High fructose consumption linked to greater risk for NAFLD

High fructose consumption should be avoided to prevent the development of non-alcoholic fatty liver disease (NAFLD), according to research being presented at ENDO 2022, the Endocrine Society's annual meeting in Atlanta, Ga.

Fructose is a natural sugar present in fruits, fruit juices, certain vegetables and honey. In these forms, fructose sugars can be part of a nutritious diet. However, fructose is also a component of high-fructose corn syrup, which manufacturers make from corn starch and add to unhealthy foods such as sodas and candies, according to a press release by Endocrine Society.

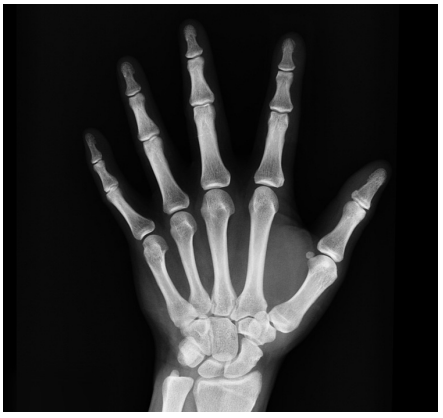
"NAFLD is a serious problem and it is increasing in the population. There is a racial/ethnic difference in the prevalence of the NAFLD. People consume high-fructose corn syrup in foods, soft drinks and other beverages. Some studies suggested that consumption of high-fructose corn syrup is related to the development of NAFLD," said lead author Theodore Friedman, M.D., Ph.D., of Charles R. Drew University in Los Angeles, Calif.

For this study, the researchers analyzed data from 3,292 participants enrolled in the National Health and Nutrition Examination Survey 2017-2018. They found the greatest proportion of those who consumed the highest fructose was Mexican Americans (48%) and non-Hispanic Blacks (44%) with a low percentage of non-Hispanic whites (33%). The highest prevalence of NAFLD was among Mexican Americans who consumed the highest amount of fructose (70%).

"We found that when adjusting for the demographics and behavioural factors (smoking, modest alcohol consumption, diet quality and physical activity), high fructose consumption was associated with a higher chance of NAFLD among the total population and Mexican Americans," Friedman said.

Increased fracture risk in patients using insulin as compared to metformin

Patients with type 2 diabetes have an increased risk for fractures, despite their normal-to-high bone mineral density, according to research being presented at ENDO 2022, the Endocrine Society's annual meeting in Atlanta, Ga. "Patients using insulin or sulfonylurea are at a high risk of fractures compared to metformin-only users, and the risk could be higher in non-obese and well-controlled diabetic patients," said Sung Hye Kong, M.D., of Seoul National University Bundang Hospital in Seongnam, South Korea.



Kong and colleagues acknowledge that anti-diabetic medications have long been suspected for an increased risk for fractures among this patient population. For their study, the researchers included 6,694 patients aged ≥50 years from the common data model (CDM) database between 2008 and 2011, which used the same anti-diabetic medications for over a year, according to a press release by Endocrine Society.

"From real-world data using the common data model, we found that insulin users were at elevated risk of major osteoporotic and hip fracture compared to metformin users, which was attenuated in users with a combination of insulin and metformin," Kong said.

This increased fracture risk among people who used insulin was exaggerated among people who are not obese and those with well-controlled diabetes. These findings suggest a need for routine fracture risk assessments in patients with diabetes.

Eyes could reveal all about ADHD and ASD

It's often said that 'the eyes tell it all', but no matter what their outward expression, the eyes may also be able to signal neurodevelopmental disorders such as attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) according to new research from Flinders University and the University of South Australia. This research was conducted in partnership with McGill University, University College London and the Great Ormond Street Hospital for Children, according to a news report by Flinders University.

Researchers found that recordings from the retina could identify distinct signals for both ADHD and ASD providing a potential biomarker for each condition.

Using the 'electroretinogram' (ERG) - a diagnostic test that measures the electrical activity of the retina in response to a light stimulus - researchers found that children with ADHD showed higher overall ERG energy, whereas children with ASD showed less ERG energy.

Research optometrist at Flinders University, Dr Paul Constable, says the preliminary findings indicate promising results for improved diagnoses and treatments in the future."ASD and ADHD are the most common neurodevelopmental disorders diagnosed in childhood. But as they often share similar traits, making diagnoses for both conditions can be lengthy and complicated," Dr Constable says.

Co-researcher and expert in human and artificial cognition at the University of South Australia, Dr Fernando Marmolejo-Ramos says that the research has potential to extend across other neurological conditions. "Ultimately, we're looking at how the eyes can help us understand the brain. While further research is needed to establish abnormalities in retinal signals that are specific to these and other neurodevelopmental disorders, what we've observed so far shows that we are on the precipice of something amazing," Dr Marmolejo-Ramos says.

Dementia associated withdeficiency of vitamin D

A study from the University of South Australia shows a direct link between dementia and a lack of vitamin D. Investigating the association between vitamin D, neuroimaging features, and the risk of dementia and stroke, according to a press release. The study found:

- Low levels of vitamin D were associated with lower brain volumes and an increased risk of dementia and stroke
- Genetic analyses supported a causal effect of vitamin D deficiency and dementia.
- In some populations as much as 17 per cent of dementia cases might be prevented by increasing everyone to normal levels of vitamin D (50 nmol/L)

Supported by the National Health and Medical Research Council, the genetic study analysed data from 294,514 participants from the UK Bio bank, examining the impact of low levels of vitamin D (25 nmol/L) and the risk of dementia and stroke. Nonlinear Mendelian randomisation (MR) – a method of using measured variation in genes to examine the causal effect of a modifiable exposure on disease - were used to test for underlying causality for neuroimaging outcomes, dementia, and stroke.

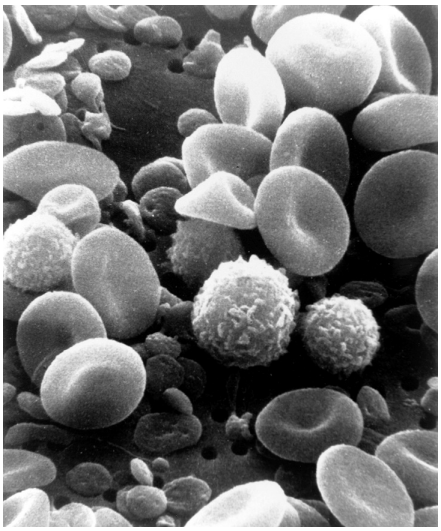
Senior investigator and Director of UniSA's Australian Centre for Precision Health, Professor Elina Hyppönen, says the findings are important for the prevention of dementia and appreciating the need to abolish vitamin D deficiency.

"Vitamin D is a hormone precursor that is increasingly recognised for widespread effects, including on brain health, but until now it has been very difficult to examine what would happen if we were able to prevent vitamin D deficiency. Most of us are likely to be ok, but for anyone who for whatever reason may not receive enough vitamin D from the sun, modifications to diet may not be enough, and supplementation may well be needed." Prof Hyppönen says.

Eosinophils vital to gut health

A Monash University collaboration has found that eosinophils, a type of white blood cell commonly associated with asthma and allergy, play an important role in maintaining a healthy gut according to a news release by Monash University. Professor Nicola Harris, from Monash's Central Clinical School, made the surprising discovery working with study co-lead, Professor Kathy McCoy from the University of Calgary, and scientists from Switzerland. Their paper was published in *Immunity*. Co-first authors on the paper were Dr Aline Ignacio from the University of Calgary and Dr Kathleen Shah from the Global Health Institute, Swiss Federal Institute of Technology, Lausanne, Switzerland.

"The study showed a critical role for eosinophils in facilitating mutualistic interactions between host and microbiota, the millions



of bacteria in the gut," Professor Harris said. "It turns our views of eosinophil function on its head and will no doubt spur a lot more research into these relatively rare cells," she said.

The scientists investigated the possible role of eosinophils in the main functions of the small intestine using germ-free animal models and advanced 3-D microscopy. They found that eosinophils co-ordinated the gut's response to bacteria.

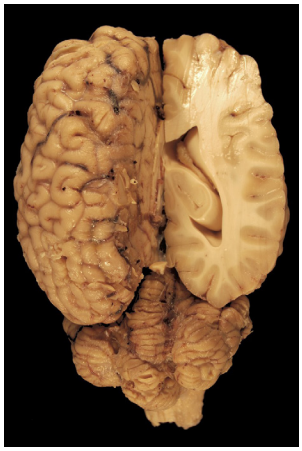
"They were limiting overt inflammation and by doing that they were limiting tissue damage," Professor Harris said. "The most important factor of this damage is the length of the villi, the finger-like projections that come up from the wall of the intestine, which absorb nutrients.

The study also found that gut motility was dysregulated in the absence of eosinophils and that they could impact the structure of tissue. "These cells are a lot more complicated than previously believed – we need to think about them in an entirely different way," Professor Harris said. "They're doing a lot that's completely unexplored."

Brain injury activates neural stem cells

One of the most devastating aspects of stroke and traumatic brain injury is that the neurons we lose are never replaced. This means that depending on the injury site, patients may suffer long-term impairments of crucial motor or cognitive functions, such as language and memory.

A study published in the journal *Developmental Cell* may offer a way forward according to a news release by Champalimaud Foundation. Scientists at the Champalimaud Foundation in Portugal discovered a novel mechanism by which neurons and glia collaborate to drive this process. "We have revealed how neural stem cells sense injury and are recruited for tissue repair. These findings may be the first step towards developing drugs to promote the formation of new neurons following brain damage", said the study's senior author Christa Rhiner.



Rhiner's team turned to the fly and mouse animal models. "Just like ours, their brains also contain neural stem cells", she explained. "In addition, many signalling molecules and forms of intercellular communication are common to humans, flies and mice. Consequently, the insights we gain from these animal models are likely to be relevant for understanding human physiology."

Anabel Simões, a doctoral student in the lab, wondered what molecules were present exclusively in the injured brain area. "It was Swim - a transporter protein that quite literally 'swims' across the tissue, helping molecules that normally act locally to spread out. Following a thorough investigation, we learned that Swim is critical for mounting a regenerative response to brain injury", she explained.

According to Simões, the next logical step was to determine which molecule Swim was carrying. An additional series of experiments uncovered the answer - Wg/Wnt, a known activator of neural stem cells in flies and mammals. "We found Wg in neurons in the dam-

aged area, which is remarkable", said Simões. "It meant that the neurons themselves sense the tissue's distress and respond to it by trying to send a wakeup signal to dormant neural stem cells." The team found that when oxygen levels drop in the injured brain area, a certain type of glial cells jumps into action. These cells produce Swim and secrete it into the extracellular space. Then, the transporter encapsulates Wg and carries it to the nearest stem cell, effectively turning it on.

"One of the more striking aspects of this mechanism is that it's collaborative. Neurons and glia in the affected brain area work together to promote tissue repair," said Simões.

New vaccine targets for rabies vaccine

La Jolla Institute (LJI) scientists, in collaboration with researchers from the Institut Pasteur in France, capture new high-resolution view of rabies virus, revealing potential vaccine targets. LJI Professor Erica Ollmann Saphire, and her team, in collaboration with a team led by Institut Pasteur Professor Hervé Bourhymay have discovered the path to better vaccine design according to the news release published by La Jolla Institute for Immunology. In a new study, published in *Science Advances*, the researchers share one of the first high-resolution looks at the rabies virus glycoprotein in its vulnerable "trimeric" form.

"The rabies glycoprotein is the only protein that rabies expresses on its surface, which means it is going to be the major target of neutralizing antibodies during an infection," says LJI Postdoctoral Fellow Heather Callaway, Ph.D., who

serves as the study's first author.

Over the course of three years, Callaway worked to stabilize and freeze the rabies glycoprotein in its trimeric form. This "pre-fusion" form is the shape the glycoprotein takes before it infects human cells. The new 3D structure highlights several key features researchers hadn't seen before. Importantly, the structure shows two key pieces of the virus structure, called the fusion peptides, the way they appear in real life. These two sequences link the bottom of the glycoprotein to the viral membrane, but project into the target cell during infection. It is very hard to get a stable image of these sequences. In fact, other rabies researchers have had to cut them off to try to get images of the glycoprotein.

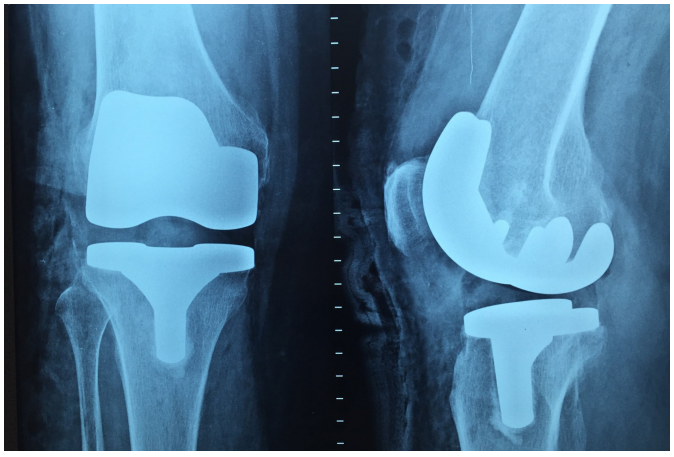
Callaway solved this problem by capturing the rabies glycoprotein in detergent molecules. "That let us see how the fusion sequences are attached before they snap upward during infection," says Saphire.

"Instead of being exposed to four-plus different protein shapes, your immune system should really just see one—the right one," says Callaway. "This could lead to a better vaccine."

Bone fracture, stroke and heart attack linked to Primary hyperparathyroidism

Primary hyperparathyroidism is a common hormone disorder, especially among the elderly. It occurs more often in women, and some 3% of postmenopausal women are affected. Rather than causing specific symptoms, it is often detected by chance in connection with blood tests, which then show elevated calcium levels and normal or elevated parathyroid hormone levels. This disturbed calcium balance in the blood can cause kidney, skeletal, and cardiovascular damage.

Previous studies have linked primary hyperparathyroidism to osteoporosis and cardiovascular disease. However, since these studies have been few and small,



the association has been debated.

This study, published in the journal *JAMA Network Open*, is based on national register data from the Swedish National Board of Health and Welfare. All the 16,374 patients included were diagnosed with primary hyperparathyroidism sometime between 2006 and 2017 according to the press release by University of Gothenburg. Each was compared with ten control individuals from the population born in the same year, of the same sex, and residing in the same county.

"We show that untreated primary hyperparathyroidism means a 51% higher risk of hip fracture and a 45% increase in heart attack or stroke risk. The kidney stone risk is almost quadrupled and, additionally, the risk of death is raised by 72%. The increased likelihood of these complications highlights the importance of identifying patients with this hormonal disease," says Kristian Axelsson, researcher at the University of Gothenburg, resident in general medicine within the public primary care in Region Västra Götaland, and the study's first author.

Manipulating the microbiome to treat acne

An international team of researchers led by Marc Güell has tried a new approach that consists of manipulating the microbiome to achieve a potential therapeutic strategy to treat acne without affecting its equilibrium. Anew study by the Translational Synthetic Biology research group at UPF presents a new approach to eliminating specific strains of a bacterium related to acne according to the news release by Universitat Pompeu Fabra, Barcelona. The paper, published in the journal *Plos Pathogens*, has also involved scientists from the company S-Biomedic and the University of Lund, in Sweden.

The bacterium *Cutibacterium* acnes (C. acnes) is the most abundant in human skin. There are different strains of this bacterium, some predominate in healthy skin and others are associated with acne, which is a multifactorial disease. In healthy skin there is a balance and in acne there is a change in the abundance of certain strains, which brings about an imbalance known as dysbiosis. Therefore, the use of antibiotic treatments is not optimal, as they usually kill the different strains of C. acnes and even other skin bacteria, thus altering the equilibrium.

"In our study we demonstrated that through bacteriophage therapy it is possible to modulate the composition of C. acnes strains over time. We can reduce the strains associated with acne without affecting the ones that have beneficial features", explains Marc Güell, study coordinator.

"Using specific bacteriophages we attack pathogenic strains, which are the ones that do not have this defence strategy. The beneficial strains do have this defensive system against bacteriophages, so they are protected against infection", explains Nastassia Knödlseder, first author of the article.

COVID-19 increases the risk of developing Parkinson's disease

Thomas Jefferson University and collaborators showed in a new study performed in mice, that the SARS-CoV-2 virus responsible for the COVID-19 pandemic could increase the risk of brain degeneration seen in Parkinson's disease.

"Parkinson's is a rare disease that affects 2% of the population above 55 years, so the increase in risk is not necessarily a cause for panic," says Richard

Smeyne, Director of the Jefferson Comprehensive Parkinson's Disease and Movement Disorder Center at the Vickie and Jack Farber Institute for Neuroscience and first author of the study in a news release. "But understanding how coronavirus impacts the brain can help us prepare for the long-term consequences of this pandemic."

The research, published in *Movement Disorders*, builds on previous evidence from the Smeyne lab showing that viruses can make

brain cells or neurons more susceptible to damage or death.

In that earlier study, the researchers found that mice infected with the H1N1 strain of influenza responsible for the 2009 flu pandemic, were more susceptible to MPTP, a toxin that is known to induce some of the characteristic features of Parkinson's: primarily the loss of neurons expressing the chemical dopamine and increased inflammation in the basal ganglia, a brain region that is critical for movement.In the current study, the researchers used mice that were genetically engineered to express the human ACE-2 receptor, which the SARS-CoV-2 virus uses to gain access to the cells in our airway. These mice were infected with SARS-CoV-2 and allowed to recover. Importantly, the dose chosen in this study corresponds to moderate COVID-19 infection in humans, with around 80% of the infected mice surviving. Thirty-eight days after the surviving animals recovered, one group was injected with a low dose of MPTP that would not normally cause any loss of neurons. The control group was given saline. Two weeks later, the animals were sacrificed and their brains examined.

The researchers found that COVID-19 infection alone had no effect on the dopaminergic neurons in the basal ganglia. However, mice that were given the low dose of MPTP after recovering from infection exhibited the classic pattern of neuron loss seen in Parkinson's disease. This increased sensitivity after COVID-19 infection was similar to what was seen in the influenza study; this suggests that both viruses could induce an equivalent increase in risk for developing Parkinson's.

"We think about a 'multi-hit' hypothesis for Parkinson's – the virus itself does not kill the neurons, but it does makes them more susceptible to a 'second hit', such as a toxin or bacteria or even an underlying genetic mutation," explains Dr. Smeyne.

While their findings thus far bolster a possible link between the coronavirus and Parkinson's disease, Dr. Smeyne says there are some important caveats. "First of all, this is preclinical work. It is too soon to say whether we would see the same thing in humans, given that there seems to a 5-10 year lag between any changes in clinical manifestation of Parkinson's in humans." This lag, he says however, could be used to our advantage. "If it does turn out that COVID-19 increases the risk of Parkinson's, it will be a major burden on our society and healthcare system. But we can anticipate that challenge by advancing our knowledge of potential 'second hits' and mitigating strategies."

Erectile Dysfunction drugs could help treat oesophageal cancer

A group of drugs commonly used to treat erectile dysfunction may be able to boost the effect of chemotherapy in oesophageal cancer, according to new research from the University of Southampton.

The research, published in *Cell Reports Medicine*, found that the drugs, known as PDE5 inhibitors can reverse chemotherapy resistance by targeting cells called cancer-associated fibroblasts (CAFs) residing in the area surrounding the tumour.

Although this is early research, PDE5 inhibitors combined with chemotherapy may be able to shrink some oesophageal tumours more than chemotherapy could alone, tackling chemotherapy resistance, which is one of the major challenges in treating oesophageal cancer.

Professor Tim Underwood, lead author of the study and a professor of gastrointestinal surgery at the University of Southampton, said in a news release, "The chemotherapy resistant properties of oesophageal tumours mean that many patients undergo intensive chemotherapy that won't work for them. Finding

a drug, which is already safely prescribed to people every day, could be a great step forward in tackling this hard-to-treat disease."

Resistance to chemotherapy in oesophageal cancer is influenced by the tumour microenvironment, the area that sounds the tumour. This is made up of molecules, blood vessels, and cells such as cancer associated fibroblasts (CAFs), which are important for tumour growth. It feeds the tumour and can act as a protective

cloak, preventing treatments like chemotherapy from having an effect.

The researchers found that levels of PDE5, an enzyme originally found in the wall of blood vessels are higher in oesophageal adenocarcinoma compared with healthy oesophageal tissue. High levels of PDE5 were found in CAFs within the tumour microenvironment. They also found that high expression of PDE5 is associated with worse overall survival, suggesting that PDE5 would be an effective target for treatment. An added benefit of using PDE5 inhibitors is that they are already proven to be a safe and well tolerated class of drug that's given to patients world-wide, even in the high doses that would be required for this treatment. The researchers also say that giving PDE5 inhibitors to people with oesophageal cancer would be extremely unlikely to cause erections without the appropriate stimulation.

With the proven safety of these drugs and the positive results from this research, the researchers' next step is a phase I/II clinical trial testing a PDE5 inhibitor in combination with chemotherapy in patients with advanced oesophageal cancer.

If successful, this treatment could be helping a significant proportion of the around 9300 people a year diagnosed with oesophageal cancer within the next 5 to 10 years. The study could pave the way for the use of PDE5 inhibitors in other cancer types.

Heart Failure severity associated with lack of gut microbe diversity

Some people who experience heart failure have less biodiversity in their gut or have elevated gut metabolites, both of which are associated with more hospital visits and greater risk of death, according to a systematic review of research findings led by Georgetown University School of Nursing & Health Studies researchers and colleagues.The gut microbiome is a delicately balanced ecosystem composed primarily of bacteria as well as viruses, fungi and protozoa. The microbiome can affect cardiovascular disease, which can be a cause of death for many.

The investigators looked at seven years of genetic, pharmacologic and other types of research findings from around the world to generate a wide perspective on how the microbiome can influence heart failure. The investigators zeroed in on one harmful metabolite, trimethylamine-N-oxide (TMAO) that can be produced by churning gut microbiota when full-fat dairy products, egg yolks and red meat are consumed.

"To diagnose and manage heart failure, we rely on certain findings and test results, but we do not know how poor heart function influences the activities of the gut, including the absorption of food and medications," says Kelley Anderson, associate professor of nursing at Georgetown and corresponding author of the study. "There is now an appreciation of a back-and-forth relationship between the heart and elements in the gut, as clearly the heart and vascular system do not work in isolation — the health of one system can directly influence the other, but clear connections are still being worked out scientifically."

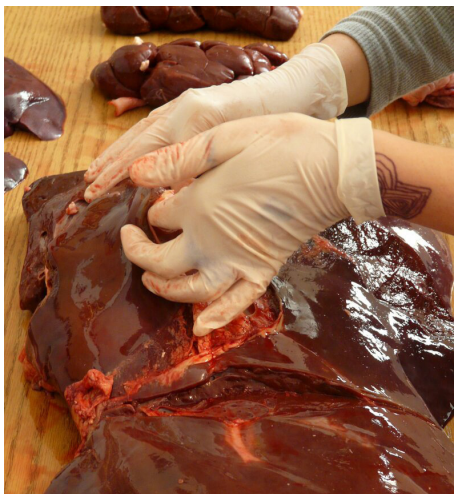
The investigators parsed 511 research articles published between 2014 and 2021 that connected the microbiome with heart failure and winnowed their focus to the 30 most relevant articles. In recent years, more advanced technology, particularly tools that can closely examine the biological roles of DNA and RNA in the body, provided more detailed insights into the gut/heart relationship and those studies were of particular interest.

"We are currently developing a forward-looking study to evaluate the microbiome in patients with heart failure. We are particularly interested in the symptomatic experience of patients with end-stage heart failure, as well as disease-related weight loss and wasting during this stage of cardiovascular disease," says Anderson.

New blood biomarker to determine status of fatty liver disease

A MedUni Vienna study team has identified the role of a specific subtype of macrophages (white blood cells) in progressive non-alcoholic fatty liver disease as reported by their news release. As part of the immune system, these cells have a protective function against fibrosis and liver cirrhosis. At the same time, they are useful as biomarkers of liver disease progression as they can be measured by a blood test. The results were recently published in the *Journal of Hepatology*.

The pathogenesis of non-alcoholic fatty liver disease, especially advanced steatohepatitis is associated with profound changes in immune cells in the liver. Recently, the increased accumulation of a subtype of macrophages that express high levels of the receptor TREM2 has been described in fatty liver disease.The MedUni Vienna research team led by Christoph Binder and Tim Hendrikx from the Department of Laboratory Medicine were able to show in an animal model that



these specific macrophages have a protective function in fibrosis - a precursor to liver cirrhosis. These cells are found in greater numbers in the affected areas of the liver upon non-alcoholic fatty liver disease-associated liver inflammation, where they accumulate particularly in areas of cellular damage and fibrosis.

The study team also demonstrated in bone marrow transplantation models that haematopoietic TREM2 deficiency prevents efficient fat storage and breakdown of excess connective tissue (extracellular matrix), leading to increased steatohepatitis, cell death and fibrosis. Hence, TREM2-positive macrophages fulfil an important protective function in non-alcoholic fatty liver disease, where they prevent fat accumulation, inflammatory processes and progression of the disease to liver fibrosis.

"It may be possible to develop new therapeutic approaches to treat fatty liver hepatitis by enhancing this protective function of TREM2-positive macrophages," said Florentina Porsch, co-first author of the study.

"The soluble form of TREM2 is an excellent biomarker for identifying and staging advanced liver disease, which can progress from fatty liver disease to incurable cirrhosis if left untreated," explains first author Tim Hendrikx from MedUni Vienna's Department of Laboratory Medicine.

Prediction of radiotherapy treatment response in case of brain metastases

A collaborated research team led by Prof. LI Hai and WANG Hongzhi from Hefei Institutes of Physical Science of Chinese Academy of Sciences (CAS) proposed an interpretable radiomic model for predicting radiotherapy treatment response in patients with brain metastases.The results were published in *European Radiology*.

Radiomics refers to extracting high-throughput radiomic features from medical images to assist clinical decision-making. These radiomic features can reflect the biological information of tumors, which cannot be obtained directly through conventional image interpretation. Therefore, machine learning-based methods can rely on in-depth data mining to obtain additional knowledge about tumor heterogeneity. Currently, there is no accurate prediction model of radiotherapy treatment response for patients with brain metastases in clinical practice.

In this research, the team proposed an interpretable radiomic model for predicting radiotherapy treatment response in patients with brain metastases by combining radiomics and SHAP methods to solve this clinical problem.WANG Yixin, the first author of the paper, ex-

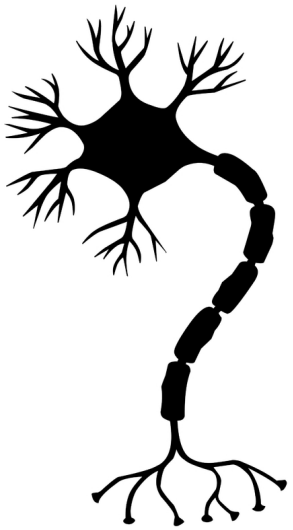
plained how they finished the whole process. At first, the research team extracted the radiomic features from the magnetic resonance imaging (MRI) images of patients with brain metastases before radiotherapy. Then they used the machine learning method to build the radiomic model. In the end, they explained the model using the game theory-based SHAP, which is helpful for the formulation of precise radiotherapy for patients with brain metastases.

This work was supported by the Key Research and Development Program of Anhui Province, the Collaborative Innovation Cultivation Fund of Hefei Big Science Center of CAS, and the Key Clinical Cultivation Specialty of Hefei Cancer Hospital of CAS.

Key factor associated with tumorigenicity of glioma stem cells found

According to research published in *Neuro-Oncology* recently, a team led by Prof. FANG Zhiyou and Prof. CHEN Xueran from Hefei Institutes of Physical Science (HFIPS), Chinese Academy of Sciences (CAS) found, for the first time, that Oct4A is the key factor in maintaining the tumorigenic activity of glioblastoma stem cells (GSCs). Palmitoylation mediated by ZDHHC17 was indispensable for keeping Oct4A from lysosomal degradation to maintain its protein stability and was beneficial to the formation of complexes between Sox4 and Oct4A.

Glioblastoma (GBM) is the most common primary intracranial tumor in adults with the highest degree of malignancy. Glioblastoma stem cells (GSCs) may be an important reason for inducing the occurrence, resistance to radiotherapy and chemotherapy, and recurrence of GBM.Oct4, also known as Pou5f1, is a member of the POU transcription factor family. This gene has multiple different transcription start sites, which can form different mRNA subtypes and be translated into different protein subtypes, participating in the regulation of physiological development. Although it has been detected in advanced



gliomas, the biological function of Oct4, and transcriptional machinery maintained by the stemness of Oct4 protein-mediated GSCs, has not been fully determined.

In this research, scientists investigate the role of the transcription factor Oct4/POU5F1 in glioma, and discovered the novel role of palmitoylation in the function of the Oct4 splicing variant Oct4A in GBM.As a result, three Oct4 variants are expressed in different types of brain tumors, and that Oct4A is particularly important for maintaining tumorigenicity in GSCs. DNA hypommethylation up-regulated the expression of OCT4 gene, which may be one of the main reasons for the up-regulation of stem cell-related gene expression in re-current gliomas.

Moreover, Oct4A palmitoylation, mediated by ZDHHC17, was found to be critical for preserving Oct4A from lysosome degradation, thereby maintaining protein levels in glioma cells in vitro. They also report that palmitoylated Oct4A interacted with Sox4. Competitive Oct4A palmitoylation inhibitors were tested as potential therapeutic compounds, and negatively affected the self-renewal ability and tumorigenicity of GSCs.

"These findings indicate that Oct4A plays a role in the tumorigenic activity of glioblastoma," explained CHEN Xueran, who conducted the research, "while Oct4A palmitoylation may be a candidate therapeutic target".

This research was supported by the National Natural Science Foundation of China, the Youth Innovation Promotion Association of the Chinese Academy of Sciences, the Innovative Program of Development Foundation of Hefei Centre for Physical Science and Technology and Hefei Institutes of Physical Science Director's Fund.

In the aftermath of the sudden death of singer 'KK'

Increasing Heart Attacks in the Young due to Stressful Lives: Experts

Change lives, take preventive measures and go for annual check-ups

The tragic death of renowned singer Krishnakumar Kunnath, known to his fans as KK, on May 31st due to myocardial infarction while performing live at Kolkata's Nazrul Mancha has sent shockwaves down through out the country, raising concerns about the rising number of deaths due to heart diseases, particularly among the young.

According to sources, 53-year-old KK had no underlying health conditions or history of cardiovascular diseases. He reportedly led a fit lifestyle, maintained a healthy diet and never indulged in smoking or alcohol consumption.

KK performing live at an event

KK had complained of feeling uneasy several times that evening, and according to sources, he even went backstage to rest. Doctors believe that those were subtle warning signs of impending peril that should not have been disregarded. If KK had cancelled his concert and sought medical attention right away, the unfortunate incident could have been prevented.

Warning signs ignored

In the final post-mortem and chemical analysis of the singer, the cause of death was cited as "myocardial infarction (MI)." "Cholesterol accumulation narrowed the posterior intramuscular artery to a great extent which affected the pumping of blood by the heart." There were blockages in the coronary artery as well, the report stated.

According to Prof. (Dr.) Anoop Misra, Executive Chairman, Fortis C-DOC Hospital for Diabetes and Allied Sciences, performing in a closed space where thousands of fans are cheering, releases a surge of adrenaline, which can adversely affect the heart if arteries are already compromised. Any such event at the venue could have been tackled if a rapid response team were in place with emergency equipment so that an ECG could have been done immediately and emergency medications administered.

A few months ago, cardiac arrest had also claimed the lives of TV actor Sidharth Shukla and famed director and stuntman, Raj Kaushal.

Evolving work cultures changing lifestyles

Sedentary lifestyles and changing work cultures have caused young individuals to lead stressful lives. Moreover, working from home during the unprecedented times owing to the Covid-19 pandemic, has led to several young people working longer shifts and late-nights, disrupting sleep-cycles. Lack of sleep often induces hormonal imbalances in the body which could contribute to heart diseases. Lack of sleep is also a risk factor for several cardiac diseases.

According to Dr. Sunil Dwivedi, Consultant - Cardiologist, Manipal Hospital Millers Road, "Heart attack is common in South Asians especially among Indians, because of conventional risk factors, like hypertension, diabetes, smoking, obesity and family history, occurring at an early age. These risk factors are more prevalent due to metabolic syndromes in a large population owing to excess calorie intake and less physical activity. Combine this with a lack of awareness about regular health checks and physical activity, people develop silent heart trouble in their middle age."

Dr. Dwivedi continues, "individuals then either abruptly start undertaking significant physical activity or engage in sports to lose weight and maintain fitness, subjecting them to stressful sessions or programmes. During such periods, stress hormones can cause sudden rupture of cholesterol plaques in the heart and

combined with the increased blood clotting tendency, a sudden blood clot in these vessels could lead to a heart attack. Rhythm disturbance during a heart attack is the cause of sudden death."

Diabetes-a huge cardiovascular risk factor

Young heart attack victims are more likely to be smokers, obese, and have high blood pressure or diabetes compared to their peers, according to research published in 2021 in the European Heart Journal. In fact, another Danish study found that children and young people with diabetes are eight times more likely to die from any type of heart disease than their peers without diabetes. The increased risk may be due to diabetes-related blood vessel abnormalities.

Dr. Anoop Misra says that it is important to screen individuals for diabetes from an early age. "We have increasingly seen young patients with multiple cardiovascular risk factors. Diabetes is one of the most important ones," he adds. "Keeping this trend in mind, we have previously stated that screening for diabetes should start at 25 years age in India. Once diagnosis of prediabetes or diabetes is made, treatment should be aggressive to aim at reversal of diabetes."

Cardiac arrest due to MIs

Meanwhile, Dr Sunil Thanvi, Senior Consultant and Head of the Department of Cardiology at Zydus Hospital, Ahmedabad informs that cardiac arrest occurs at a rate 4 to 6 times higher in patients who have had a myocardial infarction than that in the general population. "The cause of death after myocardial infarction are multifactorial and depend on the duration of time that has elapsed since the initial myocardial infarction. During the acute phase, sudden death is typically the result of ischemia that provokes lethal ventricular arrhythmias."

"Mechanical complications resulting in profound hemodynamic derangements such as ventricular or papillary muscle rupture, pericardial tamponade, septal defects, ischemic valvular dysfunction and cardiogenic shock as a result of extensive myocardial necrosis may also result in sudden death," he adds.

In admitted patients, the risk of sudden cardiac death after MI is the highest during the first month. Among 30-day survivors, the risk of sudden cardiac death declines markedly to 1.2% per year, lower than that expected in the general population.

Timing- crucial to manage the condition

Speaking about how the incidence of myocardial infarction is extremely common in younger people less than 50 years of age, Dr Sunil Kumar, Consultant-Interventional Cardiology, Manipal Hospital Hebbal has underlined several common signs and symptoms which could help diagnose and manage the condition in time. "Most commonly, sudden onset of congestion in the chest or chest pain or breathing difficulty and sometimes giddiness and sudden loss of consciousness occurs. Usually, the symptoms are associated with sweating and inability to breathe normally. The patient would not have experienced such symptoms before. So, whenever a patient develops one of these symptoms, they should immediately take rest and not exert themselves as any kind of physical activity during the time will put excessive stress on the heart. They should immediately call for medical help," advises Dr Kumar.

Dr Kumar further added, "For people with a documented heart disease, we give some medicines to keep under their tongue so as to reduce their discomfort. They can sit or lie down with the tablet under the tongue. Patients who are developing the symptoms for the first time should immediately take rest and go to a place where they can get fresh air rather than in a closed room and call for help."

Talking about how general physician or family doctors may help in such situations, Dr Kumar added, "Make sure that they immediately lie down and take rest. They should have access to adequate air and if one can, vital parameters like blood pressure and oxygen should be monitored. Aspirin can be administered immediately and if the pain is severe then one can give nitrate tablets to keep under the tongue."

"The amount of physical activity should be minimum, so once an ambulance or any help comes one must not walk around, and must sit in a wheelchair or a trolley, and must immediately undergo an ECG once at the hospital, which will determine whether the patient is having a major heart attack or not. A cardiologist would be able to evaluate and generally they will take him for an immediate angiogram to look for any block".

However, sudden cardiac arrest occurs without a warning, bringing all the functions of the heart to a standstill. If not intervened within the first six minutes, it could lead to death of the person. In order to prevent this, it is important to perform Cardiopulmonary Resuscitation (CPR) within the first six minutes. This raises the chances of survival significantly since it rapidly resumes cardiac functions and gives blood flow to the brain.

– Lavanya Kandothankandy