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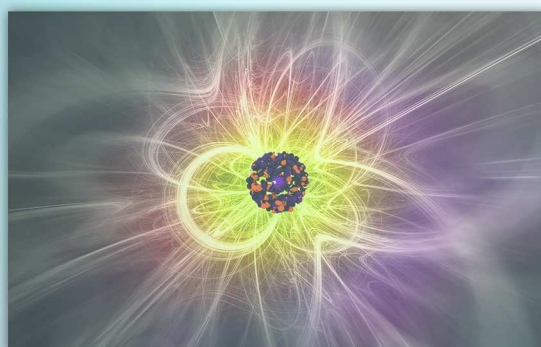
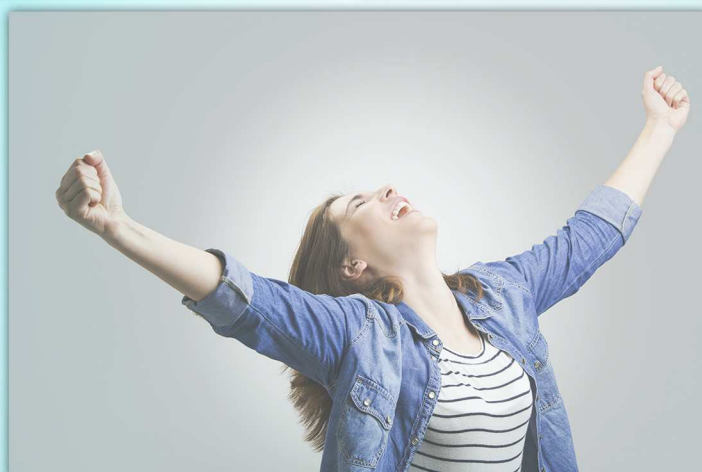
'Success Streak' is Real

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We are excited to bring nine articles on latest relevant scientific advancements which hold great potential - gene editing in uterus, cure for diabetes, novel therapy for hearing loss, effective cancer therapy and many more.

Hope you find these interesting!

Umesh Prasad

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Novel Drug Therapy to Cure Deafness

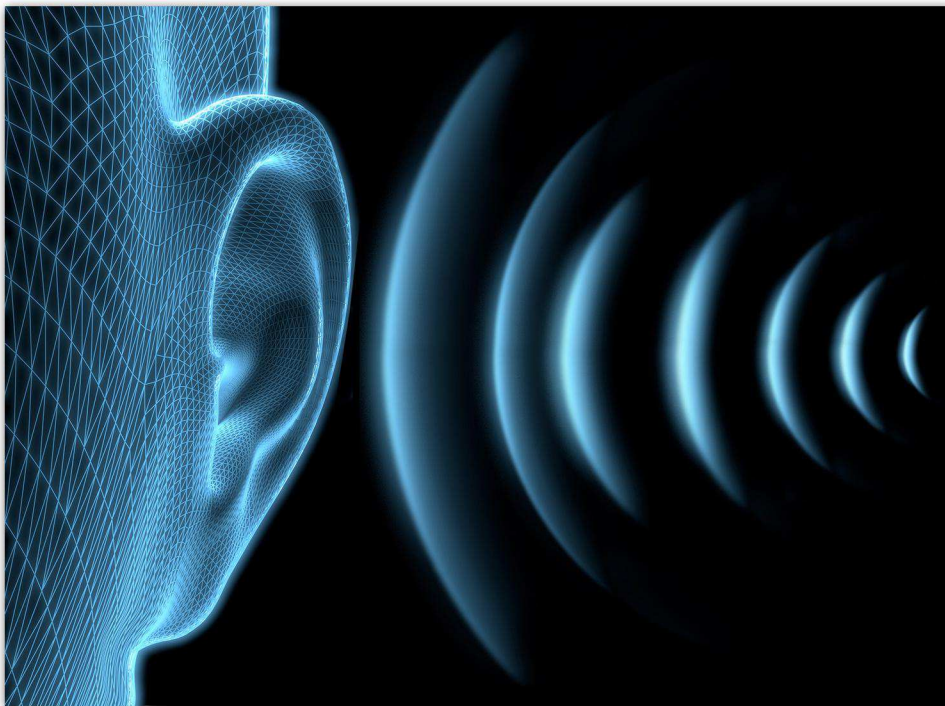
Researchers have successfully treated hereditary hearing loss in mice using a small molecule of a drug leading to hopes for new treatments for deafness

Hearing loss or deafness is caused by genetic inheritance in more than 50 percent of people. It is the most common birth defect which can unborn babies. Hereditary genetic conditions are responsible for congenital hearing loss and contribute to more 50% cases of deafness in new-borns and infants. Such hearing loss affects members within a family since a person may inherit a mutated gene or genes or an undesirable gene causing this loss to occur. The inherited hearing loss present at birth also accompanies other health issues such as problem with vision and balance in at least 30 percent of cases. Even when an offspring does not display a hearing disorder, he or she can inherit the gene mutation. This means that the person is a carrier. Even when an offspring does not display a hearing disorder, he or she can inherit the gene mutation. This means that the person is a carrier. A carrier of an undesired gene mutation can pass it along to future offspring who then might experience hearing loss. This deafness is largely incurable.

In a study published in *Cell*, scientists at the University of Iowa and the National Institute on Deafness and Other Communication Disorders, have discovered for the first time a small-molecule drug which can preserve hearing in mice suffering from hereditary progressive human deafness. Researchers were able to partly restore hearing at minor sound frequencies and also save few of the “sensory hair cells” within the inner ear. This study has not only thrown light on the exact molecular mechanism which underlines

this particular type of genetic deafness (called DNA27) but proposes a potential drug treatment for it.

The study began when researchers tried to analyse the genetic basis of this inherited form of deafness a decade ago. They looked into the genetic



information of the members of a family (referred to as LMG2). Deafness was dominant in this family i.e. they carried a dominant gene for deafness and any offspring only needed to inherit single replica of the faulty gene from mother or father to have this type

of deafness. In their investigation spanning almost a decade, researchers localised the mutation which caused the deafness onto a “region” called DFNA27. This region included around dozen genes which when altered could lead to hearing loss, therefore the exact location of the mutation still was not pointed. A later set of studies helped to point out the mice Restgene (RE1 Silencing Transcription Factor) and researchers discovered that mice Rest gene gets regulated by an uncommon process in the ear’s sensory cells and this is extremely vital for the mammal’s hearing function. Researchers then started to examine the DFNA27 region as it was seen that the human Rest gene is located in this area only. Once the location and function of Restgene was better understood, further analysis was done to see what could modulate this gene and help improve deafness.

The Restgene was then manipulated so as to create the model for deafness on which experiments could be performed. It was seen that sensory hair cells were destroyed within the mice inner ear rendering them deaf. Similar mutations were found in the LMG2 family as well. When the manipulation was reversed, REST protein switches off and many genes were switched on leading to the revival of sensory hair cells and helped the mice to listen better. Therefore, the key is the REST protein encoded by Rest gene. This protein normally suppresses genes by a method called “histone deacetylation”. Researchers used a small molecule of a drug which could “act like a switch” and could block this process of histone deacetylation and thus turn off the REST protein. Switching the Rest gene off then allowed new hair cells to be built which ultimately partially restored hearing in mice.

This is an important and relevant study in analysing the internal mechanisms which define hereditary type of deafness. Although this study has been conducted in mice, the strategies uncovered here could be utilized for human testing. It is a fine starting point to perform additional studies in which small molecule-based drugs can be shown to be effective in treating DFNA27 deafness. This study

could be also potentially be extended to other types of progressive hearing loss caused by inheriting genes. The genetic leads provide more information to uncover novel pathways for designing potential treatments for hearing loss in humans. Also, more small molecules could be used in the future to treat inherited deafness. ■

Source

Yoko Nakano, et al., 2018, ‘Defects in the Alternative Splicing-Dependent Regulation of REST Cause Deafness’, Cell, DOI: 10.1016/j.cell.2018.06.004

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Correcting *Genetic Conditions in* Unborn Babies

Study shows promise for treating genetic disease in a mammal during foetal development in the first three months of a pregnancy

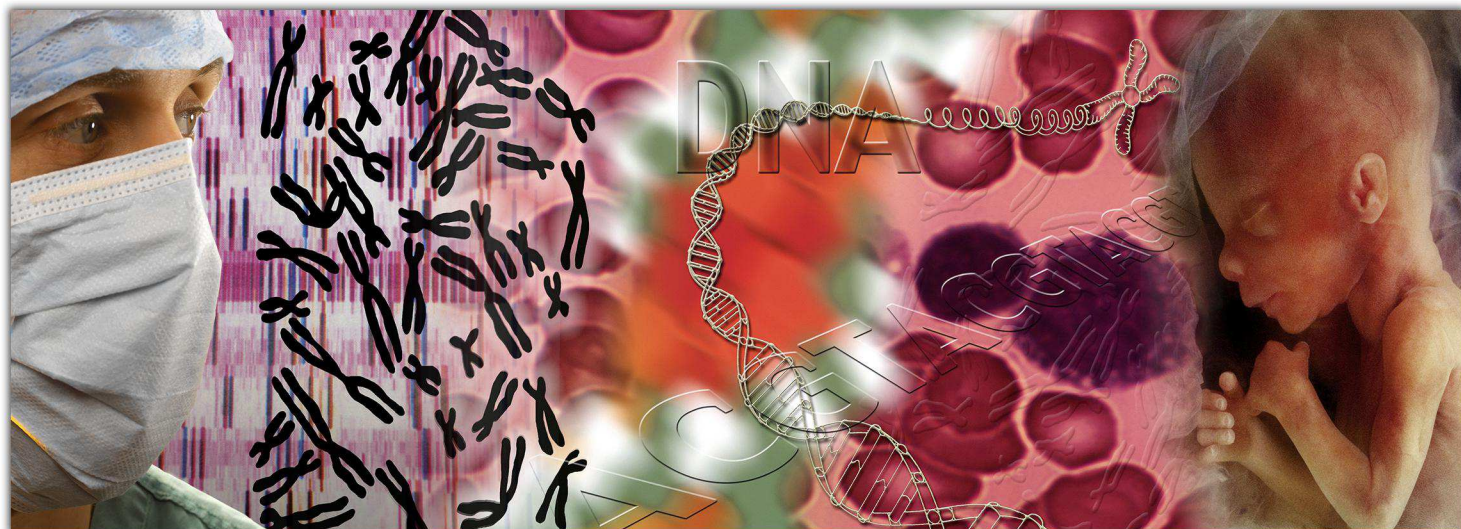
A genetic disorder is a condition or a disease which is caused by abnormal changes or mutations in a person's DNA in the gene. Our DNA provides the required code for making proteins which then perform most of the functions in our body. Even if one section of our DNA gets altered in some way, the protein associated with it can no longer carry out its normal function. Depending upon where this change happens, either it can have a little or no effect or it might alter the cells so much in our body which could then lead to a genetic disorder or illness. Such changes are caused by errors in DNA replication (duplication) during growth, or environmental factors, lifestyle, smoking and exposure to radiation. Such disorders are passed on to the offspring and start to occur when the baby is developing in mother's uterus and are therefore referred to as 'birth defects'.

These birth defects can be minor or extremely severe and may affect appearance, function of an organ and some aspect of physical or mental development. Millions of children are born annually with serious genetic conditions or most commonly called birth defects. These birth defects can be detected during pregnancy as they are evident within the first

forming. A technique called amniocentesis is available detecting genetic abnormalities in the foetus by testing the amniotic fluid which has been extracted from the uterus while the baby. However, even with amniocentesis, treating them is not possible as no options are available to make any corrections before birth of the baby. Some of the defects detected are harmless and require no intervention but some others are of a serious nature and may require long-term treatment or even be fatal for the infant. Some defects can be corrected shortly after birth of the baby – example within a week's time – but mostly it is too late for treatment.

Curing genetic condition in an unborn baby

In a first of its kind study, the revolutionary gene editing technique has been used to cure a 'genetic disorder' in mice during foetal development in the uterus in a study by researchers Carnegie Mellon University and Yale University. It is well established




now that during early development in the embryo (during first three months of a pregnancy), there are many stem cells (an undifferentiated cell type which can become any type of cell upon maturation) that are dividing at a fast rate. Therefore, this is the pertinent time point where a genetic mutation if it is corrected would reduce the impact of the mutation on embryo-to-foetal development. There are chances that a severe genetic condition could even be cured. And so, the baby is born without the unintended birth defects.

In this study published in *Nature Communications*, researchers have used a peptide nucleic acid-based gene editing technique. This same technique has been used before to treat beta thalassemia - a genetic blood disorder in which the crucial haemoglobin (HB) is produced very less in the blood is reduced considerably which then affects the normal oxygen supply to various parts of the body leading to severe abnormal consequences. In this technique, unique synthetic molecules called peptide nucleic acids (PNAs) (made of a combination of synthetic protein backbone with DNA and RNA) were created. A nanoparticle was then used to transport these PNA molecules along with "healthy and normal" donor DNA to the location of a genetic mutation. The complex of PNA and DNA identifies the designated mutation at a site, PNA molecule then

binds and unzips the double helix of the mutated or faulty DNA. Lastly, donor DNA binds with the mutated DNA and automates a mechanism to correct the DNA error. The main significance of this study is that it was done in a foetus, thus researchers had to use a method analogous to amniocentesis wherein they inserted the PNA complex into the amniotic sac (amniotic fluid) of pregnant mice whose foetuses were carrying the gene mutation which causes beta thalassemia. After one injection of PNA, 6 percent of mutations got corrected. These mice showed improvement in symptoms for the disease i.e. levels of haemoglobin were in normal range which could be interpreted as the mice being 'cured' of the condition. They also showed increased survival rate. This injection was in a very limited range but researchers are hopeful that even

Key Points

- Genetic disorders are passed on to the offspring and start to occur when the baby is developing in mother's uterus.
- The revolutionary gene editing technique has been used to cure a 'genetic disorder' in mice during foetal development in the uterus.
- The targeted quality of this study makes it ideal for therapeutics.



higher success rates can be achieved if injections were done multiple times.

The study is relevant because no off-targets were noted and only the desired DNA was corrected. This is important to note because gene editing techniques like CRISPR/Cas9 though are easier to use for research purposes, it is still controversial because it cuts the DNA and carry out off-site errors as they damage an off-target normal DNA as well. Because of this serious limitation they are not ideally suited for designing therapies. Considering this factor, the method shown in the current

study only binds to the target DNA and repairs it and shows nil offsite errors. This targeted quality makes it ideal for therapeutics. Such a method in its current design could also be potentially used to 'cure' other conditions in the future. ■

Source

Adele S. Ricciardi et al. 2018, 'In utero nanoparticle delivery for site-specific genome editing', Nature Communications, DOI: 10.1038/s41467-018-04894-2

Combination of Diet and Therapy for Cancer Treatment


The ketogenic diet (low carbohydrate, limited protein and high fat) shows improved effectiveness of a new class of cancer drugs in cancer treatment

Cancer treatment has been at the forefront of the medical and research community worldwide. 100 percent successful treatment for cancer is still not available and majority of research has been focusing on making cancer cells in the body susceptible to chemotherapy or radiation therapy or targeted medicines. An emerging new class of cancer drugs have been actively



researched upon in the recent years. These drugs target a specific molecular pathway which become faulty in many types of cancer. This is a cell signaling pathway called phosphatidylinositol-3 kinase (PI3K), which is activated by insulin. PI3K, a family of enzymes plays a key role in many internal cellular functions that are involved in cancer. Genetic mutations in PI3K enzyme is present in most cancerous tumours. It is this frequency of mutations which makes PI3K an appealing candidate to make anti-cancer drugs. Thus, inhibiting the pathway of this enzyme has been seen as a potential way to attack cancer. For

achieving this goal, more than 50 drugs have been designed and developed so far which have already been through clinical trials for testing for efficacy. Unfortunately, these clinical trials haven't been much of a success, owing to questionable efficacy of these drugs and also their high toxicity. Taking such drugs which are going to inhibit the pathway leads to a drop in the insulin in the body which only increases blood sugar level causing problems like hyperglycemia or abnormally high levels of blood sugar. The patients have to stop taking this drug because pancreas is eventually unable to make up for this loss by producing more insulin after doing it



for some time. Scientists have been trying to tackle this issue faced with new promising class of cancer drugs.

Combining keto diet with cancer therapy

A new study published in *Nature* has shown that ketogenic or keto diet is efficient for eliminating some of the side effects of new generation cancer drugs and can be very beneficial in cancer therapy. The ketogenic diet constitutes of meat, eggs and avocados as staple food items. The idea of this diet is to eat very few carbohydrates - which are quickly broken down to blood sugar - and also moderate protein - which can also get converted into blood sugar. This diet makes our body produce small fuel molecules called 'ketones' (hence the name ketogenic). These ketones are produced in the body in the liver exclusively from only fat. These ketones are like an alternative fuel for the body whenever sugar (glucose) is in limited supply, including the brain. Therefore, the body basically switches its fuel supply and 'runs' entirely on fat as no carbohydrates and limited protein is being produced. This may not be the ideal scenario but is efficient to lose weight and maintain yourself. The keto diet has been used since many decades to control insulin levels in the body.

It has been suggested that following a ketogenic (or 'keto') diet can have useful effects during cancer therapeutic treatment and side effects of new class of cancer drugs can be avoided. Researchers from Cornell University first examined the effect of PI3K-inhibiting drug called buparlisib in mice suffering from pancreatic cancer. It was seen that when the insulin levels increased as a side effect to using this drug, the PI3K pathway reactivated and cancer treatment reverses, rendering the drug as ineffective. So, to be able to control this effect of elevation of insulin which was happening whenever the drug was taken, a

follow up drug treatment needed to be done. They tried various options like blood sugar or insulin controlling drugs etc and they tested these on the mice, however, no effect was seen. Interestingly they observed that mice who were on keto diet performed way better in maintaining blood sugar and insulin check while simultaneously inhibiting tumour growth also which is the exact desired scenario. This was mainly possible because while being on a keto diet, there was reduced glycogen storage so no extra glucose was released when PI3K pathway was inhibited. Therefore, once a patient is able to control his/her sugar and insulin, the cancer drugs work much better and more efficiently in controlling the growth of tumours.

An imperative aspect of this study is that the keto diet does not have any role on its own in inhibiting or treating the cancer and if taken alone without any enzyme inhibitors, cancer still progresses at an expected pace. The diet itself could be actually harmful if taken on your own for too long. Therefore, keto diet needs to be ideally combined with the actual course of cancer treatment. As an outcome of this study, during human clinical trials for PI3K inhibitor drugs, the diet of the patients' needs to be carefully managed. Researchers definitely want to assess if combining approved PI3K inhibitor drugs and keto diet (specially prepared by nutritionists) can show a safe, efficient and improved outcome for people suffering from different types of cancer. This study is a very interesting and innovative way to improve cancer treatment. ■

Source

Benjamin D. Hopkins et al 2018, 'Suppression of insulin feedback enhances the efficacy of PI3K inhibitors', *Nature*, DOI: <https://doi.org/10.1038/s41586-018-0343-4>

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Fern Genome Decoded: Hope for Environmental Sustainability

Unlocking the genetic information of a fern could provide us potential solutions to multiple issues faced by our planet today.

In genome sequencing, DNA sequencing is done to determine the order of nucleotides in every specific DNA molecule. This exact order is of value for researchers to be able to understand the type of genetic information carried in the DNA. Since genes encode for protein which are responsible for most body functions, this information can help to understand the effect of their function in the body. Sequencing the complete genome of an organism i.e. all of its DNA is a highly complex and challenging task and has to be done bit by bit by breaking DNA into smaller pieces, sequencing them and then putting it all together. For example, the complete human genome was sequenced in 2003 took 13 years and total cost of \$3 billion. However, with advancement in technology, genomes can be sequenced relatively faster and also at a lower cost using methods like Sanger sequencing and Next-generation sequencing. Once a genome is sequenced and decoded, unlimited possibilities open up for identifying potential areas of biological research and making progress towards targeted application development.

A team of 40 researchers from Cornell University and around the world have sequenced the full genome of a water fern called *Azolla filiculoides*^{1,2}. This fern is commonly seen to be growing in warmer temperatures and tropical regions of the world. This project of unravelling the genomic secrets of the fern has been in the pipeline for a while and was backed by a \$22,160 from 123 backers through a crowdfunding site called Experiment.com. Researchers eventually received funding to carry out the sequencing from Beijing Genomics



Genomics Institute in collaboration with Utrecht University. This tiny floating fern species which fits over a finger nail has a genome size of .75 gigabases (or billion base pairs). Ferns are known to have large genomes, average of 12 gigabases in size, however none of the larger fern genomes have been decoded so far. Such an elaborate project was aimed at providing clues on what could be the potential of this fern.

Many interesting aspects of fern *Azolla* have been uncovered upon this genome sequencing study published in *Nature Plants* and have provided direction for future research on potential areas in which this fern can be beneficial. The fern *Azolla* was widespread and growing almost 50 million years ago on this planet around the Arctic Ocean. During that time earth was also warmer compared to current condition and this

fern was thought to play a significant role in keeping the planet cooler by capturing around 10 trillion tons of carbon dioxide from the atmosphere over the course of 1 million years. Thus, here we see a potential role for this fern in combating and protecting our planet from global warming resulted by climate change.

Key points

- ② Knowing exact order in DNA can tell us the type of genetic information carried in the DNA which encode for protein that are responsible for most body functions.
- ② For the first time, the full genome of a water fern called *Azolla filiculoides* has been sequenced.
- ② This genomic information from ferns is a major step in the direction of uncovering and understanding crucial plant gene and properties of this fern.

The fern is also thought to play an important role in nitrogen fixation, a process which combines free nitrogen (N₂) in the atmosphere – an inert gas available abundantly in air – with other chemical elements to create more reactive nitrogen-based compounds e.g. ammonia, nitrates etc which can then be used in various applications like fertilizer for agriculture purposes.

The genome data tells us about a symbiotic relationship (mutual benefit) of this fern with a cyanobacterium named *Nostoc azollae*. The fern leaves host these cyanobacteria in tiny holes and these bacteria fix nitrogen

thereby producing oxygen which the fern and surrounding growing plants could use. In turn, cyanobacteria gather energy through the plant photosynthesis when the fern provides it fuel. Therefore, this fern could be possibly used as a natural green fertilizer and possibly eliminate usage of nitrogen fertilizers propagating more

sustainable agriculture practices. Authors say that having both the genomes of cyanobacteria and now the fern, research can be clearly focused on developing and adopting such sustainable practices. Interestingly, fern *Azolla* has already been added in rice paddies as green manure by Asian farmers for more than 1000 years.

Researchers have also identified an important naturally modified (insecticide) gene in the fern which is seen to have the ability to provide insect resistance. This gene when transferred to cotton plants provides massive protection from insects. This 'insecticidal' gene is thought to be transferred or 'gifted' from bacteria onto the fern and is seen to be a very specific component of the fern's lineage i.e. it has been passed on successfully from generation to generation. The discovery of potential protection from insects is bound to have a very strong impact on agriculture practices.

This study shows that 'pure science' of unravelling first ever genomic information from ferns is a major step in the direction of uncovering and understanding crucial plant genes. This also helps in a better understanding of the evolutionary history of ferns i.e. how their features have evolved over the generations. Authors comment that understanding of plants is very crucial to explore and comprehend how flora and fauna exist together amicably on our planet and such research should be given importance rather than labelling it as something which is not significant enough. After sequencing *Azolla filiculoides* and *Salvinia cucullata*, more than 10 fern species are already in pipeline for further research. ■

Source

1. Fay-Wei Li et al., 2018, 'Fern genomes elucidate land plant evolution and cyanobacterial symbioses', *Nature Plants*, vol. 4, no.7, DOI: 10.1038/s41477-018-0188-8
2. Fernbase www.fernbase.org Accessed July 18, 2018.

'Success Streak' is Real

Statistical analysis has shown that “hot streak” or a string of successes is real and everyone experiences these at some time point in their careers

“Hot streak”, also called a “winning streak” is defined as consecutive wins or successes or a run of good luck. It’s somewhat of a mystery when and why do winning streaks happen in a person’s career i.e. when is the phase they are most successful in or have the best creative insights. Scientists and statisticians have pondered over this and have sometimes supported the theory of ‘probability’ for such consecutive successes. For example, in the field of sport, tossing of the coin theory is applied that if one tosses a coin several times a non-random sequence might occur at any given point. Other times it was believed that hard work could increase the possibility of a hot streak or it may at least help in continuing or maintaining it. There is still no comprehensive or logical explanation behind the concept of hot streak. Everyone wants to access the ‘secret formula’ for their elusive hot streaks because everyone chases abundant success in their careers.

The concept of “hot streak”

In a study published in *Nature*, researchers at Kellogg School of Management at Northwestern University, USA analysed and judged the careers dataset of 20,400 scientists, 6,233 motion picture/film directors and 3,480 individual artists focusing broadly on the fields of arts and sciences. For artists, researchers looked at the prices of their works which they simply charged and received at art auctions. A good way to judge film directors was looking at their ratings on the website IMDB

(Internet Movie DataBase) because their ratings climbed up and down based upon how successful they were at a timepoint. For analysing career projections of scientists and researchers, it was seen how much their research works were cited in academic journals (data gathered from Google Scholar and Web of Science). Researchers explain that a “hot streak” defined as a period of powerful creative brilliance shown by people happens at least once in someone’s career and it usually continues for a period of about five years. During this fertile period, success achieved is higher than any other time in the career. Almost a quarter of this entire pool of people had two or more winning streaks. Therefore, this winning streak is very much “real” and not an untrue concept (as sometimes it is assumed) and it generally just occurs without any forewarning. For decades, analysts have maintained that everyone generally peaks sometime in the middle of a career, example, if someone starts working at 25 years and retires at 60, they experience a peak sometime in their late forties. However, evidence in this latest research says that hot streak is more “random” and can happen at any stage of someone’s career. So, this winning streak has nothing to do with age. For instance, a scientist or even an artist could have this streak of success or “peak of creativity” in early, middle or later part of his or her career.

Nothing succeeds like success!

Also, it’s analysed that the time period of five years signifies that once a hot streak gets kick



success is achieved, this leads to more frequent subsequent successes instilling good fortune in one's career for some additional time in a sort of clustered manner. One prominent achievement can easily enhance a person's and he or she may become more focused and feel good about what they are capable of. This bestows more fame and recognition for their work thus continuing their success streak for some more time. Major contribution also occurs because of the association with

the right kind of people after the winning streak once starts. For example, a scientist who has achieved major success will get more grants/-funding and awards and an artist might be able to build his own gallery and this can further bring more fame and popularity. Likewise, film directors may get more movie deals and films to direct and at a higher remuneration and profit share, not to mention more fame with film awards. The famous painter Vincent van Gogh had a hot streak

Key points

- ⊗ Researchers analysed and judged the careers dataset of 20,400 scientists, 6,233 motion picture/film directors and 3,480 individual artists focusing broadly on the fields of arts and sciences.
- ⊗ Hot streak or a success streak is real and occurs without a warning to anyone at any point in their career and this success lasts for an average of upto 5 years.

Researchers do understand that science or art are highly subjective fields and quality of success cannot really be put out in the form of objective data. But there is still some universal method by which success can be judged. For example, scientists receive higher citations for their work when they are having a hot streak and this generally continues for up to 10 years. Similarly, film directors get higher IMDB ratings which measure up both the acclaim that they receive for their work and also the box office numbers. And, for artists, auction prices are a good indicator of their

in the year 1888 when he painted over 200 paintings and on the personal note he moved from Paris to smaller place amidst nature in South of France which made him happier and content. Albert Einstein, a famous theoretical physicist, had an extraordinary hot streak in 1905 when he discovered the theory of relativity and earned a Nobel Prize for it. Subsequently, he discovered the Brownian motion – how molecules interact with each other – marking this period a glorious time for physics discoveries.

popularity and success and most importantly value of their work. And as the saying goes, nothing succeeds like success. One success leads to more opportunities for further successes, stream of money, awards and promotion. But because researchers aimed to do a statistical analysis so they were more interested in looking at the “value” which a person received in their career. Though in reality the definition of success is relative and some people define it in the ethical context bringing in mental contentment and happiness index.

Another important aspect of the winning streak is that not only is it real but also it cannot really be predicted and can occur at any given time. After a period of time, most likely five years, the hot streak can end for a person. In this study, no connection was seen between a person’s capability and productivity and the level of success they achieved in their career. Also, there is no noticeable increase in one’s productivity “during” the hot streak. However, a thriving ego is seen as one trait which could definitely lead up to creative streaks of success. And very hopeful it may sound, every person gets their share of successive runs, example 90 percent scientists had, so did 91 percent of artists and 88 percent of film director in the dataset analysed. So, it should be prevalent across other fields because too because these three occupations are already very diverse from each other and they were chosen for analysis mainly because of the ease of assembling their dataset. The “hot streak” is definitely a universal phenomenon. ■

Source

Lu Liu et al. 2018, ‘Hot streaks in artistic, cultural, and scientific careers’, *Nature*, DOI: 10.1038/s41586-018-0315-8

A Unique Pill to Treat Type 2 Diabetes

A temporary coating that mimics the effects of gastric bypass surgery could help to treat type 2 diabetes

Gastric bypass surgery is a common choice for patients suffering from blood pressure, weight management issues and diabetes. This surgery reverses obesity by making the patient lose huge amount of weight and also helps in management of type 2 diabetes in an independent manner. Because of this successful and well understood surgery, there has been significant improvement in lifestyle and high diabetes remission in the past decades. However, this type of surgery is not the first choice to pursue for many patients because of the risks involved and also because this surgery makes irreversible changes to the gastrointestinal anatomy of the patient. Statistics point out that only 1% to 2% patients who are suitable to have this surgery will every give their nod.

A new pill to “treat” Type 2 diabetes

Researchers at the Brigham and Women’s hospital in Boston and its Centre for Weight Management and Metabolic Surgery collaborated to find a less invasive but still a highly equivalent effective treatment for reversing type 2 diabetes. Such a method could provide same benefits as by gastric bypass surgery and would also be applicable in other areas of therapy. In their work published in *Nature Materials* they have detailed a preclinical study in which an oral agent was administered in rats whose purpose was to deliver a ‘substance’ which would then neatly coat the rat’s intestine to prevent any contact between dietary nutrients (from meals) and the lining in proximal bowel by acting as a barrier. This coating then helps to

prevent any spikes in blood sugar which generally happens after eating meals. The goal was to ultimately have an oral pill which a patient of type 2 diabetes can take before consuming a meal and this temporary coating of the gut could be helpful in somewhat replicating the results of the surgery.

The creation of this kind of oral pill required a collaboration between surgeons and bioengineers who could then develop a suitable material which can be applied in a clinical manner to the patient. When searching for an appropriate material, researchers keep in mind certain properties which are a major requirement. These included having good adhesion properties to be able to adhere or “stick” to the small intestine and the ability to dissolve within few hours as it would only be a temporary coat. After screening potential candidates which were a list of approved and safe compounds, they shortlisted a candidate – a substance called sucralfate. This substance is an approved drug used for treating gastrointestinal ulcers by creating a sticky paste in the acidic environment of the stomach and it binds to the areas of gastric lining wherever required because of current malfunctioning. For their current study, researchers bioengineered this compound into a new material which could coat the intestinal lining as desired and does so without requiring the stomach acid. This novel substance or ‘luminal coating’ labelled LuCI (Luminal Coating



of the Intestine) can also be prepared in a dry power form which can be formulated into a pill. In the preclinical trial, LuCI was administered into rats and once it reached the intestine it coated the gut thereby forming a slim barrier as desired. Thus, LuCI creates a barrier emulating the most critical aspect of gastric bypass surgery but in a non-invasive manner than the actual surgery. Normally after consuming meals, blood sugar rises and stays high for some time period. But with this lining in place, the spike was avoided and blood sugar levels were lowered by almost 50 percent within 1 hour of taking LuCI. Obviously, the aim was to have a temporary coat, and once this coating self dissolves within 3 hours, the effect on blood sugar dissipates and the levels returned to normal.

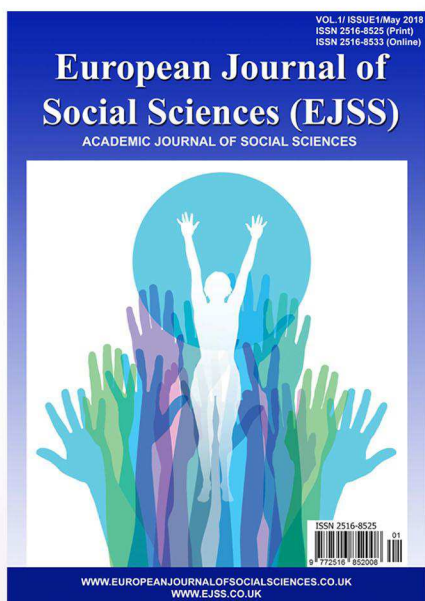
Tests have shown that this coating is safe and it has no adverse effect on the lining of the small intestine making it favourably compatible with the gastrointestinal mucosa. To gain further insights, researchers are currently testing the use of LuCI – both short and long term- on rat models which are obese and have diabetes. They have also done independent tests to show that such LuCI formulations could also be used to deliver therapeutic proteins into the gastrointestinal tract in a similar way. It could be used in nutrient absorption and to protect molecules from getting degraded by the stomach acids and intestinal fluids and degradation by stomach acid and other intestinal fluids. For controlling type 2 diabetes, this pill which could be taken before meal is a tremendous asset for patients.

Source

Yuhan Lee, Tara E. Deelman, Keyue Chen, Dawn S. Y. Lin, Ali Tavakkoli, Jeffrey M. Karp 2018, 'Therapeutic luminal coating of the intestine', Nature Materials, DOI: 10.1038/s41563-018-0106-5 ■

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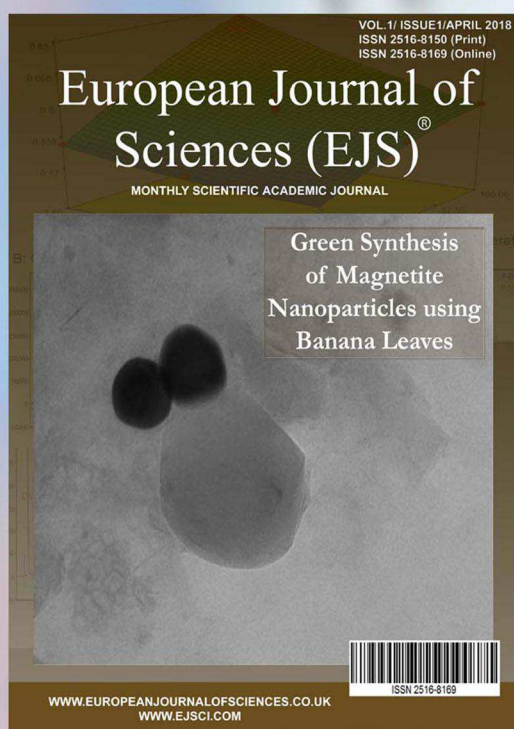
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Origin of High Energy Neutrinos Traced

The origins of high-energy neutrino have been traced for the very first time, solving an important astronomic mystery

Key points

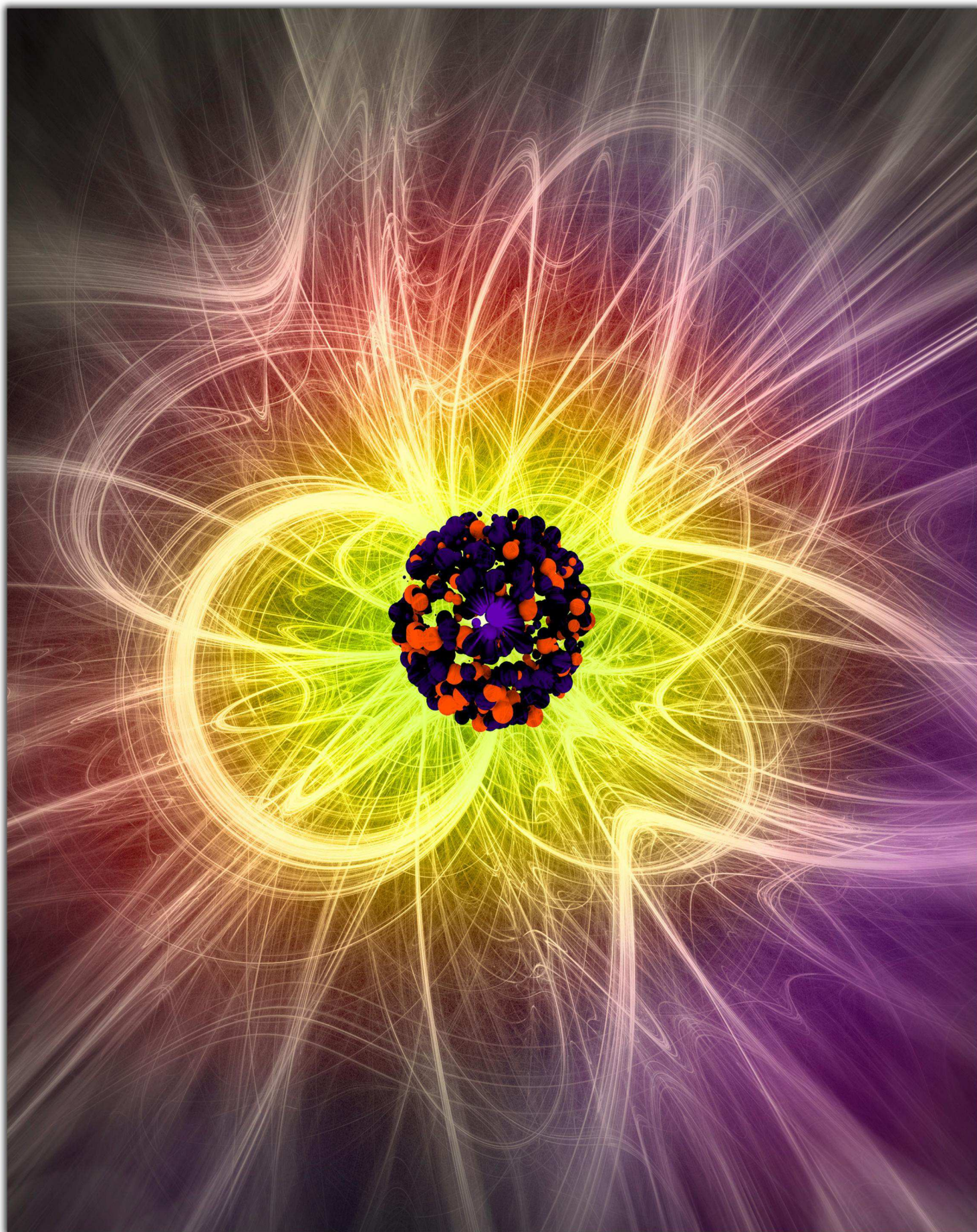
- ⊙ Researchers have for the first time traced the origin of a ghostly sub-atomic particle neutrino after it travelled 3.7 billion years to planet Earth.
- ⊙ The study of neutrinos is the most important step for any scientist interested in Physics and Astronomy as it can enable the study and observation of the universe in an unmatched manner.

To understand and learn more energy or matter, the study of the mysterious sub-atomic particles is very crucial. Physicists look at sub-atomic particles - neutrinos - to gain further understanding of the different events and processes from which they have originated. We know about stars and particularly the sun by studying neutrinos. There is so much more to be learnt about the universe and understanding how neutrinos function is the most important step for any scientist interested in Physics and Astronomy.

What are neutrinos?

Neutrinos are vaporous (and very volatile) particles with

no electric charge and they can pass through any type of matter without any alteration in themselves. Neutrinos can achieve this by withstanding extreme conditions and dense environments like stars, planet and galaxies. An important trait of neutrinos is that they never interact with the matter in their surroundings and this makes them very challenging to analyse. Also, they exist in three "flavours" - electron, tau and muon and they switch between these flavours when they are oscillating. This is called the "mixing" phenomena and this is the strangest area of study when conducting experiments on neutrinos. The strongest characteristics of neutrinos is that they carry unique information about their exact origin. This is mainly because neutrinos are though highly energetic, they possess no charge therefore they remain unaffected by magnetic fields of any power. The origin of neutrinos is not completely known. Most of them come from the sun but a small number especially the ones having high energies come from deeper regions of space. This is the reason that the exact origin of these elusive wanderers was still unknown and they are referred to as "ghost particles".



Origin of high-energy neutrino traced

In ground-breaking twin studies in astronomy published in Science, researchers have for the first time traced the origin of a ghostly sub-atomic particle neutrino which was found deep in ice in Antarctica after it travelled 3.7 billion years to planet Earth^{1,2}. This work is achieved by a collaboration of over 300 scientists and 49 institutions. High-energy neutrinos were detected by largest ever IceCube detector set up at South Pole by the IceCube Neutrino Observatory deep into the layers of ice. To achieve their goal, 86 holes were drilled into ice, each one and half miles deep, and spread over a network of more than 5000 light sensors thus covering a total area of 1 cubic kilometre. IceCube detector, managed by US National Science Foundation, is a giant detector consisting of 86 cables which are put in boreholes extending up to deep ice. The detectors record the special blue light which is emitted when a neutrino interacts with an atomic nucleus. Many high-energy neutrinos were detected but they were untraceable until a neutrino with an energy of 300 trillion electron volts was detected successfully beneath an ice cap. This energy is almost 50 times bigger than the energy of the protons which cycle through Large Hardon Collider which is the utmost powerful particle accelerator on this planet. Once this detection was done, a real time system methodically gathered and compiled data, for the entire electromagnetic spectrum, from laboratories on Earth and in space about this neutrino's origin.


The neutrino was successfully traced back to a luminous galaxy known as the "blazer". Blazer is a gigantic elliptical active galaxy with two jets which emit neutrinos and gamma rays. It has a distinctive supermassive and swiftly spinning black hole at its centre and the galaxy moves towards Earth around the speed of light. One of the jets of the blazer is of a blazing bright character and it points directly at earth giving this galaxy its name. The blazer galaxy is located to the left

of Orion constellation and this distance is about 4 billion light-years from Earth. Both neutrinos and gamma rays were detected by the observatory and also a total of 20 telescopes on Earth and in space. This first study¹ showed the detection of neutrinos and a second subsequent study² showed that the blazer galaxy had produced these neutrinos earlier also in 2014 and 2015. The blazer is definitely a source of extremely energetic neutrinos and thus of cosmic rays as well.

Ground-breaking discovery in astronomy

The discovery of these neutrinos is a major success and it can enable the study and observation of the universe in an unmatched manner. Scientists state that this discovery might help them to trace back, for the very first time, the origins of the mysterious cosmic rays. These rays are fragments of atoms which come down to Earth from outside the solar system blazing at the speed of light. They are blamed for causing problems to satellites, communications systems etc. In contrast to neutrinos, cosmic rays are charged particles thus magnetic fields keep affecting and changing their path and this makes it impossible to trace back their origins. Cosmic rays have been the subject of research in astronomy for a long time and though they were discovered in 1912, cosmic rays remain a big mystery.

In the future, a neutrino observatory on a larger scale using similar infrastructure as used in this study can achieve faster results and more detections can be made to unravel new sources of neutrinos. This study done by recording multiple observations and taking cognizance of data across the electromagnetic spectrum is crucial to further our understanding of the universe the mechanisms of physics that govern it. It's a prime illustration of "multi messenger" astronomy which uses at least two different types of signal to examine the cosmos making it more powerful and accurate in making such discoveries possible. This approach has helped discover neutron



star collision and also gravitational waves in the recent past. Each of these messengers provide us new knowledge about the universe and powerful events in the atmosphere. Also, it can assist in understanding more about the extreme events which occurred millions of years ago setting out these particles to make their journey to Earth ■

Source

The IceCube Collaboration et al., 2018, 'Multimessenger observations of a flaring blazar coincident with high-energy neutrino IceCube-170922A', Science, vol. 361, no. 6398, eaat137, DOI: 10.1126/science.aat1378

The IceCube Collaboration et al., 2018, 'Neutrino emission from the direction of the blazar TXS 0506+056 prior to the IceCube-170922A alert', Science, Vol. 361, Issue 6398, pp. 147-151, DOI: 10.1126/science.aat2890

Growing Neanderthal Brain in the Laboratory

Studying the Neanderthal brain can reveal genetic modifications which caused Neanderthals to face extinction while made us humans as a unique long-surviving species

Neanderthals were a human species (*called Neanderthal neanderthalensis*) who evolved in Asia and Europe and coexisted for some part with current human beings (*Homo Sapiens*) who evolved in Africa. These encounters had led to human brings inheriting 2% of Neanderthal DNA and thus they are the closest ancient relatives to modern day humans. Neanderthals are last known to have existed about 130000 and 40,000 years ago. Neanderthals, commonly referred to as “cavemen” had a distinctive low long skull, wide nose, no prominent chin, large teeth and short but strong muscular body frame. Their distinctive characteristics are indicative of seeking a way for the body to conserve heat amidst the cold and harsh environments they lived in. Despite their primitive living conditions, they were very bright, talented and social humans with brain size larger than modern humans today. They were excellent hunters possessing skills, strength, courage and proficient communication skills. Even though they lived in challenging environments, they were tremendously resourceful. In fact, it is believed that there might have been a very narrow gap between Neanderthals and us humans in terms of behaviour and instincts. Fossil records show that they were carnivorous (though they also ate fungi), hunters and scavengers. It is still unclear if they had their own language, but complex dynamics in their lives does suggest that they communicated with each other using a language.

The Neanderthals are now extinct for 40,000 years, however, it's still a mystery how a species

which had survived for more than 350,000 years could face extinction. Some scientists have formulated that modern humans are responsible for extinction of Neanderthals since they may not have been able to survive ably with the competition in resources posed by early ancestors of modern humans. This must have also been aggravated by rapid change in climate conditions. Neanderthals did not all quickly disappeared but were replaced by modern humans gradually through local populations. Neanderthals are the most interesting part of human evolution which has intrigued scientists mostly because of close proximity of Neanderthals to modern day humans. And to support this research, many objects and fossils, even full skeletons have been uncovered which demonstrate a glimpse of the life of Neanderthals.

Growing a Neanderthal brain in the laboratory

Researchers at University of California, San Diego are growing the Neanderthals miniature brains (resembling a cortex which is the outside layer of the brain) of the size of a ‘pea’ in petri dishes in the laboratory. Each of this “pea” carry the NOVA1 gene of the ancestors and has about 400,000 cells. The goal of growing and analysing these ‘minibrains’ of Neanderthals is to shed light on small neural lumps which can tell us why this long-surviving species became extinct and what was the reason for modern day humans to instead conquer the planet Earth. It is important to understand this because some modern-day humans do share 2% DNA with

Neanderthals through breeding and at one point we coexisted with them. The comparison of genetic differences in the brain can shed maximum light on their demise and rapid increase of homo sapiens.

To initiate the growth of the minibrain, researchers used the stem cell technology in which stem cells start to become a brain organoid (a small organ) over a period of several months. At their fully-grown size, these organoids measure 0.2 inches and are visible to the naked eye. However, their

growth is restrictive because under the laboratory circumstances as they do not get the blood supply which is required for them to grow wholly. So, minibrain cells received the nutrients for growth by the process of diffusion. It might be possible to grow them further by perhaps inculcating 3D printed artificial blood vessels in them to enable development, which is something researchers would like to attempt.

First step towards comparing Neanderthal's brain with ours

Neanderthal brains are more elongated tube-like structures compared to human rounded brains. In this exceptional work, researchers compared the available fully-sequenced genomes of Neanderthals with the modern humans. The Neanderthal genome was sequenced after retrieving it from bones in the fossils that were uncovered. A total of 200 genes showed substantial differences and from this list the researchers focused on NOVA1 – master gene expression regulator. This gene is same in humans and Neanderthals with just a slight difference (a single DNA base pair). This gene is seen to have high expression in neurodevelopment and has been linked to several

conditions like autism. On closer inspection, the Neanderthal minibrains had very few connections between neurons (called synapses) than typical and also had different neuronal networks somewhat appearing like a human brain suffering from autism researchers predicted. Its highly possible that humans had more advanced and sophisticated neural networks compared to Neanderthals which made us survive over them.

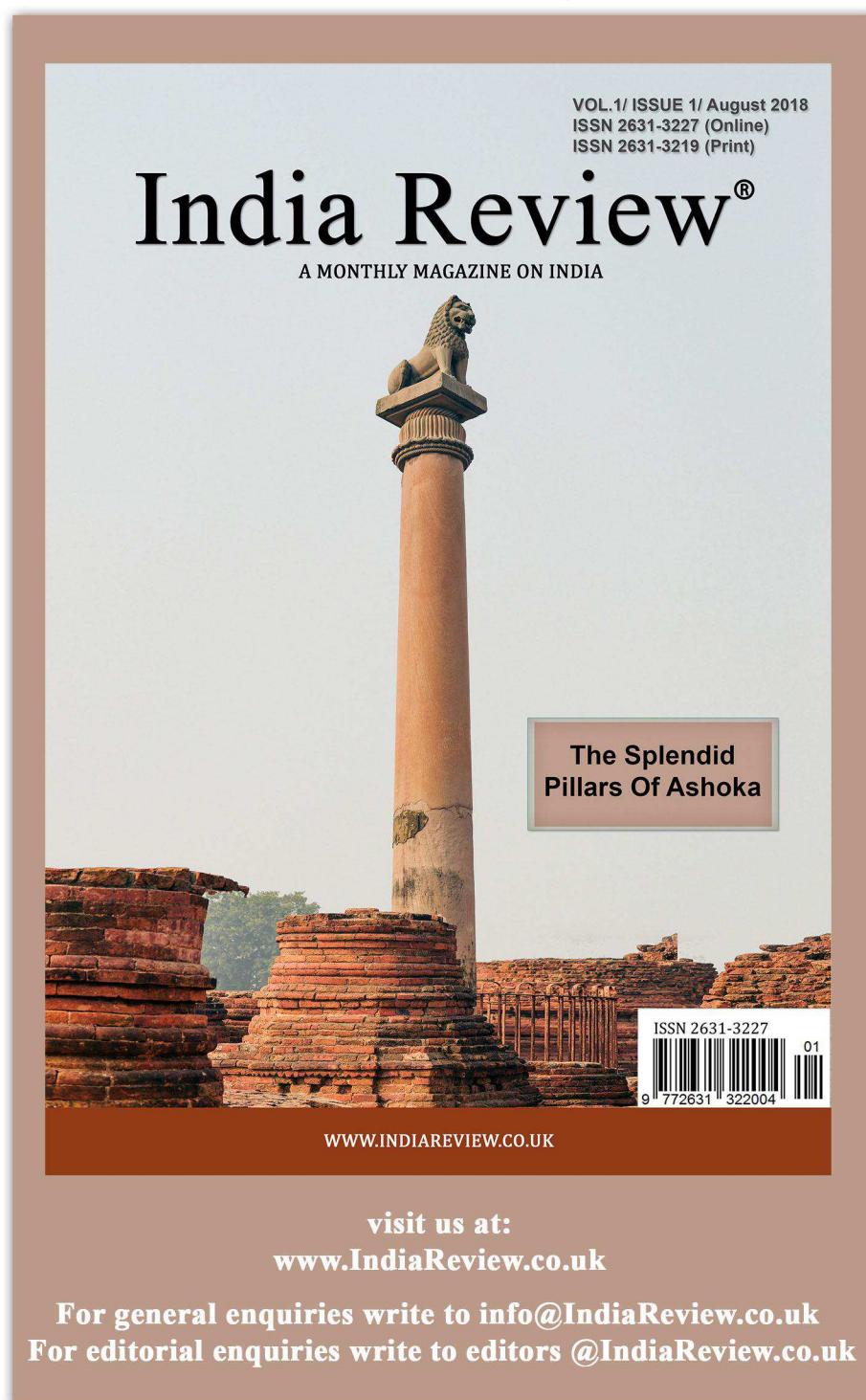


This research is still at a very early stage to arrive at a conclusion, mainly because of the nature of controlled experiments. Also, the biggest limitation of this study is that such mini brains are not “conscious minds” or a “full brain” and cannot really provide a complete picture of how an adult brain functions. However, if different regions are grown successfully, they can be fit together to gain a larger understanding of the Neanderthal

“mind”. Researchers would definitely like to explore more about the ability of the Neanderthals brains to learn things and thus they would try to put these mini brains in the robot and understand the signals. ■

Source

Neanderthal brain organoids come to life, Jon Cohen, Science, Vol. 360, Issue 6395, pp. 1284, DOI: 10.1126/science.360.6395.1284



A New Approach to Treat Obesity

Researchers have studied an alternative approach to regulate immune cell function to treat obesity


Obesity is a chronic illness which affects 30% of the world's total population. The main cause of obesity is higher consumption of fat rich food and limited physical activity or exercise. The surplus amount of high energy consumed (mainly from fat and sugars) is then stored as fat in the body leading to high body weight. The Body Mass Index (BMI) of an obese person is between 25 and 30 which is very high. Many factors affect and contribute to obesity like genetics, body's metabolism rate, lifestyle, environmental factors etc. Obesity or high body weight then leads to other negative outcomes in the body by causing harmful inflammation. Obese or overweight people are at a

higher risk of developing severe illnesses or conditions, including heart disease because of clogged arteries, Type 2 diabetes and serious bone and joint conditions.

A study published in *Proceedings of National Academy of Sciences USA* sheds light on the reason why immune cells inside our fat tissue become harmful when someone is suffering from obesity. These immune cells in our body otherwise considered to be useful start to cause undesired inflammation and changes in the metabolic system. Free radicals are produced in our body during normal metabolic processes or due to exposure to outside sources like

harmful radiation, smoking, environmental pollution etc. These free radicals are unstable and harmful atoms which can damage cells in our body and cause ageing and illness. Researchers of the current study from University of Virginia School of Medicine say that these free radicals are highly reactive and in an obese person as they react with lipids inside





the fat tissue. Once lipids - which are considered an attractive target by the free radicals - combine with free radicals, normal immune response occurs in the body causing inflammation and results in 'lipid oxidation'. The small oxidized lipids are pretty harmless and are found in healthy cells. However, longer full length oxidized lipids, found generally in obese tissue, cause excessive harmful inflammation which propagates the obesity disease within the fat tissue.

The knowledge of these problematic oxidized lipids can be used to devise a method to block them which can then prevent harmful inflammation. Example, a drug which could either diminish or completely eliminate the longer and damaging oxidized lipids.

Such a therapy would be extremely beneficial for a chronic disease like obesity. However, as scientists point out, eradicating all inflammation may not be the right approach because some of it is useful for the body. Such targeting of the metabolic of immune cells in our immune system is an approach which is already being used for cancer. ■

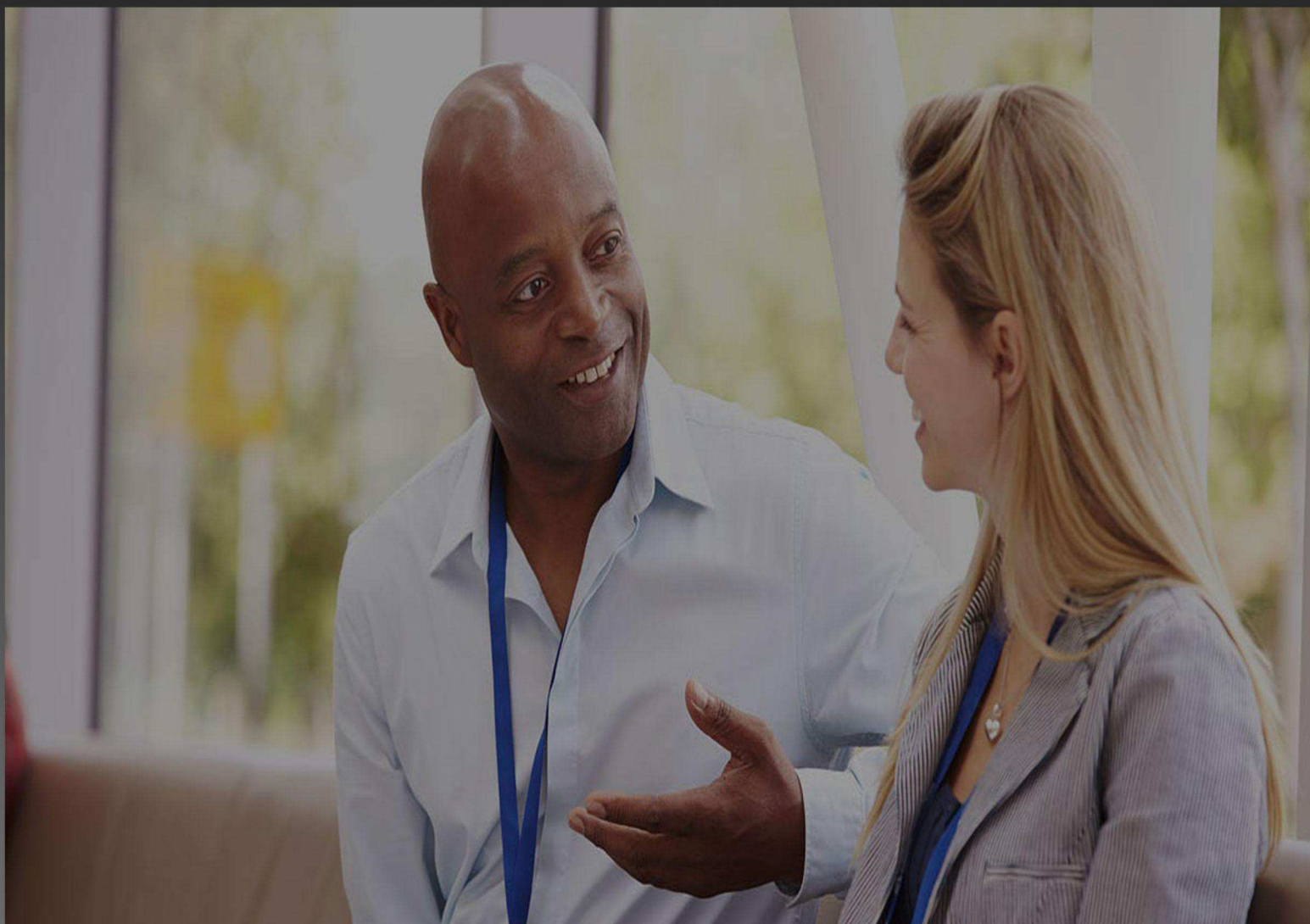
Source

Vlad Serbulea, et al 2018, 'Macrophage phenotype and bioenergetics are controlled by oxidized phospholipids identified in lean and obese adipose tissue', Proceedings of the National Academy of Sciences, vol. 115, no. 27, DOI: 10.1073/pnas.1800544115



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