CHEMWATCH

Bulletin Board

Contents

MAY. 10, 2024

(click on page numbers for links)

CONTACT US

subscribers@chemwatch.net
tel +61 3 9572 4700
fax +61 3 9572 4777

1227 Glen Huntly Rd
Glen Huntly
Victoria 3163 Australia

*** While Chemwatch has taken all efforts to ensure the accuracy of information in this publication, it is not intended to be comprehensive or to render advice. Websites rendered are subject to change.**

CURIOSITIES

TECHNICAL NOTES

ASIA PACIFIC

The final regulatory decision for the reconsideration of malathion

2024-05-02

The Australian Pesticides and Veterinary Medicines Authority (APVMA) has published the final regulatory decision for the reconsideration of malathion (also known as maldison), an insecticide used for the control of pests in various broadacre and horticultural crops, vegetables and ornamental plants, and for veterinary and domestic uses.

The APVMA has decided to vary and affirm malathion active constituent approvals, chemical product registrations, and associated label approvals. These variations include:

- changing the name of the active constituent from 'maldison' to 'malathion' to harmonise with the name specified in ISO 1750-1981
- removing uses to control mosquito larvae and prohibiting direct application to water due to the risks to aquatic species
- updating the instructions for use, including protection statements, restraints, spray drift buffer zones, re-entry and withholding periods, safety directions, and storage conditions
- including a provision for all products containing malathion as the active constituent to have a shelf life and for the associated expiry date to be included on labels

The APVMA's decision includes consideration of all current active constituents, chemical products and associated labels. A summary of the underlying risk assessments has also been published in the final malathion Review Technical Report. This technical report also includes the APVMA's consideration of submissions received during the public consultation on the malathion proposed regulatory decision.

The APVMA has determined that a 2-year phase out period will apply to malathion products bearing the previously approved labels. After the 2-year phase out period ends, these products must be supplied with the new label that contains updated instructions.

Read More

APVMA, 02-05-24

https://www.apvma.gov.au/sites/default/files/2024-05/APVMA%20Special%20Gazette%2C%202%20May%202024.pdf

U.S. EPA Designates PFOA and PFOS as Hazardous Substances under CERCLA

2024-04-23

Obligated entities shall report releases of PFOA or PFOS exceeding one pound to NRC in 24 hours.

On April 17, 2024, the US Environmental Protection Agency (EPA) published a rule to designate perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), including their salts and structural isomers, as hazardous substances under section 102(a) of the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA). The list of hazardous substances specified in Table 302.4 of 40 CFR part 302 is amended to include PFOA, PFOS and their salts and structural isomers. This rule shall take effect 60 days after publication in the Federal Register.

Background

PFAS, including PFOA and PFOS, are a nationwide concern due to their association with significant adverse health effects on humans, their widespread usage, and their persistence and mobility in the environment once released.

This designation is justified based solely on the EPA's determination that the release of PFOA and PFOS into the environment may pose substantial risks to public health, welfare, or the environment. It aligns with CERCLA's primary goals of remediating contaminated sites and ensuring that the responsible parties bear the financial burden of cleanup efforts, adhering to the principle of "Polluter Pays." This designation enables the

CHEMWATCH
Bulletin Board
Regulatory Update
MAY. 10, 2024

EPA to enforce the responsibility of those accountable for significant contamination to cover the costs associated with its remediation.

Read More

Chemlinked, 23-04-24

https://chemical.chemlinked.com/news/chemical-news/us-epa-designates-pfoa-and-pfos-as-hazardous-substances-under-cercla

CP nº 1,235/2024 - RDC proposal - sanitary requirements applicable to silicones used in contact with food

2024-05-01

Proposal for a Resolution of the Collegiate Board of Directors - RDC that provides for the sanitary requirements applicable to silicones used in materials, packaging, coatings and equipment intended to come into contact with food.

This proposal for regulatory intervention is the result of negotiations that took place within the scope of Mercosul and aims to harmonize the sanitary requirements of silicone materials intended to come into contact with food.

This proposition was discussed within the scope of the Food Commission of Working Subgroup No. 3 (CA/SGT No. 3), following the procedures for the preparation, review or revocation of Mercosur Technical Regulations (RTM) established in GMC/MERCOSUR Resolution No. 45, of 2017, and is supported by Draft Resolution (P. RES) No. 6/2022, approved at the LXXXII Ordinary Meeting of Working Subgroup No. 3 (SGT No. 3) of Mercosul.

In accordance with the harmonized procedures in Mercosur, this project must be submitted to internal consultation with the States Parties, in order to confirm its technical and legal convenience and to establish the procedures and deadlines necessary for its incorporation, before its submission to the Common Market Group (GMC).

The Public Consultation is not a vote, referendum or poll! The main objective is to collect critical and well-founded evaluations, from different segments of society, on the proposed standard under discussion.

Contributions recorded in the electronic form will only be considered valid after the participant clicks the SEND button, available at the end of the questionnaire.

Read More

ANVISA, 01-05-24

https://pesquisa.anvisa.gov.br/index.php/672465?lang=pt-BR

EUROPE

France Moves Forward with PFAS Ban Amid Industry Pushback

2024-04-22

France proposes to ban PFAS in cosmetics, wax and textile products, with the exception of cookware.

Despite opposition from the government and industries, French National Assembly nodded through a proposed bill aimed at protecting the population from the risks linked to per- and polyfluoroalkyl substances (PFAS) on April 4, 2024. The bill will proceed to the Senate for deliberation.

The bill came as Europe is on track to develop an initiative which will result in a broad PFAS restriction. However, this initiative is conditioned on a long decision-making process and could succeed, in the most favorable scenario, by 2027-2028. Highlighting the urgent need to address the irreversible accumulation of these substances in the environment, Greens MP Nicolas Thierry, the proponent of the bill, emphasized that France should take proactive measures without delay to combat these persistent pollutants.

Unsurprisingly, the bill faced strong opposition from industries, particularly SEB, the global leader in non-stick frying pans, which sought an exemption for cookware initially included in the text. After negotiations, a unanimous agreement was reached, resulting in the removal of "products that come into contact with foodstuff" from the bill.

Accordingly, from January 1, 2026, the manufacture, import, export and placing on the market, free of charge or for a fee, of the following products containing PFAS shall be prohibited:

- Any cosmetic product containing PFAS;

CHEMWATCH
Bulletin Board
Regulatory Update
MAY. 10, 2024

- Any wax product containing PFAS;
- Any textile product containing PFAS, with the exception of protective clothing for security and civil safety professionals.

This ban shall extend to all textile product containing PFAS from 2030.

Read More

Chemlinked, 22-04-24

https://chemical.chemlinked.com/news/chemical-news/france-moves-forward-with-pfas-ban-amid-industry-pushback

Expiry of the approval of the active substance abamectin in GB

2024-05-01

The approval of abamectin was not supported for GB renewal. The approval of abamectin has now expired as a pesticide active substance in GB.

The statutory approvals register has been updated to reflect this change.

There are several products authorised in GB containing abamectin, which will expire with grace periods for the sale, distribution, storage, disposal and use of existing stocks.

Details of authorised products and their grace periods can be found on the pesticides register.

The expiry of the approval of abamectin has no immediate impact on the GB Maximum Residue Levels (GB MRLs) which will remain in force unless HSE decides to take specific regulatory action; no such action is currently planned, but the GB MRLs will be reviewed and this will be based on a priority of protecting UK consumers.

Read More

HSE UK, 01-05-24

https://www.hse.gov.uk/index.htm

Call for EU to ban sale of pesticides already outlawed in the bloc

2024-05-02

The EU should ban the production and export of pesticides that it has prohibited in the bloc, a coalition of citizen groups has urged. Contrary to what the agrochemical sector argues, they say that an export ban would not endanger employment or have significant economic effects.

The EU has not acted on its 2020 commitment to ban the export of such pesticides, which include Syngenta's paraquat, Bayer's acetochlor and various neonicotinoids. However, some member states have acted independently. A Belgian law will come into force in 2025 but it covers a limited number of substances. France has banned the export of products, rather than active substances, meaning that some banned substances may still be exported. German discussions on an export ban have stalled.

Read More

Chemistry World, 02-05-24

https://www.chemistryworld.com/news/call-for-eu-to-ban-sale-of-pesticides-already-outlawed-in-the-bloc/4019425.article

Denmark will ban clothing with 'forever chemicals'

2024-04-30

Regulations take effect in 2026.

The Danish government is sending a message on PFAS, a class of artificial substances known as "forever chemicals," as they don't break down easily in nature.

Denmark's Ministry of the Environment said it plans to ban all clothes, shoes, and waterproofing agents that contain Per and Polyfluoroalkyl Substances, citing myriad health risks linked to the oil, water, and stain repellents. Developed in the 1930s, PFAS became widely used in the '50s, appearing in everything from cars and carpets to food packaging and beauty products. Studies have linked PFAS to reproductive health problems, child developmental delays, cancers, and high cholesterol, per the EPA.

Denmark intends for its PFAS clothing ban to kick in on July 1, 2026, in order to offer businesses a "transition period," the environmental regulator said in an April 25 announcement. The ban will encompass both imported

CHEMWATCH
Bulletin Board
Regulatory Update
MAY. 10, 2024

and Danish-made clothing, but it won't affect "professional" or "safety clothing." Denmark had already banned PFAS in food packaging as of 2020.

"The proposal for a ban will be subject to consultation," the Ministry said in a statement. "It will be possible for companies to register if there are special challenges that must be taken into account."

Read More

Popular Science, 30-04-24

https://www.popsci.com/health/forever-chemicals-clothing-ban/

INTERNATIONAL

Rapidly rising levels of TFA 'forever chemical' alarm experts

2024-05-02

Rapidly rising levels of TFA, a class of "forever chemical" thought to damage fertility and child development, are being found in drinking water, blood and rain, causing alarm among experts.

TFA, or trifluoroacetic acid, is a type of per- and polyfluoroalkyl substance (PFAS), a group of human-made chemicals used widely in consumer products that do not break down for thousands of years. Many of the substances have been linked to negative effects on human health.

Studies from across the world are reporting sharp rises in TFA. A major source is F-gases, which were brought in to replace ozone-depleting CFCs in refrigeration, air conditioning, aerosol sprays and heat pumps. Pesticides, dyes and pharmaceuticals can also be sources.

"Everywhere you look it's increasing. There's no study where the concentration of TFA hasn't increased," said David Behringer, an environmental consultant who has studied TFA in rain for the German government.

"If you're drinking water, you're drinking a lot of TFA, wherever you are in the world … China had a 17-fold increase of TFA in surface waters in a decade, the US had a sixfold increase in 23 years." TFA in rainwater in Germany has been found to have increased fivefold in two decades.

"I'm worried about this because we've never seen in recent history a chemical that's accumulating in so many media at such a high rate,"

said Hans Peter Arp from the Norwegian Geotechnical Institute and the Norwegian University of Science and Technology. "It's accumulating in our tap water, the food we're eating, plants, trees, the sea, and all in the past few decades."

He added: "We all have been experiencing rising TFA concentrations in our blood since the Montreal protocol [banned CFCs]. Future generations will have increasing concentrations in their blood until some kind of global action is taken. Accumulation [in the environment] is essentially irreversible and I'm afraid the impact on humans and the environment won't be recognised by scientists until it is too late."

Read More

The Guardian, 02-05-24

https://www.theguardian.com/environment/2024/may/01/rapidly-rising-levels-of-tfa-forever-chemical-alarm-experts#:~:text=TFA%2C%20or%20trifluoroacetic%20acid%2C%20is,negative%20effects%20on%20human%-20health

Airlines lobby against EU plan to monitor non-CO2 emissions from flights

2024-04-30

Contrails or condensation trails are created when ice crystals form around tiny particles of carbon emitted by a plane's engines.

Airlines have hit back against EU plans to monitor contrails from aircraft, claiming too little is known about their climate impact to regulate them.

The International Air Transport Association (IATA) says it's too soon to implement regulations as there are still "gaps" in scientific knowledge about their impact.

New EU regulations will see airlines required to measure and report non-CO2 emissions from flights from January 2025. That would include contrails, nitrogen oxides and sulphur.

Contrails or condensation trails are created when ice crystals form around tiny particles of carbon emitted by a plane's engines when they fly through layers of humidity. Depending on the atmospheric conditions, they can hang around for between a few minutes and 18 hours.

Why are contrails a problem?

CHEMWATCH
Bulletin Board
Regulatory Update
MAY. 10, 2024

Research has shown contrails may play a significant role in the climate impact of aviation. The first piece of evidence highlighting the non-CO2 impacts of flights came from the IPCC in 1999.

Since then, contrails have been shown to disrupt the balance between the sun's incoming solar radiation and the heat being emitted from the Earth's surface. This essentially means when these clouds persist they can trap heat in the atmosphere.

Read More

Euronews, 30-04-24

https://www.euronews.com/green/2024/04/30/airlines-lobby-against-eu-plan-to-monitor-non-co2-emissions-from-flights

IUCLID major release (version 8.0.1) including format updates

2024-04-29

A new major version of IUCLID, including format changes, is available for download from the IUCLID website.

The format changes include updates relevant to all IUCLID users such as:

- The extension of the format of the Robust Study Summaries, which are part of the OECD Harmonised Templates (OHTs), to include fields relevant to the OECD QSAR Assessment Framework
- The OHTs have also been updated to follow the evolution of the OECD Test Guidelines
- The completion of the harmonisation of the Use and exposure information templates between EU REACH and the OECD

Format changes that are relevant to specific stakeholders are also included, for example:

- Updates of the Classification and Labelling information following the latest changes in the CLP Regulation
- Further improvements for several dossier types under the EU Biocidal Products Regulation: Summary of Product Characteristics (SPC), Biocidal product authorisation and Active substance application
- Finalisation of a first version of the format supporting the future notifications and applications under the EU Drinking Water Directive
- Improvements for EFSA-related information in the domain of the EU Plant Protection Products legislation

The full documentation of the format (v8) can be found on the website.

All fixes and improvements for this release are listed in the release notes. For example the report templates and the validation rules were adapted to the format changes and improved. In addition, a known migration issue detected with the previous IUCLID release has been solved. Before upgrading to the new version, we recommend to check the list of known issues and the latest fixes in the FAQ section of the website.

CHEMWATCH
Bulletin Board
REACH Update
MAY. 10, 2024

The update of instances of IUCLID in the ECHA Cloud Services will start during the week of the release.

Read More

ECHA, 29-04-24

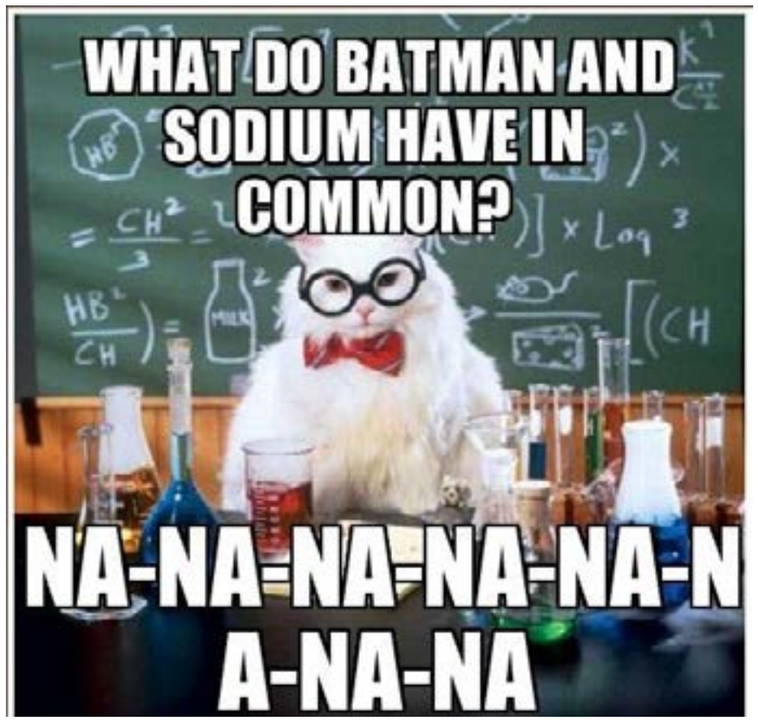
https://iuclid6.echa.europa.eu/view-article/-/journal_content/title/new-iuclid-version-including-format-updates#msdynttrid=TnYVCltZlQY50QsDO62gnPPvZqDvZNTqBQraZHoQwDE

Janet's Corner

MAY. 10, 2024

Batman & Sodium

2024-05-10



Hazard Alert

MAY. 10, 2024

Acetamide

2024-05-10

Acetamide (IUPAC: ethanamide) is an organic compound with the formula CH3CONH2. It is the simplest amide derived from acetic acid. [1] It is a colourless, deliquescent hexagonal crystal. Acetamide is odourless when pure, but frequently has a mousy odour. It is soluble in water, alcohol, chloroform, glycerol, hot benzene, and slightly soluble in ether. Acetamide is combustible and when heated to decomposition, it emits toxic fumes of oxides of nitrogen. [1,2]

USES [2,3]

Acetamide is used in organic synthesis as a reactant, a solvent, and a peroxide stabiliser. It is also used as a general solvent, a hygroscopic agent, wetting agent, penetrating agent, in lacquers, in explosives, in soldering flux, as a solubiliser, and a plasticiser. Acetamide is also used in the manufacture of methylamine and the denaturing of alcohol.

EXPOSURE SOURCES & ROUTES OF EXPOSURE [3]

Exposure Sources

Occupational exposure to acetamide may occur for those workers in the plastics and chemical industries.

Routes of Exposure

Probable routes of human exposure to acetamide are inhalation of vapours or dusts and dermal contact.

HEALTH EFFECTS [4]

Acute Health Effects

- Acetamide causes mild skin irritation in humans from acute exposure.
- Tests involving acute exposure of rats and mice have shown acetamide to have low to moderate acute toxicity from oral exposure.

Carcinogenicity

- No information is available on the carcinogenic effects of acetamide in humans.
- Animal studies have reported liver tumours from oral exposure to acetamide.

- EPA has not classified acetamide for carcinogenicity.
- The International Agency for Research on Cancer (IARC) has classified acetamide as a Group 2B, possible human carcinogen.

Other Effects

- No information is available on the carcinogenic effects of acetamide in humans.
- Animal studies have reported liver tumours from oral exposure to acetamide.

SAFETY

First Aid Measures [5]

- No information is available on the carcinogenic effects of acetamide in humans.
- Animal studies have reported liver tumours from oral exposure to acetamide.
- EPA has not classified acetamide for carcinogenicity.
- The International Agency for Research on Cancer (IARC) has classified acetamide as a Group 2B, possible human carcinogen.

Workplace Controls & Practices [4]

Control measures include:

- Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits.
- If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protective Equipment [5]

- Splash goggles
- Lab coat
- Dust respirator (be sure to use an approved/certified respirator or equivalent)
- Gloves
- Splash goggle
- Full suit
- Dust respirator
- Boots

CHEMWATCH
Bulletin Board
Hazard Alert
MAY. 10, 2024

- A self-contained breathing apparatus should be used to avoid inhalation of the product.
- Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

REGULATION

No occupational exposure limits have been set for acetamide. However, it may pose a health risk. Safe work practices should be followed when handling this substance.

REFERENCES

1. https://en.wikipedia.org/wiki/Acetamide
2. http://scorecard.goodguide.com/chemical-profiles/html/acetamide.html
3. https://www3.epa.gov/ttn/atw/hlthef/acetamid.html
4. http://www.sciencelab.com/msds.php?msdsId=9927059
5. http://nj.gov/health/eoh/rtkweb/documents/fs/2890.pdf

Copper coating turns touchscreens into bacteria killers

2024-05-03

If there's one thing that needs to be antibacterial, it's the public touchscreen displays that everyone paws at with their filthy fingers. Well, help is on the way, in the form of a newly developed copper coating.

While copper is known for its ability to kill bacteria on contact, it's also opaque and electrically conductive … neither of which are good qualities for something that will be covering a touchscreen.

The new "transparent nanostructured copper surface" (TANCS) was developed with these limitations in mind. It was created by a team of scientists from Spain's Catalan Institution for Research and Advanced Studies (ICREA), Institute of Photonic Sciences (ICFO) and the Corning corporation.

The researchers started by depositing a 3.5-nanometer-thick copper film onto a Corning Gorilla Glass substrate. In a process known as rapid thermal annealing, they then heated that film to 390 ºC (734 ºF), held it at that temperature for 10 minutes, then cooled it. Doing so caused the previously uniform film to "dewet" into a myriad of individual evenly-spaced copper nanoparticles.

The resulting altered film retained the copper's antibacterial qualities but became transparent, color-neutral and electrically non-conductive. Layers of silicon dioxide and fluorosilanes (water-and oil-repelling chemicals) were finally added over top of the film for added durability and environmental protection.

In tests performed under dry real-world conditions, the TANCS was found to kill 99.9% of applied Staphylococcus aureus bacteria within two hours. It also remained intact and effective after being subjected to the equivalent of being wiped down with cleansers twice a day for two years.

"While further development is necessary for full-fledged commercial deployment, this is a step in the right direction to enable antimicrobial touchscreens for public or personal displays," says Corning researcher Prantik Mazumder, co-author of a paper on the study.

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

That paper was recently published in the journal Communications Materials.

New Atlas, 03 May 2024

https://newatlas.com

Common Diabetes Drug Reduces the Chance of COVID-19 Reinfection

2024-05-03

A team of University of Minnesota researchers found that metformin, a drug commonly used to treat diabetes, can decrease the amount of COVID-19 virus in the body and lower the chances of the virus coming back strongly after initial treatment. The study was published in Clinical Infectious Diseases.

A higher viral load — the amount of virus in a person's body — usually indicates a greater concentration of the virus, which can be important in understanding the severity of an infection and monitoring the effectiveness of treatments.

"The results of the study are important because COVID-19 continues to cause illness, both during acute infection and for months after infection," said Carolyn Bramante, MD, principal investigator and an assistant professor at the U of M Medical School. She is also an internist and pediatrician with M Health Fairview.

In this phase 3 randomized clinical trial, the researchers tested metformin against a placebo in 1,323 adults infected with COVID-19. The group treated with metformin had a viral load that was about four times lower than the placebo at day 10. The metformin group also had less viral rebound than the placebo group.

The research team concludes that metformin treatment for adults recently infected with COVID-19 is an effective way to reduce the amount of the virus in the nose and to keep the amount of virus from becoming elevated again.

"Among the volunteers in this randomized trial, there was a more than 41% reduction of long COVID among those receiving metformin and a 58% reduction in hospitalization by 28 days. This new study explains why this occurred. Metformin reduced the amount of SARS-CoV-2 virus present, which likely accounts for why this $1 medication reduced hospitalizations and long COVID," said David Boulware, MD, MPH, an infectious disease

physician and professor at the U of M Medical School and M Health Fairview.

None of the outpatient treatments in current guidelines have been tested in adults who had prior infection. Further research is needed to understand how metformin works in those who had the virus before.

A computer simulator developed by U of M Medical School and College of Science and Engineering faculty accurately predicted metformin's effectiveness against COVID-19 — helping steer the direction of the clinical trial. Similarly, the simulation also predicted the failure of medications such as hydroxychloroquine.

"These results are consistent with the model predictions for viral replication that we developed to identify antiviral drugs at the beginning of the pandemic," said David Odde, PhD, co-author and biomedical engineering professor in the College of Science and Engineering. "This is another great example of how engineering tools can be used to predict clinical outcomes, steer research efforts and ultimately add to the body of knowledge around disease treatments."

Technology Networks, 03 May 2024

https://technologynetworks.com

Non-Coding DNA Could Explain Childhood Cancer's Radiotherapy Resistance

2024-05-02

St. Jude Children's Research Hospital scientists have identified specific DNA variants in the non-coding regions of the genome contributing to chemotherapy resistance in acute lymphoblastic leukemia (ALL). The results guided the team to unravel the mechanism behind a previously unknown contributor to therapeutic resistance. The discovery was enabled by combining new technologies to overcome previous limitations in understanding the non-coding genome, which could be adapted to other types of cancer and diseases. The findings were published today in Nature Communications.

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer. Survival rates are over 94% due to modern therapy. However, those with relapsed or recurrent disease, often due to chemotherapy resistance, have a much poorer 30-40% survival rate.

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

The researchers studied resistance variants found in the non-coding genome, which makes up 98% of DNA and does not contain genes. Previous attempts to identify resistance mechanisms to chemotherapy focused on DNA that encoded genes. Looking directly at genes is simpler because non-coding DNA can have complex relationships with gene function, but the St. Jude group showed it is possible.

"We demonstrated that we now have the tools to find relevant non-coding genetic factors that contribute to chemotherapy resistance," said corresponding author Daniel Savic, PhD, St. Jude Department of Pharmacy and Pharmaceutical Sciences. "The end goal is to understand the mechanisms of drug resistance so we can develop novel therapeutics and optimize existing chemotherapies based on the individual's unique genetic makeup."

Sorting through non-coding DNA to find the root of chemotherapy resistance

"The non-coding 98% of the genome contains instructions," said co-first author Jackson Mobley, PhD, St. Jude Department of Pharmacy and Pharmaceutical Sciences. "If we are making a building, genes encode the iron bars, wires and concrete; non-coding DNA are the blueprints. We found the small changes in the blueprints that impact how well you respond to certain therapies."

The group explored novel non-coding resistance variants by combining state-of-the-art technologies to examine patient samples and clinical data on treatment outcomes. In the past, research focused on a single gene or variant. However, combining high-throughput DNA sequencing methods allowed the St. Jude researchers to perform massively parallel variant screens. Those large screens enabled the testing of over 1,600 variants simultaneously to identify which were functional. That huge increase made the results more comprehensive, leading to the discovery of over 500 functional non-coding DNA variants associated with chemotherapy resistance.

"Our work represents the largest functional investigation of inherited non-coding variants associated with pharmacological traits, especially in ALL," said co-first author Kashi Raj Bhattarai, PhD, St. Jude Department of Pharmacy and Pharmaceutical Sciences. "We verified that identified variants also have a similar effect in cell lines and patient samples."

A novel resistance mechanism

By surveying many non-coding variants at once, the researchers could find the most impactful ones across different subtypes of ALL and connect them to a specific gene using innovative 3D genome mapping technologies. By finding the mechanism behind how variants in the non-coding genome affect target gene activity, they can figure out how it affects cancer's response to treatment.

For example, the top variant from the screen led to the discovery of a new resistance mechanism. The resistance was to the chemotherapy drug vincristine. The researchers examined how DNA containing the functional variant physically looped to its target gene and which transcription factors, proteins that guide gene expression, were involved. The scientists found the variant bound near the gene for EIF3A, which is known to be involved in cell proliferation and survival. When they deleted the DNA containing the variant or reverted the mutation to the original sequence, they could alter the cells' sensitivity to the chemotherapeutic agent vincristine.

The study serves as a proof of principle of how to take non-coding DNA variants and mechanistically connect them to a trait, such as chemotherapy resistance. That has been a long-standing issue holding back genomics research on inherited variants, from cancer to neurological issues.

"In any genome-wide association study, nearly all associated variants reside in the non-coding genome," Savic said. "Therefore, connecting that variation to gene function and then to an actual trait, such as chemotherapy resistance or disease predisposition, is challenging. We showed that we have harnessed tools and technologies to systematically examine the non-coding genome and understand what it's doing. We hope that our findings can be utilized to improve clinical outcomes in ALL patients."

Technology Networks, 02 May 2024

https://technologynetworks.com

Geologists, biologists unearth the atomic fingerprints of cancer

2024-05-06

Scientists at the University of Colorado Boulder and Princeton University have, for the first time, employed a tool often used in geology to detect the atomic fingerprints of cancer.

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

In a case of medicine meets Earth science, the researchers discovered that cancer cells may be made from a different assortment of hydrogen atoms than healthy tissue. The findings could give doctors new strategies for studying how cancer grows and spreads—and may even, one day, lead to new ways to spot cancer early on in the body.

The team, led by CU Boulder geochemist Ashley Maloney, published the findings in the Proceedings of the National Academy of Sciences.

"This study adds a whole new layer to medicine, giving us the chance to look at cancer at the atomic level," said Maloney, a research associate in the Department of Geological Sciences.

She explained that in nature, hydrogen comes in two main flavors, or isotopes. Some hydrogen atoms, called deuterium, are a little heavier, while others, usually just known as hydrogen, are a little lighter. On Earth, hydrogen atoms outnumber deuterium atoms by a ratio of about 6,420 to one.

For decades, scientists from a number of fields have turned to the natural distribution of these atoms to reveal clues about the history of our planet. Climate scientists, for example, examine the hydrogen atoms trapped in the ice on Antarctica to infer how hot or cool Earth was hundreds of thousands of years ago.

In the new study, Maloney and her colleagues wondered: Could those same, tiny atoms provide hints about the lives of complex biological organisms?

To find out, the team grew cultures of yeast and mouse liver cells in the lab, then analyzed their hydrogen atoms. The team found that cells that are growing really fast, such as cancer cells, contain a much different ratio of hydrogen versus deuterium atoms. Think of it like cancer leaving a fingerprint on the doorknob of a crime scene.

The research is still in its early stages, and the team isn't sure how this signal might appear, or not, in the bodies of real cancer patients. But the potential could be big, said Sebastian Kopf, a co-author of the study and an assistant professor in geological sciences.

"Your chances of survival are so much higher if you catch cancer early on," Kopf said. "If this isotopic signal is strong enough that you could detect it through something like a blood test, that could give you an important hint that something is off."

In a case of medicine meets Earth science, the researchers discovered that cancer cells may be made from a different assortment of hydrogen atoms than healthy tissue. The findings could give doctors new strategies for studying how cancer grows and spreads—and may even, one day, lead to new ways to spot cancer early on in the body.

The team, led by CU Boulder geochemist Ashley Maloney, published the findings in the Proceedings of the National Academy of Sciences.

“This study adds a whole new layer to medicine, giving us the chance to look at cancer at the atomic level,” said Maloney, a research associate in the Department of Geological Sciences.

She explained that in nature, hydrogen comes in two main flavors, or isotopes. Some hydrogen atoms, called deuterium, are a little heavier, while others, usually just known as hydrogen, are a little lighter. On Earth, hydrogen atoms outnumber deuterium atoms by a ratio of about 6,420 to one.

For decades, scientists from a number of fields have turned to the natural distribution of these atoms to reveal clues about the history of our planet. Climate scientists, for example, examine the hydrogen atoms trapped in the ice on Antarctica to infer how hot or cool Earth was hundreds of thousands of years ago.

In the new study, Maloney and her colleagues wondered: Could those same, tiny atoms provide hints about the lives of complex biological organisms?

To find out, the team grew cultures of yeast and mouse liver cells in the lab, then analyzed their hydrogen atoms. The team found that cells that are growing really fast, such as cancer cells, contain a much different ratio of hydrogen versus deuterium atoms. Think of it like cancer leaving a fingerprint on the doorknob of a crime scene.

The research is still in its early stages, and the team isn’t sure how this signal might appear, or not, in the bodies of real cancer patients. But the potential could be big, said Sebastian Kopf, a co-author of the study and an assistant professor in geological sciences.

“Your chances of survival are so much higher if you catch cancer early on,” Kopf said. “If this isotopic signal is strong enough that you could detect it through something like a blood test, that could give you an important hint that something is off.”

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

The metabolism of cancer

The study centers around a concept that has intrigued cancer researchers for years: metabolism.

Under normal conditions, the cells of organisms like yeast and animals generate energy through a process called respiration, in which they take in oxygen and release carbon dioxide. But that’s not the only way to get a sugar high. Colonies of baker’s yeast (Saccharomyces cerevisiae), for example, can produce energy via fermentation, in which organisms break down sugars without help from oxygen and produce alcohol. It’s the same process that gives you beer.

“In humans, if an athlete performs beyond their aerobic limit, their muscles will also start fermenting, which doesn’t use oxygen,” Kopf said. “That gives you a quick energy boost.”

As it turns out, many cancer cells also fuel their growth through a similar get-rich-quick strategy.

Scientists have long searched for more ways to track these metabolic changes in cancer cells. Maloney, who led the new study as a Harry Hess Postdoctoral Fellow at Princeton, and her advisor Xinning Zhang developed an idea: Track hydrogen.

Inside the cell

Today, Maloney manages CU Boulder’s Earth Systems Stable Isotope Lab, one of more than 20 Core Facilities on campus. As a graduate student, she explored hydrogen atoms in algae from tropical islands. Her current work was inspired by an unlikely source: her father, a dermatologist.

“He takes skin cancer cells off people all the time,” Maloney said. “I wondered how the metabolism of those cells might be different from the cells growing next to them.”

To understand that question, it helps to know how hydrogen winds up in cells in the first place. In some cases, those atoms come from a hard-to-pronounce, but critically important, enzyme known as nicotinamide adenine dinucleotide phosphate (NADPH). Among its many roles in cells, NADPH collects hydrogen atoms then passes them to other molecules in the process of making fatty acids, an important building block for life.

NADPH, however, doesn’t always draw from the same pool of hydrogen. Previous research led by Zhang and focusing on bacteria suggested

that, depending on what other enzymes in a cell are doing, NADPH may sometimes use different hydrogen isotopes more or less often.

Which raised the question: If cancer rewires a cell's metabolism, could it also alter how NADPH gets its hydrogen, ultimately altering the atomic makeup of a cell?

Window into cancer

To begin to find out, the researchers set up jars filled with flourishing colonies of yeast in labs at Princeton and CU Boulder. Separately, biologists at Princeton conducted an experiment with colonies of healthy and cancerous mouse liver cells. The researchers then pulled the fatty acids from the cells and used a machine called a mass spectrometer to identify the ratio of hydrogen atoms within.

"When we started the study, I thought, 'Ooh, we have a chance to see something cool,'" Maloney said. "It ended up creating a huge signal, which I didn't expect."

Fermenting yeast cells, the kind that resemble cancer, contained roughly 50% fewer deuterium atoms on average than the normal yeast cells, a startling change. Cancerous cells exhibited a similar but not quite as strong shortage in deuterium.

Zhang, the study's senior author and an assistant professor of geosciences at Princeton, lost her own father to cancer. She's hopeful that the results could one day help families like her own.

"Cancer, and other illnesses, are unfortunately a huge theme in many people's lives. Seeing Ashley's data was a special, profound moment," Zhang said. "It meant that a tool used to track planetary health might also be applied to track health and disease in lifeforms, hopefully one day in humans. Growing up in a family challenged by cancer, I hope to see this area expand."

Phys Org, 06 May 2024

https://phys.org

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

Tweaking isotopes sheds light on promising approach to engineer semiconductors

2024-05-03

Partly because of semiconductors, electronic devices and systems become more advanced and sophisticated every day. That's why for decades researchers have studied ways to improve semiconductor compounds to influence how they carry electrical current. One approach is to use isotopes to change the physical, chemical and technological properties of materials.

Isotopes are members of a family of an element that all have the same number of protons but different numbers of neutrons and thus different masses. Isotope engineering has traditionally focused on enhancing so-called bulk materials that have uniform properties in three dimensions, or 3D. But new research led by ORNL has advanced the frontier of isotope engineering where current is confined in two dimensions, or 2D, inside flat crystals and where a layer is only a few atoms thick. The 2D materials are promising because their ultrathin nature could allow for precise control over their electronic properties.

"We observed a surprising isotope effect in the optoelectronic properties of a single layer of molybdenum disulfide when we substituted a heavier isotope of molybdenum in the crystal, an effect that opens opportunities to engineer 2D optoelectronic devices for microelectronics, solar cells, photodetectors and even next-generation computing technologies," said ORNL scientist Kai Xiao.

Yiling Yu, a member of Xiao's research team, grew isotopically pure 2D crystals of atomically thin molybdenum disulfide using molybdenum atoms of different masses. Yu noticed small shifts in the color of light emitted by the crystals under photoexcitation, or stimulation by light.

"Unexpectedly, the light from the molybdenum disulfide with the heavier molybdenum atoms was shifted farther to the red end of the spectrum, which is opposite to the shift one would expect for bulk materials," Xiao said. The red shift indicates a change in the electronic structure or optical properties of the material.

Xiao and the team, working with theorists Volodymyr Turkowski and Talat Rahman at the University of Central Florida, knew that the phonons, or crystal vibrations, must be scattering the excitons, or optical excitations, in unexpected ways in the confined dimensions of these ultrathin crystals. They discovered how this scattering shifts the optical bandgap to the red

end of the light spectrum for heavier isotopes. "Optical bandgap" refers to the minimum amount of energy needed to make a material absorb or emit light. By adjusting the bandgap, researchers can make semiconductors absorb or emit different colors of light, and such tunability is essential for designing new devices.

ORNL's Alex Puretzky described how different crystals grown on a substrate can show small shifts in emitted color caused by regional strain in the substrate. To prove the anomalous isotope effect and measure its magnitude to compare with theoretical predictions, Yu grew molybdenum disulfide crystals with two molybdenum isotopes in one crystal.

"Our work was unprecedented in that we synthesized a 2D material with two isotopes of the same element but with different masses, and we joined the isotopes laterally in a controlled and gradual manner in a single monolayer crystal," Xiao said. "This enabled us to observe the intrinsic anomalous isotope effect on the optical properties in the 2D material without the interference caused by an inhomogeneous sample."

The study demonstrated that even a small change of isotope masses in the atomically thin 2D semiconductor materials can influence optical and electronic properties -- a finding that provides an important basis for continued research.

"Previously, the belief was that to make devices such as photovoltaics and photodetectors, we had to combine two different semiconductor materials to make junctions to trap excitons and separate their charges. But actually, we can use the same material and just change its isotopes to create isotopic junctions to trap the excitons," Xiao said. "This research also tells us that through isotope engineering, we can tune the optical and electronic properties to design new applications."

For future experiments, Xiao and the team plan to collaborate with the experts at the High Flux Isotope Reactor and the Isotope Science and Engineering Directorate at ORNL. These facilities can provide various highly enriched isotope precursors to grow different isotopically pure 2D materials. The team can then further investigate the isotope effect on spin properties for their application in spin electronics and quantum emission.

This work was supported by DOE's Office of Science, Basic Energy Sciences, Materials Sciences and Engineering Division and was performed at the Center for Nanophase Materials Sciences, or CNMS, at ORNL, an Office of

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

Science user facility. The CNMS supported the TOF-SIMS, STEM and optical spectroscopy measurements.

ScIENCE Daily, 03 May 2024

https://sciencedaiy.com

Common Sweetener Neotame Damages Gut Cells

2024-04-27

Sweeteners and human health

In our increasingly health-conscious society, artificial sweeteners are widely used by individuals looking to reduce their sugar consumption without sacrificing sweetness in their food and beverages. Most artificial sweeteners – also known as non-sugar sweeteners (NSS) – are at least very low in calorie content, if not completely calorie-free.

It's perhaps no surprise, therefore, that the predicted global market value of artificial sweeteners is estimated to reach $3 billion by 2025.

Despite many sweeteners having been on the market for decades, their effects on human health remain under active research. At present, there doesn't appear to be a global consensus on whether these first-generation sweeteners can be deemed "good" or "bad" for our health. Last July, the World Health Organization (WHO) listed aspartame as a possible carcinogen, but the US Food and Drug Administration (FDA) stated that it disagreed with the report that ultimately led to this decision.

As studies continue to probe the effects of traditional artificial sweeteners such as saccharin and aspartame, researchers are turning their attention to more recently developed sweeteners, like neotame. Neotame was developed in the 1990s and authorized as safe for the general population by the FDA in 2002. It is derived from and is chemically similar to aspartame, but it is roughly 30–60 times sweeter.

Dr. Aparna Shil, associate professor in the Department of Botany at Jahangirnagar University in Bangladesh, and Dr. Havovi Chichger, associate professor in Biomedical Science at Anglia Ruskin University (ARU) in the UK, have published their findings from an in vitro study assessing neotame's effects on the gut epithelium and microbiome.

Neotame acceptable daily intake

The acceptable daily intake (ADI) of neotame is 2 mg per kg of body weight per day. In an individual of average weight, this would be equivalent to 10 mM per day.

"We use a model of the intestinal epithelium (Caco-2) and microbiota (Escherichia coli and Enterococcus faecalis) to investigate how physiologically-relevant exposure of neotame impacts intestinal epithelial cell function, gut bacterial metabolism and pathogenicity and gut epithelium–microbiota interactions," the authors explained in Frontiers in Nutrition.

Neotame negatively affects intestinal epithelium

Chichger's previous work demonstrated that sucralose, saccharin and aspartame reduce the viability of epithelial cells. In the new study, the researchers tested cell viability up to the recommended ADI of neotame (10 mM) and found that this sweetener also reduced viability at higher concentrations. At low concentrations (1–100 µM), it caused leaks across the epithelial monolayer.

Exploring whether this effect was because of a direct interaction between neotame and the sweet taste receptor, T1R3, the researchers transfected cells with siRNA targeting T1R3. This attenuated some of the cytotoxic and pro-apoptotic effects of the sweetener on the cell models.

Neotame also caused indirect damage to the intestinal epithelium via its pathogenic effects on the common gut bacteria E.coli and E. faecalis. In co-cultures, neotame had pathogenic effects at 100 Mm concentrations, which is lower than typical concentrations found in food and beverage products, as well as the ADI.

"The negative effect of neotame on the epithelium–microbiota relationship in the gut has the potential to influence a range of gut functions resulting in poor gut health which impacts a range of conditions including metabolic and inflammatory diseases, neuropathic pain and neurological conditions," the authors described.

"Understanding the impact of these pathogenic changes occurring in the gut microbiota is vital. Our findings also demonstrate the need to better understand common food additives more widely and the molecular mechanisms underlying potential negative health impacts," Chichger said.

The researchers note that the analyses were performed after 24 hours of exposure to neotame, whereas it normally takes around five hours to pass through the intestine. This is a limitation to the translation of the research,

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

as cells in the epithelium and the gut bacteria may not, in reality, be exposed to the sweetener for such long periods of time.

Technology Networks, 27 April 2024

https://technologynetworks.com

Engineers solve 'catalysis vs corrosion' mystery in electrochemical ozone production

2024-05-06

Researchers at the University of Pittsburgh and Drexel University in Philadelphia, along with Brookhaven National Laboratory, are working to solve a multipart mystery to make water disinfection treatments more sustainable.

Scalable electrochemical ozone production (EOP) technologies to disinfect dirty water may someday replace centralized chlorine treatments used today, whether in modern cities or remote villages. However, little is understood about EOP at the molecular level and how technologies that make it possible can be made to be efficient, economical, and sustainable.

Their research, "Interplay between Catalyst Corrosion and Homogeneous Reactive Oxygen Species in Electrochemical Ozone Production," was published recently in the journal ACS Catalysis.

The lead author is Drexel Ph.D. student Rayan Alaufey, with contributing researchers from Drexel, including co-PI Maureen Tang, associate professor of chemical and biological engineering, postdoctoral researcher Andrew Lindsay, Ph.D. student Tana Siboonruang, and Ezra Wood, associate professor of chemistry; co-PI John A. Keith, associate professor of chemical and petroleum engineering, and graduate student Lingyan Zhao from Pitt; and Qin Wu from Brookhaven.

"People have used chlorine to treat drinking water since the 19th century, but today we better understand that chlorine may not always be the best option. EOP for example can generate ozone, a molecule with about the same disinfecting power as chlorine, directly in water.

"Unlike chlorine which stably persists in water, ozone in water naturally decomposes after about 20 minutes, meaning it is less likely to damage people when consuming from water at a tap, when swimming in a pool, or when cleaning wounds in a hospital," explained Keith, who is also R.K. Mellon Faculty Fellow in Energy at Pitt's Swanson School of Engineering.

"EOP for sustainable disinfection would make a lot of sense in some markets, but doing it requires a good enough catalyst, and because nobody has found a good enough EOP catalyst yet, EOP is too expensive and energy-intensive for broader use.

"My colleagues and I thought if we could decode at the atomic level what makes a mediocre EOP catalyst work, maybe we could engineer an even better EOP catalyst."

Solving the mystery of how EOP catalysts work is crucial in understanding how to better engineer one of the most promising and least toxic EOP catalysts known to date: nickel- and antimony-doped tin oxide (Ni/Sb–SnO2, or NATO).

Therein, said Keith, lies the conundrum: what is every atom's role in NATO doing to help EOP? Is ozone getting formed catalytically in ways we want it to, or does it form because the catalyst is decomposing, and future work needs to be done to make NATO catalysts more stable?

Surprisingly, the researchers discovered that it is probably a mix of both.

By using experimental electrochemical analyses, mass spectrometry, and computational quantum chemistry modeling, the researchers created an "atomic-scale storyline" to explain how ozone is generated on NATO electrocatalysts.

For the first time, they identified that some of the nickel in NATO is probably leaching out of the electrodes via corrosion, and these nickel atoms, now floating in the solution near the catalyst, can promote chemical reactions that eventually generate ozone.

"If we want to make a better electrocatalyst, we need to understand what parts are working and not working. Factors like metal ion leaching, corrosion, and solution phase reactions can give the appearance that a catalyst is working one way when actually it is working another way."

Keith noted that identifying the prevalence of corrosion and chemical reactions occurring away from the catalyst are important steps to clarify before other researchers can pursue improvements to EOP and other electrocatalytic processes.

In their conclusion, they note, "Identifying or refuting the existence of such fundamental technological constraints will be critical to any future applications of EOP and other advanced electrochemical oxidation processes."

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

"We know that electrochemical water treatment works on small scales, but the discovery of better catalysts will boost it to a global scale. The next step is finding new atomic combinations in materials that are more resistant to corrosion but also promote economically and sustainably viable EOP," Keith said.

Phys Org, 06 May 2024

https://phys.org

Microbial enzymes cut a path towards universal blood for transfusions

2024-05-03

A Scandinavian collaboration has taken another step towards generating universal blood that is suitable for everyone receiving a transfusion or an organ transplant with the use of microbial enzymes. The enzymes come from a bacterium that feeds on mucus in the gut and can prune the A and B antigens from red blood cells.

Blood types in humans are partly the result of the ABO gene coming in two forms, with the A gene producing one enzyme (N-acetylgalactosaminyl-transferase) and B another (α-galactosyltransferase). These enzymes add the A- and B-specific sugars to the glycolipids and glycoproteins on red blood cells. Those with O-type blood have neither enzyme and can donate blood and organs to all ABO blood groups.

Mismatched blood can cause lethal immune responses. 'Everyone has natural antibodies against the antigens you miss,' explains Martin Olsson, a blood expert at Lund University, Sweden, who co-led the new study. 'If you tried to transplant a lung, liver or kidney against the ABO barrier, it would be destroyed within minutes.'

Almost 120 million units of blood are donated globally every year. Every unit must be blood-group matched with the patient. When a patient's blood group in an emergency is unknown or cannot be determined, O-type blood is used. Demand for this universal blood type therefore outstrips supply.

In the early 1980s, a group at the New York Blood Center used α-galactosidase enzymes from coffee beans to modify B antigens to H antigens, which are those on O-type blood, a landmark advance. More recently, a screen of gut microbes identified an enzyme pair that can

convert from A antigens to H antigens. None of these advances completely removed the cross-reactivity between blood groups, however.

Olsson says he now knows why. 'We've uncovered new antigens linked to ABO,' he says. 'The textbooks were wrong. There are at least four other ABO-related antigens that cause the enigmatic reactivity when A and B are gone.'

These antigens can be pictured as extensions to the glycan tree on a red blood cell's surface. Previous efforts to remove the glycan only trimmed the treetops. 'We cut off the trees and for the first time see the shrubs and bushes underneath, which harboured these unknown antigens,' says Olsson.

The enzymes were discovered in the lab of Maher Abou Hachem, a chemical engineer at the Technical University of Denmark, with a long-time interest in Akkermansia muciniphila. This gut microbe exclusively feeds on the densely glycosylated mucin, the main component of the mucosal layer lining our gut.

It turns out the glycans in mucin share similarities to those on red blood cells. 'They are capped by terminal epitopes which resemble the blood antigen groups,' says Abou Hachem, who co-led the research. 'Both are gel-like and insoluble, negatively charged and complex glycan surfaces.' After evaluating 22 hydrolases from the microbe, exoglycosidase combinations were identified that could efficiently trim A and B antigens and the four newly discovered carbohydrate extensions.

An estimated 95% of group O plasmas were compatible with group B blood converted with the new method, indicating that it may be acceptable for transfusion across the ABO barrier, says Olsson. Group A red cells are more complex and more work is needed to make enzyme-converted A blood that fits all patients.

This group's work 'led to significant compatibility improvements of treated red blood cells', says Marcelo Guerin, a glycobiologist at the Institute of Molecular Biology of Barcelona. 'These are truly outstanding discoveries that brings the [universal blood] concept much closer to clinical application.'

Biochemist Stephen Withers at the University of British Columbia, Canada, who has researched enzyme conversion of blood, says it will still take time to generate an approved universal blood product. 'We all want to say

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

it'll be there in five years, but in reality I don't think it will because safety studies take a long time,' he says.

His group formed a company – Avivo – that is working with the US Food and Drug Administration on eliminating the blood-matching barrier. 'They're trying to understand what they would need us to do for a clinical trial,' says Withers. 'The regulatory agencies aren't quite sure how to deal with this. This isn't a normal drug, a biologic or a small molecule. Is it a medical device? They'll need to decide.'

Chemistry World, 05 May 2024

https://chemistryworld.com

UC San Diego's open source AI platform revolutionizes multi-target drug discovery

2024-05-06

Scientists at UC San Diego have developed a machine learning algorithm to simulate the time-consuming chemistry involved in the earliest phases of drug discovery, which could significantly streamline the process and open doors for never-before-seen treatments. Identifying candidate drugs for further optimization typically involves thousands of individual experiments, but the new artificial intelligence (AI) platform could potentially give the same results in a fraction of the time. The researchers used the new tool, described in Nature Communications, to synthesize 32 new drug candidates for cancer.

The technology is part of a new but growing trend in pharmaceutical science of using AI to improve drug discovery and development.

The new platform, called POLYGON, is unique among AI tools for drug discovery in that it can identify molecules with multiple targets, while existing drug discovery protocols currently prioritize single target therapies. Multi-target drugs are of major interest to doctors and scientists because of their potential to deliver the same benefits as combination therapy, in which several different drugs are used together to treat cancer, but with fewer side effects.

"It takes many years and millions of dollars to find and develop a new drug, especially if we're talking about one with multiple targets." said Ideker. "The rare few multi-target drugs we do have were discovered largely by chance, but this new technology could help take chance out of the equation and kickstart a new generation of precision medicine."

The researchers trained POLYGON on a database of over a million known bioactive molecules containing detailed information about their chemical properties and known interactions with protein targets. By learning from patterns found in the database, POLYGON is able to generate original chemical formulas for new candidate drugs that are likely to have certain properties, such as the ability to inhibit specific proteins.

"Just like AI is now very good at generating original drawings and pictures, such as creating pictures of human faces based off desired properties like age or sex, POLYGON is able to generate original molecular compounds based off of desired chemical properties," said Ideker. "In this case, instead of telling the AI how old we want our face to look, we're telling it how we want our future drug to interact with disease proteins."

To put POLYGON to the test, the researchers used it to generate hundreds of candidate drugs that target various pairs of cancer-related proteins. Of these, the researchers synthesized 32 molecules that had the strongest predicted interactions with the MEK1 and mTOR proteins, a pair of cellular signaling proteins that are a promising target for cancer combination therapy. These two proteins are what scientists call synthetically lethal, which means that inhibiting both together is enough to kill cancer cells even if inhibiting one alone is not.

The researchers found that the drugs they synthesized had significant activity against MEK1 and mTOR, but had few off-target reactions with other proteins. This suggests that one or more of the drugs identified by POLYGON could be able to target both proteins as a cancer treatment, providing a list of choices for fine-tuning by human chemists.

"Once you have the candidate drugs, you still need to do all the other chemistry it takes to refine those options into a single, effective treatment," said Ideker. "We can't and shouldn't try to eliminate human expertise from the drug discovery pipeline, but what we can do is shorten a few steps of the process."

Despite this caution, the researchers are optimistic that the possibilities of AI for drug discovery are only just being explored.

"Seeing how this concept plays out over the next decade, both in academia and in the private sector, is going to be very exciting." said Ideker. "The possibilities are virtually endless."

News Medical Life Sciences, 06 May 2024

https://news-medical.net

CHEMWATCH
Bulletin Board
Gossip
MAY. 10, 2024

Scientists use high pressure NMR spectroscopy to study structure of dynamic proteins

2024-05-06

A pressure of 3,000 bar is applied to the cold shock protein B of Bacillus subtilis in a small tube in the NMR spectroscopy laboratory at the University of Konstanz. This is roughly three times the water pressure at the deepest point of the ocean. The pressure is so intense that the highly dynamic protein shows structural features that would not be sufficiently visible under normal pressure.

But why do scientists apply such high pressure, which does not occur anywhere else on our planet under natural conditions? The answer is: To study processes and properties that are too volatile to be observed under normal conditions.

"This high pressure allows us to make states visible that actually do exist at 1 bar, but which we can only observe directly at 3,000 bar," explains Frederic Berner, University of Konstanz. Literally "under high pressure," the doctoral researcher investigates the properties of a protein determined by its structure, and how changes in the structure in turn influence its properties.

In the research group Physical Chemistry and Nuclear Magnetic Resonance at the University of Konstanz, led by Michael Kovermann, he recently implemented a new method for analyzing the structural properties of proteins at 3,000 bar with as little influence as possible from surrounding effects.

The two researchers now present their new methodological approach in the journal Angewandte Chemie International Edition.

Proteins: How structure influences their properties

Proteins are the basic building blocks of life. They consist of amino acid chains whose three-dimensional structure can take on a wide variety of formations. They "fold" in the same way as a long paper ribbon can be folded into different shapes.

The functional properties of a protein depend largely on its folding, so that the same protein can have very different effects in the cell, depending on the form in which it is folded. "What is important for proteins is their structure, which in turn is linked to functionalities. If you want to identify biochemical mechanisms, you need information about their structure," says Berner.

Scientists aim to capture the properties of the protein structure in its "pure" form—as unclouded as possible by influences from its environment. For two reasons, however, that is not so easy: First, there are almost always interactions with the solvent surrounding the protein and with neighboring sections of its molecular chain.

Second, proteins are highly dynamic, their folding is always in motion. For example, there are proteins that constantly fold apart and go back like scissors. In the fraction of the second it opens, a chemical reaction takes place. This happens far too quickly for researchers to be able to examine it directly.

Under high pressure

And this is where the pressure of 3,000 bar comes in: The molecule is pressed into a certain state—its structure is manipulated: The scissors remain open. Using magnetic resonance spectroscopy, the researchers can now study specific structural properties of the protein that are not directly visible under normal pressure.

Previous analysis methods often have accepted the environmental effects and try to factor them out afterward. Kovermann's and Berner's new high-pressure method, in contrast, can suppress or "correct" the environmental effects from the outset ("intrinsically") and thus allows a view of the protein that is affected as little as possible. It makes particular sense to use and compare the new method in combination with existing methods, as this way the various influencing factors become visible in detail.

The high-pressure process invented at the University of Konstanz has brought about very good results even in the early phase of its application. Berner and Kovermann explain that further experiments and computer simulations will now take place to further test and potentially refine the process.

Phys Org, 06 May 2024

https://phys.org

CHEMWATCH
Bulletin Board

Study reveals flaw in long-accepted approximation used in water simulations

2024-05-07

Computational scientists at the Department of Energy's Oak Ridge National Laboratory have published a study in the Journal of Chemical Theory and Computation that questions a long-accepted factor in simulating the molecular dynamics of water: the 2-femtosecond (one quadrillionth of a second) time step. The femtosecond is a timescale used by scientists to measure the ultrafast processes of atoms and molecules.

According to the team's findings, using anything greater than a 0.5 femtosecond time step—the time interval at which a computer simulation is analyzed—can introduce errors in both the dynamics and thermodynamics when simulating water using a rigid-body description.

Because water is the most prevalent component of biomolecular simulations—from protein ensembles to nucleic acids—the team's recommendation of a 0.5-femtosecond time step for better accuracy could cause some waves in the scientific community. The 2-femtosecond time step has been accepted as a standard in water simulations for almost 50 years.

"This has broad implications because water is the active constituent in cell biology. Water is the matrix of life, and all the simulations that we do on biological systems are always in water. But if you are simulating that fluid in a way that breaks a fundamental tenet of equilibrium statistical mechanics, that's a problem," said co-author Dilip Asthagiri, a senior computational biomedical scientist in ORNL's Advanced Computing for Life Sciences and Engineering group.

Molecular simulations solve Newtonian equations of motion to elucidate how the molecules evolve over time. Of particular interest to researchers conducting such calculations is the determination of the resulting system temperatures.

One of the tenets of statistical mechanics is that if a system is in equilibrium, then the temperatures associated with its translational motion (movement along a line) and rotational motion should be the same. If those two temperatures differ, then the simulation is not in equilibrium. According to the team's findings, that is the essential problem with using time steps longer than 0.5 femtoseconds to simulate water.

The use of the 2-femtosecond time step in simulations arose from a paper published in 1977, when computing time was far more computationally expensive. Because the flexible bond between oxygen and hydrogen vibrates rapidly, the time steps necessary to accurately calculate that vibration are very small, requiring more computing time to capture enough intervals to study. Because that motion is the most rapid, that time step is the one that must be used in the evolution to obtain the right answer.

The paper's authors wanted to know whether there was a way to use longer time steps and allow for fewer intervals and longer simulations. Those researchers proposed a rigid-body description of water to do just that.

"The 1977 work basically said that the vibrations of the oxygen-hydrogen bond can be decoupled from translation and rotation, and therefore freezing the vibrations by treating water as a rigid body should allow one to take a big time step," Asthagiri said. "Since that time, the rigid-bond model has become the standard—the canonical way that scientists look at this."

But Asthagiri discovered that using this method can cause discrepancies in the temperatures between the water molecules' translational and rotational motions, meaning the simulation may be producing incorrect results.

"What Dilip found is that going with too long of a time step, you tend to get inaccurate values for both the thermodynamics and the dynamics of the motion of water, which is the medium in which all these molecules move. In effect, you can get a false friction, either too large or too small, due to this approximation of too long of a time step. And if you have the friction off, that means the motion of these molecules is going be off, too," said co-author Tom Beck, section head of Science Engagement in the National Center for Computational Sciences at ORNL.

Asthagiri first noted this disparity in temperatures as a research professor at Rice University in 2021. He and a graduate student were simulating water in the supercooled regime and found that the average temperature in the log file was lower than the setpoint temperature.

"It was a 1 Kelvin difference, and you can easily ignore it, but it was systematically seen at different temperatures. And that was the clue that there was something off—okay, maybe one temperature, but multiple

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

temperatures with the same behavior? There must be something wrong," Asthagiri said.

After joining ORNL in 2022, Asthagiri began examining rotation and translation separately rather than using the site coordinates and velocities, which are standard quantities that biomolecular simulation codes produce.

Incidentally, formulating the equations of those motions separately was the approach used by the authors of the very first paper ever written on simulating water in 1971. Those authors recommended a time step of 0.4 femtoseconds.

"We need to go back to the original work in terms of being careful. There is nothing wrong with doing site velocities, but if you do it as site velocities, then you need to take a time step that is small enough that temperatures between translation and rotation are the same, on average," Asthagiri said.

Computational scientists can easily make the change to 0.5-femtosecond time steps, should they choose to do so, although it would also result in shorter simulations because of longer computing times.

"It's just one flag in the input script—2 to 0.5. It's a very simple switch, but now the problem is you have to use more computing time, that's all. But the computing power is available now," Asthagiri said.

Asthagiri has presented the study's findings to colleagues at the Telluride Science & Innovation Center and the online Statistical Thermodynamics & Molecular Simulations Seminar Series.

"When I presented the work to an online statistical thermodynamics seminar series, the first reaction was a little bit of a shock. It's going to take time to sink in," Asthagiri said.

Asthagiri will present the results at another workshop co-organized by Beck for the Centre Européen de Calcul Atomique et Moléculaire on May 6–8 in Pisa, Italy.

Phys Org, 07 May 2024

https://phys.org

Ban on most uses of dichloromethane finalised in US

2024-05-07

The US Environmental Protection Agency (EPA) has signed off on a rule banning most uses of dichloromethane, also known as methylene chloride.

The chemical is commonly used as a paint stripper and has been linked to dozens of deaths, as well as cancers and other serious health issues. The action, announced on 30 April under the Toxic Substances Control Act (Tsca) that governs US chemical policy, followed the agency's proposal about a year ago.

Dichloromethane is used by the public for degreasing and as a paint stripper, and commercially in products like adhesives and sealants. Industrially, the substance is used to make other chemicals like more environmentally-friendly refrigerants. At least 88 people have died from acute dichloromethane exposure in the US since 1980, and most of those fatalities were members of the public refinishing bathtubs or stripping paint, according to the EPA. Often, these individuals are fully trained and wearing personal protective equipment, the agency said.

Back in 2019, the EPA banned consumer use of dichloromethane and limited commercial applications, but the chemical nevertheless continues to be used widely. The agency's new final risk management rule requires companies to rapidly reduce manufacturing, processing and distribution of this chemical for all consumer uses and most industrial and commercial uses. Consumer use will be phased out within a year, and most industrial and commercial uses will be prohibited within two years.

The EPA's new regulation also establishes worker protections under Tsca for some industrial uses of the chemical, including strict exposure limits, monitoring requirements, and worker training and notification requirements.

The uses of dichloromethane that will continue under the final rule are those considered important to the country's national security and economy. These include making other chemicals like refrigerants important for phasing out climate-damaging hydrofluorocarbons, producing battery separators for electric vehicles and laboratory use. In addition, other specific uses of the chemical required by Nasa, the Department of Defense and the Federal Aviation Administration will also be allowed to go on with strict workplace safety oversight intended to reduce exposure and minimise the risks to workers.

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

The EPA's new rule has faced some backlash from the chemical industry. The American Chemistry Council, a trade group that represents US chemical companies, is arguing that dichloromethane is 'a critical chemical' used in many industrial and commercial applications. 'ACC continues to be disappointed with EPA's approach to establishing occupational exposure limits,' the organisation said in a statement. 'EPA's methodology and approach need to be revised before being applied in subsequent risk management rules. Without making these improvements, these limits will be unworkable, unmeetable examples of unnecessary overregulation.' The organisation says that it will work with the EPA as stakeholders move into the compliance phase.

Chemistry World, 07 May 2024

https://chemistryworld.com

Scientists Discover Protein Complex That Controls Cell Division

2024-05-03

"We have gained in-depth knowledge of how cell division is controlled, which is important for understanding the causes of various diseases that are due to errors in cell division, such as various tumour diseases," says Stefan Björklund, professor at the Department of Medical Biochemistry and Biophysics at Umeå University and lead author of the study.

In each cell there is a machinery called the ribosome. It uses DNA as a template to produce proteins, which are necessary for virtually all processes in the cell. First, however, the cells must make a copy of the instructions in the form of mRNA through a process called transcription.

The research team at Umeå University has discovered how the Mediator, a protein complex in the cell nucleus, can bind to DNA and interact with another protein complex, Lsm1-7, to regulate the production of proteins that make up the ribosomes. The study shows that when cells grow too densely, cell division slows down. When this happens, the mediator moves to the end of the genes where it interacts with Lsm1-7. This has the dual effect of both slowing down the reading of the genes and interfering with the maturation of mRNA. This, in turn, leads to a reduced production of ribosomal proteins and thus a slower cell division.

A possible direction of future research may be to study whether it is possible to control the position of the mediator, in order to inhibit rapid cell division, for example in tumours.

"We are still early in the research in the field, so more studies are needed before we can say that this is a viable path, but it is an exciting opportunity," says Stefan Björklund.

The study has been conducted in yeast cells that serve as a good model when it comes to understanding basic mechanisms that work in a similar way in more complex systems such as animal and plant cells.

Technology Networks, 03 May 2024

https://technologynetworks.com

80% of Americans exposed to harmful chemicals found in both Cheerios and Quaker Oats

2024-04-23

Animal studies have linked chlormequat to various reproductive issues, including reduced fertility, altered fetal growth, and harm to the reproductive system.

"We detected the chemical in 92 percent of oat-based foods purchased in May 2023, including Quaker Oats and Cheerios," stated a report released alongside the study. "The fact that so many people are exposed raises concerns about its potential impact on public health."

To obtain their findings, researchers collected 96 urine samples from individuals between 2017 and 2023 and tested them for chlormequat. They found that 77 out of 96 people tested positive for the chemical. Researchers inferred that their exposure must have been recent, as chlormequat typically exits the bloodstream within 24 hours.

"We found a greater number of people were exposed in 2023, compared to earlier years, and at higher concentrations," noted the researchers, suggesting that exposure is increasing rapidly.

Regarding sources of exposure, researchers discovered high levels of chlormequat in oat-based products. Out of the 20 products examined, seven were organic, and 13 were non-organic. Additionally, nine wheat-based products were tested.

"Detectable levels of chlormequat were found in 92 percent of non-organic oat-based foods, while only two samples of wheat-based foods—both bread—had low levels. Only one of the seven organic samples had low levels of chlormequat," the study determined.

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

Chlormequat is used to make plants more rigid, facilitating easier harvest.

Although the Environmental Protection Agency (EPA) prohibits the use of chlormequat on food crops grown in the United States, it is permitted on food and grains imported into the country.

"Chlormequat was not permitted on oats sold in the U.S. before 2018, when the Trump-era EPA granted initial approval for some amount of the chemical on imported oats. The same administration increased the allowable level in 2020," explained the report. These regulatory changes may help explain why we are observing more frequent and higher detections of the chemical in Americans tested."

What are the effects of chlormequat exposure on human health?

Chlormequat is a plant growth regulator commonly used in agriculture to control the growth of various crops such as cereals, fruits, and vegetables. Exposure to chlormequat can occur through inhalation, skin contact, or ingestion, particularly among agricultural workers or individuals living near treated fields.

While chlormequat is considered to have low acute toxicity, chronic exposure or high doses can lead to various health effects:

Skin Irritation: Direct contact with chlormequat can cause skin irritation, including redness, itching, and dermatitis.

Eye Irritation: Exposure to chlormequat can lead to eye irritation, causing redness, tearing, and discomfort.

Respiratory Irritation: Inhalation of chlormequat dust or spray may irritate the respiratory tract, leading to symptoms such as coughing, sore throat, and difficulty breathing, particularly in cases of high exposure or inadequate ventilation.

Allergic Reactions: Some individuals may develop allergic reactions to chlormequat upon repeated exposure, leading to symptoms such as skin rash, hives, or respiratory difficulties.

Endocrine Disruption: Chlormequat has been found to interfere with hormonal regulation in animal studies, although the extent of this effect in humans is not fully understood. Prolonged exposure to chlormequat may potentially disrupt hormone balance, leading to reproductive or developmental issues.

Carcinogenicity: There is limited evidence suggesting that chlormequat may have carcinogenic properties. Studies on animals have shown an increased incidence of tumors in certain organs following prolonged exposure to high doses of chlormequat. However, more research is needed to determine its carcinogenic potential in humans.

Neurotoxicity: High levels of chlormequat exposure may have neurotoxic effects, leading to symptoms such as headaches, dizziness, and incoordination. Chronic exposure to chlormequat has been associated with neurological symptoms in animal studies, but the relevance to human health is uncertain.

Reproductive and Developmental Effects: Animal studies have suggested that chlormequat exposure may impact reproductive function and fetal development. However, the evidence in humans is limited, and further research is needed to establish the potential risks to human reproductive health and development.

It's important to note that the health effects of chlormequat exposure can vary depending on factors such as the duration and intensity of exposure, individual susceptibility, and the presence of other chemicals or environmental factors.

Proper safety precautions and regulatory measures should be followed to minimize exposure to chlormequat in occupational and environmental settings. If exposure occurs, prompt medical attention should be sought to manage any symptoms and prevent further complications.

Brighter Side of News, 23 April 2024

https://thebrighterside.com

Chemists produce new-to-nature enzyme containing boron

2024-05-07

Boronic acid has been used in organic chemistry for decades, even though it is not present in any organism. "It gives rise to different chemical reactions than those we find in nature," explains Gerard Roelfes, Professor of Biomolecular Chemistry & Catalysis at the University of Groningen.

His group created an enzyme with boronic acid at its reactive center and then used directed evolution to make it more selective and to improve its catalytic power. Furthermore, enzymatic reactions are more sustainable than classical chemical reactions, as they take place at low temperatures

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

and without toxic solvents. The study was published online in the journal Nature on 8 May.

The application of boron in organic chemistry dates back some seventy years and was awarded a Nobel Prize for Chemistry in 1979. In recent years, the interest in boron as a catalyst has grown, but as yet, its use in the chemical industry is limited.

Roelfes explains, "So far, boron catalysis is too slow and it is not very suitable for enantioselective reactions. These types of reactions are used to create chiral molecules, which can exist in two versions that are mirror images of each other, like a left and a right hand.

"In many drugs, both hands can have a different effect. It is, therefore, important to selectively produce the proper hand, especially for the pharmaceutical industry."

Expanded genetic code

"To make this possible, we set out to introduce boron into an enzyme. Our group has a long history of designing enzymes that don't exist in nature," says Roelfes. The Roelfes group used an expanded genetic code to introduce a non-natural amino acid that contains a reactive boronic acid group into an enzyme. "Using this technique, we can determine at the DNA level where we place the amino acid in a protein."

Once they made an enzyme with boronic acid at its reactive center, they could use directed evolution to increase its efficiency, resulting in faster catalysis. Roelfes adds, "Furthermore, by placing the boronic acid in the chiral context of an enzyme, we were able to achieve highly enantioselective catalysis. The reaction that is described is a proof of principle and shows the way to harnessing the catalytic power of boron in enzymes."

Biocatalysis

Using enzymes to create organic compounds is important for the pharmaceutical industry. "In their push towards greener and more sustainable ways of producing drugs, they are looking at biocatalysis to replace conventional chemical reactions," Roelfes says.

At the University of Groningen, concerted efforts are being made towards this goal. Roelfes concludes, "We have a number of research groups at the Faculty of Science and Engineering engaged in this kind of work, using

different approaches to create biocatalytic solutions for the chemical industry."

In this context, Roelfes and his team will continue to develop their boronic acid enzymes and create other such new-to-nature enzymes.

Phys Org, 07 May 2024

https://phys.org

BASF's electric cracker demonstrator goes online

2024-05-07

Steam cracking, the thermal process used by the chemical industry to transform hydrocarbons into useful smaller molecules such as ethylene and propylene, is very energy-intensive. The amount of energy required varies according to the feedstock and plant design, but is typically more than 30GJ per ton of ethylene produced. Burning natural gas to provide this energy also creates 1.5–2 tons of CO_2 emissions per ton of ethylene, meaning greenhouse gas targets will be difficult to achieve with existing cracker designs.

There has been a lot of interest in using electrically powered furnaces to achieve the 850°C temperatures required. This would also avoid energy losses from hot flue gases that make the process inefficient, even if much of the heat is recovered.

A demonstration plant for electric cracking is now running at BASF's giant complex in Ludwigshafen, Germany, with the hope of proving its feasibility. If that electricity came from renewable sources rather than burning gas, the overall CO_2 emissions burden could be cut by as much as 90%, BASF said.

The plant is a collaboration between BASF, Sabic and Linde, and backed by a grant from the German government. Chemistry World reported that BASF was working on the idea back in 2019, when the company said it hoped the demonstrator would be on stream before 2025. Linde now plans to commercialise the technology from the end of 2024, under the brand name Starbridge.

The plant has two furnaces with different designs running in parallel. One uses direct heating, with an electric current applied to the process tubes inside the reactor. Resistive heating inside the tube wall, caused by the electrical resistivity of the material, provides the required thermal energy for the chemical reaction.

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

The second uses electricity to power resistive heating elements around the cracker coils, followed by radiative heat transfer from the heating elements and the insulated walls placed around the tubes. This gives indirect heating. Together, the two furnaces can process about 4 tons of hydrocarbon feedstock an hour, using 6MW of electrical power.

'We want to test and demonstrate the reliability of key components, like materials of construction and custom-made components, for use in this type of high-temperature reactor,' says Michael Reitz, steam cracker/eFurnace technology manager at BASF. 'We expect that both heating concepts have their own advantages.'

The main environmental advantage is the reduction in direct carbon emissions compared to a fossil-fired furnace, Reitz says. The only heat losses from the eFurnace are to the insulation, he says, with none of the additional flue gas losses that occur in a conventional furnace. This makes the furnace boxes more efficient, lowering their overall energy demand as well as running on cleaner energy sources.

The next step is to construct industrial-scale furnaces, he says, although timelines also depend on securing supplies of renewable energy at competitive prices. BASF already meets 20% of its global electricity demand with wind and solar energy, and Reitz says this should rise to at least 60% by 2030, both by making its own and buying in more. The company recently agreed to buy a 49% stake in Vattenfall's Nordlicht wind farm project in the German North Sea, adding to existing wind farm investments in the Netherlands and China.

Reitz says that developing new technologies is always risky, and the consortium with Sabic and Linde has been important to its success. 'It would not have been possible to complete the project so quickly and in such a target-oriented way without the contribution of the various resources and competencies,' he says. 'We are optimistic. The use of electricity is the most reasonable alternative among the potential measures to reduce CO_2 emissions.'

Chemistry World, 07 May 2024

https://chemistryworld.com

Simulated chemistry: New AI platform designs tomorrow's cancer drugs

2024-05-06

The technology is part of a new but growing trend in pharmaceutical science of using AI to improve drug discovery and development.

"A few years ago, AI was a dirty word in the pharmaceutical industry, but now the trend is definitely the opposite, with biotech startups finding it difficult to raise funds without addressing AI in their business plan," said senior author Trey Ideker, professor in the Department of Medicine at UC San Diego School of Medicine and adjunct professor of bioengineering and computer science at the UC San Diego Jacobs School of Engineering. "AI-guided drug discovery has become a very active area in industry, but unlike the methods being developed in companies, we're making our technology open source and accessible to anybody who wants to use it."

The new platform, called POLYGON, is unique among AI tools for drug discovery in that it can identify molecules with multiple targets, while existing drug discovery protocols currently prioritize single target therapies. Multi-target drugs are of major interest to doctors and scientists because of their potential to deliver the same benefits as combination therapy, in which several different drugs are used together to treat cancer, but with fewer side effects.

"It takes many years and millions of dollars to find and develop a new drug, especially if we're talking about one with multiple targets." said Ideker. "The rare few multi-target drugs we do have were discovered largely by chance, but this new technology could help take chance out of the equation and kickstart a new generation of precision medicine."

The researchers trained POLYGON on a database of over a million known bioactive molecules containing detailed information about their chemical properties and known interactions with protein targets. By learning from patterns found in the database, POLYGON is able to generate original chemical formulas for new candidate drugs that are likely to have certain properties, such as the ability to inhibit specific proteins.

"Just like AI is now very good at generating original drawings and pictures, such as creating pictures of human faces based off desired properties like age or sex, POLYGON is able to generate original molecular compounds based off of desired chemical properties," said Ideker. "In this case, instead of telling the AI how old we want our face to look, we're telling it how we want our future drug to interact with disease proteins."

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

To put POLYGON to the test, the researchers used it to generate hundreds of candidate drugs that target various pairs of cancer-related proteins. Of these, the researchers synthesized 32 molecules that had the strongest predicted interactions with the MEK1 and mTOR proteins, a pair of cellular signaling proteins that are a promising target for cancer combination therapy. These two proteins are what scientists call synthetically lethal, which means that inhibiting both together is enough to kill cancer cells even if inhibiting one alone is not.

The researchers found that the drugs they synthesized had significant activity against MEK1 and mTOR, but had few off-target reactions with other proteins. This suggests that one or more of the drugs identified by POLYGON could be able to target both proteins as a cancer treatment, providing a list of choices for fine-tuning by human chemists.

"Once you have the candidate drugs, you still need to do all the other chemistry it takes to refine those options into a single, effective treatment," said Ideker. "We can't and shouldn't try to eliminate human expertise from the drug discovery pipeline, but what we can do is shorten a few steps of the process."

Despite this caution, the researchers are optimistic that the possibilities of AI for drug discovery are only just being explored.

"Seeing how this concept plays out over the next decade, both in academia and in the private sector, is going to be very exciting." said Ideker. "The possibilities are virtually endless."

This study was funded, in part, by the National Institutes of Health (Grants CA274502, GM103504, ES014811, CA243885, CA212456).

Science Daily, 06 May 2024

https://sciencedaily.com

Cheap Catalyst Made Out of Sugar Has the Power To Destroy CO2

2024-05-08

New catalyst may provide a potential solution for utilizing captured carbon.

A new catalyst made from an inexpensive, abundant metal and common table sugar has the power to destroy carbon dioxide (CO_2) gas.

In a new Northwestern University study, the catalyst successfully converted CO2 into carbon monoxide (CO), an important building block to produce a variety of useful chemicals. When the reaction occurs in the presence of hydrogen, for example, CO2 and hydrogen transform into synthesis gas (or syngas), a highly valuable precursor to producing fuels that can potentially replace gasoline.

With recent advances in carbon capture technologies, post-combustion carbon capture is becoming a plausible option to help tackle the global climate change crisis. But how to handle the captured carbon remains an open-ended question. The new catalyst potentially could provide one solution for disposing of the potent greenhouse gas by converting it into a more valuable product.

The study will be published in the May 3 issue of the journal Science.

"Even if we stopped emitting CO2 now, our atmosphere would still have a surplus of CO2 as a result of industrial activities from the past centuries," said Northwestern's Milad Khoshooei, who co-led the study. "There is no single solution to this problem. We need to reduce CO2 emissions and find new ways to decrease the CO2 concentration that is already in the atmosphere. We should take advantage of all possible solutions."

"We're not the first research group to convert CO2 into another product," said Northwestern's Omar K. Farha, the study's senior author. "However, for the process to be truly practical, it necessitates a catalyst that fulfills several crucial criteria: affordability, stability, ease of production, and scalability. Balancing these four elements is key. Fortunately, our material excels in meeting these requirements."

An expert in carbon capture technologies, Farha is the Charles E. and Emma H. Morrison Professor of Chemistry at Northwestern's Weinberg College of Arts and Sciences. After starting this work as a Ph.D. candidate at the University of Calgary in Canada, Khoshooei now is a postdoctoral fellow in Farha's laboratory.

Solutions from the pantry

The secret behind the new catalyst is molybdenum carbide, an extremely hard ceramic material. Unlike many other catalysts that require expensive metals, such as platinum or palladium, molybdenum is an inexpensive, non-precious, Earth-abundant metal.

To transform molybdenum into molybdenum carbide, the scientists needed a source of carbon. They discovered a cheap option in an

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

unexpected place: the pantry. Surprisingly, sugar — the white, granulated kind found in nearly every household — served as an inexpensive, convenient source of carbon atoms.

"Every day that I tried to synthesize these materials, I would bring sugar to the lab from my home," Khoshooei said. "When compared to other classes of materials commonly used for catalysts, ours is incredibly inexpensive."

Successfully selective and stable

When testing the catalyst, Farha, Khoshooei, and their collaborators were impressed by its success. Operating at ambient pressures and high temperatures (300-600 degrees Celsius), the catalyst converted CO2 into CO with 100% selectivity.

High selectivity means that the catalyst acted only on the CO2 without disrupting surrounding materials. In other words, industry could apply the catalyst to large volumes of captured gases and selectively target only the CO2. The catalyst also remained stable over time, meaning that it stayed active and did not degrade.

"In chemistry, it's not uncommon for a catalyst to lose its selectivity after a few hours," Farha said. "But, after 500 hours in harsh conditions, its selectivity did not change."

This is particularly remarkable because CO2 is a stable — and stubborn — molecule.

"Converting CO2 is not easy," Khoshooei said. "CO2 is a chemically stable molecule, and we had to overcome that stability, which takes a lot of energy."

Tandem approach to carbon clean-up

Developing materials for carbon capture is a major focus of Farha's laboratory. His group develops metal-organic frameworks (MOFs), a class of highly porous, nano-sized materials that Farha likens to "sophisticated and programmable bath sponges." Farha explores MOFs for diverse applications, including pulling CO2 directly from the air.

Now, Farha says MOFs and the new catalyst could work together to play a role in carbon capture and sequestration.

"At some point, we could employ a MOF to capture CO2, followed by a catalyst converting it into something more beneficial," Farha suggested.

"A tandem system utilizing two distinct materials for two sequential steps could be the way forward."

"This could help us answer the question: 'What do we do with captured CO2?'" Khoshooei added. "Right now, the plan is to sequester it underground. But underground reservoirs must meet many requirements in order to safely and permanently store CO2. We wanted to design a more universal solution that can be used anywhere while adding economic value."

SciTechDaily, 08 May 2024

https://scitechdaily.com

Is hyaluronic acid as effective at hydration and moisturising as skincare brands claim?

2024-03-23

Hyaluronic acid has become a huge buzzword in the beauty industry, with everything from creams and cleansers to shampoos containing it.

Often, these products are marketed to consumers with the promise that hyaluronic acid will boost hydration — important for keeping the skin looking its best.

Hyaluronic acid is ubiquitous in our organs and tissues, playing a crucial role in the function of our cells and tissues. It has been in clinical use for decades, for example, as an injectable between joints to help lubricate cartilage.

But at the turn of the century, cosmetic companies began using it as a moisturising ingredient in cosmetic products.

Topically, it's thought that hyaluronic acid works by holding and retaining water molecules in order to hydrate the skin and restore elasticity, preventing wrinkles.

When combined with sunscreen, hyaluronic acid may be capable of protecting the skin against ultraviolet radiation as it has antioxidant properties (meaning it prevents damage caused by oxidising agents, such as ultraviolet radiation).

Is it just hyaluronic hype?

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

One of the most frequent marketing claims used to sell hyaluronic acid is the long-held belief that hyaluronic acid holds 1,000 times its weight in water.

This means it can maintain moisture and reduce moisture loss.

But this claim has been called into question recently, with numerous publications recently discussing the findings of a pre-print paper which suggests this claim is not true.

The authors of the pre-print, researchers from the University of California, looked into the molecule-binding properties of hyaluronic acid and water to test the claim that it can hold 1,000 times its weight in water.

To do this, the researchers created a solution containing 1g of hyaluronic acid and 1,000g of water (0.1 per cent of hyaluronic acid), which was compared with just water.

They then applied heat to both solutions, measuring the thermal changes that occurred.

They found that there was not much difference in the changes that occurred in the 0.1 per cent hyaluronic acid solution compared with the pure water. They therefore concluded that the long-held claim is not true.

These findings may have consumers wondering how well their hyaluronic acid products actually work if it doesn't hydrate the skin as much as previously claimed.

How hyaluronic acid works

While there's no disputing the experimental results obtained, the conclusion on hyaluronic acid's water-holding capacity is not applicable to all forms of hyaluronic acids.

Hyaluronic acid comes in different molecular sizes. This pre-print only looked at one medium-sized hyaluronic acid molecule in their experiments. This means the results may only be true for products containing medium and smaller hyaluronic acid molecules.

When hylauronic acid interacts with water, its water-loving and water-hating parts lead to electrostatic repulsion. This enables large numbers of hyaluronic acid molecules to form networks, which look a bit like honeycombs, and expand.

The larger the hyaluronic acid's molecule size, the more capable it is of forming these honeycomb structures — and also the more able it is to retain water relative to its own weight.

Hyaluronic acid with larger molecular sizes will form these networks at a concentration of 0.1 per cent, meaning it can hold 1,000 times its own weight in water. Some very large molecules will even form these networks at a concentration as low as 0.05 per cent. This means it can hold 2,000 times its weight in water.

It's also worth noting that hyaluronic acid doesn't just hold moisture and hydrate the skin. Because of its hydrating and antioxidant effects, it also promotes cell regeneration and stimulates collagen production. So hyaluronic acid's benefits go beyond its ability to retain water.

Although this paper may have partially debunked one popular claim about hyaluronic acid's moisturising abilities, that doesn't mean you should stop using it.

The research still shows there's no doubt about hyaluronic acid's moisturising abilities, which can leave skin softer, smoother and with fewer wrinkles. Plus, hyaluronic acid's antioxidant effects promote the growth of new skin cells and collagen.

But if you want to make sure you're getting the most effective product possible, look for one containing multiple weights of hyaluronic acid molecules (sometimes labelled as "triple weight", "multiweight" or "multi-molecular weight").

Also look for a product containing a minimum hyaluronic acid concentration of 0.1 per cent.

This is because research suggests products containing a formulation of multiple sizes of hyaluronic acid molecules could be more beneficial for skin than formulations containing only one molecule size. This is partly due to smaller molecules permeating skin better, while the larger ones hold more water.

ABC News, 23 March 2024

https://abc.net.au

CHEMWATCH
Bulletin Board
Curiosities
MAY. 10, 2024

Century-Old Chemistry Puzzle Solved: Researchers Unveils Game-Changing Compound

2024-05-08

Harnessing these molecules can significantly impact agriculture, pharmaceuticals, and electronics.

Chemists at the University of Minnesota Twin Cities College of Science and Engineering have successfully synthesized a highly reactive chemical compound that has eluded sicentists for over 120 years. This breakthrough may pave the way for the development of innovative drug treatments, safer agricultural products, and enhanced electronics.

For decades, researchers have been investigating molecules called N-heteroarenes, which are ring-shaped chemical compounds that contain one or more nitrogen atoms. Bio-active molecules having a N-heteroarene core are widely used for numerous medicinal applications, lifesaving pharmaceuticals, pesticides and herbicides, and even electronics.

"While the average person does not think about heterocycles on a daily basis, these unique nitrogen-containing molecules are widely applied across all facets of human life," said Courtney Roberts, the senior author of the study and a University of Minnesota Department of Chemistry assistant professor who holds the 3M Alumni Professorship.

Challenges in Chemical Synthesis

These molecules are highly sought out by many industries, but are extremely challenging for chemists to make. Previous strategies have been able to target these specific molecules, but scientists have not been able to create a series of these molecules. One reason for this is that these molecules are extremely reactive. They are so active that chemists have used computational modeling to predict that they should be impossible to make. This has created challenges for more than a century and prevented a solution to create this chemical substance.

"What we were able to do was to run these chemical reactions with specialized equipment while getting rid of elements commonly found in our atmosphere," said Jenna Humke, a University of Minnesota chemistry graduate student and lead author on the paper. "Luckily, we have the tools to do that at the University of Minnesota. We ran experiments under nitrogen in a closed-chamber glovebox, which creates a chemically inactive environment to test and move samples."

Curiosities

These experiments were accomplished by using organometallic catalysis—the interaction between metals and organic molecules. The research required collaboration between both organic and inorganic chemists. This is something that is common at the University of Minnesota.

"We were able to solve this long-standing challenge because the University of Minnesota Department of Chemistry is unique in that we don't have formal divisions," Roberts added. "This allows us to put together a team of experts in all fields of chemistry, which was a vital component in completing this project"

After introducing the chemical compound in this paper, the next steps will be to make it widely available to chemists across multiple fields to streamline the creation process. This could help solve important problems like preventing food scarcity and treating illnesses to save lives.

Reference: "Nickel binding enables isolation and reactivity of previously inaccessible 7-aza-2,3-indolynes" by Jenna N. Humke, Roman G. Belli, Erin E. Plasek, Sallu S. Kargbo, Annabel Q. Ansel and Courtney C. Roberts, 25 April 2024, Science.

DOI: 10.1126/science.adi1606

Along with Roberts and Humke, the University of Minnesota research team included postdoctoral researcher Roman Belli, graduate students Erin Plasek, Sallu S. Kargbo, and former postdoctoral researcher Annabel Ansel.

This work was primarily funded by the National Institutes of Health and the National Science Foundation. Funding was also provided by four University of Minnesota-sponsored graduate research fellowships and start-up funding provided by the Department of Chemistry.

SciTechDaily, 08 May 2024

https://scitechdaily.com

CHEMWATCH
Bulletin Board

Technical Notes

(NOTE: OPEN YOUR WEB BROWSER AND CLICK ON HEADING TO LINK TO SECTION)

CHEMICAL EFFECTS

Advanced applications of hydroxyapatite nanocomposite materials for heavy metals and organic pollutants removal by adsorption and photocatalytic degradation: A review

Marine degradation and ecotoxicity of conventional, recycled and compostable plastic bags

Development of an Automated Morphometric Approach to Assess Vascular Outcomes following Exposure to Environmental Chemicals in Zebrafish

ENVIRONMENTAL RESEARCH

Presence of polycyclic aromatic hydrocarbons and persistent organochlorine pollutants in human Milk: Evaluating their levels, association with Total antioxidant capacity, and risk assessment

Co-composting of green waste and biogas waste: physical, chemical parameters and quality of ripe compound

PHARMACEUTICAL/TOXICOLOGY

Can on-site leachate treatment facilities effectively address the issue of perfluoroalkyl acids (PFAAs) in leachate?

Oxidation of chromium( ): A potential risk of using chemical oxidation processes for the remediation of 2-chlorophenol contaminated soils

OCCUPATIONAL

Occupational radiation exposure among medical personnel in university and general hospitals in Japan

Maternal-Fetal Exposure to Antibiotics: Levels, Mother-to-Child Transmission, and Potential Health Risks

Association between long-term exposure to fine particulate matter and its chemical constituents and premature death in individuals living with HIV/AIDS