Bio News – June, 2022

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

5/1　BMS の待望の心筋症薬 Camzyos を米国 FDA が承認

単独や合剤での年間売上が 40 億ドルに達すると Bristol-Myers Squibb（BMS）が見込む心筋症薬 Camzyos（mavacamten、マバカムテン）が心不全を引き起こしうるとの強調警告（Boxed Warning）付きで米国 FDA に承認された。

5/2　1 型糖尿病を治療する移植細胞 VX-880 の順調な Ph1/2 試験を米国 FDA が差し止め

Vertex Pharmaceuticals（本社：マサチューセッツ州ボストン）の膵島細胞移植による 1 型糖尿病治療 VX-880 の Ph1/2 試験の見張り番・Independent Data Monitoring Committee は最初の被験者 2 人の経過をみて高用量投与のパート B 段階に進むように指示したが、米国 FDA の見解は真反対で、情報不足のためより多くはまだ投与できないとして試験を差し止めた。

5/4　Biogen がアルツハイマー病薬 Aduhelm の営業廃止

Biogen が現在の Michel Vounatsos 氏に代わる新たな CEO 探しを始め、売り上げがほぼ皆無のアルツハイマー病薬 Aduhelm（アデュヘルム；aducanumab）の営業を 5 億ドル程の年間経費削減の一環として廃止する。

5/5　田辺三菱製薬のカナダの子会社 Medicago の植物が作る COVID-19 ワクチンの効果 70%の Ph3 試験結果論文報告

5/6　住友ファーマの Ph1 段階のナルコレプシー薬候補の欧米権利を Jazz（本社：カリフォルニア州パロアルト）が取得

Jazz Pharmaceuticals が住友ファーマにひとまず 5,000 万ドルを払う。

5/6　炭素で O157 を無毒化？　特効薬開発にも期待　群馬大研究 G が発表

重度の食中毒を引き起こす腸管出血性大腸菌 O（オー）157 を、炭素を用いることで無毒化することに成功したと、群馬大学が 6 日発表した。大学院医学系研究科の平川秀忠准教授らの研究グループによる成果で、「根本的な治療方法が確立されていない O157 への有効な薬などの開発が期待できる」という。
研究を進める中で、活性炭よりも大きい平均直径 150 ナノメートルのマクロ孔を持つ「多孔質炭素」が、O157 が生み出す病原性たんぱく質の大きさにあっていることが判明。この炭素を O157 の培養液に添加すると、病原性たんぱく質を強く吸着し、無毒化することが確認できた。O157 の代替菌に感染させたマウスを使った実験でも、多孔質炭素を経口投与したグループには治療効果がみられ、副作用などもみられなかったという。

5/7　ここ 7 か月間に米国の小児 109 人に原因不明の肝炎が発生～7 人に 1 人が肝移植

米国の 25 の州や地域でここ 7 か月間に小児 109 人に発端不明の急な肝炎が生じており、7 人に 1 人（14%）は肝臓移植を必要とし、5 人は死亡した。

5/7　原因不明の小児肝炎、日本でも 7 人の可能性報告　米国で 5 人死亡

国内外で報告が続く原因不明の子どもの肝炎について、米疾病対策センター（CDC）は 6 日、患者 109 人の調査を進めていると発表した。このうち十数人が肝臓移植を受け、5 人は死亡したという。日本でもこれまでに、該当する可能性のある患者 7 人が報告されている。

5/7　子どもの肝炎症状に注意喚起　米 CDC、衛生対策も

5/9　冬眠中クマの血清がヒトの筋肉を増強？　広大と北大の研究グループが解明

広島大と北大の研究グループは、冬眠期のツキノワグマの血清にヒトの筋肉細胞量を増強する効果があるとする論文を発表した。冬眠中のクマやリスなどは長期間活動しないのに筋肉が衰えないことで知られているが、研究グループはクマの血液中の特定物質が筋肉の分解を抑制していることも確認した。要因物質が特定されれば、高齢者の寝たきり防止やリハビリへの応用が期待できるという。
論文は 1 月に米国のオンライン科学誌「PLOS　ONE」に掲載された。

5/11　Pfizer、片頭痛薬メーカーBiohaven（本社：コネチカット州ニューヘイブン）を 116 億ドルで買収

5/11　ラマ起源の抗 COVID-19 抗体 XVR011 の第 1/2 相試験をベルギーの ExeVir が中止

5/11　佐賀大のダイヤモンド半導体、世界最高出力を記録　米国学会が注目

佐賀大理工学部の嘉数誠教授（61）=半導体工学=らの研究グループは 10 日、作製したダイヤモンドのパワー半導体が 1 平方センチ当たりの出力電力で 875 メガワットを記録したと発表した。ダイヤモンドとしては世界最高で、電子工学で権威のある米国電気電子学会の学術論文誌 5 月号に掲載され、注目論文として表紙を飾った。

5/12　DNA や RNA に含まれる核酸塩基 5 種類、炭素質隕石から初めて同時検出

北海道大学の大場康弘准教授を筆頭とする研究グループは、地球に落下した「炭素質コンドライト」（有機物に富む炭素質隕石）を分析した結果、デオキシリボ核酸（DNA）やリボ核酸（RNA）に含まれている 5 種類の核酸塩基がすべて検出されたとする研究結果を発表した。

5/12　米国の小児への Moderna の COVID-19 ワクチンの取り急ぎの認可の申請が完了

5/12　Moderna の最高財務責任者（CFO）Jorge Gomez 氏が前職での問題の調べを背景に就任日の翌日に辞任

5/12　オミクロン株の変異系統 BA.4 と BA.5 を初確認、空港検疫で　現在の系統より感染力高め

厚生労働省は 12 日、新型コロナウイルスのオミクロン株の変異の系統「BA.4」「BA.5」を、国内の検疫で初めて確認したと発表した。いずれも、国内で現在主流の BA.2 系統よりも感染が広がりやすいとの研究結果がある。
BA.4 は、4 月 22 日の南アフリカからの入国者から、BA.5 は、4 月 29 日のスペインからの入国者とザンビアからの入国者からそれぞれ見つかった。3 人ともワクチンを 3 回接種していたという。

5/13　Seagen（Seattle Genetics －本社：ワシントン州）の CEO・Clay Siegall 氏、妻への暴行で先月 23 日に逮捕されていた

5/13　海水を飲み水に変える「極細チューブ」 東京大学が開発

東京大学の研究チームが、塩分は通さず水だけを高速で通す、極細チューブを開発した。こげつかないフライパンのように、フッ素で内側が覆われているのが特徴だ。海水を淡水化し、飲み水などに変える次世代の水処理技術に役立つ可能性がある。13 日付の米科学誌サイエンスに発表した。

5/13　月の砂で植物栽培 米大学、初めて成功

米フロリダ大学（University of Florida）の研究チームは 12 日、アポロ（Apollo）計画で月から持ち帰った砂で植物の栽培に初めて成功したとする実験結果を、科学誌「コミュニケーションズ・バイオロジー（Communications Biology）」で発表した。
研究チームは、アポロ 11 号、12 号、17 号が月の複数の場所から採取した、「レゴリス」と呼ばれる砂計 12 グラムを使用。約 1 グラムずつ指ぬき程度の大きさの容器に入れ、水を加えて種をまき、養液を毎日与えた。
栽培する植物にはシロイヌナズナが選ばれた。カラシナの仲間で育てるのが容易。最も重要なのは、これまで広く研究に使われてきた点にある。遺伝子情報が解析されており、宇宙を含む厳しい環境への適応能力があることでも知られる。

5/13　チンパンジーも夜間に勃起　京大の研究チームが発表　他の研究中に偶然発見　ヒト以外の動物で確認は初 -京大

5/14　余るモデルナ、止まらぬ廃棄　融通できず悩む自治体

5/14　田辺三菱製薬の ALS 薬エダラボンの経口剤 Radicava ORS を米国が承認

5/16　塩野義、12～19 歳に治験開始　開発中のコロナワクチン

5/16　上海ロックダウン 50 日経過　いつまで続く厳しい制限

5/17　昆虫のゲノム編集に手軽な新手法　京大などの研究チームが開発

多くの昆虫に使える簡単なゲノム編集の手法を京都大学などの研究チームが開発した。これまで難しかったゴキブリでもうまくいくことを確認した。昆虫食などへの技術の応用が期待できる一方、手軽さゆえに悪用の恐れも懸念される。論文は米科学誌に 17 日、オンライン掲載される。

5/19　すべてのコロナウイルスに対応 ～画期的な新抗体創出に成功―国立研究所など～

国立研究開発法人医療基盤・健康・栄養研究所（NIBIOHN）と塩野義製薬との共同研究で、オミクロン株を含むさまざまな変異株に対応できる新たな抗ウイルス抗体の創出に成功した。この基礎研究の成果を基に、一刻も早い「広域型抗ウイルス抗体薬」の開発に期待がかかる。

5/19　上海市、6 月中に生産・生活の秩序を全面回復させる方針

5/19　新型コロナ対策のエアカーテン　深紫外線でウイルス不活化　病院用に卓上型開発・名古屋大など

新型コロナウイルスが付着した空気中の微粒子の流れを遮断する卓上型エアカーテン装置を病院用に開発したと、名古屋大や国立病院機構名古屋医療センターなどの研究チームが 19 日までに発表した。
エアカーテンで流した空気は別の箱型装置に送り、含まれているかもしれないウイルスを発光ダイオード（LED）の深紫外線で不活化する。同センターで実験し、ウイルスを検出限界まで不活化できることを確認した。深紫外線の種類は人の目などに当たると危険な UV―C であるため、エアカーテンとパイプで接続した箱型のウイルス不活化装置の内部に LED を収納した。実用化に向けて、この不活化装置を小さくし、できればエアカーテンと一体化させる方針。
研究チームには青色 LED の開発でノーベル物理学賞を受賞した天野浩名大教授も参加し、論文は米物理学協会の専門誌「AIP アドバンシズ」に掲載された。

5/20　米国が 5-11 歳小児に COVID-19 ワクチン追加接種が必要とした

5/20　昆虫の遺伝子操作が簡便に　雌の成虫に注射　京大

昆虫の遺伝子操作を簡便に行う方法を開発し、チャバネゴキブリや穀物の害虫「コクヌストモドキ」で実証したと、京都大とスペインの進化生物学研究所の研究チームが 20 日までに米科学誌セル・リポーツ・メソッズ電子版に発表した。害虫対策などに役立つと期待される。
哺乳類のマウスなどの遺伝子操作に広く使われる「ゲノム編集」技術のうち、2020 年にノーベル化学賞の授与対象になった「クリスパー・キャス 9」は、昆虫に使う際、DNA を切断するたんぱく質などを受精直後の卵に注射する必要があり、技術的に難しかった。京大大学院農学研究科の大門高明教授らは雌の成虫に注射するだけで卵に取り込まれることを発見し、遺伝子を壊したり、改変したりできることを示した。
この新技術は卵の形成に必要な卵黄たんぱく質などが体液から取り込まれる仕組みを利用する。このため遺伝子操作実験によく使われるショウジョウバエなど、一部の種には適用できない。しかし、卵が硬い卵鞘（らんしょう）に覆われ、注射が困難だったゴキブリでは非常に有効だという。

5/20　マウス、運動で「仲間への共感性が向上」 群馬大研究グループ発表

群馬大共同教育学部の島孟留（たける）講師らの研究グループが、マウスに軽い運動を継続的にさせると仲間のマウスに対する共感性が向上するとの研究結果を発表した。「BDNF」と呼ばれる神経細胞の生存や成長に関わる栄養因子などが関係していることもわかった。島講師は「いじめなどの諸課題解決、学校での体育授業やスポーツ活動の価値の再考などにつなげられれば」としている。
研究は脳神経科学の国際ジャーナル「Brain　Research」（オンライン版）で公開された。島講師らは今後、島皮質での働きについてさらに詳しく調べるという。

5/21　WHO がサル痘流行の緊急会議を開催

- WHO calls emergency meeting as monkeypox cases top 100 in Europe | Reuters

5/22　スペインでのサル痘感染が 30 人に達した

5/23　サル痘疑い患者、届け出求める　厚労省通知　国内での報告はなし

5/24　天然痘に似た症状の「サル痘」が欧米などで拡大 厚労省、国内流入を警戒

5/24　ALS 患者の筋肉内神経に特定たんぱく質蓄積　広大などが発見

運動神経が異常を起こし全身の筋力が低下する難病「筋萎縮性側索硬化症」（ALS）について、広島大と徳島大、国立病院機構呉医療センターは 23 日、患者の筋肉内の神経に、病気の初期段階からたんぱく質が蓄積することを発見したと発表。
特有の異常として、早期診断や新たな治療法の開発につながる可能性があるという。研究成果は米医学雑誌「ジャマ・ニューロロジー」オンライン版に掲載された。

5/24　低所得～中の低所得の国での抗癌剤の普及を助ける製薬会社多数参加の連盟発足

国民総所得を一人当たりに換算した額（GNI per capita）が 1,000 ドルほど以下の低所得国や 1,000～4,000 ドルほどの中の低所得国での抗癌剤の普及を促す製薬会社多数参加の連盟 Access to Oncology Medicines (ATOM) が発足。

5/25　サル痘ワクチンを欲しい多くの国とデンマークの Bavarian Nordic が交渉中

5/26　新型コロナ感染を 9 分で判定、精度は PCR 以上　理研などが装置開発

5/26　Pfizer が 23 の薬やワクチンを 45 の貧困国に利益を求めず提供

5/26　Lilly が 21 億ドルを投じて本拠地インディアナ州に工場建設～最大 500 人新規雇用

5/26　Moderna の CEO・Stephane Bancel 氏が約 3 億 5,500 万ドルを慈善活動に寄付

5/27　サル痘拡大「異例」と警戒　WHO、患者 200 人に

世界保健機関（WHO）は 27 日の総会で、動物由来のウイルス感染症「サル痘」が従来継続的に発生してきたアフリカ以外で感染が広がっていることは「異例」として、警戒を訴えた。欧米を中心に 20 カ国以上で約 200 人の患者が確認されたとし、今後の見通しは不透明としながらも、増加の恐れがあるとした。

5/28　病因不明の急な肝炎の WHO 基準を満たす小児患者の 5 月 26 日までの報告数 650 人

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. マウスの記憶を保存しアルツハイマー病に対する免疫に有望な新基盤を提供する研究

2. カロリーを減らし適切な時間に食すことによって長生きする -マウス実験

3. 炎症の遮断が慢性的な痛みに繋がる可能性 -マウス研究

4. 単一のホルモンが低タンパク食に対する体の反応を管理
   FGF21 の存在により、マウスは長生きし、体重を減らしながらより多くの食事をする

5. 腸は遺伝子の使用法を調整し、腸内微生物はその調整をサポート
   腸内微生物のないマウスは、脂肪消化のために全く異なる遺伝子セットに依存

6. CRISPR-Cas9 遺伝子編集アプローチが動物の社会的行動を変える可能性 -ハムスター実験

7. 食餌性コレステロールがインフルエンザ マウスの病状を悪化させる

8. 人工知能を利用してイヌの生命を脅かす細菌感染症を予測

9. メスのマウスは妊娠するとバナナ臭の尿を出してオスを阻止
   オスにストレスを与え遠ざけることによって子殺しをさせないと考えられる

1. マウスの記憶を保存しアルツハイマー病に対する免疫に有望な新基盤を提供する研究

日付：2022 年 5 月 3 日
ソース：カンザス大学
概要：

カンザス大学の研究者らは、マウスモデルの実験で、アルツハイマー病（AD）に対する免疫化の新アプローチを発見した。この研究で彼らは、トウモロコシ由来の組換えメチオニン（Met）に富むタンパク質を使用、このタンパク質を in vitro で酸化、抗原であるメチオニンスルホキシド（MetO）に富むタンパク質を生成した。この抗原は、体に注入されると、免疫系を刺激して、脳細胞に毒性があり、アルツハイマー病の特徴と見なされるタンパク質のベータアミロイドの MetO 成分に対する抗体を生成する。調査結果は、査読付きのオープンアクセスジャーナル「Antioxidants」に掲載されている。
2011 年に発表された同研究チームの研究では、アルツハイマー病のマウスモデルに同様の MetO に富むタンパク質を注射し、アルツハイマー病による損傷が発生する主要な領域である海馬でアミロイド斑の負荷が約 30%減少することを示していた。
今回の新しい追跡調査では、家族性のアルツハイマー病を発症するように遺伝子組み換えされた生後 4 か月の AD マウスモデルに MetO に富むタンパク質を注射し、その後のテストで、このアプローチがマウスの免疫系を刺激して、高齢（10 か月齢）のマウスでの AD 表現型の存在を軽減できる抗体を産生することが示された。この治療によって、マウスの記憶が、対照と比較して約 50%改善した。又、短期記憶の改善に加えて、より優れた長期記憶能力、血漿と脳の両方でのベータアミロイドレベルの低下を示した、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＞Study preserves memory in mice, offering prom | EurekAlert!

NEWS RELEASE 3-MAY-2022

Study preserves memory in mice, offering promising new basis for active immunization against Alzheimer's disease

Peer-Reviewed Publication

UNIVERSITY OF KANSAS

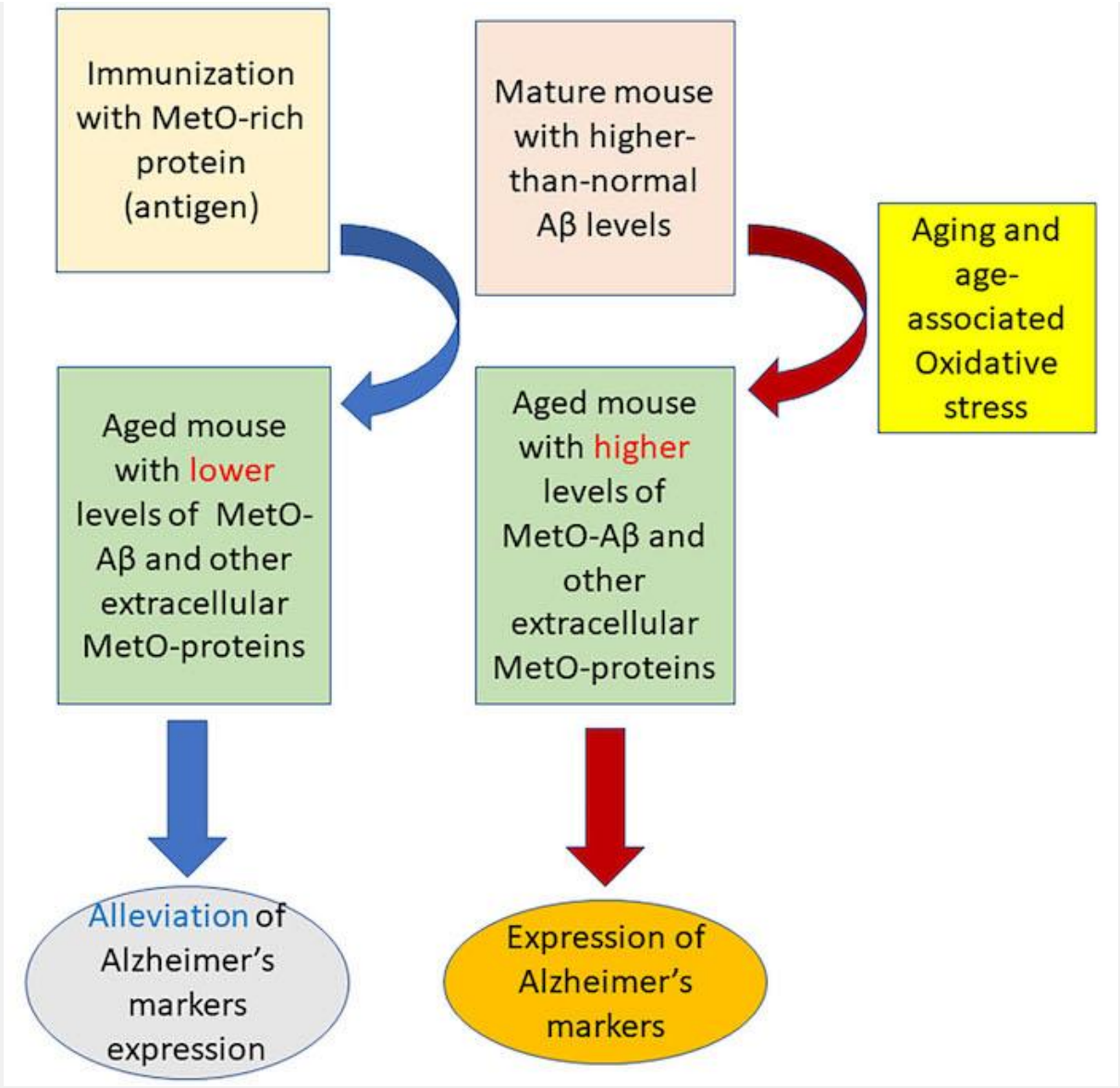


IMAGE: IN A SERIES OF TESTS, KU RESEARCHERS ASSESSED THE MEMORY OF INJECTED MICE AGAINST SIMILAR MICE THAT DIDN'T RECEIVE THE CORN-BASED METHIONINE SULFOXIDE. view more

CREDIT: SMITH, ET AL.

LAWRENCE — During experiments in animal models, researchers at the University of Kansas have discovered a possible new approach to immunization against Alzheimer's disease (AD).

Their method uses a recombinant methionine (Met)-rich protein derived from corn that was then oxidized in vitro to produce the antigen: methionine sulfoxide (MetO)-rich protein. This antigen, when injected to the body, goads the immune system into producing antibodies against the MetO component of beta-amyloid, a protein that is toxic to brain cells and seen as a hallmark of Alzheimer's disease. The findings have been just published in the peer-reviewed open-access journal *Antioxidants*.

“As we age, we have more oxidative stress, and then beta-amyloid and other proteins accumulate and become oxidized and aggregated – these proteins are resistant to degradation or removal,” said lead researcher Jackob Moskovitz, associate professor of pharmacology & toxicology at the KU School of Pharmacy. “In a previous 2011 published study, I injected mouse models of Alzheimer’s disease with a similar methionine sulfoxide-rich protein and showed about 30% reduction of amyloid plaque burden in the hippocampus, the main region where damage from Alzheimer’s disease occurs.”

The MetO-rich protein used by Moskovitz for the vaccination of AD-model mice is able to prompt the immune system to produce antibodies against MetO-containing proteins, including MetO-harboring beta-amyloid. The introduction of the corn-based MetO-rich protein (antigen) fosters the body’s immune system to produce and deploy the antibodies against MetO to previously tolerated MetO-containing proteins (including MetO-beta-amyloid), and ultimately reduce the levels of toxic forms of beta-amyloid and other possible proteins in brain.

In the new follow-up study, Moskovitz and his co-authors injected the MetO-rich protein into 4-month-old AD-model mice that were genetically modified to develop the familial form of Alzheimer’s disease. Subsequent testing showed that this approach provoked the mice’s immune systems into producing antibodies that could alleviate the presence of AD phenotypes at an older age (10-month-old mice).

“This treatment induced the production of anti-MetO antibody in blood-plasma that exhibits a significant titer up to at least 10 months of age,” according to the authors.

Moskovitz’s KU co-authors on the Antioxidants study are Adam Smith, assistant professor of pharmacology & toxicology; Kyle Gossman and Benjamin Dykstra, graduate students in Smith’s lab; and Philip Gao, director of the Protein Production Group at the Del Shankel Structural Biology Center.

In a series of tests, the KU researchers assessed the memory of injected mice against similar mice that didn’t receive the corn-based methionine sulfoxide.

“We measured short-term memory capability through a ‘Y’ maze, and that's very important in Alzheimer’s disease — because when people get Alzheimer’s, their short-term memory is going away, while the old memories are still there,” Moskovitz said. “You put a mouse in a maze shaped like a ‘Y’ so they can go either the left or right arm. But then you introduce a third arm in the middle and if they recognize the third arm as new, they’ll spend more time exploring that new arm because they have curiosity. If they don't even notice there’s a third arm — because they forget it the minute after they saw it — they will spend more time in right or left.”

According to Moskovitz, there was a roughly 50% improvement in the memory of mice injected with the methionine sulfoxide (MetO)-rich protein versus the control.

In another experiment, mice were tasked with locating a platform in a water maze.

“We gave them six days to learn, and even the ones with Alzheimer’s eventually learn the location of the platform — but we found after the second day there was a big difference, the injected mice with the antigen learn much faster than the nonimmunized mice,” Moskovitz said. “Then we remove the platform to see if they remember where the platform was just by memory, not by looking. And again, we saw a big difference. The antigen-immunized mice remember and spend more time in the vicinity of the platform they were trained on compared to the nonimmunized control mice.”

In addition to short-term memory improvement, the study showed the antigen-injected mice exhibited better long memory capabilities, reduced beta-amyloid levels in both blood-plasma and the brain, as well as “reduced beta-amyloid burden and MetO accumulations in astrocytes in hippocampal and cortical regions; reduced levels of activated microglia; and elevated antioxidant capabilities (through enhanced nuclear localization of the transcription factor Nrf2) in the same brain regions.”

The researchers found the data collected in the study likely are translational, suggesting active immunization “could give a possibility of delaying or preventing AD onset.”

Moskovitz said such an immunization could be given to people as the risk of Alzheimer’s disease increases later in life, “around the time people are told to go get a colonoscopy for the first time in their 50s or 60s,” he said. “Further booster shots could maintain immunization, a process which people are so familiar with from the COVID vaccines.”

An active immunization would represent an improvement over current passive immunization regimes because the methionine sulfoxide antigen prods the immune system into producing its own antibodies. In passive immunization, antibodies are directly injected into the body but can have severe toxic side effects (such as brain encephalitis) as well as being prone to rejection by the immune system as non-self-antibodies over time.

Moskovitz said the next steps in this line of research would be to conduct pre-clinical and clinical trials in humans in conjunction with the sponsorship of interested pharmaceutical companies.

JOURNAL

Antioxidants

DOI

10.3390/antiox11040775

2. カロリーを減らし適切な時間に食すことによって長生きする –マウス実験

日付：2022 年 5 月 5 日
ソース：ハワード ヒューズ医学研究所
概要：

寿命を延ばすためのレシピの 1 つは単純で、食べる量を減らすことである。さまざまな動物を対象とした研究では、カロリーを制限することで、より長く健康的な生活を送ることができる、と既に示されている。
今回のハワード ヒューズ医学研究所の研究者らによる新しい研究は、体の毎日のリズムがこの長寿効果に大きな役割を果たしていることを示唆している。彼らは、1 日の最も活発な時間帯にのみ食事をすると、低カロリー食でマウスの寿命が大幅に延びたと、5 月 5 日の「Science」誌で報告している。
研究チームによる 4 年間にわたる数百匹のマウスの研究では、低カロリー食だけで動物の寿命を 10% 延長したが、マウスが最も活発な時間である夜間のみに食餌を与えたところ、寿命は 35% 伸びた。また、時間制限のある食事では、減量を促進しなくても、寿命には大きな違いが見られた、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＞Cutting calories and eating at the right time of day leads to longer life in mice -- ScienceDaily

Cutting calories and eating at the right time of day leads to longer life in mice

Date:

May 5, 2022

Source:

Howard Hughes Medical Institute

Summary:

In a study that followed hundreds of mice over their lifespans, calorie restriction combined with time-restricted eating boosted longevity.

FULL STORY

One recipe for longevity is simple, if not easy to follow: eat less. Studies in a variety of animals have shown that restricting calories can lead to a longer, healthier life.

Now, new research suggests that the body's daily rhythms play a big part in this longevity effect. Eating only during their most active time of day substantially extended the lifespan of mice on a reduced-calorie diet, Howard Hughes Medical Institute Investigator Joseph Takahashi and colleagues report May 5, 2022, in the journal *Science*.

In his team's study of hundreds of mice over four years, a reduced-calorie diet alone extended the animals' lives by 10 percent. But feeding mice the diet only at nighttime, when mice are most active, extended life by 35 percent. That combo -- a reduced-calorie diet plus a nighttime eating schedule -- tacked on an extra nine months to the animals' typical two-year median lifespan. For people, an analogous plan would restrict eating to daytime hours.

The research helps disentangle the controversy around diet plans that emphasize eating only at certain times of day, says Takahashi, a molecular biologist at the University of Texas Southwestern Medical Center. Such plans may not speed weight loss in humans, as a recent study in the *New England Journal of Medicine* reported, but they could prompt health benefits that add up to a longer lifespan.

Takahashi's team's findings highlight the crucial role of metabolism in aging, says Sai Krupa Das, a nutrition scientist at the Jean Mayer USDA Human Nutrition Research Center on Aging who was not involved with the work. "This is a very promising and landmark study," she says.

Fountain of youth

Decades of research has found that calorie restriction extends the lifespan of animals ranging from worms and flies to mice, rats, and primates. Those experiments report weight loss, improved glucose regulation, lower blood pressure, and reduced inflammation.

Butit has been difficult to systematically study calorie restriction in people, who can't live in a laboratory and eat measured food portions for their entire lives, Das says. She was part of the research team that conducted the first controlled study of calorie restriction in humans, called the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy, or CALERIE. In that study, even a modest reduction in calories "was remarkably beneficial" for reducing signs of aging, Das says.

Scientists are just beginning to understand how calorie restriction slows aging at the cellular and genetic level. As an animal ages, genes linked to inflammation tend to become more active, while genes that help regulate metabolism become less active. Takahashi's new study found that calorie restriction, especially when timed to the mice's active period at night, helped offset these genetic changes as mice aged.

Question of time

Recent years have seen the rise of many popular diet plans that focus on what's known as intermittent fasting, such as fasting on alternate days or eating only during a period of six to eight hours per day. To unravel the effects of calories, fasting, and daily, or circadian, rhythms on longevity, Takahashi's team undertook an extensive four-year experiment. The team housed hundreds of mice with automated feeders to control when and how much each mouse ate for its entire lifespan.

Some of the mice could eat as much as they wanted, while others had their calories restricted by 30 to 40 percent. And those on calorie-restricted diets ate on different schedules. Mice fed the

low-calorie diet at night, over either a two-hour or 12-hour period, lived the longest, the team discovered.

The results suggest that time-restricted eating has positive effects on the body, even if it doesn't promote weight loss, as the *New England Journal of Medicine* study suggested. Takahashi points out that his study likewise found no differences in body weight among mice on different eating schedules -- "however, we found profound differences in lifespan," he says.

Rafael de Cabo, a gerontology researcher at the National Institute on Aging in Baltimore says that the *Science* paper "is a very elegant demonstration that even if you are restricting your calories but you are not [eating at the right times], you do not get the full benefits of caloric restriction."

Takahashi hopes that learning how calorie restriction affects the body's internal clocks as we age will help scientists find new ways to extend the healthy lifespan of humans. That could come through calorie-restricted diets, or through drugs that mimic those diets' effects.

In the meantime, Takahashi is taking a lesson from his mice - he restricts his own eating to a 12-hour period. But, he says, "if we find a drug that can boost your clock, we can then test that in the laboratory and see if that extends lifespan."

Story Source:

Materials provided by **Howard Hughes Medical Institute**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Victoria Acosta-Rodríguez, Filipa Rijo-Ferreira, Mariko Izumo, Pin Xu, Mary Wight-Carter, Carla B. Green, Joseph S. Takahashi. **Circadian alignment of early onset caloric restriction promotes longevity in male C57BL/6J mice**. *Science*, 2022; DOI: 10.1126/science.abk0297

---

3. 炎症の遮断が慢性的な痛みに繋がる可能性 –マウス研究

日付：2022 年 5 月 12 日
ソース：マギル大学
概要：

マギル大学を中心とする研究チームは、抗炎症薬とステロイドで痛みを和らげると、その後慢性的な痛みを発症する可能性が高くなるとして、痛みを和らげるために使用される従来の慣行に疑問を投げかけている。痛みを伴う怪我からの通常の回復には炎症が含まれるが、その炎症を薬でブロックすることによって、後々治療が困難な痛みに繋がる可能性がある、としている。
「Science Translational Medicine」誌に掲載された研究で、研究者らは人間とマウスの両方の痛みのメカニズムを調べた。彼らは、好中球（体が感染と戦うのを助ける白血球の一種）が痛みを解決する上で重要な役割を果たすことを発見した。
マウスで実験的に好中球をブロックすると、痛みは通常の 10 倍まで延長された。デキサメタゾンやジクロフェナクなどの抗炎症薬やステロイドで痛みを治療しても、初期の痛みには効果があったものの、同じ結果が得られた。
これらの発見は、英国の 50 万人の別の分析によっても裏付けられており、痛みを治療するために抗炎症薬を服用している人は、2～10 年後に痛みを感じる可能性が高く、アセトアミノフェンや抗うつ薬を服用している人には見られない効果がある、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＞Discovery reveals blocking inflammation may lead to chronic pain (medicalxpress.com)

MAY 11, 2022

Discovery reveals blocking inflammation may lead to chronic pain

by McGill University

Credit: Pixabay/CC0 Public Domain

Using anti-inflammatory drugs and steroids to relieve pain could increase the chances of developing chronic pain, according to researchers from McGill University and colleagues in Italy. Their research puts into question conventional practices used to alleviate pain. Normal recovery from a painful injury involves inflammation and blocking that inflammation with drugs could lead to harder-to-treat pain.

"For many decades it's been standard medical practice to treat pain with anti-inflammatory drugs. But we found that this short-term fix could lead to longer-term problems," says Jeffrey Mogil, a Professor in the Department of Psychology at McGill University and E. P. Taylor Chair in Pain Studies.

The difference between people who get better and don't

In the study published in *Science Translational Medicine*, the researchers examined the mechanisms of pain in both humans and mice. They found that neutrophils—a type of white blood cell that helps the body fight infection—play a key role in resolving pain.

"In analyzing the genes of people suffering from lower back pain, we observed active changes in genes over time in people whose pain went away. Changes in the blood cells and their activity seemed to be the most important factor, especially in cells called neutrophils," says Luda Diatchenko a Professor in the Faculty of Medicine, Faculty of Dentistry, and Canada Excellence Research Chair in Human Pain Genetics.

Inflammation plays a key role in resolving pain

"Neutrophils dominate the early stages of inflammation and set the stage for repair of tissue damage. Inflammation occurs for a reason, and it looks like it's dangerous to interfere with it," says Professor Mogil, who is also a member of the Alan Edwards Centre for Research on Pain along with Professor Diatchenko.

Experimentally blocking neutrophils in mice prolonged the pain up to ten times the normal duration. Treating the pain with anti-inflammatory drugs and steroids like dexamethasone and diclofenac also produced the same result, although they were effective against pain early on.

These findings are also supported by a separate analysis of 500,000 people in the United Kingdom that showed that those taking anti-inflammatory drugs to treat their pain were more likely to have pain two to ten years later, an effect not seen in people taking acetaminophen or anti-depressants.

Reconsidering standard medical treatment of acute pain

"Our findings suggest it may be time to reconsider the way we treat acute pain. Luckily pain can be killed in other ways that don't involve interfering with inflammation," says Massimo Allegri, a Physician at the Policlinico of Monza Hospital in Italy and Ensemble Hospitalier de la Cote in Switzerland.

"We discovered that pain resolution is actually an active biological process," says Professor Diatchenko. These findings should be followed up by clinical trials directly comparing anti-inflammatory drugs to other pain killers that relieve aches and pains but don't disrupt inflammation."

"Acute inflammatory response via neutrophil activation protects against the development of chronic pain" by Marc Parisien et al. was published in *Science Translational Medicine*.

Explore further

Newly discovered pathway for pain processing could lead to new treatments

---

More information: Marc Parisien et al, Acute inflammatory response via neutrophil activation protects against the development of chronic pain, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abj9954. www.science.org/doi/10.1126/scitranslmed.abj9954

Journal information: Science Translational Medicine

Provided by McGill University

4. 単一のホルモンが低タンパク食に対する体の反応を管理

FGF21 の存在により、マウスは長生きし、体重を減らしながらより多くの食事をする

日付:2022 年 5 月 13 日
ソース:ペニントン生物医学研究センター
概要:

「Nature Communications」誌に掲載されたペニントン生物医学研究センターの新しい研究では、食事中のタンパク質の量を減らすと、寿命の延長を含む一連の好ましい健康上の結果がもたらされること、また、これらの効果は肝臓由来の線維芽細胞成長因子 21（FGF21）と呼ばれる代謝ホルモンに依存すること、が示されている。
食べる量を減らすと健康が増進し、寿命が延びることは古くから知られており、たんぱく質やアミノ酸の摂取量を減らすことがこの有益な効果に寄与する可能性への関心が高まっている。最近のいくつかの研究は、タンパク質が少ないが栄養失調を引き起こすほど低くない食事で健康を改善できること、逆に、高タンパク食の過剰摂取は、特定の年齢層の死亡率の増加に関連している、ことが示唆されている。
数年前、ペニントンのニューロシグナリング研究所は、代謝ホルモン FGF21 が、タンパク質制限中に体と脳をつなぐ重要な信号になっていることを発見した。この信号がなければ、若いマウスは低タンパク食を与えられたときに摂食行動や代謝を変えることができなかった。
このグループの最新の研究では、低タンパク食が老齢マウスに有益な代謝効果をもたらし、代謝の健康を改善し、虚弱を減らし、寿命を延ばすことを示した。これらの有益な効果は、中年マウスがタンパク質の摂取量が減らした時にも明らかであり、肥満の悪影響からさえ保護していた。重要なことに、これらの有益な効果は FGF21 を欠いたマウスでは失われた。

研究関連ニュース/他のトップページに戻る

＜英文＞A single hormone directs body's responses to low-protein diet: Mice live longer and lose weight while eating more when FGF21 is present -- ScienceDaily

A single hormone directs body's responses to low-protein diet

Mice live longer and lose weight while eating more when FGF21 is present

Date:

May 13, 2022

Source:

Pennington Biomedical Research Center

Summary:

A single hormone appears to coordinate the lifespan extension produced by a low-protein diet. Low-protein diets produce beneficial metabolic effects in aged mice, improving metabolic health, reducing frailty, and extending lifespan. These beneficial effects were also apparent when protein intake was reduced in middle-aged mice, even protecting against the detriments of obesity. Importantly, these beneficial effects were lost in mice that lacked FGF21, suggesting that its action in the brain is critical for the increase in health and lifespan.

FULL STORY

A single hormone appears to coordinate the lifespan extension produced by a low-protein diet.

A new study from Pennington Biomedical Research Center, published in the journal *Nature Communications*, found that reducing the amount of protein in the diet produced an array of favorable health outcomes, including an extension of lifespan, and that these effects depend on a liver-derived metabolic hormone called Fibroblast Growth Factor 21 (FGF21).

It has long been known that reducing the amount you eat improves health and extends lifespan, and there has been increasing interest in the possibility that reducing protein or amino acid intake contributes to this beneficial effect. Several recent studies suggest that diets that are low in protein, but not so low that they produce malnutrition, can improve health. Conversely, overconsumption of high-protein diets has been linked to increased mortality in certain age groups.

A few years ago, Pennington Biomedical's Neurosignaling Laboratory discovered that the metabolic hormone FGF21 was a key signal linking the body to the brain during protein restriction. Without this signal, young mice failed to change their feeding behavior or metabolism when placed on a low-protein diet.

"Our data suggest that FGF21 talks to the brain, and that without this signal the mouse doesn't 'know' that it is eating a low-protein diet. As a result, the mouse fails to adaptively change its metabolism or feeding behavior," said Christopher Morrison, Ph.D., Professor and Director of the Neurosignaling Lab.

The group's newest work, led by postdoctoral researcher Cristal M. Hill, Ph.D., demonstrates that low-protein diets produce beneficial metabolic effects in aged mice, improving metabolic health, reducing frailty, and extending lifespan. These beneficial effects were also apparent when protein intake was reduced in middle-aged mice, even protecting against the detriments of obesity. Importantly, these beneficial effects were lost in mice that lacked FGF21, suggesting that its action in the brain is critical for the increase in health and lifespan.

"We previously showed that FGF21 acts in the brain to improve metabolic health in young mice fed a low-protein diet. These new data extend this work by demonstrating that FGF21 also improves metabolic health and extends lifespan. Collectively, these data provide clear evidence that FGF21 is the first known hormone that coordinates feeding behavior and metabolic health to improve lifespan during protein restriction," Dr. Hill said.

However, Dr. Hill said several questions remain. It's unclear exactly how these observations will translate to aging humans, but the hope is that this work will uncover novel molecular and neural pathways that can be leveraged to improve health in people.

"This groundbreaking research has important implications for extending the health and lifespan of people. If scientists can better understand how diets and nutritional hormones like FGF21 act to extend lifespan, these discoveries could offset many of the health issues that occur in middle age and later," said Pennington Biomedical Executive Director John Kirwan, Ph.D.

This work was supported by the National Institutes of Health grants R01DK105032, R01DK121370, R01DK123083, and F32DK115137. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Story Source:

Materials provided by **Pennington Biomedical Research Center**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Cristal M. Hill, Diana C. Albarado, Lucia G. Coco, Redin A. Spann, Md Shahjalal Khan, Emily Qualls-Creekmore, David H. Burk, Susan J. Burke, J. Jason Collier, Sangho Yu, David H. McDougal, Hans-Rudolf Berthoud, Heike Münzberg, Andrzej Bartke, Christopher D. Morrison. **FGF21 is required for protein restriction to extend lifespan and improve metabolic health in male mice**. *Nature Communications*, 2022; 13 (1) DOI: 10.1038/s41467-022-29499-8

---

5. 腸は遺伝子の使用法を調整し、腸内微生物はその調整をサポート
腸内微生物のないマウスは、脂肪消化のために全く異なる遺伝子セットに依存

日付：2022 年 5 月 13 日
ソース：デューク大学
概要：

微生物から腸の細胞に届くメッセージの解析を開始するに当たり、ノースカロライナ州ダーラムのデューク大学の研究者らは、腸内微生物なしで飼育されたマウスと正常な腸内微生物叢を持つマウスを比較した。研究者らは、RNA 転写（DNA が RNA にコピーされる）と、脂肪や他の栄養素のほとんどの取り込みが起こる小腸でこのコピープロセスをオンまたはオフにするタンパク質との間のクロストークに焦点を当てた。
無菌マウスと正常マウスの両方が高脂肪食で脂肪酸を代謝することができたが、驚くべき発見は、無菌動物が高脂肪食を処理するために非常に異なる遺伝子セットを使用したことであった。すなわち、腸上皮が食餌性脂肪に反応するために使用する遺伝子プレイブックは、微生物が存在するかどうかによって異なる。
また、微生物は腸が脂肪を吸収するのを助けることができることを発見した。これに対して、無菌マウスでは、腸の細胞に燃料を供給するために、酪酸の酸化、文字通り酪酸の燃焼に関与する遺伝子活性の増加が見られた。研究者らは、無菌動物が珍しいように見えるあらゆる点において、それは我々が「正常な」動物生物学であると考えるものに対する微生物叢の大きな影響について何かを教えてくれるものだ、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＞Microbes help orchestrate how the gut uses it | EurekAlert!

NEWS RELEASE 13-MAY-2022

Microbes help orchestrate how the gut uses its genes

Mice without microbes rely on an entirely different set of genes to digest fat

Peer-Reviewed Publication

DUKE UNIVERSITY

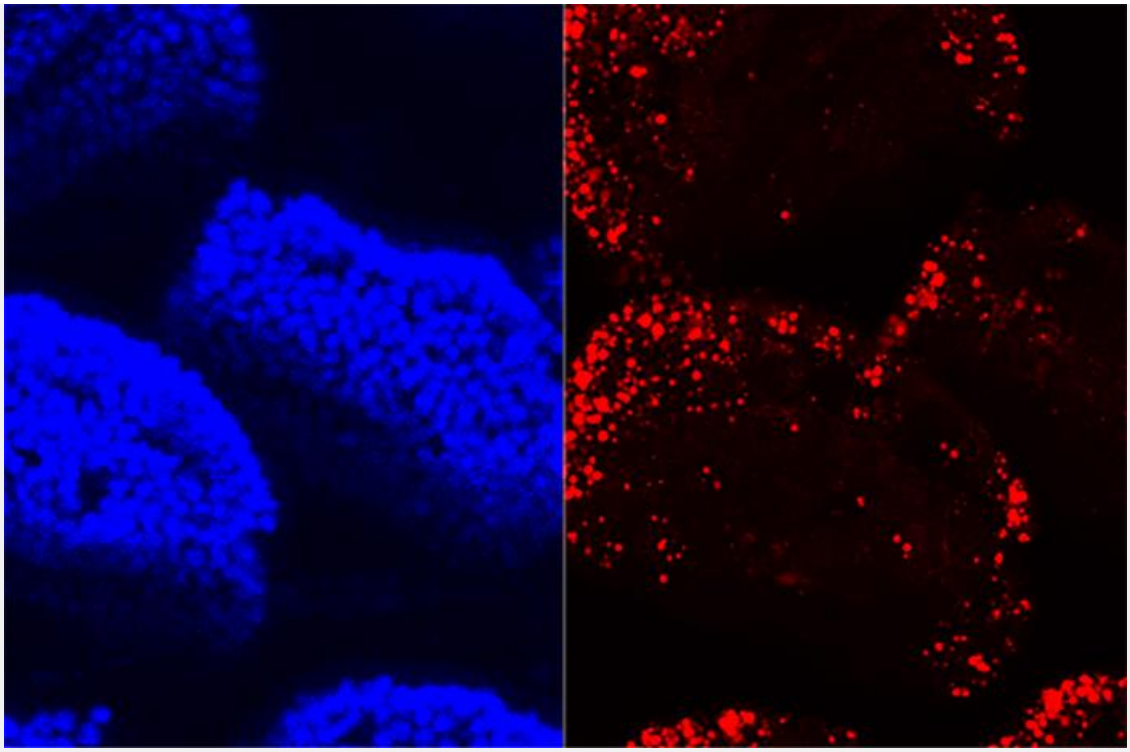


IMAGE: A CONFOCAL MICROSCOPY IMAGE OF SMALL VILLI IN THE SMALL INTESTINE SHOWS CELL NUCLEI IN BLUE AND ABSORBED DIETARY FAT IN RED. view more

CREDIT: JOHN RAWLS LAB, DUKE MICROBIOME CENTER

DURHAM, N.C. –The microbes that help break down food actually tell the gut how to do its job better, according to a new study in mice at Duke.

The researchers said it appears that the microbes are able to influence which of the gut's genes are being called into action, and in turn, that interaction might lead to a remodeling of the epithelial cells lining the gut so that they match the diet.

"The gut is a fascinating interface between an animal and the world it lives in, and it receives information from both the diet and the microbes it harbors," said John Rawls, Ph.D., a professor of molecular genomics and microbiology at Duke and director of the Duke Microbiome Center.

The study appeared May 6 in the open access journal *Cellular and Molecular Gastroenterology and Hepatology*.

To begin to parse the messages coming from the microbes to the cells of the gut, the Duke researchers compared mice raised without any gut microbes and those with a normal gut microbiome. The researchers focused on the crosstalk between RNA transcription – DNA being copied to RNA -- and the proteins that turn this copying process on or off in the small intestine, where most uptake of fat and other nutrients occurs.

While both the germ-free and normal mice were able to metabolize fatty acids in a high-fat diet, the striking finding was that the germ-free animals used a very different set of genes to deal with a high-fat meal.

“We were surprised to find that the gene playbook that the gut epithelium uses to respond to dietary fat is different depending on whether or not microbes are there,” Rawls said.

The researchers also saw that the microbes can help the gut absorb fats.

“It’s a relatively consistent finding across multiple studies, from our lab and others, that microbes actually promote lipid absorption,” said Colin Lickwar, Ph.D., a senior research associate in Rawls’ lab and first author on the paper. “And that, at some level, also impacts systemic processes like weight gain.”

The germ-free mice saw an increase in activity of the genes involved in fatty acid oxidation, literally burning of fatty acids, to provide fuel for the gut’s cells.

“Typically we think about the gut just doing its job absorbing dietary nutrients across the epithelium to share with the rest of the body, but the gut has to eat too,” Rawls said. “So what we think is going on in germ-free animals, is that the gut is consuming more of the fat than it would if the microbes were there.“

And that may reflect differences in the composition of the gut’s epithelial cells.

“There are a bunch of recent papers showing that there is a substantial capacity to change the larger architecture of the intestine as well as in the individual gene programs,” Lickwar said. “There is a remarkable amount of plasticity in the intestine. We largely don’t understand it, but some of it is elucidated by this paper.”

The researchers focused their effort on a transcription factor called HNF4-Alpha, which is known to regulate genes involved in lipid metabolism and genes that respond to microbes. “We thought that it might represent an interface or a crossroads between interpreting information that comes from either microbial sources or from dietary fat,” Lickwar said.

“It’s certainly complicated, but we do appear to identify that HNF4-Alpha is important in simultaneously integrating multiple signals within the intestine,” Lickwar said.

“For every way that germ-free animals seem unusual, that teaches us something about the large impact of the microbiome on what we consider to be ‘normal’ animal biology,” Rawls said.

This research was supported by the National Institutes of Health (R01-DK093399, P01-DK094779, R01-DK113123, R01-DK111857, R01-DK081426, P01-HL020948), as well as the Nuclear Receptor Signaling Atlas consortium (NURSA, U24-693 DK09774).

CITATION: “Transcriptional Integration of Distinct Microbial and Nutritional Signals by the Small Intestinal Epithelium,” Colin Lickwar, James Davison, Cecelia Kelly, Gilberto Padilla Mercado, Briana Davis, Matthew Tillman, Ivana Semova, Sarah Andres, Goncalo Vale, Jeffrey McDonald and John Rawls. *Cellular and Molecular Gastroenterology and Hepatology*, online May 2, 2022. DOI: 10.1016/j.jcmgh.2022.04.013

JOURNAL

Cellular and Molecular Gastroenterology and Hepatology

DOI

10.1016/j.jcmgh.2022.04.013

METHOD OF RESEARCH

Experimental study

SUBJECT OF RESEARCH

Animals

ARTICLE TITLE

Transcriptional Integration of Distinct Microbial and Nutritional Signals by the Small Intestinal Epithelium

ARTICLE PUBLICATION DATE

2-May-2022

6. CRISPR-Cas9 遺伝子編集アプローチが動物の社会的行動を変える可能性 -ハムスター実験

日付:2022 年 5 月 16 日
ソース:ジョージア州立大学
概要:

国立科学アカデミー紀要(PNAS)に掲載された新しい研究で、ジョージア州立大学の科学者らは、社会神経科学の研究のために遺伝子編集されたハムスターを作成し、社会的行動の背後にある生物学が以前に考えられていたよりも複雑である可能性がある、と発表している。
研究者らは、CRISPR-Cas9 テクノロジーを使用して、哺乳類の社会的行動の調節に重要な役割を果たす神経化学的シグナル伝達経路の作用を排除した。バソプレシンとそれが作用する受容体である Avpr1a は、ペアボンディング、協力、社会的コミュニケーションから優性や攻撃性に至るまでの社会現象を調節する。この研究では、ハムスターの Avpr1a 受容体をノックアウトし、バソプレシンの作用を効果的に排除することで、ハムスターの社会的行動表現が劇的に変化することを発見した。驚くことに、受容体のないハムスターは、受容体のあるハムスターよりもはるかに高いレベルの社会的コミュニケーション行動を示した。さらに興味深いことに、攻撃性で観察された典型的な性差は、他の同性の個体に対して高レベルの攻撃性を示すオスとメスのハムスターの両方で排除された。
研究に使用されたハムスターは、社会的行動、攻撃性、コミュニケーションの研究にとってますます重要になっている。それらは、バソプレシンが社会性に影響を与えることが最初に示された種である。また、ハムスターは、マウスが最も一般的に使用される実験動物である中、その社会組織はマウスで観察されるものよりもはるかに人間に類似しているため、社会的行動の研究のための強力なモデルである、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＞CRISPR-Cas9 gene editing approach can alter the social behavior of animals -- ScienceDaily

CRISPR-Cas9 gene editing approach can alter the social behavior of animals

Date:

May 16, 2022

Source:

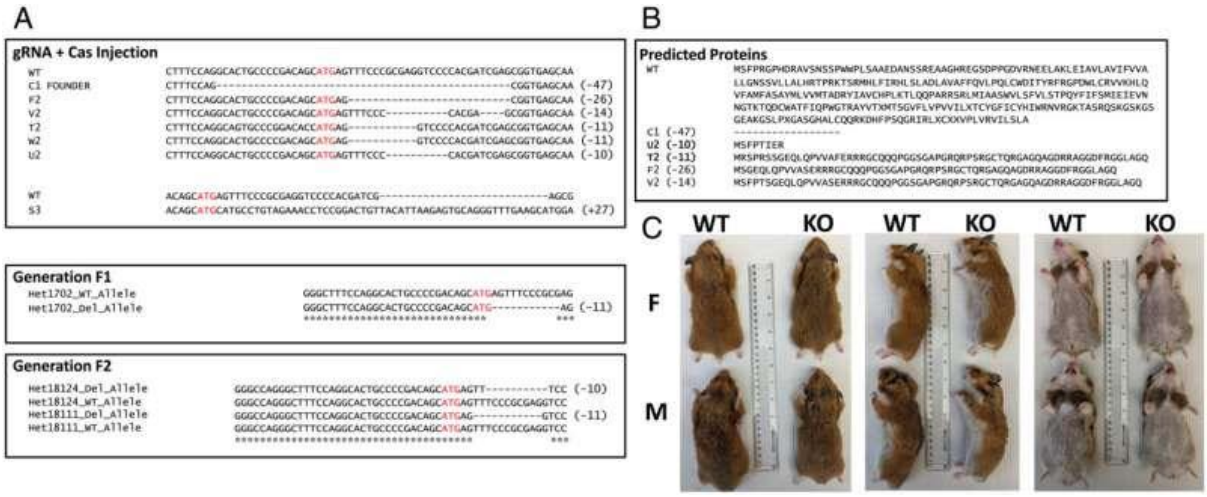
Georgia State University

Summary:

New gene-editing techniques are shedding light on how hormones impact social behavior in animals and possibly, humans.

FULL STORY

Georgia State University scientists have created gene-edited hamsters for studies of social neuroscience and have found that the biology behind social behavior may be more complex than previously thought.



Injections of sgRNA/Cas9 plasmid targeting the Avpr1a gene into hamster embryos. (A) Alignments of various indels produced by CRISPR-Cas9 editing. Only C1 FOUNDER was able to produce offspring resulting in generations F1 and F2. (B) Predicted proteins produced by indels. (C) F (Top of each photo) and M (Bottom of each photo) Avpr1a KOs (Right side of each photo) exhibit no obvious physical differences compared to WT (Left side of each photo).

Credit: *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2121037119

A team of Georgia State University researchers led by Regents' Professor of Neuroscience H. Elliott Albers and Distinguished University Professor Kim Huhman used CRISPR-Cas9 technology to eliminate the actions of a neurochemical signaling pathway that plays a critical role in regulating social behaviors in mammals. Vasopressin and the receptor that it acts on called Avpr1a regulates social phenomena ranging from pair bonding, cooperation, and social communication to dominance and aggression. The new study, published in the *Proceedings of the National Academy of Sciences (PNAS)*, finds that knocking out the Avpr1a receptor in hamsters, and thus effectively eliminating vasopressin's action on it, dramatically altered the expression of social behavior in unexpected ways.

"We were really surprised at the results," Albers said. "We anticipated that if we eliminated vasopressin activity, we would reduce both aggression and social communication. But the opposite happened."

Instead, the hamsters without the receptor showed much higher levels of social communication behavior than did their counterparts with intact receptors. Even more interesting, the typical sex differences observed in aggressiveness were eliminated with both male and female hamsters displaying high levels of aggression towards other same-sex individuals.

"This suggests a startling conclusion," Albers said. "Even though we know that vasopressin increases social behaviors by acting within a number of brain regions, it is possible that the more global effects of the Avpr1a receptor are inhibitory.

"We don't understand this system as well as we thought we did. The counterintuitive findings tell us we need to start thinking about the actions of these receptors across entire circuits of the brain and not just in specific brain regions."

The hamsters used in the research were Syrian hamsters, which have become increasingly important for studies of social behavior, aggression and communication. They are the species in which vasopressin was first demonstrated to influence sociality. Hamsters provide a powerful model for the studies of social behavior because their social organization is far more similar to humans than that observed in mice, even though mice are the most common laboratory animal used. Hamsters are unique research animals in other ways as well, explained Huhman, who is Associate Director of the Neuroscience Institute at Georgia State.

"Their stress response is more like that of humans than it is other rodents. They release the stress hormone cortisol, just as humans do. They also get many of the cancers that humans get," she said. "Their susceptibility to the SARS-CoV-2 virus that causes COVID-19 makes them the rodent species of choice because they are vulnerable to it just as we are."

The work using CRISPR in hamsters was a significant step forward, say both researchers. "Developing gene-edited hamsters was not easy," Albers said. "But it is important to understand the neurocircuitry involved in human social behavior and our model has translational relevance for human health. Understanding the role of vasopressin in behavior is necessary to help identify potential new and more effective treatment strategies for a diverse group of neuropsychiatric disorders ranging from autism to depression."

Story Source:

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

Journal Reference:

1. Jack H. Taylor, James C. Walton, Katharine E. McCann, Alisa Norvelle, Qian Liu, Jacob W. Vander Velden, Johnathan M. Borland, Michael Hart, Chengliu Jin, Kim L. Huhman, Daniel N. Cox, H. Elliott Albers. **CRISPR-Cas9 editing of the arginine–vasopressin V1a receptor produces paradoxical changes in social behavior in Syrian hamsters**. *Proceedings of the National Academy of Sciences*, 2022; 119 (19) DOI: 10.1073/pnas.2121037119

---

7. 食餌性コレステロールがインフルエンザ マウスの病状を悪化させる

日付:2022 年 5 月 19 日
ソース:イリノイ大学農学・消費者・環境科学部
概要:

イリノイ大学の新しい研究によると、高レベルの食餌性コレステロールはインフルエンザに感染するとマウスを病気にすることが示唆されている。この研究は、食餌性コレステロールをウイルス感染の悪化と関連付ける最初の研究で、「Journal of Immunology」誌に掲載されている。
これまでの研究では、一般的に高脂肪食と血中コレステロールの上昇が感染症への感受性の増加と免疫応答の低下と関連付けられていた。例えば、肥満は COVID やインフルエンザの重症疾患では危険因子とされている。しかし、これらの感染症におけるコレステロールの寄与を分離した研究はほとんどなく、食事中のコレステロールの影響を描写したものはなかった。
研究者らは、標準的な齧歯動物用飼料、あるいは同一の飼料に 2% コレステロールを添加したものをマウスに与えた。食餌を与えてから 5 週間後、マウスをマウスに適応したヒトインフルエンザ A ウイルスに感染させ、体重減少、食餌摂取、病気の行動など、病気の進行を追跡した。また、血清コレステロールレベルと免疫応答を追跡し、感染過程の複数の時点で肺のウイルス量を測定した。
彼らのデータは、食餌性コレステロールがインフルエンザに感染したマウスの罹患率を増加させたことをまとめて示しており、それはウイルス自体の影響ではなく、肺で発生する異常な免疫応答の結果であるように見えたとしており、これらの結果については、更なる考慮が必要である、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＞Dietary cholesterol worsens inflammation, sickness in mice with influenza -- ScienceDaily

Dietary cholesterol worsens inflammation, sickness in mice with influenza

Date:

May 19, 2022

Source:

University of Illinois College of Agricultural, Consumer and Environmental Sciences

Summary:

New research suggests high levels of dietary cholesterol make mice sicker when infected with influenza. This study links cholesterol in the diet with exacerbation of a viral infection.

FULL STORY

New research from the University of Illinois suggests high levels of dietary cholesterol make mice sicker when infected with influenza. The study is the first to link cholesterol in the diet with exacerbation of a viral infection.

Previously, scientists linked high-fat diets and elevated blood cholesterol with increased susceptibility to infection and lowered immune response. For example, obesity is a well-known risk factor for severe disease in COVID and influenza. But few studies have separated out the contribution of cholesterol in these infections, and none have delineated the effect of dietary cholesterol.

"We knew high serum cholesterol levels can lead to higher risk of sepsis in influenza infections and that statins -- cholesterol-lowering medications -- can improve survival during influenza pneumonia, SARS-CoV-2 infection, and sepsis. But it wasn't clear whether or how dietary cholesterol was involved," says Allison Louie, lead author on the *Journal of Immunology* study and doctoral student in the Neuroscience Program at Illinois.

Cholesterol is essential in the body. It's part of our cell membranes, helps us make hormones and vitamin D, and allows for proper immune cell function. Our bodies manufacture it for us, requiring little to come in through dietary sources. In fact, for healthy people, dietary cholesterol does not substantially affect circulating cholesterol levels nor increase risk of cardiovascular disease. That's part of the reason limits on cholesterol intake were lifted from the Dietary Guidelines for Americans in 2015.

But when it comes to infectious disease in mice, Louie's study suggests dietary cholesterol may make a difference, even without increasing dietary fat.

Louie, along with co-authors Andrew Steelman and Joseph Tingling, fed mice a standard rodent chow or an identical diet supplemented with 2% cholesterol. After five weeks on the diets, mice were infected with a mouse-adapted human influenza A virus. The research team tracked disease progression, including weight loss, food intake, and sickness behavior. They also tracked serum cholesterol levels and immune responses and measured viral load in the lungs at multiple time points over the course of the infection.

"Across four cohorts, the cholesterol-fed mice had consistently higher morbidity," Louie says. "They exhibited greater weight loss and sickness behavior."

Because viruses also require cholesterol for cell entry and replication, there was a chance the high-cholesterol diet would boost viral load in the lungs. But that's not what the researchers found.

"Our plaque assay did not show a significant difference in viral load in the lungs of the two groups of mice," says Tingling, a postdoctoral researcher in the Department of Animal Sciences at Illinois. "It's very important to consider not just the infectious agent, but the host immune system."

Speaking of the host, the researchers determined mice fed a high-cholesterol diet were sicker because their immune systems went awry. Fat can have an immunosuppressive effect, which is detrimental during the course of an infection. But an underactive immune system is not what the researchers observed in the cholesterol-fed mice. Instead, cholesterol increased the number of cytokine-producing immune cells in the lungs.

"A so-called cytokine storm during severe disease results in excessive inflammation that can be damaging to the host. Along those lines, we found that more cytokine-producing cells had infiltrated the lungs of the mice fed cholesterol, which may have contributed to them being sicker," Louie says. "It's a double-edged sword. You want to be able to mount an effective immune response, but excessive inflammation is detrimental."

Unfortunately, the effects of dietary cholesterol on influenza morbidity lasted long after mice stopped eating it. The researchers took mice that consumed a high-cholesterol diet initially and then gave them a normal diet for five weeks. When those mice were exposed to influenza, they still got sicker than mice that had never consumed a high cholesterol diet.

"We were thinking this dietary component is a highly modifiable factor. Perhaps it would only have a transient effect. But ultimately we found that five additional weeks on a normal diet was not enough time to fully reverse the detrimental effects of cholesterol," Louie says.

Surprisingly, inflammatory changes in the lungs were detectable in the high-cholesterol mice even before they were infected with influenza.

"Some of the changes in the lungs' immune function were already present before infection. It would be interesting to see exactly how dietary cholesterol increased inflammation prior to infection," says corresponding author Steelman, associate professor in the Department of Animal Sciences, the Neuroscience Program, and the Division of Nutritional Sciences at Illinois.

"Nevertheless, our data collectively show that dietary cholesterol increased morbidity in influenza-infected mice. The response appeared to be a result of an aberrant immune response occurring in the lungs rather than an effect of the virus itself. These results demonstrate the need to consider how host factors contribute to disease outcome."

Department of Animal Sciences and the Division of Nutritional Sciences are in the College of Agricultural, Consumer and Environmental Sciences at the University of Illinois Urbana-Champaign.

Story Source:

Materials provided by **University of Illinois College of Agricultural, Consumer and Environmental Sciences**. Original written by Lauren Quinn. *Note: Content may be edited for style and length.*

Journal Reference:

1. Allison Y. Louie, Joseph Tingling, Evan Dray, Jamal Hussain, Daniel B. McKim, Kelly S. Swanson and Andrew J. Steelman. **Dietary Cholesterol Causes Inflammatory Imbalance and Exacerbates Morbidity in Mice Infected with Influenza A Virus**. *Journal of Immunology*, 2022 DOI: 10.4049/jimmunol.2100927

---

8. 人工知能を利用してイヌの生命を脅かす細菌感染症を予測

日付:2022 年 5 月 23 日
ソース:カリフォルニア大学デービス校
概要:

カリフォルニア大学デービス校の獣医師と研究者のチームは、今回人工知能を介してレプトスピラ症を予測する技術を開発した。レプトスピラ症は、レプトスピラ菌で汚染された飲料水を犬が飲むことで発症する可能性のある病気で、腎不全、肝臓病、肺への重度の出血を引き起こす可能性がある。病気の早期発見が非常に重要で、生命を脅かす可能性のある細菌性疾患である。
レプトスピラ症の伝統的な検査は、病気の初期段階では感度が不足おり、また、血液サンプル中の抗体レベルの上昇を実証する必要があるため、検出にも 2 週間以上かかる場合がある。彼らの AI モデルは、迅速かつ正確な診断へのこれら 2 つの障害を排除するとして、この画期的な発見を、「Journal of Veterinary Diagnostic Investigation」誌で発表している。

研究関連ニュース/他のトップページに戻る

＜英文＞Using artificial intelligence to predict life-threatening bacterial disease in dogs -- ScienceDaily

Using artificial intelligence to predict life-threatening bacterial disease in dogs

Date:

May 23, 2022

Source:

University of California - Davis

Summary:

Veterinarians and researchers have developed a technique to predict leptospirosis in dogs through artificial intelligence. Leptospirosis is a life-threatening bacterial disease dogs can get from drinking contaminated water.

FULL STORY

Leptospirosis, a disease that dogs can get from drinking water contaminated with *Leptospira* bacteria, can cause kidney failure, liver disease and severe bleeding into the lungs. Early detection of the disease is crucial and may mean the difference between life and death.

Veterinarians and researchers at the University of California, Davis, School of Veterinary Medicine have discovered a technique to predict leptospirosis in dogs through the use of artificial intelligence. After many months of testing various models, the team has developed one that outperformed traditional testing methods and provided accurate early detection of the disease. The groundbreaking discovery was published in Journal of Veterinary Diagnostic Investigation.

"Traditional testing for *Leptospira* lacks sensitivity early in the disease process," said lead author Krystle Reagan, a board-certified internal medicine specialist and assistant professor focusing on infectious diseases. "Detection also can take more than two weeks because of the need to demonstrate a rise in the level of antibodies in a blood sample. Our AI model eliminates those two roadblocks to a swift and accurate diagnosis."

The research involved historical data of patients at the UC Davis Veterinary Medical Teaching Hospital that had been tested for leptospirosis. Routinely collected blood work from these 413 dogs was used to train an AI prediction model. Over the next year, the hospital treated an additional 53 dogs with suspected leptospirosis. The model correctly identified all nine dogs that were positive for leptospirosis (100% sensitivity). The model also correctly identified approximately 90% of the 44 dogs that were ultimately leptospirosis negative.

The goal for the model is for it to become an online resource for veterinarians to enter patient data and receive a timely prediction.

"AI-based, clinical decision making is going to be the future for many aspects of veterinary medicine," said School of Veterinary Medicine Dean Mark Stetter. "I am thrilled to see UC Davis veterinarians and scientists leading that charge. We are committed to putting resources behind AI ventures and look forward to partnering with researchers, philanthropists, and industry to advance this science."

Detection model may help people

Leptospirosis is a life-threatening zoonotic disease, meaning it can transfer from animals to humans. As the disease is also difficult to diagnose in people, Reagan hopes the technology behind this groundbreaking detection model has translational ability into human medicine.

"My hope is this technology will be able to recognize cases of leptospirosis in near real time, giving clinicians and owners important information about the disease process and prognosis," said Reagan. "As we move forward, we hope to apply AI methods to improve our ability to quickly diagnose other types of infections."

Reagan is a founding member of the school's Artificial Intelligence in Veterinary Medicine Interest Group comprising veterinarians promoting the use of AI in the profession. This research was done in collaboration with members of UC Davis' Center for Data Science and Artificial Intelligence Research, led by professor of mathematics Thomas Strohmer. He and his students were involved in the algorithm building.

Reagan's group is actively pursuing AI for prediction of outcome for other types of infections, including a prediction model for antimicrobial resistant infections, which is a growing problem in veterinary and human medicine. Previously, the group developed an AI algorithm to predict Addison's disease with an accuracy rate greater than 99%.

Funding support comes from the National Science Foundation.

Story Source:

Materials provided by **University of California - Davis**. Original written by Rob Warren. *Note: Content may be edited for style and length.*

Journal Reference:

1. Krystle L. Reagan, Shaofeng Deng, Junda Sheng, Jamie Sebastian, Zhe Wang, Sara N. Huebner, Louise A. Wenke, Sarah R. Michalak, Thomas Strohmer, Jane E. Sykes. **Use of machine-learning algorithms to aid in the early detection of leptospirosis in dogs**. *Journal of Veterinary Diagnostic Investigation*, 2022; 104063872210967 DOI: 10.1177/10406387221096781

9. メスのマウスは妊娠するとバナナ臭の尿を出してオスを阻止
オスにストレスを与え遠ざけることによって子殺しをさせないと考えられる

日付：2022 年 5 月 20 日
ソース：マギル大学
概要：

妊娠中または最近出産したメスのマウスは、尿中にバナナ臭の化学物質を生成し、オスにストレスを与え、子犬を殺すのを防ぐ可能性がある。モントリオールのマギル大学の研究チームが、この行動を偶然発見し、「Science Advances」誌に発表している。
気付きを確認するために研究者らは、別のオスのマウス、妊娠していないマウス（メス）、新しく妊娠したマウス（メス）、出産を間近に控えたマウス（メス）、最近出産して授乳中のマウス（メス）、過去に出産して授乳していないマウス（メス）の近くのケージに入れられたときのオスのマウスのストレスレベルをテストした。オスのマウスは、妊娠中または授乳中のメスのマウスの近くでケージに入れられたとき、痛みの感受性の低下とコルチコステロイドレベルの上昇を示した。これらは両方ともストレスの兆候だが、他のマウスの近くでは生じなかった。
研究者らは、これは妊娠中および授乳中の女性が、バナナ臭の酢酸アミルと呼ばれる化学物質を尿中に生成したためであることを発見した。これがオスの近くのケージの中に漂い、彼らがそれを嗅いだときに彼らにストレスを与えた、としている。
妊娠中または授乳中のメスがいない場合でも、オスをこの化学物質にさらすだけでストレスが溜まった。また、妊娠中および授乳中のメスは、見知らぬオスにさらされたとき、子供の父親にさらされたときよりも多くの尿痕を残した。
研究者らは、この化学物質を嗅ぐことで実際にオスが子供を殺すのを阻止したかどうかをテストしてはいない。しかし、一部の科学者らは、妊娠中のメスの近くにオスのマウスを飼育している場合、無意識のうちにストレスを受けたマウスを実験に使用している可能性があるため、この調査結果は他のマウス研究に影響を及ぼす。これが、異なるラボが同じ実験から異なる結果を得ることがある理由の 1 つである可能性がある、と指摘している。

研究関連ニュース/他のトップページに戻る

＜英文＞Animal behaviour: Female mice release banana-scented urine when pregnant to deter males | New Scientist

Female mice release banana-scented urine when pregnant to deter males

Pregnant and lactating female mice release a banana-smelling chemical in their urine that is thought to stress out males so they don't commit infanticide

LIFE 20 May 2022

By **Alice Klein**

A pregnant harvest mouse (Micromys minutus) and a pup: females will fight to protect their young, and use their urine to remind males of the fact

Klein and Hubert/NaturePL

Female mice that are heavily pregnant or have recently given birth produce a banana-smelling chemical in their urine that stresses out males, possibly to stop them from killing their pups.

Jeffrey Mogil at McGill University in Montreal and his colleagues discovered this behaviour by accident. "We were doing experiments with pregnant female mice and noticed that male mice that were being used for other experiments in the same room were acting a bit crazy," he says.

To explore further, they tested the stress levels of male mice when they were placed in a cage near that of another male mouse or a female that was either not pregnant, newly pregnant, heavily pregnant, had recently given birth and was lactating, or had given birth in the past and was no longer lactating.

The male mice showed reduced pain sensitivity and elevated corticosteroid levels - which are both signs of stress - when they were caged near female mice that were heavily pregnant or lactating, but not when they were near the other mice.

The researchers discovered that this was because heavily pregnant and lactating females produced a chemical in their urine called amyl acetate, which smells of bananas. This wafted into the males' nearby cages and made them stressed when they sniffed it.

Just exposing the males to this chemical alone made them stressed, even when there were no pregnant or lactating females around.

Females probably release this chemical when they are about to have pups or have just had them to let males know, "if you come any closer, I'll beat the crap out of you", says Mogil.

This is because male mice try to kill pups that have been fathered by other males, he says.

In line with this, pregnant and lactating females left more urine marks when they were exposed to stranger males than when they were exposed to the father of their pups.

"Females are known to unleash serious aggression if males try to attack their pups so we think that when males smell this chemical in their urine, the prospect that there might be a fight causes their stress response," says Mogil.

The researchers didn't test if sniffing this chemical did in fact stop males from killing pups because it would be unethical to conduct that kind of experiment, says Mogil.

The findings have implications for other mouse research since some scientists may unwittingly be using stressed mice in their experiments if they house male mice near pregnant females, says Mogil. This could be one reason why different labs sometimes get different results from the same experiments, he says. "It's something we need to pay more attention to."

Journal reference: *Science Advances*, DOI: 10.1126/sciadv.abi9366

More on these topics: