Health Matters

Damaging impact of heat waves on vital organs

Researchers from the University of California, Irvine have found evidence of the molecular causes of the damaging impact heat stress causes on the gut, liver and brain in the elderly. These findings point to the potential of developing precise prognostic and therapeutic interventions.

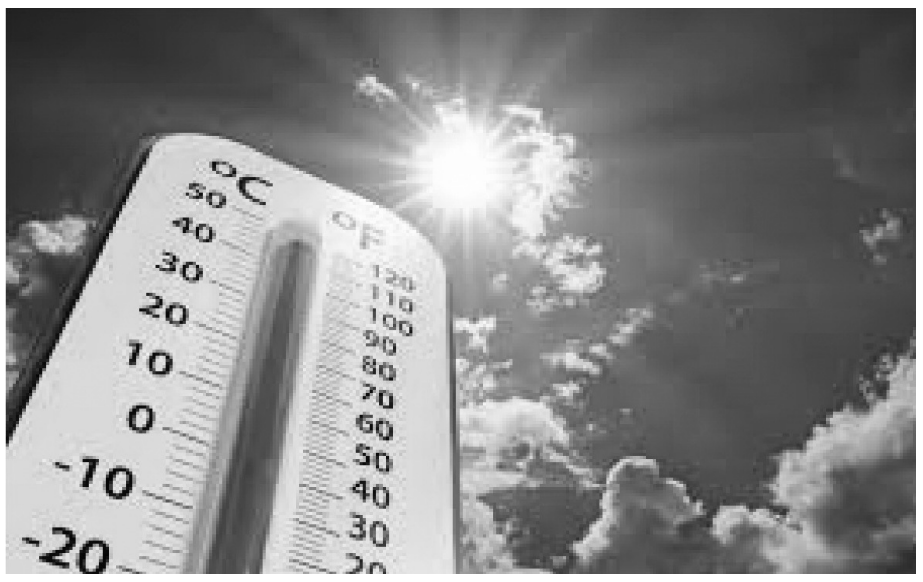
These organs have a complex and multidirectional communication system that touches everything from our gastrointestinal tract to the nervous system. Whether it is our brain affecting hunger or the liver influencing mental health, understanding the gut-liver-brain communication or "axis" is crucial to protecting human health.

Their study, which was conducted on mouse models, is one of the first to fill the knowledge gap on the effects of heat stress on a molecular level of this crucial biological conversation.

"Inflammation in the brain and spine contributes to cognitive decline, compromises the ability to form new neurons and exacerbates age-related diseases," said corresponding author, Saurabh Chatterjee, a professor of environmental & occupational health at the UC Irvine Program in Public Health. "By investigating the effects of heat stress on the gut-liver-brain crosstalk, we can better protect our increasingly vulnerable aging population."

Using RNA analysis and bioinformatics to analyze elderly, heat-stressed mice, Chatterjee and his team found evidence of heat stress-affected genes in the brain and liver. A significant increase in the production of ORM2, a liver-produced protein, was observed in the heat-stressed mice. The control group of unstressed mice did not show a change, providing proof of organ dysfunction in the heat-stressed mice.

Researchers believe that increased secretion of ORM2 is a coping



mechanism that may be due to gut inflammation and imbalance. In addition, ORM2 may impact the brain through a leaky blood-brain barrier, emphasizing intricate multi-organ crosstalk.

Additionally, the study shows the potential to use ORM2 for targeted biomarker interventions to prevent liver disease in heat exposure. This observation advances molecular insights into the pathophysiology of adverse heat events and will serve as a foundation for future research.

"Our findings have the potential to be used for the development of prognostic and therapeutic markers for precise interventions," said Chatterjee. "In a dynamically changing global landscape, the imminent threat of climate change is evident in rising temperatures, raising concerns about intermittent heat waves. Our heating planet is undoubtedly leading to acute and chronic heat stress that harms the health of our aging population."

Additional authors from UCI Public Health include members of the Environmental Health and Disease Laboratory: doctoral students Subhajit Roy (the first author), Punnag Saha, Dipro Bose, Ayushi Trivedi and Madhura More; and Christina Lin, Jie Wu and Melanie Oakes with the UCI genomics high-throughput facility.

Yogurt reduces Type 2 diabetes risks

Sharp-eyed grocery shoppers may notice new labels in the dairy aisle touting yogurt as way to reduce the risk of Type 2 diabetes.

That's because the U.S. Food and Drug Administration recently said it's OK for producers of yogurt to make that claim — even though the agency acknowledged that it's based on limited evidence.

Danone North America, the U.S. branch of the French firm that makes several popular yogurt brands, asked the FDA in 2018 for clearance to make what is known as a "qualified health claim." FDA gave Danone the nod in March.

The way FDA sees it, there's some support — but not significant scientific agreement — that eating at least 2 cups of yogurt per week may reduce the risk of developing the disease that affects about 36 million Americans.

Those are claims that lack full scientific support but are permitted as long as the product labels include disclaimers to keep from misleading the public.

They have been allowed for dietary supplements since 2000 and for foods since 2002, ever since the FDA faced lawsuits challenging the standard of requiring scientific agreement for product claims. Back then, lawyers successfully argued that such standards violated free speech rights guaranteed in the U.S. Constitution.

Rather than fight proposed label changes in court, the FDA created a new category, separate from authorized health claims, in which products must prove significant scientific agreement among qualified experts that they reduce the risk of a disease or a health-related condition.

Examples of qualified health claims include reports that consuming some types of cocoa may reduce heart disease and that cranberry juice might cut the risk of recurrent urinary tract infections in women.

Danone submitted information from studies that observed participants over time and found a link between eating yogurt and lower markers of diabetes. The FDA agreed that there is "some credible evidence" of benefit of eating yogurt as a whole food, but not because of any particular nutrient in it.

In other words, there is no direct evidence that yogurt can prevent diabetes — only weak evidence that eating yogurt may be associated with reducing certain biomarkers that are related to increase risk of the disease.

Critics questioned approval of the claim, saying it's not based on gold-standard randomized controlled trials that could have proven whether yogurt actually reduces Type 2 diabetes risk.

No single food can reduce the risk of a disease tied to overall diet, the advocacy group Center for Science in the Public Interest said. In fact, the label change might raise the risk of diabetes by encouraging consumption of yogurt types that include added sugars and mix-ins such as cookies and pretzels.

Marion Nestle, a food policy expert, said qualified health claims based on limited evidence are "ridiculous on their face."

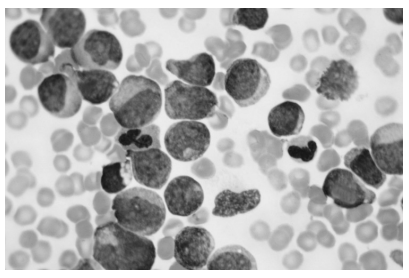
New target for potential leukemia therapy

Boston - A team of Dana-Farber Cancer Institute investigators discovered that a subset of myeloid and lymphoid leukemias depend on a molecular complex called PI3Kgamma for survival. The study provides both mechanistic and preclinical evidence supporting the rapid initiation of clinical trials for patients with acute myeloid leukemia (AML) to test an existing medicine that inhibits the complex, called eganelisib, both alone and in combination with the most used AML chemotherapy, cytarabine.

"Given what we've observed, we can move very quickly to take these medicines, which appear to be safe and well tolerated, to patients with AML. We are planning clinical trials to start hopefullywithin the next year," says principal investigator Andrew Lane, MD, PhD, a clinician-scientist in the Adult Leukemia Program at Dana-Farber.

Treatment for AML has advanced in the last decade, but most patients ultimately relapse after treatment. Therapies that target AML-related mutations have provided options for subsets of patients, though the cancer eventually evolves to evade the therapy.

The Dana-Farber team took a different approach to searching for therapeutic targets. Rather than focusing on mutations, first author Qingyu Luo, MD, PhD, a research



fellow in Lane's lab, used genome wide CRISPR interference to search for genes that AML cells rely on to grow.

He found a promising hit. A subset of leukemia cells relied on a gene called PI3KR5 to survive. That gene produces an important portion of the PI3Kgamma complex.

This hit was attractive in part because the PI3Kgamma complex had been studied before, though not in AML. In addition, a medicine already existed to inhibit it. This drug, eganelisib, has been tested in trials for certain solid tumors to enhance cancer immunotherapy.

What Luo and Lane had found, however, was a completely different mechanism of action in which the drug might work directly on leukemia cells to stop their growth.

To validate this hypothesis, the team treated animal models harboring patient-derived leukemia xenografts with eganelisib. They found that the leukemia xenografts predicted to be highly dependent on PI3Kgamma shrank, and the animal models survived longer when treated with eganelisib.

Looking at The Cancer Genome Atlas Data (TCGA), the team found that patients with AML predicted to be sensitive to eganelisib don't do as well in terms of survival on existing therapies compared to those with negative biomarkers. This finding suggests that this patient group, which can be identified by high levels of PI3KR5 expression, has a need for new medicines and could potentially benefit from treatment with eganelisib.

"This is a drug that is ready to be tested in patients with AML," says Lane. "It's already been used in clinical trials for many patients with solid tumors."

Luo, who initiated this research to improve existing therapies for AML, also treated animal models of leukemia with cytarabine alone and with eganelisib plus cytarabine. The team found that those treated with a combination of eganelisib and cytarabine survived longer than those treated with cytarabine alone, regardless of the leukemia's sensitivity to PI3Kgamma inhibition alone.

"We want synergy, where two drugs mesh with each otherx. Through inhibition of PI3Kgamma, eganelisib has this downstream effect of suppressing an energy pathway important in AML relapse," says Luo.

Enough sleep can help prevent osteoporosis?

As part of the University of Colorado Department of Medicine's annual Research Day, held recently, faculty member Christine Swanson, MD, MCR, described her National Institutes of Health-funded clinical research on whether adequate sleep can help prevent osteoporosis.

"Osteoporosis can occur for many reasons such as hormonal changes, aging, and lifestyle factors. But some patients I see don't have an explanation for their osteoporosis," said Swanson, an associate professor in the Division of Endocrinology, Metabolism, and Diabetes.

"Therefore, it's important to look for novel risk factors and consider what else changes across the lifespan like bone does - sleep is one of those," she added.

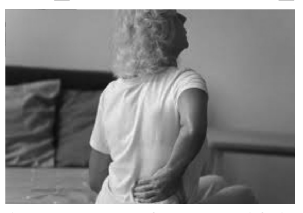
In people's early- to mid-20s, they reach what is called peak bone mineral density, which is higher for men than it is for women, Swanson said. This peak is one of the main determinants of fracture risk later in life.

After reaching this peak, a person's bone density remains roughly stable for a couple of decades. Then, when women enter the menopausal transition, they experience accelerated bone loss. Men also experience bone density decline as they age.

Sleep patterns also evolve over time. As people get older, their total sleep time decreases, and their sleep composition changes. For instance, sleep latency, which is the time it takes to fall asleep, increases with age. On the other hand, slow wave sleep, which is deep restorative sleep, decreases as we age.

"And it's not just sleep duration and composition that change. Circadian phase preference also changes across the lifespan in both men and women," Swanson said, referring to people's preference for when they go to sleep and when they wake up.

These markers of bone resorption and formation follow a daily rhythm. The amplitude of this rhythm is larger for markers of



bone resorption - which refers to the process of breaking down bones - than it is for markers of bone formation, she said.

"This rhythmicity is likely important for normal bone metabolism and suggests that sleep and circadian disturbance could directly affect bone health," she said.

To further understand this relationship, Swanson and colleagues researched how markers of bone turnover responded to cumulative sleep restriction and circadian disruption.

For this study, participants lived in a completely controlled inpatient environment. The participants did not know what time it was, and they were put on a 28-hour schedule instead of a 24-hour day.

"This circadian disruption is designed to simulate the stresses endured during rotating night shift work and is roughly equivalent to flying four time zones west every day for three weeks," she said. "The protocol also caused participants to get less sleep."

The research team measured bone turnover markers at the beginning and end of this intervention and found significant detrimental changes in bone turnover in both men and women in response to the sleep and circadian disruption. The detrimental changes included declines in markers of bone formation that were significantly greater in younger individuals in both sexes compared to the older individuals.

In addition, young women showed significant increases in the bone resorption marker.

If a person is forming less bone while still resorbing the same amount -- or even more -- then, over time, that could lead to bone loss, osteoporosis, and increased fracture risk, Swanson said.

"And sex and age may play an important role, with younger women potentially being the most susceptible to the detrimental impact of poor sleep on bone health," she said.

Research in this area is ongoing, she added.

Risks of neuropathy unveiled in study

Neuropathy, the nerve damage that causes pain and numbness in the feet and hands and can eventually lead to falls, infection and even amputation, is very common and underdiagnosed, according to a study published recently.

"More than one-third of people with neuropathy experience sharp, prickling or shock-like pain, which increases their rates of depression and decreases quality of life," said study author Melissa A. Elafros, MD, PhD, of the University of Michigan in Ann Arbor and a member of the American Academy of Neurology. "People with neuropathy also have an increased risk of earlier death, even when you take into account other conditions they have, so identifying and treating people with or at risk for neuropathy is essential."

The study involved 169 people from an outpatient internal medicine clinic serving mainly Medicaid patients in Flint, Michigan. The participants had an average age of 58 years and 69% were Black people. One-half of the people had diabetes, which can cause neuropathy. A total of 67% had metabolic syndrome, which is defined as having excess belly fat plus two or more of the following risk factors: high blood pressure, higher than normal triglycerides (a type of fat found in the blood), high blood sugar and low high-density lipoprotein (HDL) cholesterol, or "good" cholesterol. These risk factors are also associated with neuropathy.

All participants were tested for distal symmetric polyneuropathy. Information about other health conditions was also collected.

A total of 73% of the people had neuropathy. Of those, 75% had not been previously diagnosed with the condition. Nearly 60% of those with neuropathy were experiencing pain.

Of those with neuropathy, 74% had metabolic syndrome, compared to 54% of those who did not have neuropathy.

After adjusting for other factors that could affect the risk of neuropathy, researchers found that people with metabolic syndrome were more than four times more likely to have neuropathy than people who did not have the syndrome.

Researchers were also looking for any relationship between race and income and neuropathy, as few studies have been done on those topics. There was no relationship between low income and neuropathy. For race, Black people had a decreased risk of neuropathy. Black people made up 60% of those with neuropathy and 91% of those without neuropathy.

"The amount of people with neuropathy in this study, particularly undiagnosed neuropathy, was extraordinarily high with almost three fourths of the study population," Elafros said. "This highlights the urgent need for interventions that improve diagnosis and management of this condition, as well as the need for managing risk factors that can lead to this condition." A limitation of the study is that it is a snapshot in time; it did not follow people to see who developed neuropathy over time. It also did not look at reasons why people were not able to manage risk factors that can lead to neuropathy.

SALE NOTICE

M/s. DEIVAANAI SINTER METALS PRIVATE LIMITED

(In Liquidation)

Reg. Off : NO 4/1 82A SRINAGAR RAMAN NAGAR, METTUR DAM, SALEM-TN 636403

Liquidator: CHANDRAMOULI RAMASUBRAMANIAM

(C RAMASUBRAMANIAM, INSOLVENCY PROFESSIONAL)

Liquidator Address: 'RAJI' 3B1, 3rd Floor, Gaiety Palace, No. 1L, Blackers Road, Mount Road, Chennai - 600002 **Email:** srinidhicra@gmail.com

Telephone No: +91 9884068292 |+91 9962568292| 044-28528292

Registration No: IBBI/IPA-002/IP-N00052/2016-17/10096

E- Auction

Sale of Assets under Insolvency and Bankruptcy Code, 2016

Date and Time of Auction: Saturday, 1st June , 2024 at 3:00 P.M to 4 P.M

(With unlimited extension of 5 minutes each)

Sale of assets and properties owned by M/s. DEIVAANAI SINTER METALS PRIVATE LIMITED (In Liquidation) forming part of Liquidation Estate by the Liquidator, appointed by the Hon'ble National Company Law Tribunal, Chennai Bench vide order MA/23/2018 IN CP/595/IB/CB/2017 dated 03rd May 2018. The sale will be done by the undersigned through the e-auction platform WWW.BANKAUCTIONS.IN

Asset	Reserve Price	Earnest Money Amount
LAND with Industrial sheds LAND EXTENT 2.15 ACRES Asset No.1: Survey Nos.36/4B1, Salem Main Road, Periyasathappadi Village, Mettur Taluk, Salem District – 636451. Asset No.2: Plant & Machineries ALL LYING At Factory - Survey Nos.36/4B1, Salem Main Road, Periyasathappadi Village, Mettur Taluk, Salem District – 636451.	Rs. 7,57,17,500/-	Rs. 75,71,750/-

Terms and Condition of the E-Auction are as under:

1.E-Auction will be conducted on **"AS IS WHERE IS", "AS IS WHAT IS" AND "WHATEVER THERE IS BASIS"** as such sale is without any kind of warranties and indemnities through approved service provider M/s. 4CLOSURE.

2.The auction comprises of single batch, wherein the entire lot of assets are being auctioned in Single Batch. The Liquidator reserves the right in announcing the successful bidder based on the highest bid received

3.The EMD shall be payable through DD/NEFT/RTGS in the account of Deivaanai Sinter Metals Private Limited in Liquidation, A/c. No. 3713010521, Bank and Branch: Central Bank of India - Mettur Branch – Salem District and IFSC Code: CBIN0282563.

4.The Bids can be submitted through email or can be submitted at the Liquidator's office before 6.00 p.m. on Thursday 30th May 2024. The bid form can be downloaded from the website of WWW.BANKAUCTIONS.IN

5.Last date and time of submission of EMD & Tender documents is 6.00 p.m on Thursday, 30th May , 2024

6.The date and time of e-Auction on Saturday , 1st June, 2024 between 03.00 P.M and 04.00 P.M.

7.If any offer is received within the last 5 minutes of closure time, the biding time will be extended automatically by another 5 minutes and if no higher bid is received within in the extended 5 minutes, the auction will automatically get closed at the extended 5 minutes.

8.The intended bidder who have deposited EMD and require assistance in creating login id and password may contact the liquidator office on phone +91 9884068292, +91 9962568292, 044-28528292 or through email at srinidhicra@gmail.com and for technical support, you can contact Mr. Prakash @ 08142000064.

9.The EMD amount of unsuccessful Bidders will be refunded within one week.

10.The bidder who submits highest offer (more than Reserve Price) on closure of online auction shall be declared successful bidder subject to approval by the Liquidator. The liquidator reserves his rights to reject any or all of the offers or accept offer for one or more properties received without assigning any reasons whatsoever at any stage.

11.If none of the intended bidder participating in the E-Auction has not increasing the bid amount, the EMD amount of the bidders will be forfeited.

12.Upon confirmation of sale, the purchaser shall deposits 25% of sale price (including EMD) immediately and the balance sale consideration within 90 days of the date of such demand, provided that payment made after 30 days shall attract interest @ the rate of 12% as per Sub-clause 12 of Clause 1 of Schedule I of IBBI (Liquidation Process) Regulations 2016 as amended from time to time.

13.The sale shall be cancelled if the payment is not received within 90 days and the amount paid will be forfeited. For more particulars about e-auction, the bidders are requested to go through the tender form thoroughly.

14.The Liquidator will not be responsible for any charge, lien under sale. The Liquidator has absolute right to accept or reject the bid or adjourn, postpone, extend the auction without assigning any reasons whatsoever. No objections will accrue to the Liquidator in such an event.

15.In addition to the final auction value, the successful bidders have to pay 18% of GST for Plant & machinery and 9 % of Stamp duty for registration of the Land & Buildings with Sub Registrar office.

16.Upon payment of the full amount of sale consideration and GST @ 18% / Taxes (if any), the Liquidator shall deliver the possession of the property sold (Plant & Machinery) to the purchaser. On receipt of possession from the Liquidator, the purchaser has to remove Property from the Factory Premises.

17.The properties mentioned above can be inspected by the prospective bidders at the site with prior appointment contacting Mr. C. Ramasubramaniam, Liquidator +91 9884068292, +91 9962568292, 044-28528292

18.Further inquiries, if any and/or terms and conditions for sale can be obtained from the Liquidator office at phone numbers mentioned above.

19.The advertisement will be valid for 90 days from the date of advertisement. The properties mentioned above can be inspected by the prospective bidders at the site with prior appointment contacting Mr. C. Ramasubramaniam (+91 9884068292).

Date : 14.05.2024

Place: Chennai

Sd/-

CHANDRAMOULI RAMASUBRAMANIAM

(C.RAMASUBRAMANIAM)

LIQUIDATOR- DEIVAANAI SINTER METALS PRIVATE LIMITED

IBBI Reg No. IBBI/IPA-002/IP-N00052/2016-17/10096

Email: srinidhicra@gmail.com

Contact No: 9884068292, +91 9962568292, 044-28528292