however, the exact mechanism has been unclear until now. A study published in *Cell* on April 25, 2019 proposes that blood-sugar regulating hormone insulin and insulin growth factors (IGF-1) act as a primary signal which communicate eating time to our body clock. Insulin is normally released when we eat food. In this study, researchers subjected mice to insulin and IGF-1 at a 'wrong time' i.e. when it was dark and animals were asleep. Results showed a disruption in mice's circadian rhythm due to induction of period circadian proteins (PERIOD proteins) at the wrong time when mice didn't need to be active. The three PERIOD homologous proteins PER1, PER2 and PER3 are the chief components of the mammalian circadian clock. This untimely increase in PER proteins affected mice's circadian physiology, behaviour and clock gene expression. Mice's perceived differences between day and night were blurred.

Insulin and IGF-1 have been implicated in affecting body clock in previous studies but their mechanism was not well known. It was thought that their action might be limited to few particular tissues in the body. The factors which hindered establishment of their role was their broad distribution, poor viability and the partial redundancy between insulin and IGF-1.

Key points

- It is proposed that blood-sugar regulating hormone insulin and insulin growth factors (IGF-1) act as a primary signal which communicate eating time to our body clock.
- Irregular insulin secretion associated with untimely eating disrupts body's rhythm and affects one's health.
- The disruption of body clock is associated with increased risk and severity of chronic diseases

This new study shows that irregular insulin secretion associated with untimely eating disrupts body's rhythm and affects one's health. This disruption of body clock is associated with increased risk and severity of chronic diseases including type 2 diabetes, obesity and cardiovascular ailments. Thus, eating timing and light exposure is important to maintain a healthy body clock. Understanding how our body clock responds and adapts to changes in light and eating time is crucial for night-shift workers, sleep-deprived individuals especially young people and the ageing population.

Source(s)

Crosby P. 2019. Insulin/IGF-1 Drives PERIOD Synthesis to Entrain Circadian Rhythms with Feeding Time. *Cell*.
DOI:10.1016/j.cell.2019.02.017

■

Ultrahigh *Ångström-Scale* Resolution Imaging *of Molecules*

Highest level resolution (Angstrom level) microscopy developed that could observe vibration of molecule

The science and technology of microscopy has come a long way since Van Leeuwenhoek achieved magnification of about 300 in late 17th century using a simple single lens microscope. Now the limits of standard optical imaging techniques is no barrier and ångström-scale resolution has recently been achieved and used to image the motion of a vibrating molecules.

The magnifying power or resolution of a modern standard optical microscope is about few hundreds of nano-meter. Combined with electron microscopy, this has seen improvement to few nano-meter. As reported by Lee et al. recently, this has seen further improvement to few ångström (one tenth of nano-meter) which they used to image vibrations of molecules.

Lee and his colleagues have employed "tip-enhanced Raman spectroscopy (TERS) technique" which involved Illuminating the metal tip by a laser to create a confined hotspot at its apex, from which the surface enhanced Raman spectra of a

molecule can be measured. A single molecule was anchored firmly on a copper surface and an atomically sharp metallic tip was positioned above the molecule with ångström-scale accuracy. They were able to obtain images of extremely high resolutions in ångström range.

The mathematical computational method notwithstanding, this is the first time spectroscopic method yielded such an ultrahigh resolution images.

There are questions and limitations of the experiments such as the conditions of experiments of ultrahigh vacuum and extremely low temperature (6 kelvin), etc. Nevertheless, Lee's experiment has opened up many opportunities, for example ultra-high resolution imaging of biomolecules.

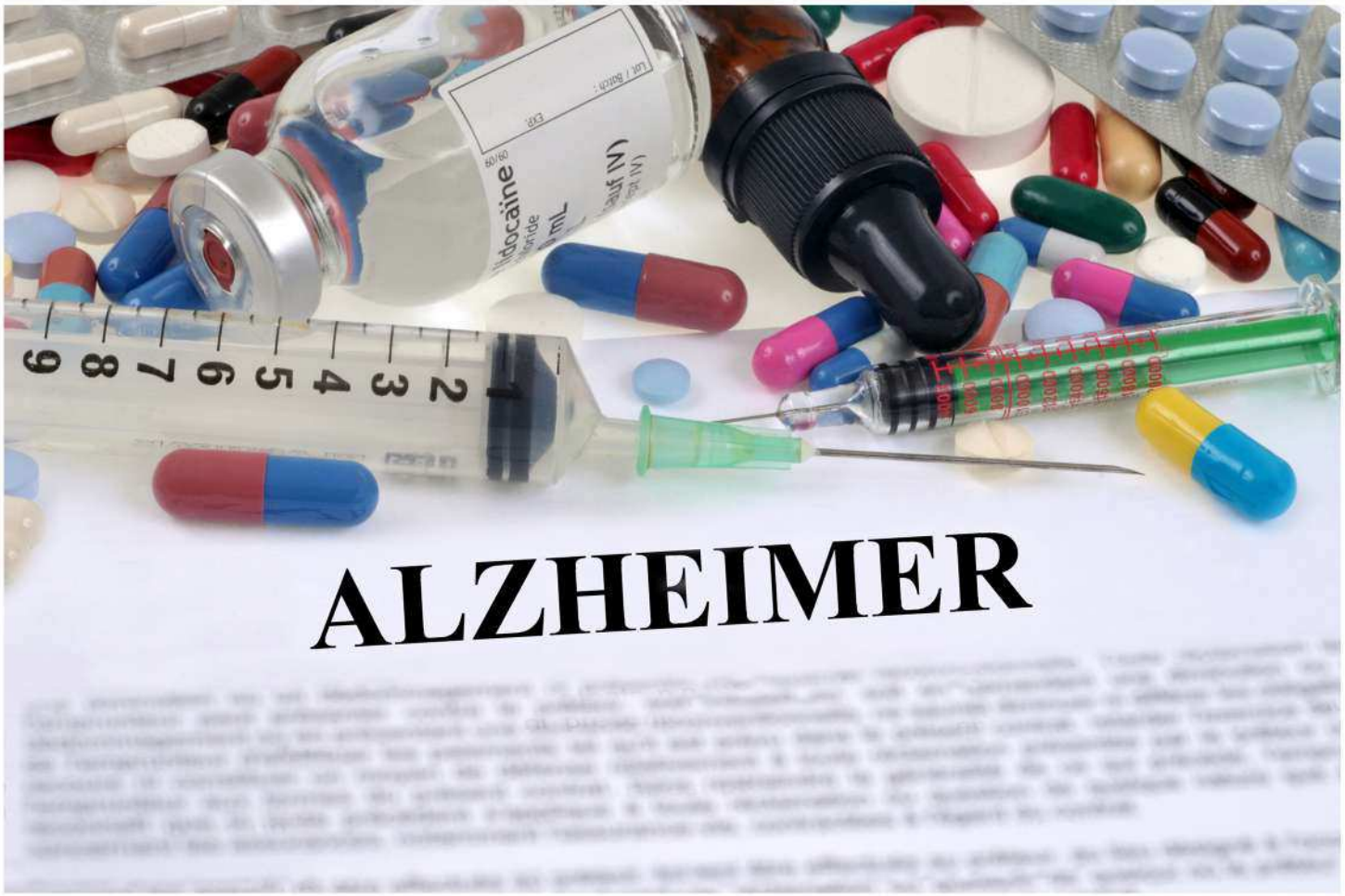
Source(s)

Lee et al 2019. Snapshots of vibrating molecules. Nature. 568. DOI:10.1038/d41586-019-00987-0 ■

A New Combination *Therapy for Alzheimer's* Disease: Animal Trial *Shows Encouraging* Results

Study shows a new combination therapy of two plant-derived compounds to reverse cognitive impairment in mice

At least 50 million people are living with Alzheimer's disease worldwide. The total number of patients of Alzheimer's disease could exceed 152 million by 2050. The first signs of cognitive impairment in Alzheimer's disease (AD) patients is memory problems and impaired decision-making. As the disease progresses, patients experience significant memory loss and cognitive difficulties. There is no cure for Alzheimer's disease and also no means to stop or slow down the progression of this disease. Limited drugs and other options are available which can relieve some of the symptoms. In Alzheimer's disease, amyloid plaques accumulate between neurons in the brain of patients. In healthy people, protein fragments called amyloid beta protein are broken down and removed. But in case of Alzheimer's, these fragments accumulate to form hard, insoluble amyloid plaques which contribute to impaired transmission of impulses across neurons and cause subsequent symptoms of Alzheimer's disease.



In a study published in *Journal of Biological Chemistry*, researchers have shown that a combination therapy could reverse symptoms of Alzheimer's disease in mice who were genetically predisposed to develop Alzheimer's. Two promising plant-derived compounds were explored which have complimentary amyloidogenic properties, firstly EGCG (epigallocatechin-3-gallate) an important component of green tea and secondly FA (ferulic acid) which is present in tomatoes, rice, oats and carrots. Such natural dietary compounds are called 'nutraceuticals' – compounds which are well-tolerated natural supplements, have drug-like properties and could be simply incorporated into one's diet.

For the analysis, 32 mice having Alzheimer's like symptoms were randomly assigned into four groups. Each group had equal number of males and females and also healthy mice. When mice were 12 months old, they were given either (a) EGCG and FA (b) EGCG or FA or (c) a placebo once daily for a period of 3 months. The dosage given was 30 mg per kg of body weight as this dose is well-tolerated by humans and can be consumed as portion of a healthy dietary supplement. Before and after this special diet administration, researchers conducted neuropsychological tests which can analyze thinking and memory and thus make assessments about the disease. One of the tests done for memory assessment was the 'Y-shaped maze' which can test a mouse's spatial working memory analogous to a human finding a way out of a building. Mice with Alzheimer's like symptoms cannot navigate such a maze with ease as compared to healthy counterparts.

After administration of special diet for three months, mice having Alzheimer's like symptoms

performed similar to healthy mice in learning and memory tests. This suggested that combination therapy of EGCG-FA reverses cognitive impairment in mice having Alzheimer's like symptoms. Mice treated with combination of EGCG-FA exhibited reduced abundance of amyloid-beta proteins when compared with individual treatment of these compounds. The underlying mechanism could be the ability of these compounds to prevent amyloid precursor proteins from breaking down into smaller protein fragments - amyloid beta - which accumulate in an Alzheimer's patient's brain as plaques. EGCG and FA together reduced neuroinflammation and oxidative stress in the brain – both of which are important part of Alzheimer's in humans. Research which is successful in mice may not translate in humans but such plant-derived substances or supplements offer significant promise towards Alzheimer's therapeutics in humans.

This successful research in mice may pave the way for human trials. Such plant-derived substances or supplements offer significant promise towards Alzheimer's therapy.

Source(s)

Mori T et al. 2019. Combined treatment with the phenolics (−)-epigallocatechin-3-gallate and ferulic acid improves cognition and reduces Alzheimer-like pathology in mice. *Journal of Biological Chemistry*. 294(8). DOI:10.1074/jbc.RA118.004280

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Revival of Pigs Brain after Death : An Inch *Closer to Immortality*

Scientists have revived pigs brain four hours after its death and kept alive outside the body for several hours

Of all organs, brain is most susceptible to continuous supply of blood to meet its immense non-stop requirement of oxygen and glucose. Any disruption beyond few minutes is known to cause irreparable damage to the brain or even death of the brain. The cessation of activity in the brain or 'brain death' occurs when neural activity comes to a halt. This is fate of all life and is fundamental for legal and medical purposes for defining death; cessation of breathing or stopping of heart beats alone are not adequate.

Scientists have preserved and maintained cellular and histological features of brain after death by perfusion and chemical fixation. But the functions are not preserved. Rouleau N et al. in 2016 reported preservation of some functional capacity of brain. They showed patterns similar to living condition were elicited by temporal lobe structure of the preserved brain.

Things have moved bit further now.

As published on 17 April in *Nature*, scientists at Yale University have reported significant functional preservation. They successfully revived the disembodied brains of pigs four hours after the death of animals. Their technique restored important functions like cellular respiration, waste removal and maintaining the brain's internal structures.

This research challenges the notion that brain

death is final and questions the nature of death and consciousness and could very well be an advance in the direction of immortality.

Apparently, neuroscience is moving towards a point when brain could be revived after death and lifetime of information- experiences, knowledge and wisdom stored in the brain could be read out and one could live with the deceased person again. However this does not seem likely in foreseeable future.

Researchers at ***Alcor Life Extension Foundation in Arizona*** are working towards giving the dead a chance to live again by preserving the brain in liquid nitrogen at -300 degree using cryonic suspension technique which could allow thawing and reanimation in future when appropriate new technology is invented.

Key points

- The cessation of activity in the brain or 'brain death' occurs when neural activity comes to a halt.
- Scientists have successfully revived the disembodied brains of pigs four hours after the death of animals.
- The research challenges the notion that brain death is final and questions the nature of death and consciousness and could very well be an advance in the direction of immortality.

But, the biological brain per se may not be important for immortality because what really matters are the computations that are running on this. The mind is what brain does. The computational hypotheses (that it's only the interactions in the brain that makes a person who they are) offers a possibility for existing and living digitally by running as a simulation. There could be a functional version without the biological brain.

Blue Brain Project is actually attempting to build a full working simulation of a brain and aims to come up with the software and hardware infrastructure capable of running a brain simulation by 2023. The final product of this project would be a thinking, self aware mind living on computer. Possibly, even the 'single unified experience' called consciousness if it is an emergent property of vast neural population of the brain interacting in right way.

Source(s)

1. Vrselja Z et al 2019. Restoration of brain circulation and cellular functions hours post-mortem. *Nature*. 568. DOI:10.1038/s41586-019-1099-1
2. Reardon S. 2019. Pig brains kept alive outside body for hours after death. *Nature*. 568. DOI:10.1038/d41586-019-01216-4
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Advances in *Treatment of HIV* Infection by Bone *Marrow Transplantation*

New study shows a second case of successful HIV remission after a bone marrow transplant

At least one million people die due to HIV-related causes every year and almost 35 million are living with HIV. HIV-1 (Human Immunodeficiency Virus) is responsible for majority of HIV infections worldwide and is transmitted through direct contact with HIV-infected body fluids. The virus attacks and kills crucial infection fighting cells of our immune system. There is no cure for HIV. Currently, HIV can only be treated using medications which have the ability to suppress the HIV virus. These drugs have to be taken life long and it is challenging plus a cost burden on the health system especially in low-and-middle-income countries. Only 59 percent of patients of HIV worldwide are receiving Antiretroviral therapy (ARV) and HIV virus is fast becoming resistant from many known drugs which itself is a major concern.

Bone marrow transplant (BMT) is a treatment used for leukemia, myeloma, lymphoma etc. Bone marrow, the soft tissue inside bones,


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makes blood-forming cells including the infection fighting white blood cells. A bone marrow transplant replaces unhealthy marrow with a healthy one. In the first case of successful HIV remission, an HIV-infected individual called 'Berlin Patient' who later revealed his name received a bone marrow transplant a decade ago when he was targeted to treat acute leukemia. He received two transplants along with total body irradiation which led to long-term HIV remission.

In a new study published in *Nature* led by UCL and Imperial College London, the only second person has been shown to experience sustained remission from HIV-1 after a bone marrow transplant and stoppage of treatment. The anonymous adult male patient from UK was diagnosed with HIV infection in 2003 and was on antiretroviral therapy treatment since 2012. He was subsequently diagnosed with Hodgkin's Lymphoma in the same year and he underwent chemotherapy. In 2016, he was given stem cell transplant from a donor who carried a genetic mutation which prevents expression of a most commonly used HIV receptor protein called CCR5. Such a donor is resistant to HIV-1 strain of the virus which specifically uses CCR5 receptor and thus the virus now cannot enter host cells. Since chemotherapy kills cells which are dividing, HIV could be targeted. From this understanding if one's immune cells are replaced by cells which do not have CCR5 receptor, HIV can be prevented from rebounding after the treatment.

The transplant was carried out with minor side effects like a mild complication common in transplants in which recipient's immune cells are attacked by donor immune cells. Antiretroviral treatment was continued for 16 months after the transplant before making a decision to halt the treatment in order to evaluate remission of HIV-1. Post this, viral load of the patient

This is a second case of a patient exhibiting sustained remission of HIV-1 following a bone marrow transplant. One important difference in this second patient being that 'Berlin Patient' had received two transplants along with total body irradiation while this UK patient received only a single transplant and underwent less aggressive and lesser toxic approach of chemotherapy. Mild complications of similar nature were seen in both patients i.e. graft versus host disease. Achieving success in two different patients points towards developing strategies based on preventing CCR5 expression which might even cure HIV.

Authors state that they are monitoring the patient's condition and cannot say with affirmation yet if he has been cured of HIV. This may not be a generalized appropriate treatment for HIV because of adverse effects and toxicity of chemotherapy. Also, bone-marrow transplants are expensive and carry risks. Nevertheless, it is a better approach with reduced intensity conditioning and no irradiation. Research could also focus on knocking out the CCR5 receptor using gene therapy in people with HIV.

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First Successful *Gene Editing in* Lizard Using CRISPR *Technology*

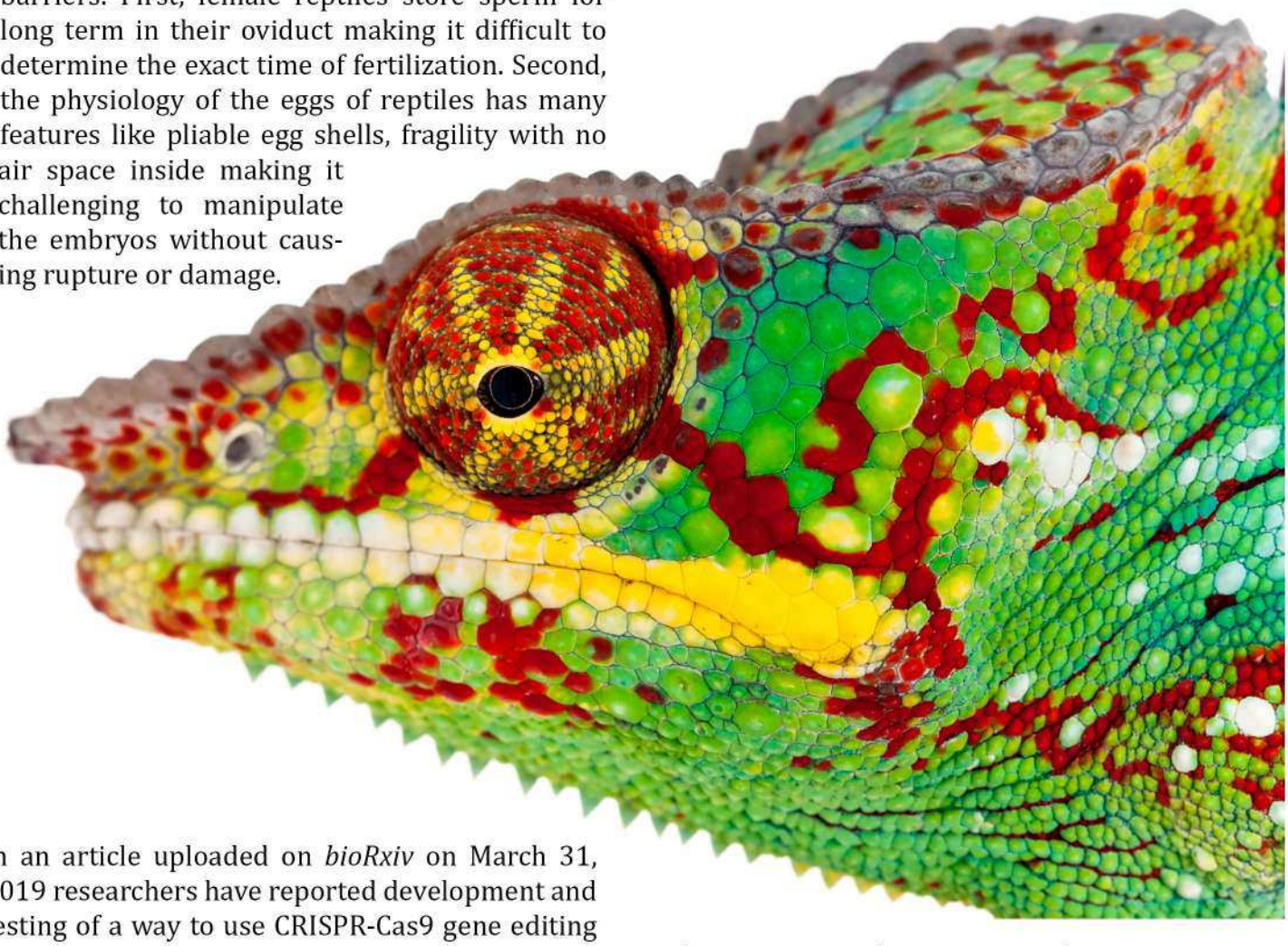
This first case of genetic manipulation in a lizard has created a model organism that could help gain further understanding of reptile evolution and development

CRISPR-Cas9 or simply CRISPR is a unique, fast and inexpensive gene editing tool which enables editing of a genome by deleting, adding or altering DNA. CRISPR acronym stands for 'Clustered Regularly Inter-Spaced Palindromic Repeats'. This tool is simple and more precise than previous methods used for editing DNA.

CRISPR-Cas9 tool injects organisms at zygote (one-cell) stage with a DNA construct made of (a) Cas9 enzyme which acts as 'scissors' and can cut or delete a part of DNA, (b) guide RNA – a sequence which matches the target gene and thus guides Cas9 enzyme to the target location. Once a target section of DNA is cut, cell's DNA repair machinery will re-join the remaining strand and, in the process, silence the targeted gene. Or the gene could be 'corrected' by using a new modified DNA template in a process called as homology directed repair. Thus, CRISPR-Cas9 tool allows for genetic modifications by injecting gene-editing solutions into a single-celled fertilized egg. This process

causes a genetic alteration (mutation) in all subsequent cells which are produced thus affecting gene function.

Though CRISPR-Cas9 is routinely used in many species including fish, birds and mammals, so far it has not been successful in genetically manipulating reptiles. This is primarily because of two barriers. First, female reptiles store sperm for long term in their oviduct making it difficult to determine the exact time of fertilization. Second, the physiology of the eggs of reptiles has many features like pliable egg shells, fragility with no air space inside making it challenging to manipulate the embryos without causing rupture or damage.



In an article uploaded on *bioRxiv* on March 31, 2019 researchers have reported development and testing of a way to use CRISPR-Cas9 gene editing in reptiles for the first time. The reptile species chosen in the study was a tropical lizard called *Anolis sagrei* or more commonly brown anole which is widespread in the Caribbean. The lizards in the study were collected from a wild region in Florida, USA. This species is ideally suited for the study because of its miniature size, long breeding season and relatively short average time between two generations.

To overcome the limitations currently faced with reptiles, researchers microinjected CRISPR components into immature unfertilized eggs while the eggs were still in female lizards' ovaries before fertilization. They targeted tyrosinase gene which produces an enzyme that controls skin pigmentation in lizards and if this gene is removed the lizard would be born an albino. This clear pigmentation phenotype was the reason to choose tyrosinase gene. The microinjected eggs then mature inside the female and are subsequently naturally fertilized with an introduced male or stored sperm.

As a result, four albino lizards were born few weeks later confirming that gene tyrosinase was

deactivated and the gene editing process was successful. Since the offspring contained edited gene from both parents it was clear that CRISPR components remained active much longer in mother's immature oocyte and post fertilization it mutated paternal genes. Thus, mutant albino lizards exhibited manipulated tyrosinase in genes inherited from both mother and father as albinism is a trait inherited from both parents.

This is the first ever study to effectively produce genetically modified reptiles. The research could work in a similar manner in other lizard species like snakes for which current approaches have been unsuccessful so far. This work could help gain further understanding of reptile evolution and development.

Source(s)

Rasys AM et al. 2019. Preprint. CRISPR-Cas9 Gene Editing in Lizards Through Microinjection of Unfertilized Oocytes. bioRxiv.
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Scientific European Connects General *Readers to the Original* Research

By Rajeev Soni

***Scientific European* is a magazine reporting significant recent advances in science to general audience.**

They identify relevant original research articles published in reputed peer reviewed journals in the recent months and present the breakthrough discoveries in a simple language that is appreciable to general readers. The stories of recent advances in science and technology thus can reach to a general reader. This platform aids in disseminating the scientific information in a manner that is easily accessible and comprehensible to a general audience who would otherwise might be oblivious to its existence.

This propagation of scientific knowledge to general people, particularly students and the young generation will contribute in popularizing science and may stimulate them intellectually to choose scientific research as a career.

The USP of the magazine is the availability at the end of the article of a list of sources with details and links to the original research articles, so that anyone interested can go and read the relevant research paper simply by clicking the link provided.

A potential area of improvement for the magazine would be to introduce videos and blogs related to the various discoveries and inventions as that will attract more young readers. The application of the news articles in everyday life can also be introduced.

This is a free access magazine; all articles and issues including the current one is freely downloadable from the website.

The topics covered are mostly from biological and medical sciences. At times, articles in physical and environmental sciences are also seen. However, articles related to general improvement of mind and body in relation to medical sciences can also be included to provide an overall health improvement perspective to the readers.

The focus is mainly to spread information and awareness and not unsurprisingly, there are no advertisements, sponsored contents or promotional materials.

Rajeev Soni PhD (Cambridge)

Dr Rajeev Soni holds a PhD in Molecular Biology from University of Cambridge where he was Cambridge Nehru and Schlumberger scholar. He is an experienced biotech professional and has held several senior roles in academia and industry. ■

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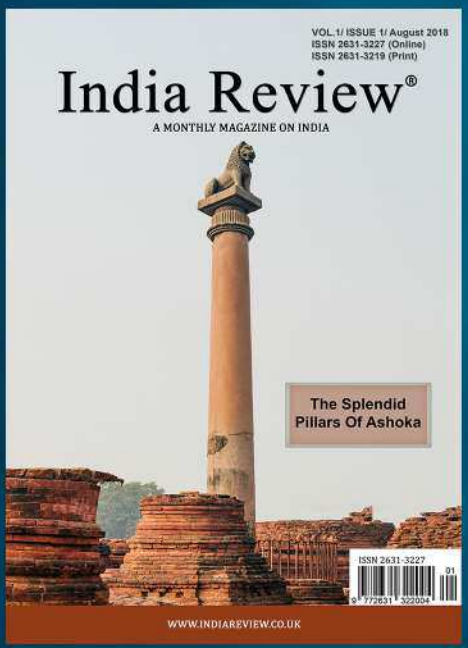

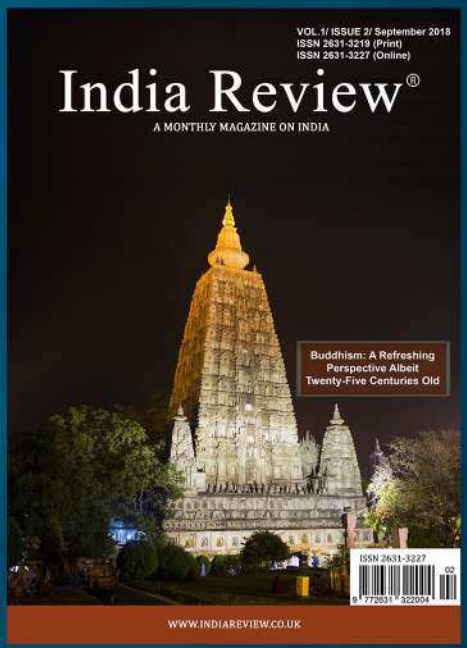

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