Bio News – February, 2020

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

1/3　明けまして。パンダマウス　日本産 生物遺伝資源　江戸時代からはるかな旅

https://newstsukuba.jp/?p=20825

1/3　卵巣の黄体を詳しく調査　オオヤマネコ繁殖に応用へ -独ライプニッツ動物園野生動物研究所

https://www.jiji.com/jc/article?k=2020010300395&g=int

1/4　破産した uBiome の資産を韓国の Macrogen が取得～微生物情報事業の主軸に

1/4　Illumina（カリフォルニア州サンディエゴ）が Pacific Biosciences（PacBio）（カリフォルニア州メンローパーク）を約 12 億ドルで買収する合意が取り消しに

Illumina は PacBio を買収することによって米国の次世代 DNA 配列読み取り装置（NGS）市場独占を非合法的に維持しようとしているとしてアメリカ連邦取引委員会（FTC）が先月その買収を阻止する決定を発表。

https://www.pacb.com/press_releases/illumina-and-pacific-biosciences-announce-termination-of-merger-agreement/

https://www.fiercebiotech.com/medtech/illumina-calls-it-quits-after-ftc-blocks-its-1-2b-offer-for-pacbio

1/6　AI搭載ロボが執刀と予測も　普及広がるロボット支援手術　次世代型開発へ競争激化

https://feedclass.com/posts/Bw5FMVpb

1/6　10 万人の患者の全ゲノム解析がスタート がんや難病の新治療法開発を目指す -国立がん研究センターなど国内の医療研究機関が連携

https://seiyakuonlinenews.com/news/223250/

1/7　免疫細胞活性化、鍵は「繊維」 仕組み一端解明、がん治療活用つながる可能性 -京大グループ

https://www.kyoto-np.co.jp/articles/-/113985

1/8　iPS 細胞分化時に異常　がん化関連も　容器、機関で差

https://mainichi.jp/articles/20200107/k00/00m/040/434000c

1/8　武田薬品がマサチューセッツ工科大学（MIT）に AI 創薬拠点を開設

人工知能（AI）技術をヒトの健康や薬の開発に役立てる武田薬品とマサチューセッツ工科大学（MIT）の提携 MIT–Takeda Program が発足。

http://news.mit.edu/2020/mit-school-engineering-takeda-join-to-advance-artificial-intelligence-health-research-0106

1/9　知の統合を目指す nference（マサチューセッツ州ケンブリッジ）– メイヨークリニックなどから 6,000 万ドルを調達

https://aitimes.media/2020/01/13/3920/

1/9　米国の若い成人の HPV ワクチン接種率が 2018 年までの 6 年間に約 2 倍の 40%に上昇

1/10　米国の癌死亡率がピークの 1991 年から 2017 年に 29%低下～肺癌死亡率低下が貢献

https://www.statnews.com/2020/01/08/u-s-cancer-death-rate-drops-by-largest-annual-margin-ever-report-says/

1/11　Pfizer が Scripps Research Institute（フロリダ州）の微生物収蔵に 21 万株を超える微生物を寄贈

1/13　iPS 細胞の一部で異常　京大提供、研究機関で培養

1/13　武漢に続き深センで新たな「新型ウイルス」か　肺炎の女性重症
中国外初、タイでも新型ウイルス検出

https://www.sciencemag.org/news/2020/01/mystery-virus-found-wuhan-resembles-bat-viruses-not-sars-chinese-scientist-says?utm_campaign=news_daily_2020-01-10&et_rid=375979900&et_cid=3159080

1/14　全ゲノム配列データ、「量子暗号」で伝送に成功 –東芝と東北大

https://headlines.yahoo.co.jp/hl?a=20200114-00000000-mai-sctch

1/15　睡眠中には脳内から“毒素”が洗い流される：米研究チームがメカニズムを解明、アルツハイマー病の治療に光

https://headlines.yahoo.co.jp/article?a=20200115-00010001-wired-sctch

1/16　遺伝子編集企業 Emendo に提携会社・武田薬品や AnGes 等が 6,100 万ドル投資

1/16　腹膜と一定距離で再発リスク高まる　胃がん手術後の患者 –大阪市立大

https://www.jiji.com/jc/article?k=20200116008999&g=soc

1/16　大腸菌の代謝系を改変し、ナイロン原料の生産性 8 倍 –神戸大など

https://headlines.yahoo.co.jp/hl?a=20200116-00010000-sportal-sctch

1/17　Biogen が数週間以内にアルツハイマー病薬を承認申請か？

1/17　Concerto Health AI が Pfizer、J&J と提携し、1 億 5,000 万ドル調達

1/17　ドイツの BioNTech が抗癌 T 細胞治療の Neon Therapeutics を 6,700 万ドルで取得

1/18　世界の死亡数の 5 分の 1 が敗血症による

新たな解析の結果、全世界でこれまでの予想より 2 倍多い 4,890 万人が 2017 年に敗血症を被り、世界の全死亡数の約 20%を占める 110 万人が敗血症で死亡したと推定された。

世界の敗血症の発現率や敗血症による死亡率は 1990 年から 2017 年にそれぞれ 37%と 53%低下したとはいえ、1 分間あたり 20 人以上が敗血症で亡くなっている。

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32989-7/fulltext

1/20　新型肺炎患者 韓国で初確認　武漢から入国の中国人女性
北京と広東省でも 3 人の発症確認

1/21　脳内の重要分子を可視化　治療法開発に期待 -横浜市大など

https://headlines.yahoo.co.jp/hl?a=20200121-00000004-jij-sctch

1/21　人工タンパク貼り難治性潰瘍を治療　京都大など素材開発

1/22　「赤ちゃんの頭の形外来」新設 -福岡の病院

1/23　液体のり成分、がん治療に　効果大幅向上 -東工大など

https://headlines.yahoo.co.jp/hl?a=20200123-00000004-jij-sctch

1/23　ストレスで白髪、メカニズム解明 -ハーバード大研究チーム

https://headlines.yahoo.co.jp/hl?a=20200123-00000055-jij-sctch

1/23　活性酸素少ない細胞からヒト iPS 細胞作製で、DNA 損傷抑えられる -日・カナダの研究チームが発表

https://headlines.yahoo.co.jp/hl?a=20200123-00000056-mai-sctch

1/23　Moderna が新種コロナウイルスへのワクチンに米国と協力して取り組んでいる

去年の暮れから中国を始めとするアジアで広がっている新種のコロナウイルス（2019 Novel Coronavirus；2019-nCoV）感染に対向するワクチンに Moderna（マサチューセッツ州ケンブリッジ）が米国政府と協力して取り組んでいる。米国立衛生研究所（NIH）がワクチン開発に着手しており、臨床試験が始まるのは数カ月先になると CNN に話している。
2019-nCoV は米国にも既に到達しており、同国で初の 2019-nCoV 感染例を CDC が 21 日に発表。その感染は、中国の流行地・湖北省武漢市から帰国した男性に認められた。
また、当初 2019-nCoV 感染は動物から人に広まっているとされていたが、人から人にも広まりうることが分かっている。

https://www.fiercepharma.com/vaccines/vaccine-researchers-kick-off-work-against-new-coronavirus-cnn

1/23　Eli Lilly が 4 億 7,000 万ドルを投じてノースカロライナ州に注射剤工場を建設

1/24　アステラス製薬との日本での合弁会社 Amgen Astellas BioPharma を Amgen が完全に取得

1/24　「新型肺炎の感染規模は SARS の 10 倍」香港の専門家、「武漢はすでに制御不能」と絶望

https://headlines.yahoo.co.jp/hl?a=20200124-00000002-binsiderl-sctch

1/24　iPS 軟骨の膝移植、厚労省が承認　京大、今年中にも移植術

1/24　新型肺炎 日本国内で 2 例目 中国で感染拡大、WHO は各国に警戒呼びかけ

1/25　受精卵検査、拡大を議論　治療法ない遺伝病に −産科婦人科学会

1/27　iPS 心筋移植を実施　重症心臓病患者に世界初 −阪大

1/28　O157 新薬開発に期待　大腸菌の「呼吸酵素」構造解明 −九州工業大らグループ

1/28　米食品大手ケロッグ、除草剤グリホサート段階的廃止へ 2025 年目標

https://headlines.yahoo.co.jp/hl?a=20200128-00000026-jij_afp-sctch

1/28　J&J が中国の新型コロナウイルスに対するワクチンに取り組んでいる

Moderna や Gilead Sciences 等と同様に J&J も中国の新型コロナウイルス 2019-nCoV に取り組んでおり、できるだけ早く新たなワクチンを作るつもりだと同社最高科学責任者（CSO）Paul Stoffels 氏が米国の放送 CNBC に話している。

1/28　中国が新型コロナウイルス 2019-nCoV に AbbVie の HIV 薬 Aluvia を試している

中国で広がる新型コロナウイルス 2019-nCoV による肺炎への対処法として同国政府が AbbVie の抗ウイルス薬 lopinavir/ritonavir（商品名 Aluvia または Kaletra）服用や α インターフェロン吸入を示唆しており、AbbVie は HIV 治療に使われている lopinavir/ritonavir を中国に 150 万ドル相当分寄付する。

1/29　中国での新型コロナウイルス感染者数はおよそ 6,000 人に増え、132 人が死亡

1/30　WHO、新型肺炎で緊急委再招集

1/30　がん免疫療法の効果有無、事前に判定　ノーベル賞の本庶氏らグループ発見

https://headlines.yahoo.co.jp/hl?a=20200130-00249056-kyt-sctch

1/30　iPS 免疫細胞でがん治療　理研などが治験計画を千葉大に申請

https://headlines.yahoo.co.jp/hl?a=20200130-00000531-san-sctch

1/30　中国との間柄について虚偽のあったハーバード大学トップ化学者 Charles Lieber 氏を米国が逮捕

1/31　新型肺炎 日本国内の感染者 14 人に

1/31　何年か下がり続けた米国人の寿命が上向き始めた～2018 年の寿命は 2017 年から 0.1 年延びて 78.7 歳

1/31　Accenture の生命科学企業向け情報サービスと Google の解析/AI 技術が合体

1/31　WHO、緊急事態を宣言　渡航・貿易制限は勧告せず　新型肺炎

【ベルリン時事】世界保健機関（WHO）は 30 日、中国を中心に拡大している新型コロナウイルス感染による肺炎について緊急委員会を開き「国際的に懸念される公衆衛生上の緊急事態」に当たると宣言した。
中国での感染者の急増に加え、日本や米国、ドイツなどでも人から人への感染が発生していることを重く見て、これまで見送っていた宣言に踏み切った。

テドロス事務局長は 30 日、ジュネーブで記者会見し、WHO が確認した中国外での感染例は 98 件とまだ限定的なものの「これ以上の感染拡大阻止のため一致して行動すべき時だ」と表明した。一方で「不必要に人やモノの移動を制限する理由はない」として、感染地への渡航や貿易を制限する勧告は行わないと強調した。
今回の勧告では、こうした措置を加盟国が取る場合「リスクと費用対効果の分析」を行った上で判断すべきだと促す内容にとどめた。事実上各国の裁量に任せている。このほか感染源特定に向けた研究での国際協力や、低所得国への支援などを求めた。緊急事態が宣言されると、加盟各国は情報共有の義務を負うが、勧告に拘束力はない。
また、テドロス氏は、中国は感染封じ込めに「並外れた措置を取った」などと高く評価した。中国に対しては、国民への情報公開や国際社会との情報共有、WHO の専門家チームと協力した調査などの継続を勧告した。
宣言に踏み切った理由としては「医療制度の弱い国に広がったらどうなるか、この危険性を最も懸念している」とテドロス氏は指摘した。中国と経済的な結び付きを持たない国は世界にほとんどなくなった。感染者が確認された国が日々増える事態に一定の危機意識を示した。
WHO による緊急事態宣言は、現在の制度が整備された 2005 年以来で 6 件目となった。過去には、09 年の新型インフルエンザや、昨年のエボラ出血熱などで宣言が出されている。

企業関連ニュース/他のトップページに戻る

今月の研究関連ニュース/他

1. ドーパミン、体内時計とスナック、過食、肥満との関連

2. 米国の肥満蔓延は加工食品摂取と多いに関連

3. 後期敗血症の新治療法

4. 母親の腸内微生物に由来する抗体 −マウス研究
   母親の腸内微生物に由来する抗体が新生児を大腸菌感染から保護

5. 分子「ドアマン」が潜在的な肥満治療への道を開く

6. 運動の代わりになる？

7. アルコール依存によって脳全体の機能構造が改造される −マウス実験

8. 大豆油は脳に遺伝的変化をもたらす −マウス実験
   代謝や神経学的変化にもリンク

9. ケトダイエットに関するマウス研究

1. ドーパミン、体内時計とスナック、過食、肥満との関連

日付：2020 年 1 月 3 日
ソース：バージニア大学
概要：

バージニア大学の新しい研究では、脳の快楽の中枢と脳の体内時計は結び付いており、脳に快楽をもたらす高カロリーの食物が通常の摂食スケジュールを混乱させ、結果として過剰摂取を引き起こす、としている。
1976 年から 1980 年の間、米国成人の 15%が肥満であった。それが現在では、成人の約 40%が肥満、そして 33%は肥満とまではいかなくても過体重だとされる。また、この体重増加と並行して、高血圧など肥満によって引き起こされる心臓病、糖尿病、癌、合併症も増加している。アルツハイマー病でさえ、肥満と身体的不活性に一部起因している可能性がある。
1 月 2 日の *Current Biology* 誌に発表された研究で、バージニア大学の生物学教授のアリ・ギュラー氏と彼の同僚らは、化学ドーパミンを生成する脳の快楽センターと、毎日の生理学的リズムを調節する脳の独立した生物時計がリンクしていること、脳に快楽をもたらす高カロリー食品が通常の食餌スケジュールを混乱させ、過剰消費をもたらすことをマウスを用いて実証している。研究者らは、カロリーと脂肪において野生の食餌に匹敵するものを与えられたマウスは、通常の食餌と運動スケジュール、および適切な体重を維持していることを発見、また脂肪や糖分を多く含んだ高カロリー食を与えられたマウスは、全ての時間で「スナッキング」を始め肥満になった、としている。更に、ドーパミンシグナル伝達が絶たれた所謂「ノックアウト」マウスは、高脂肪食による快楽を求めず、通常の食餌スケジュールを維持し肥満にはならなかった。
加えて、ギュラー教授は、電力社会の到来によって、我々は昼夜を問わず仕事、遊び、食事をしており、これが、日中の活動、適度な食事、夜間の休憩に合わせた睡眠覚醒サイクルで動作するように進化した体内時計に影響を与えているとも、言っている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200103111717.htm

Study finds dopamine, biological clock link to snacking, overeating and obesity

Date:

January 3, 2020

Source:

University of Virginia

Summary:

A new study finds that the pleasure center of the brain and the brain's biological clock are linked, and that high-calorie foods -- which bring pleasure -- disrupt normal feeding schedules, resulting in overconsumption.

FULL STORY

Clock and eating concept (stock image).

Credit: © nehopelon / Adobe Stock

During the years 1976 through 1980, 15% of U.S. adults were obese. Today, about 40% of adults are obese. Another 33% are overweight.

Coinciding with this increase in weight are ever-rising rates of heart disease, diabetes, cancer and health complications caused by obesity, such as hypertension. Even Alzheimer's disease may be partly attributable to obesity and physical inactivity.

"The diet in the U.S. and other nations has changed dramatically in the last 50 years or so, with highly processed foods readily and cheaply available at any time of the day or night," Ali Güler, a professor of biology at the University of Virginia, said. "Many of these foods are high in sugars, carbohydrates and calories, which makes for an unhealthy diet when consumed regularly over many years."

In a study published Thursday in the journal *Current Biology*, Güler and his colleagues demonstrate that the pleasure center of the brain that produces the chemical dopamine, and the brain's separate biological clock that regulates daily physiological rhythms, are linked, and that high-calorie foods -- which bring pleasure -- disrupt normal feeding schedules, resulting in overconsumption. Using mice as study models, the researchers mimicked the 24/7 availability of a high-fat diet, and showed that anytime snacking eventually results in obesity and related health problems.

Güler's team found that mice fed a diet comparable to a wild diet in calories and fats maintained normal eating and exercise schedules and proper weight. But mice fed high-calorie diets laden with fats and sugars began "snacking" at all hours and became obese.

Additionally, so-called "knockout" mice that had their dopamine signaling disrupted -- meaning they didn't seek the rewarding pleasure of the high-fat diet -- maintained a normal eating schedule and did not become obese, even when presented with the 24/7 availability of high-calorie feeds.

"We've shown that dopamine signaling in the brain governs circadian biology and leads to consumption of energy-dense foods between meals and during odd hours," Güler said.

Other studies have shown, Güler said, that when mice feed on high-fat foods between meals or during what should be normal resting hours, the excess calories are stored as fat much more readily than the same number of calories consumed only during normal feeding periods. This eventually results in obesity and obesity-related diseases, such as diabetes.

Speaking of the modern human diet, Güler said, "The calories of a full meal may now be packed into a small volume, such as a brownie or a super-size soda. It is very easy for people to over-consume calories and gain excessive weight, often resulting in obesity and a lifetime of related health problems.

"Half of the diseases that affect humans are worsened by obesity. And this results in the need for more medical care and higher health care costs for individuals, and society."

Güler said the human body, through thousands of years of evolution, is hard-wired to consume as much food as possible as long as it's available. He said this comes from a long earlier history when people hunted or gathered food and had brief periods of plenty, such as after a kill, and then potentially lengthy periods of famine. Humans also were potential prey to large animals and so actively sought food during the day, and sheltered and rested at night.

"We evolved under pressures we no longer have," Güler said. "It is natural for our bodies as organisms to want to consume as much as possible, to store fat, because the body doesn't know when the next meal is coming.

"But, of course, food is now abundant, and our next meal is as close as the kitchen, or the nearest fast-food drive-through, or right here on our desk. Often, these foods are high in fats, sugars, and therefore calories, and that's why they taste good. It's easy to overconsume, and, over time, this takes a toll on our health."

Additionally, Güler said, prior to the advent of our electricity-powered society, people started the day at dawn, worked all day, often doing manual labor, and then went to sleep with the setting of the sun. Human activity, therefore, was synchronized to day and night. Today, we are working, playing, staying connected -- and eating -- day and night. This, Guler said, affects our body clocks, which were evolved to operate on a sleep-wake cycle timed to daytime activity, moderate eating and nighttime rest.

"This lights-on-all-the-time, eat-at-any-time lifestyle recasts eating patterns and affects how the body utilizes energy," he said. "It alters metabolism -- as our study shows -- and leads to obesity, which causes disease. We're learning that when we eat is just as important as how much we eat. A calorie is not just a calorie. Calories consumed between meals or at odd hours become stored as fat, and that is the recipe for poor health."

The National Institute of General Medical Sciences and University of Virginia Brain Institute funded the research.

Story Source:

Materials provided by **University of Virginia**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Ryan M. Grippo, Qijun Tang, Qi Zhang, Sean R. Chadwick, Yingnan Gao, Everett B. Altherr, Laura Sipe, Aarti M. Purohit, Nidhi M. Purohit, Meghana D. Sunkara, Krystyna J. Cios, Michael Sidikpramana, Anthony J. Spano, John N. Campbell, Andrew D. Steele, Jay Hirsh, Christopher D. Deppmann, Martin Wu, Michael M. Scott, Ali D. Güler. **Dopamine Signaling in the Suprachiasmatic Nucleus Enables Weight Gain Associated with Hedonic Feeding**. *Current Biology*, 2020; DOI: 10.1016/j.cub.2019.11.029

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2. 米国の肥満蔓延は加工食品摂取と多いに関連

日付：2020 年 1 月 6 日
ソース：ジョージワシントン大学
概要：

米国で消費される食品がますます加工化されるにつれて、肥満が蔓延する可能性がある。ジョージワシントン大学（GW）の研究者、Leigh A. Frame（PhD、MHS）は、食品の全体的な傾向をレビューすることで、より安くて便利ではあるが同時に高度に加工されている食品を優先する消費者には、食事の質と全体的な栄養を改善するための詳細な推奨事項が必要であると結論付けた。この結論は、*Current Treatment Options in Gastroenterology* 誌のレビュー記事として掲載されている。
米国で増加している肥満の蔓延とそれに関連する慢性疾患は、超加工食品の消費の増加と相関している。体重増加に最も関連する食品には、ポテトチップス、砂糖入り飲料、お菓子やデザート、精製された穀物、赤身の肉、加工肉が含まれ、その対極は、全粒穀物、果物、野菜である。報告書で概説されている他の食品トレンドには、食物繊維の摂取不足、乳化剤などの食品添加物の劇的な増加、特に女性における高い肥満有病率が含まれている。
マウスおよび in vitro 試験では、加工食品に含まれる乳化剤が、腸内微生物の組成を変化させ、空腹時血糖を上昇させ、過食を引き起こし、体重増加と脂肪過多を増加させ、肝臓脂肪症を誘発することがわかっている。最近のヒトでの試験では、超加工食品が、満腹感の低下、食事摂取率の増加（速度）、炎症やコレステロールを含む生化学マーカーの悪化、および体重増加と関連することが分かった。対照的に、肉が少なく、繊維が多く、加工食品が最小限の「ブルーゾーン」の人口は、慢性疾患、肥満率がはるかに少なく、無病生活が長くなる、ともしている。
著者らは、肥満や関連疾患の症状を薬物治療だけで治療するのではなく、食物を薬として使用する努力を含める必要があり、慢性疾患はライフスタイルと食事の影響を強く受けるため、米国の肥満と慢性疾患の減少には、加工食品の制限と野菜、豆類、ナッツ、果物、水の摂取量の増加が必要だ、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-01/gwu-pfh010620.php

NEWS RELEASE 6-JAN-2020

Processed foods highly correlated with obesity epidemic in the US

GEORGE WASHINGTON UNIVERSITY

WASHINGTON (Jan. 6, 2020) -- As food consumed in the U.S. becomes more and more processed, obesity may become more prevalent. Through reviewing overall trends in food, George Washington University (GW) researcher Leigh A. Frame, PhD, MHS, concluded that detailed recommendations to improve diet quality and overall nutrition are needed for consumers, who are prioritizing food that is cheaper and more convenient, but also highly processed. Her conclusions are published in a review article in *Current Treatment Options in Gastroenterology*.

"When comparing the U.S. diet to the diet of those who live in "blue zones" - areas with populations living to age 100 without chronic disease - the differences are stark," said Frame, co-author of the article, program director for the Integrative Medicine Programs, executive director of the Office of Integrative Medicine and Health, and assistant professor of clinical research and leadership at the GW School of Medicine and Health Sciences. "Many of the food trends we reviewed are tied directly to a fast-paced U.S. lifestyle that contributes to the obesity epidemic we are now facing."

The rising obesity epidemic in the U.S., as well as related chronic diseases, are correlated with a rise in ultra-processed food consumption. The foods most associated with weight gain include potato chips, sugar sweetened beverages, sweets and desserts, refined grains, red meats, and processed meats, while lower weight gain or even weight loss is associated with whole grains, fruits, and vegetables. Other food trends outlined in the report include insufficient dietary fiber intake, a dramatic increase in food additives like emulsifiers and gums, and a higher prevalence of obesity, particularly in women.

In mice and in vitro trials, emulsifiers, found in processed foods, have been found to alter microbiome compositions, elevate fasting blood glucose, cause hyperphagia, increase weight gain and adiposity, and induce hepatic steatosis. Recent human trials have linked ultra-processed foods to decreased satiety (fullness), increased meal eating rates (speed), worsening biochemical markers, including inflammation and cholesterol, and more weight gain. In contrast, populations with low meat, high fiber, and minimally processed foods -- the "blue zones" -- have far less chronic diseases, obesity rates, and live longer disease-free.

"Rather than solely treating the symptoms of obesity and related diseases with medication, we need to include efforts to use food as medicine," said Frame. "Chronic disease in later years is not predestined, but heavily influenced by lifestyle and diet. Decreasing obesity and chronic disease in the U.S. will require limiting processed foods and increasing intake of whole vegetables, legumes, nuts, fruits, and water. Health care providers must also emphasize lifestyle medicine, moving beyond 'a pill for an ill.' "

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Janese Laster, MD, a gastroenterologist in Washington, D.C., also co-authored the report. The project was conducted independently and did not receive outside funding.

"Beyond the Calories--Is the Problem in the Processing?" was published in *Current Treatment Options in Gastroenterology* and is available at link.springer.com/article/10.1007%2Fs11938-019-00246-1.

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3. 後期敗血症の新治療法

日付:2020 年 1 月 6 日
ソース:オハイオ州立大学
概要:

敗血症は、感染に対する身体の極端な反応に起因する致命的な疾患である。特に後期になると、免疫系が損なわれ、侵入細菌を除去できなくなる。
今回オハイオ州立大学の研究者らは、ナノテクノロジーを用いて、健康な免疫細胞を細菌を殺す力が強化された薬に変換し、この後期敗血症との闘いを可能にすることに成功した。敗血症のマウスを治療する実験では、人工免疫細胞が血液および主要臓器の細菌を除去し、生存率を劇的に改善した、としている。
この研究では、脂質ナノ粒子を作るための主成分としてビタミンを使用することと、新しい抗菌薬の作成において天然の細胞プロセスを利用するためにそれらのナノ粒子を使用することの 2 つの主要な技術を組み合わせている。
この研究は、1 月 6 日の *Nature Nanotechnology* 誌で発表されている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200106122000.htm

Finding a new way to fight late-stage sepsis

Researchers manipulate natural process to boost cells' antibacterial properties

Date:

January 6, 2020

Source:

Ohio State University

Summary:

Researchers have developed a way to prop up a struggling immune system to enable its fight against sepsis, a deadly condition resulting from the body's extreme reaction to infection.

FULL STORY

Researchers have developed a way to prop up a struggling immune system to enable its fight against sepsis, a deadly condition resulting from the body's extreme reaction to infection.

The scientists used nanotechnology to transform donated healthy immune cells into a drug with enhanced power to kill bacteria.

In experiments treating mice with sepsis, the engineered immune cells eliminated bacteria in blood and major organs, dramatically improving survival rates.

This work focuses on a treatment for late-stage sepsis, when the immune system is compromised and unable to clear invading bacteria. The scientists are collaborating with clinicians specializing in sepsis treatment to accelerate the drug-development process.

"Sepsis remains the leading cause of death in hospitals. There hasn't been an effective treatment for late-stage sepsis for a long time. We're thinking this cell therapy can help patients who get to the late stage of sepsis," said Yizhou Dong, senior author and associate professor of pharmaceutics and pharmacology at The Ohio State University. "For translation in the clinic, we believe this could be used in combination with current intensive-care treatment for sepsis patients."

The study is published today (Jan. 6, 2020) in *Nature Nanotechnology*.

Sepsis itself is not an infection -- it's a life-threatening systemic response to infection that can lead to tissue damage, organ failure and death, according to The Centers for Disease Control and Prevention. The CDC estimates that 1.7 million adults in the United States develop sepsis each year, and one in three patients who die in a hospital have sepsis.

This work combined two primary types of technology: using vitamins as the main component in making lipid nanoparticles, and using those nanoparticles to capitalize on natural cell processes in the creation of a new antibacterial drug.

C Cells called macrophages are one of the first responders in the immune system, with the job of "eating" invading pathogens. However, in patients with sepsis, the number of macrophages and other immune cells are lower than normal and they don't function as they should.

In this study, Dong and colleagues collected monocytes from the bone marrow of healthy mice and cultured them in conditions that transformed them into macrophages. (Monocytes are white blood cells that are able to differentiate into other types of immune cells.)

The lab also developed vitamin-based nanoparticles that were especially good at delivering messenger RNA, molecules that translate genetic information into functional proteins.

The scientists, who specialize in messenger RNA for therapeutic purposes, constructed a messenger RNA encoding an antimicrobial peptide and a signal protein. The signal protein enabled the specific accumulation of the antimicrobial peptide in internal macrophage structures called lysosomes, the key location for bacteria-killing activities.

From here, researchers delivered the nanoparticles loaded with that messenger RNA into the macrophages they had produced with donor monocytes, and let the cells take it from there to "manufacture" a new therapy.

"Macrophages have antibacterial activity naturally. So if we add the additional antibacterial peptide into the cell, those antibacterial peptides can further enhance the antibacterial activity and help the whole macrophage clear bacteria," Dong said.

After seeing promising results in cell tests, the researchers administered the cell therapy to mice. The mouse models of sepsis in this study were infected with multidrug-resistant Staphylococcus aureus and E. coli and their immune systems were suppressed.

Each treatment consisted of about 4 million engineered macrophages. Controls for comparison included ordinary macrophages and a placebo. Compared to controls, the treatment resulted in a

significant reduction in bacteria in the blood after 24 hours -- and for those with lingering bacteria in the blood, a second treatment cleared them away.

Dong considers the lipid nanoparticle delivery of messenger RNA into certain kinds of immune cells applicable to other diseases, and his lab is currently working on development of cancer immunotherapy using this technology.

Story Source:

Materials provided by **Ohio State University**. Original written by Emily Caldwell. *Note: Content may be edited for style and length.*

Journal Reference:

1. Xucheng Hou, Xinfu Zhang, Weiyu Zhao, Chunxi Zeng, Binbin Deng, David W. McComb, Shi Du, Chengxiang Zhang, Wenqing Li, Yizhou Dong. **Vitamin lipid nanoparticles enable adoptive macrophage transfer for the treatment of multidrug-resistant bacterial sepsis**. *Nature Nanotechnology*, 2020; DOI: 10.1038/s41565-019-0600-1

Cite This Page:

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4. 母親の腸内微生物に由来する抗体 -マウス研究

母親の腸内微生物に由来する抗体が新生児を大腸菌感染から保護

日付:2020 年 1 月 8 日
ソース:ハーバード大学医学部
概要:

母乳が新生児へ有益な効果をもたらすこと、また、乳児を特定の感染症から保護する力があることについては、長年言われている。今回マウスで行われたハーバード大学医学部の研究は、その保護効果の少なくとも一部が驚くべきソース -母親の腸内微生物- から来ていることを示している。
Nature 誌で 1 月 8 日に公開された新しい研究では、母親の腸内の特定の 1 つの生物に反応して作られた抗体が、少なくとも 1 つの病気 -致命的ともされる大腸菌感染- による感染から新生児を保護するために、母乳と胎盤の両方を介して子孫に渡されることが示されている。更に母親が感染症に事前に罹ったことがない場合でも、腸内微生物叢が免疫を保護し、子孫に保護抗体を構築して渡すことができることを示唆している。
感染性下痢は、最も一般的には大腸菌やロタウィルスによるものであり、栄養失調の主原因で、5 歳未満の子供の世界的死因の第 2 位である。世界保健機構によると、年間 17 億人が感染し、52 万人以上の命が奪われている。
研究者らは、免疫システムの抗体産生工場である B 細胞を欠くように遺伝子操作された新生児マウスを使って研究。生まれたばかりのマウスの一部は、抗体産生 B 細胞なしで生まれた母親によって育てられたため、保護抗体を欠いていた。他の新生児マウスは、正常な免疫システムを持っている母親によって育てられた。すると、母親からの保護抗体にさらされたマウスは、そのような抗体にさらされなかったマウスよりも大腸菌感染に対してはるかに抵抗力があった。実際、彼らの腸には、母体抗体を欠く新生児マウスよりも大腸菌が 33 倍少なかった。対照的に、保護抗体にさらされなかった新生児マウスは、播種性大腸菌疾患を発症した、としている。

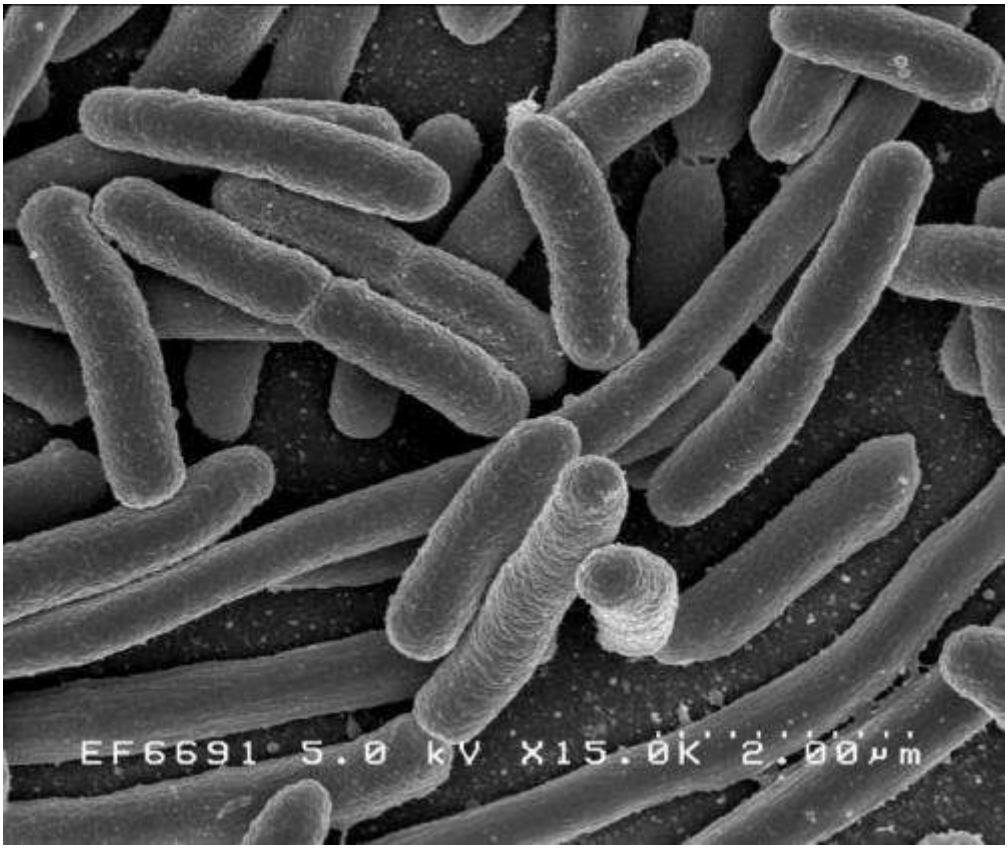
研究関連ニュース/他のトップページに戻る

＜英文＞https://medicalxpress.com/news/2020-01-mice-antibodies-derived-mom-gut.html

JANUARY 8, 2020

Research in mice shows antibodies derived from mom's gut microbes protect newborns from E. coli infection

by Harvard Medical School



Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH

Mother's milk has been long touted for its salutary effects on the newborn and its ability to shield infants from certain infections.

Now research from Harvard Medical School conducted in mice shows that at least part of its protective effects come from a surprising source: the microbes residing in maternal intestines.

The new study, published Jan. 8 in *Nature*, shows that antibodies made in response to one particular organism in the maternal gut are passed on to the offspring both via milk and through the placenta to protect newborn pups from infection by at least one disease-causing, and potentially lethal, microbe, *E. coli*.

The findings add to a growing body of evidence pointing to the potent role of the microbiota—the trillions of microbes that dwell in the gut, skin, mouth and other parts of the bodies of mammals, including humans—in disease and health.

But the new research goes a step further—it specifically identifies maternal microbiota as source of newborn immunity. It further suggests that the intestinal microbiota could offer immune protection even when mothers have had no prior encounters with an infection that allows them to build and pass on protective antibodies to their offspring.

"Our results help explain why newborns are protected from certain disease-causing microbes despite their underdeveloped immune systems and lack of prior encounters with these microbes," said study senior investigator Dennis Kasper, professor of

immunology in the Blavatnik Institute at Harvard Medical School. "Moreover, they raise the possibility that mothers can confer immune protection to their offspring even to pathogens that they haven't themselves encountered in the past."

If affirmed through further studies, the findings could inform the design of microbial therapies against dangerous infections such as *E. coli* and other disease-causing organisms, the researchers said.

"Albeit preliminary, we are hopeful these insights could inform the development of vaccines derived from commensal microbial molecules as a way to prevent infectious diseases," said Kasper, who is also the William Ellery Channing Professor of Medicine at Brigham and Women's Hospital. "Another therapeutic avenue could be the use of commensal microbes as probiotics that protect against diarrheal disease."

Infectious diarrhea—most commonly due to *E. coli* or rotavirus—is the leading cause of malnutrition and the second leading cause of death globally in children under age 5. It causes 1.7 billion infections and claims more than 520,000 lives a year worldwide, according to the World Health Organization.

Without any prior exposure to microbes, a newborn's immune system is a blank slate. For the first three weeks, a newborn's immune protection is derived entirely from maternal antibodies passed onto the fetus during pregnancy via the placenta, during birth via the birth canal, and shortly after birth via breastfeeding.

In the current study, researchers worked with newborn mice genetically engineered to lack B cells—the antibody-producing factories of the immune system. Some of the newborn mice were subsequently raised by mothers that were also born without antibody-making B cells, and therefore, lacked protective antibodies. The other newborn mice were raised by mothers that had normal immune systems.

Mice exposed to protective antibodies from their mothers were far more resistant to *E. coli* infection than mice that were not exposed to such antibodies. It was as if the pups repelled the pathogen, the researchers observed. Indeed, their intestines had 33 times fewer *E. coli* bacteria than newborn mice lacking maternal antibodies. By contrast, mice pups that were not exposed to protective antibodies developed disseminated *E. coli* disease.

The researchers were also able to pinpoint the specific organism responsible for inducing the formation of the protective antibodies—a microbe called Pantoea, member of the Enterobacteriaceae bacterial family, which resides in the intestines of mice and other mammals, including humans.

Furthermore, the experiments showed that the antibodies enter both the intestines and bloodstream of newborns via the neonatal Fc receptor, a molecular channel on the placenta that helps ferry protective antibodies from the mother to the growing fetus. Thus far, the receptor has been known to transfer antibodies through the placenta. However, the experiments conducted in the new study show this receptor also absorbs antibodies derived from milk and ferries them from the intestines and into the bloodstream of the newborn mice, ensuring wider, systemic protection beyond the gut.

Adult mice, in which this neonatal receptor loses its function with age, did not transfer protective antibodies from their gut to the bloodstream, the experiments showed.

Explore further

Antibodies in breast milk help newborn mice tolerate good gut microbes

More information: Microbiota-targeted maternal antibodies protect neonates from enteric infection, *Nature* (2020). DOI: 10.1038/s41586-019-1898-4 , https://nature.com/articles/s41586-019-1898-4

Journal information: Nature

Provided by Harvard Medical School

5. 分子「ドアマン」が潜在的な肥満治療への道を開く

日付：2020 年 1 月 10 日
ソース：イェール大学
概要：

脂肪細胞は、ホテルのドアマンのように機能する分子でコーティングされた滴で満たされている。これらの「ドアマン」は、栄養素や脂質と呼ばれるエネルギー供給分子の出口への細胞アクセスを制御する。健康な人では、脂肪細胞の出入りの交通量はバランスが取れており、エネルギーを供給しながら、腹部への望ましくない脂肪の過剰な拡散を防ぐ。ところが、肥満の人では、これらの細胞のドアマンは、内臓脂肪細胞として知られる特定の重要な脂肪細胞に対して非常に広くゲートを開き、最初に脂質を燃やすことなく炭水化物を過剰に入れた。これは、腹部の内臓脂肪細胞の大きさのバルーニングにつながり、その肥満が、心臓病、糖尿病、慢性肝疾患、およびその他の障害のリスク増加に関連している。
イェール大学の研究者らは、1 月 10 日、*Nature Communications* 誌で、この脂肪滴のドアマンの分子調節因子と、痩せた人に見られる健康的なバランスの回復に基づく肥満の新治療法を発見した、と報告している。
研究チームによると、これらの脂肪滴の歩哨の司令官は、O-GlcNAc トランスフェラーゼ（OGT）と呼ばれる酵素で、この酵素を欠くマウスは痩せており、脂肪細胞のサイズの劇的な減少を示し、より多くの炭水化物燃料を摂取するのではなく、最初に脂質を燃やす傾向がある。逆に、マウスでの OGT の過剰発現は、過剰な脂質を燃やさずに炭水化物の摂取量を増やすことで肥満を引き起こす、としている。研究者らは、OGT が肥満を薬学的に治療するための非常に魅力的なターゲットになる、と結論している。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200110073742.htm

Molecular 'doormen' open the way to potential obesity treatment

Date:

January 10, 2020

Source:

Yale University

Summary:

Fat cells are filled with droplets coated by molecules that act like hotel doormen: These 'doormen' control cellular access for nutrients as well as for the exit of energy-supplying molecules called lipids. In healthy individuals, outgoing and incoming traffic in fat cells is finely balanced, supplying energy while preventing excessive spread of undesirable fat in the belly.

FULL STORY

Fat cells are filled with droplets coated by molecules that act like hotel doormen: These "doormen" control cellular access for nutrients as well as for the exit of energy-supplying molecules called lipids. In healthy individuals, outgoing and incoming traffic in fat cells is finely balanced, supplying energy while preventing excessive spread of undesirable fat in the belly.

But in obese individuals, these cellular doormen have opened the gates far too wide in certain key fat cells, known as visceral fat cells, letting in too many carbohydrates without first burning off lipids. This leads to a ballooning of the size of visceral fat cells in the belly.

Obesity is linked to increased risk of heart disease, diabetes, and chronic liver disease, as well as other disorders.

Yale researchers report Jan. 10 in the journal *Nature Communications* that they have found the molecular regulator of this fat droplet doorman, and potential new treatments for obesity based on restoring healthy balance found in lean individuals.

The regulator, or commander, of these fat droplet sentinels is an enzyme called O-GlcNAc transferase (OGT), according to the research team. Mice lacking the enzyme are lean, exhibit a dramatic reduction in the size of fat cells and tend to burn off lipids first rather than taking in more carbohydrate fuel.

Conversely, the overexpression of OGT in mice triggers obesity by increasing intake of carbohydrates without burning off excess lipids.

"The commander of this doorman makes it easier for nutrients to get in, but harder for lipids to get out," said senior author Xiaoyong Yang, associate professor of comparative medicine and of cellular and molecular physiology at Yale University School of Medicine.

In previous studies, Yang's team found that overexpression of OGT in fat cells has another side effect -- it signals the brain to consume more calories (essentially asking the brain to order another pizza).

"This makes OGT a very attractive target to pharmaceutically treat obesity," Yang said.

Yale's Yunfan Yang is first author of the study, which was primarily funded by the National Institutes of Health.

Story Source:

Materials provided by **Yale University**. Original written by Bill Hathaway. *Note: Content may be edited for style and length.*

Journal Reference:

1. Yunfan Yang, Minnie Fu, Min-Dian Li, Kaisi Zhang, Bichen Zhang, Simeng Wang, Yuyang Liu, Weiming Ni, Qunxiang Ong, Jia Mi, Xiaoyong Yang. **O-GlcNAc transferase inhibits visceral fat lipolysis and promotes diet-induced obesity**. *Nature Communications*, 2020; 11 (1) DOI: 10.1038/s41467-019-13914-8

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6. 運動の代わりになる？

日付:2020 年 1 月 13 日
ソース:ミシガン大学医学部
概要:

公園を散歩したり、ジムで集中トレーニングをしたりと、運動は体に良い効果をもたらす。しかし、筋肉を動かさずに良いトレーニングの利点を活用できるとしたらどうだろう？
セストリンと呼ばれる天然に存在するタンパク質のクラスを研究しているミシガン大学医学部の研究者らは、セストリンがハエやマウスの運動の効果の多くを模倣できることを発見した。
運動後にセストリンが筋肉に蓄積することは以前から観察されていた。そこで彼らは、テストチューブを上ったり出たりというショウジョウバエの通常の本能を利用してハエを 3 週間訓練し、走行能力と飛行能力について、通常のハエとセストリンを作る能力を欠くように飼育されたハエを比較した。ハエはこの時点で約 4〜6 時間走ることができ、通常のハエの能力はその期間中に改善されたのに対して、セストリンのないハエでは運動しても改善されなかった。さらに、通常のハエの筋肉でセストリンを過剰発現させ、セストリンのレベルを最大にすると、それらのハエは訓練されたハエを超えて運動しなくても能力を持っていることがわかった。実際、過剰発現したセストリンを含むハエは、運動しても耐久性が向上しなかった。
セストリンの有益な効果には、持久力の向上以上のものが含まれる。セストリンのないマウスは、一般的に運動に関連する好気性能力、呼吸および脂肪燃焼の改善に欠けていた。
この独立した研究は、セストリンだけで運動の多くの利点を生み出すのに十分であることを強調しているものの、セストリンは小分子ではないため、セストリンのサプリメント開発のために、研究者らはその小分子モジュレーターを見付けるべく取り組んでいる、としている。また、運動がどのように体内でセストリンを生成するのかは分かっておらず、これが将来の研究にとって非常に重要であり、運動できない人の治療につながる可能性がある、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200113075830.htm

A replacement for exercise?

A protein called Sestrin might be responsible for many of the benefits of a good workout

Date:

January 13, 2020

Source:

Michigan Medicine - University of Michigan

Summary:

Researchers recently found that Sestrin, a naturally occurring protein in the body, mimicked the benefits of exercise in flies and mice.

FULL STORY

Mouse in exercise wheel (stock image).

Credit: © Emilia Stasiak / Adobe Stock

Whether it be a brisk walk around the park or high intensity training at the gym, exercise does a body good. But what if you could harness the benefits of a good workout without ever moving a muscle?

Michigan Medicine researchers studying a class of naturally occurring protein called Sestrin have found that it can mimic many of exercise's effects in flies and mice. The findings could eventually help scientists combat muscle wasting due to aging and other causes.

"Researchers have previously observed that Sestrin accumulates in muscle following exercise," said Myungjin Kim, Ph.D., a research assistant professor in the Department of Molecular & Integrative Physiology. Kim, working with professor Jun Hee Lee, Ph.D. and a team of researchers wanted to know more about the protein's apparent link to exercise. Their first step was to encourage a bunch of flies to work out.

Taking advantage of *Drosophila* flies' normal instinct to climb up and out of a test tube, their collaborators Robert Wessells, Ph.D. and Alyson Sujkowski of Wayne State University in Detroit developed a type of fly treadmill. Using it, the team trained the flies for three weeks and compared the running and flying ability of normal flies with that of flies bred to lack the ability to make Sestrin.

"Flies can usually run around four to six hours at this point and the normal flies' abilities improved over that period," says Lee. "The flies without Sestrin did not improve with exercise."

What's more, when they overexpressed Sestrin in the muscles of normal flies, essentially maxing out their Sestrin levels, they found those flies had abilities above and beyond the trained flies, even without exercise. In fact, flies with overexpressed Sestrin didn't develop more endurance when exercised.

The beneficial effects of Sestrin include more than just improved endurance. Mice without Sestrin lacked the improved aerobic capacity, improved respiration and fat burning typically associated with exercise.

"We propose that Sestrin can coordinate these biological activities by turning on or off different metabolic pathways," says Lee. "This kind of combined effect is important for producing exercise's effects."

Lee also helped another collaborator, Pura Muñoz-Cánoves, Ph.D., of Pompeu Fabra University in Spain, to demonstrate that muscle-specific Sestrin can also help prevent atrophy in a muscle that's immobilized, such as the type that occurs when a limb is in a cast for a long period of time. "This independent study again highlights that Sestrin alone is sufficient to produce many benefits of physical movement and exercise," says Lee.

Could Sestrin supplements be on the horizon? Not quite, says Lee. "Sestrins are not small molecules, but we are working to find small molecule modulators of Sestrin."

Additionally, adds Kim, scientists still don't know how exercise produces Sestrin in the body. "This is very critical for future study and could lead to a treatment for people who cannot exercise."

Story Source:

Materials provided by **Michigan Medicine - University of Michigan**. Original written by Kelly Malcom. *Note: Content may be edited for style and length.*

Journal Reference:

1. Myungjin Kim, Alyson Sujkowski, Sim Namkoong, Bondong Gu, Tyler Cobb, Boyoung Kim, Allison H. Kowalsky, Chun-Seok Cho, Ian Semple, Seung-Hyun Ro, Carol Davis, Susan V. Brooks, Michael Karin, Robert J. Wessells, Jun Hee Lee. **Sestrins are evolutionarily conserved mediators of exercise benefits**. *Nature Communications*, 2020; 11 (1) DOI: 10.1038/s41467-019-13442-5

- Chicago

Michigan Medicine - University of Michigan. "A replacement for exercise? A protein called Sestrin might be responsible for many of the benefits of a good workout." ScienceDaily. ScienceDaily, 13 January 2020. <www.sciencedaily.com/releases/2020/01/200113075830.htm>.

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7. アルコール依存によって脳全体の機能構造が改造される -マウス実験

日付:2020 年 1 月 14 日
ソース:カリフォルニア大学サンディエゴ校医学部
概要:

カリフォルニア大学サンディエゴ校医学部の研究者らは、単一細胞の解像度で全脳のイメージングを可能にする高度な技術を駆使して、アルコール依存症のマウスモデルにおいては、その脳の機能構造が大幅に改造されている、と 1 月 14 日のオンライン版 PNAS で報告している。また、アルコールを奪われた時、依存症のマウスは、非飲酒あるいは依存症ではないマウスと比較して、協調的脳活動が増加しモジュール性が低下した、ともしている。
依存症の神経科学は飛躍的な進歩を遂げたが、焦点は常に限られた数の脳回路と神経伝達物質、主にドーパミン作動性ニューロン、扁桃体および前頭前野にあった。しかし、この研究によって、今回アルコール消費に関して以前は疑わなかったいくつかの領域が特定され、ヒトのアルコール依存症のより良い理解と治療のための新しい研究目標が提供された、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200114173106.htm

In mice, alcohol dependence results in brain-wide remodeling of functional architecture

Date:

January 14, 2020

Source:

University of California - San Diego

Summary:

Using novel imaging technologies, researchers produce first whole-brain atlas at single-cell resolution, revealing how alcohol addiction and abstinence remodel neural physiology and function in mice.

FULL STORY

Employing advanced technologies that allow whole brain imaging at single-cell resolution, researchers at University of California San Diego School of Medicine report that in an alcohol-dependent mouse model, the rodent brain's functional architecture is substantially remodeled. But when deprived of alcohol, the mice displayed increased coordinated brain activity and reduced modularity compared to nondrinker or casual drinker mice.

The findings, published in the January 14, 2020 online issue of *PNAS*, also identified several previously unsuspected regions of the brain relevant to alcohol consumption, providing new research targets for better understanding and treatment of alcohol dependence in humans.

"The neuroscience of addiction has made tremendous progress, but the focus has always been on a limited number of brain circuits and neurotransmitters, primarily dopaminergic neurons, the amygdala and the prefrontal cortex," said senior author Olivier George, PhD, associate professor in the Department of Psychiatry at UC San Diego School of Medicine.

"Research groups have been fighting for years about whether 'their' brain circuit is the key to addiction. Our results confirm these regions are important, but the fact that we see such a massive remodeling of the functional brain architecture was a real shock. It's like studying the solar system and then discovering that there is an entire universe behind it. It shows that if you really want to understand the neurobiological mechanisms leading to addiction, you can't just look at a handful of brain regions, you need to look at the entire brain, you need to take a step back and consider the whole organ."

George said the findings further undermine the idea that addiction is simply a psychological condition or consequence of lifestyle. "You would be surprised at how prevalent this view remains," he said. "The brain-wide remodeling of the functional architecture observed here is not 'normal.' It is not observed in a naïve animal. It is not observed in an animal that drinks recreationally. It is only observed in animals with a history of alcohol dependence and it is massive. Such a decrease in brain modularity has been observed in numerous brain disorders, including Alzheimer's disease, traumatic brain injury and seizure disorders."

Brain modularity is the theory that there are functionally specialized regions in the brain responsible for different, specific cognitive processes. For example, the frontal lobes of the human brain are involved in executive functions, such as reasoning and planning, while the fusiform face area located in the lower rear of the brain is involved in recognizing faces.

Reduced modularity, said George, likely interferes with "normal neuronal activity and information processing and contributes to cognitive impairment, emotional distress and intense craving observed in mice during abstinence from alcohol."

Due to the format of the testing, George said it was not clear if the reduced modularity was permanent. "So far, we only know that it lasts at least one week into abstinence. We have not tested longer durations of abstinence, but it's one of our goals."

George and colleagues used multiple new and emerging imaging technologies to create their whole-brain atlas of mouse brains, capable of being viewed at the level of single cells. The result was a first, they said, providing unprecedented data and insights.

"This new approach allows us to explore an entirely new universe. It can answer so many questions. What I am most interested in now is figuring out how early these brain changes start and how long do they last for. This would be critical to understanding when the switch to addiction happens and when does your brain come back to normal, if it ever does. We are also very interested in comparing the brain network of alcohol dependence with other drugs, such as cocaine, nicotine and methamphetamines."

The imaging approach cannot yet be used with human brains, which are far larger and more complex. "I don't think that it is possible to do it in humans now, the technology is just not there," said George. "But when I started doing this research 15 years ago, this technique didn't exist at all and I never ever imagined it would be possible, so who knows what the future will bring."

Story Source:

Materials provided by **University of California - San Diego**. Original written by Scott LaFee. *Note: Content may be edited for style and length.*

Journal Reference:

1. Adam Kimbrough, Daniel J. Lurie, Andres Collazo, Max Kreifeldt, Harpreet Sidhu, Giovana Camila Macedo, Mark D'Esposito, Candice Contet, Olivier George. **Brain-wide functional architecture remodeling by alcohol dependence and abstinence**. *Proceedings of the National Academy of Sciences*, 2020; 201909915 DOI: 10.1073/pnas.1909915117

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University of California - San Diego. "In mice, alcohol dependence results in brain-wide remodeling of functional architecture." ScienceDaily. ScienceDaily, 14 January 2020. <www.sciencedaily.com/releases/2020/01/200114173106.htm>.

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8. 大豆油は脳に遺伝的変化をもたらす –マウス実験
代謝や神経学的変化にもリンク

日付:2020 年 1 月 17 日
ソース:カリフォルニア大学リバーサイド校
概要:

UC リバーサイドの新しい研究は、大豆油が肥満や糖尿病を引き起こすだけでなく、自閉症、アルツハイマー病、不安、うつ病などの神経疾患にも影響を与える可能性があることを示している。
米農務省によると、大豆油は、ファーストフードのフライに使用され、包装された食品に加えられ、家畜に与えられ、米国では断然最も幅広く生産され消費されている食用油だ。
今月ジャーナル内分泌学で発表された新しい研究では、3 つの異なる油、すなわち大豆油、低リノール酸に変更された大豆油、およびココナッツ油、による 3 つの異なる食餌を与えられたマウスで比較した。
同じ UCR 研究チームは 2015 年に、大豆油がマウスの肥満、糖尿病、インスリン抵抗性、脂肪肝を誘発することを発見。その後、2017 年の研究で、同じグループは、大豆油がリノール酸が少なくなるように精製されている場合、肥満とインスリン抵抗性が低下することも発見。
しかし、今月リリースされた研究では、研究者は脳に対する変更大豆油と非変更大豆油の効果の違いはなかった、としている。具体的には、多くの重要なプロセスが行われる視床下部に対する油の顕著な影響を発見した。視床下部は、代謝を通じて体重を調節し、体温を維持し、生殖および身体成長ならびにストレスへの反応に重要である。
更に、研究チームは、大豆油を与えられたマウスの多くの遺伝子が正しく機能していないとも判断した。そのうちの 1 つは、「愛」ホルモンであるオキシトシンを生成する遺伝子で、大豆油飼育マウスでは、視床下部のオキシトシンのレベルが低下した。
この研究では雄マウスが使用されたが、オキシトシンは母体の健康にとって非常に重要であり、母子の結合を促進するため、雌のマウスを使用して同様の研究を行う必要がある、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://medicalxpress.com/news/2020-01-america-widely-consumed-oil-genetic.html

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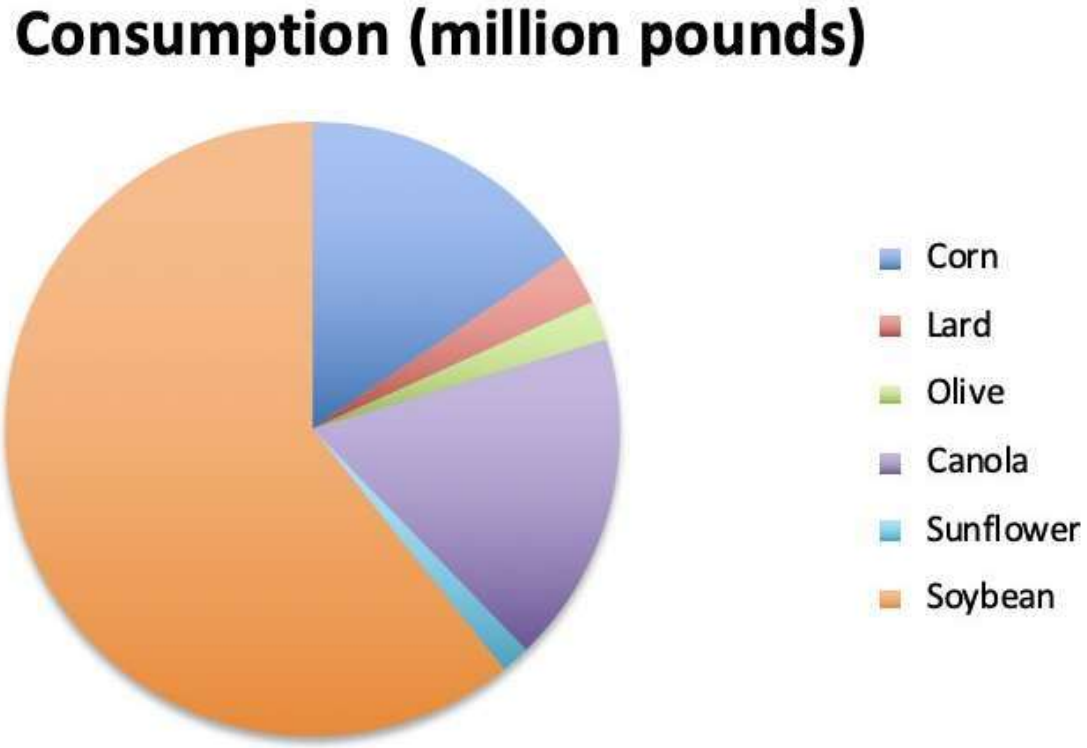
JANUARY 17, 2020

America's most widely consumed oil causes genetic changes in the brain

by University of California - Riverside



Edible fats and oils consumed in the U.S., 2017/18. Credit: USDA

New UC Riverside research shows soybean oil not only leads to obesity and diabetes, but could also affect neurological conditions like autism, Alzheimer's disease, anxiety, and depression.

Used for fast food frying, added to packaged foods, and fed to livestock, soybean oil is by far the most widely produced and consumed edible oil in the U.S., according to the U.S. Department of Agriculture. In all likelihood, it is not healthy for humans.

It certainly is not good for mice. The new study, published this month in the journal *Endocrinology*, compared mice fed three different diets high in fat: soybean oil, soybean oil modified to be low in linoleic acid, and coconut oil.

The same UCR research team found in 2015 that soybean oil induces obesity, diabetes, insulin resistance, and fatty liver in mice. Then in a 2017 study, the same group learned that if soybean oil is engineered to be low in linoleic acid, it induces less obesity and insulin resistance.

However, in the study released this month, researchers did not find any difference between the modified and unmodified soybean oil's effects on the brain. Specifically, the

scientists found pronounced effects of the oil on the hypothalamus, where a number of critical processes take place.

"The hypothalamus regulates body weight via your metabolism, maintains body temperature, is critical for reproduction and physical growth as well as your response to stress," said Margarita Curras-Collazo, a UCR associate professor of neuroscience and lead author on the study.

The team determined a number of genes in mice fed soybean oil were not functioning correctly. One such gene produces the "love" hormone, oxytocin. In soybean oil-fed mice, levels of oxytocin in the hypothalamus went down.

The research team discovered roughly 100 other genes also affected by the soybean oil diet. They believe this discovery could have ramifications not just for energy metabolism, but also for proper brain function and diseases such as autism or Parkinson's disease. However, it is important to note there is no proof the oil causes these diseases.

Additionally, the team notes the findings only apply to soybean oil—not to other soy products or to other vegetable oils.

"Do not throw out your tofu, soymilk, edamame, or soy sauce," said Frances Sladek, a UCR toxicologist and professor of cell biology. "Many soy products only contain small amounts of the oil, and large amounts of healthful compounds such as essential fatty acids and proteins."

A caveat for readers concerned about their most recent meal is that this study was conducted on mice, and mouse studies do not always translate to the same results in humans.

Also, this study utilized male mice. Because oxytocin is so important for maternal health and promotes mother-child bonding, similar studies need to be performed using female mice.

One additional note on this study—the research team has not yet isolated which chemicals in the oil are responsible for the changes they found in the hypothalamus. But they have ruled out two candidates. It is not linoleic acid, since the modified oil also produced genetic disruptions; nor is it stigmasterol, a cholesterol-like chemical found naturally in soybean oil.

Identifying the compounds responsible for the negative effects is an important area for the team's future research.

"This could help design healthier dietary oils in the future," said Poonamjot Deol, an assistant project scientist in Sladek's laboratory and first author on the study.

"The dogma is that saturated fat is bad and unsaturated fat is good. Soybean oil is a polyunsaturated fat, but the idea that it's good for you is just not proven," Sladek said.

Indeed, coconut oil, which contains saturated fats, produced very few changes in the hypothalamic genes.

"If there's one message I want people to take away, it's this: reduce consumption of soybean oil," Deol said about the most recent study.

Explore further

GM soybean oil causes less obesity and insulin resistance but is harmful to liver function

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More information: Poonamjot Deol et al, Dysregulation of Hypothalamic Gene Expression and the Oxytocinergic System by Soybean Oil Diets in Male Mice, *Endocrinology* (2020). DOI: 10.1210/endocr/bqz044

Journal information: Endocrinology

Provided by University of California - Riverside

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9. ケトダイエットに関するマウス研究

日付:2020 年 1 月 27 日
ソース:イェール大学
概要:

イェール大学の研究者らは、ケトジェニックダイエット –このダイエットではカロリーの 99%を脂肪から摂取し、炭水化物からのカロリーはわずか 1%に抑えるというもの– は短期的には糖尿病のリスクや炎症を低下させることで健康的利点をもたらすが、約 1 週間以降はマイナスの効果をもたらす、ことをマウス実験で発見。有名人が減量療法として宣伝してますます人気が高まっているケトダイエットに警笛を鳴らしている。
Nature Metabolism 誌の 1 月 20 日号に掲載されたこの研究で、研究者らは、この食事療法のプラスとマイナスの両方の影響が、糖尿病のリスクと炎症を低下させる組織保護細胞であるガンマデルタ T 細胞と呼ばれる免疫細胞関連していることを発見した。
食事の炭水化物含有量が低いせいで身体のグルコースレベルが低下すると。身体は飢餓状態にあるように動作し(実際に飢餓状態ではなくても)、炭水化物の代わりに脂肪を燃やし始める。この過程で、代替燃料源としてケトン体と呼ばれる化学物質が生成される。身体がケトン体を燃やすと、組織を保護するガンマデルタ T 細胞が身体全体に広がるり、これにより糖尿病のリスクと炎症が軽減され、身体の代謝が改善される。実際にこのケトダイエットを 1 週間続けたマウスの血糖値と炎症が減少した。ところが、身体がこの“実際には飢餓状態ではない飢餓状態”にあるとき、脂肪の崩壊と同時に蓄積も起こっている、ということが今回分かった。実際にマウスが1週間以上高脂肪・低炭水化物の食餌をし続けた場合、マウスは燃焼できるよりも多くの脂肪を摂取し、ガンマデルタ T 細胞を失い、糖尿病や肥満を発症する、としている。
研究者らは、ケトダイエットの健康上の利点について逸話的な主張を検証するには、ヒトにおける長期臨床研究が必要だ、としている。

研究関連/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200127134741.htm

Keto diet works best in small doses, mouse study finds

Date:

January 27, 2020

Source:

Yale University

Summary:

> A ketogenic diet -- which provides 99 percent of calories from fat and only 1 percent from carbohydrates -- produces health benefits in the short term, but negative effects after about a week, researchers found in a study of mice.

FULL STORY

Mouse with cheese (stock image).

Credit: © Emilia Stasiak / Adobe Stock

A ketogenic diet -- which provides 99% of calories from fat and only 1% from carbohydrates -- produces health benefits in the short term, but negative effects after about a week, Yale researchers found in a study of mice.

The results offer early indications that the keto diet could, over limited time periods, improve human health by lowering diabetes risk and inflammation. They also represent an important first step toward possible clinical trials in humans.

The keto diet has become increasingly popular as celebrities, including Gwyneth Paltrow, Lebron James, and Kim Kardashian, have touted it as a weight-loss regimen.

In the Yale study, published in the Jan. 20 issue of *Nature Metabolism*, researchers found that the positive and negative effects of the diet both relate to immune cells called gamma delta T-cells, tissue-protective cells that lower diabetes risk and inflammation.

A keto diet tricks the body into burning fat, said lead author Vishwa Deep Dixit of the Yale School of Medicine. When the body's glucose level is reduced due to the diet's low carbohydrate content, the body acts as if it is in a starvation state -- although it is not -- and begins burning fats instead of

carbohydrates. This process in turn yields chemicals called ketone bodies as an alternative source of fuel. When the body burns ketone bodies, tissue-protective gamma delta T-cells expand throughout the body.

This reduces diabetes risk and inflammation, and improves the body's metabolism, said Dixit, the Waldemar Von Zedtwitz Professor of Comparative Medicine and of Immunobiology. After a week on the keto diet, he said, mice show a reduction in blood sugar levels and inflammation.

But when the body is in this "starving-not-starving" mode, fat storage is also happening simultaneously with fat breakdown, the researchers found. When mice continue to eat the high-fat, low-carb diet beyond one week, Dixit said, they consume more fat than they can burn, and develop diabetes and obesity.

"They lose the protective gamma delta T-cells in the fat," he said.

Long-term clinical studies in humans are still necessary to validate the anecdotal claims of keto's health benefits.

"Before such a diet can be prescribed, a large clinical trial in controlled conditions is necessary to understand the mechanism behind metabolic and immunological benefits or any potential harm to individuals who are overweight and pre-diabetic," Dixit said.

There are good reasons to pursue further study: According to the Centers for Disease Control, approximately 84 million American adults -- or more than one out of three -- have prediabetes (increased blood sugar levels), putting them at higher risk of developing type 2 diabetes, heart disease, and stroke. More than 90% of people with this condition don't know they have it.

"Obesity and type 2 diabetes are lifestyle diseases," Dixit said. "Diet allows people a way to be in control."

With the latest findings, researchers now better understand the mechanisms at work in bodies sustained on the keto diet, and why the diet may bring health benefits over limited time periods.

"Our findings highlight the interplay between metabolism and the immune system, and how it coordinates maintenance of healthy tissue function," said Emily Goldberg, the postdoctoral fellow in comparative medicine who discovered that the keto diet expands gamma-delta T cells in mice.

If the ideal length of the diet for health benefits in humans is a subject for later studies, Dixit said, discovering that keto is better in small doses is good news, he said: "Who wants to be on a diet forever?"

The research was funded in part by grants from the National Institutes of Health.

Story Source:

Materials provided by **Yale University**. Original written by Brita Belli. *Note: Content may be edited for style and length.*

Journal Reference:

1. Emily L. Goldberg, Irina Shchukina, Jennifer L. Asher, Sviatoslav Sidorov, Maxim N. Artyomov, Vishwa Deep Dixit. **Ketogenesis activates metabolically protective γδ T cells in visceral adipose tissue**. *Nature Metabolism*, 2020; 2 (1): 50 DOI: 10.1038/s42255-019-0160-6

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Yale University. "Keto diet works best in small doses, mouse study finds." ScienceDaily. ScienceDaily, 27 January 2020. <www.sciencedaily.com/releases/2020/01/200127134741.htm>.
