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In-Vivo Science International, Inc.

今月の企業関連ニュース/他

12/3　オミクロン株、欧で 79 例確認　数カ月以内に欧州感染の半分超に＝EU

欧州疾病予防管理センター（ECDC）は 2 日、新型コロナウイルスの新変異株「オミクロン」が数カ月以内に、欧州での感染の半分超に達するという見通しを示した。見通しには欧州連合（EU）加盟の 27 カ国のほか、アイスランド、ノルウェー、リヒテンシュタインが含まれる。

12/5　人の疑似胚盤胞で「着床」再現　iPS 細胞など利用　オーストリア研究所

人の受精卵が分裂して成長した胚盤胞が子宮内膜に着床する過程を、人工多能性幹細胞（iPS 細胞）などを利用して模倣し、実験容器内でほぼ再現できたと、オーストリア科学アカデミー分子生物工学研究所（IMBA）などの研究チームが発表した。「生殖補助医療（不妊治療）の成功率を高める物質を発見する一方、副作用の少ない避妊薬の開発につながる物質も見つけた」という。論文は 3 日、英科学誌ネイチャー電子版に掲載された。

12/6　米国が自宅での COVID-19 検査を無料で受けられるようにする

新型コロナウイルス（SARS-CoV-2）オミクロン（Omicron）株感染の重症度の見きわめに科学者が取り組み、保健部門がこれからの寒い季節の感染増加への対策の準備を進めるなか、米国政府はワクチン接種を引き続き推進することに加えて海外旅行での検査を拡大し、飛行機やバスなどの公共交通でのマスク着用義務を継続する。

12/7　脳の視床下部の一部に食欲を抑える神経細胞 北大グループが確認

食後に活性化して食欲を抑える働きのある神経細胞が脳の視床下部の「背内側核」という部分にあることを突き止めた、と北海道大学の研究グループが発表した。同グループはこの神経細胞の活動を人工的に増やすと食事量が低下したことも確認した。肥満の予防・治療開発への貢献が期待できるという。北海道大学大学院獣医学研究院の戸田知得助教らの研究グループは、活性化した神経細胞を蛍光タンパク質で標識できるマウスを作ることに成功。このマウスを使って食後に視床下部のどの部分の神経細胞が活性化するかを調べた。

12/8　オミクロン株、Pfizer 製ワクチンの効果「大幅に低下」…南アの民間研究機関

南アフリカの民間研究機関は 7 日、新型コロナウイルスの変異株「オミクロン株」が米 Pfizer 製ワクチンの効果を大幅に低下させるとの研究結果を発表した。南アでは、ワクチン接種後に感染する「ブレイクスルー感染」が相次いでいる。米政府のアンソニー・ファウチ首席医療顧問は 7 日、AFP通信に対し、オミクロン株の重症化率について「ほぼ確実にデルタ株よりは深刻ではない」との見方を示した。感染力についてはデルタ株を上回る可能性が高いとの認識を示した。

12/8　オミクロン株、52 カ国・地域に拡大　デンマークで 398 件

欧州連合（EU）の欧州疾病予防管理センター（ECDC）は 7 日、新型コロナウイルスの新たな変異株「オミクロン株」の感染が確認された国・地域が 52 に広がったと発表した。クロアチア、フィジーなどで新たに確認された。ロイター通信によると、デンマークではオミクロン株の感染が急拡大し、これまでに 398 件の感染が報告された。大規模コンサートやクリスマスパーティーで市中感染が広がったという。

12/8　「尿一滴でがんがわかる」で話題　線虫がん検査「精度 86%」は問題だらけ

CM で「尿一滴で、精度 86%のがん検査」を謳っている、HIROTSU バイオサイエンス（以下、H 社）の線虫がん検査を巡って、関係者から検査方法に疑義の声が上がっていることが「週刊文春」の取材でわかった。

12/8　「最後は研究者として…」 山中伸弥さん、iPS 研究所の所長退任へ

京都大学は 8 日、山中伸弥教授が iPS 細胞研究所の所長を 2022 年 3 月末で退任すると発表。後任の所長には iPS 細胞を使ったパーキンソン病治療を研究する高橋淳教授が就任する。山中教授は教授職として iPS 研に残り、研究を続ける。

12/9　南アのコロナ新規感染者、2 万人に迫る　オミクロン検出以来の高水準

12/9　ワクチンが不向きな人用の AstraZeneca の COVID-19 予防抗体 Evusheld を米国認可

ワクチンが不向きな人の新型コロナウイルス（SARS-CoV-2）感染（COVID-19）を予防する AstraZeneca の長く効く抗体 Evusheld （エブシェルド、AZD7442） が米国で取り急ぎ認可された。持病や治療で免疫が衰えていて COVID-19 ワクチンで十分な免疫を備えることができそうにない人や COVID-19 ワクチン接種でひどく体を壊した経験があって決められた通りの COVID-19 ワクチン接種が不適切な人への投与が認められた。

12/9　Humira 後発品の Alvotech が SPAC 取り引きで 4 億 5,000 万ドルを手にして上場

AbbVie の売り上げ世界一の薬 Humira（ヒュミラ；adalimumab、アダリムマブ）の高濃度模倣品（バイオシミラー）AVT02 を米国 FDA に承認申請済みのアイスランド拠点の Alvotech が Oaktree Acquisition との SPAC 取り引きで 4 億 5,000 万ドルを手にして米国ナスダック市場に上場する。

12/10　追加接種の加速で WHO「高所得国がワクチンため込む」「地球規模の視点が必要」

新型コロナウイルスの新たな変異株「オミクロン株」の世界的な広がりを受け、各国がワクチン追加接種を進めていることについて、世界保健機関（WHO）の専門家は 9 日、高所得国がワクチン確保を急ぐ動きを控えるよう訴えた。さらに、すべての国にワクチンが行き渡らない限り感染予防対策はうまくいかないと指摘し、「パンデミック（世界的大流行）を食い止めるため、各国は合理的で地球規模の視点をもつ必要がある」と、追加接種よりも未接種者へのワクチン分配を進めるよう訴えた。

12/10　J&J が社内安全性部門が明るみに出すべきとした糖尿病薬の害を約 10 年黙殺

Reuters の調べによると、Johnson & Johnson（J&J）は 10 年ほど前の 2013 年 3 月に米国 FDA に承認された糖尿病薬 Invokana（canagliflozin、カナグリフロジン）使用に伴う血中の酸蓄積・ケトアシドーシスの発生を把握しながら米国 FDA が気付くまでだんまりを決め込んでいた。

12/10　オミクロン株関連 COVID-19 流行の南アでの新規感染数 2 万人超 (12/9) ～死亡は 22 人のみ

12/10　COVID-19 のみならずどのコロナウイルスも始末しうる飲み薬を Novartis が開発中

12/11　米のオミクロン感染者、多くがワクチン完全接種済み＝CDC

米疾病対策センター（CDC）が 10 日に公表した報告書によると、これまでに米国で新型コロナウイルスのオミクロン型変異株への感染が確認された 43 人のうち、ほとんどがワクチン接種を完全に済ませていた。また、そのうち 3 分の 1 は追加接種（ブースター接種）も済ませていたという。

12/11　ワクチンで老化細胞除去　マウスで成功、治療応用期待　順大など

加齢に伴い蓄積され、動脈硬化などの原因となる「老化細胞」を除去するワクチンの開発に成功したと、順天堂大大学院の南野徹教授らの研究グループが発表した。マウスに接種後、老化細胞が除去され、動脈硬化部分の縮小が確認された。南野氏は「動脈硬化や糖尿病など加齢関連疾患の治療に応用が期待できる」と話している。論文は 10 日付の科学誌ネイチャー・エイジング電子版に掲載された。

12/12　Pfizer の COVID-19 ワクチン 3 回目接種の効果を裏付けたイスラエル試験の論文報告

Pfizer の新型コロナウイルス（SARS-CoV-2）ワクチン BNT162b2 の 3 回目接種で SARS-CoV-2 感染（COVID-19）、重症の COVID-19、COVID-19 による死亡がより減ることを示したイスラエルでの試験 2 つが論文になった。
又 2 回接種してから 5-6 か月経つ人の血液はオミクロン（Omicron）株にまるで歯が立たなかったが、3 回目接種してから間もない人の血液は幸いにもオミクロン株を食い止めた、としている。

https://www.nejm.org/doi/full/10.1056/NEJMoa2115926
https://www.nejm.org/doi/full/10.1056/NEJMoa2115624

12/13 「唾液に柿渋　重症化と感染抑制」 新型コロナ　ハムスター実験

奈良県立医大（橿原市）の研究グループは 13 日、柿から抽出した柿タンニン（柿渋）が唾液中に含まれていると、新型コロナウイルスに感染しても重症化しにくく、感染抑制効果もあることを、ハムスターの実験で確かめたと発表。8 日付の英科学誌「サイエンティフィック・リポーツ」電子版に掲載された。

12/13　妊娠 25 週、胎内で心臓手術　国内初、重い先天性の病気

国立成育医療研究センターは 13 日、重い先天性の心臓の病気「重症大動脈弁狭窄症」と診断された赤ちゃんの手術を母親のおなかの中にいる妊娠 25 週で行い、成功させたと発表。この病気の胎内での手術は欧米では実績があったが、国内では初。無事に生まれ、経過も良好という。

12/13　南アのラマポーザ大統領が新型コロナ陽性－軽症、自主隔離に

12/13　英、オミクロン株で死者　世界で初確認か

12/13　WHO「デルタ株からオミクロン株に置き換わる」

WHO は 12 日、オミクロン株についての最新の知見を公開。免疫を回避する力によるものなのか、感染力の強さによるものなのか不明なものの、市中感染が発生しているところではデルタ株からオミクロン株に置き換わるだろうと指摘。デルタ株の割合が高かったイギリスのような国でも、オミクロン株はデルタ株より速く感染が拡大しているとみられることを理由に挙げている。また、多くの変異があることなどから、ワクチンがオミクロン株の感染を防ぐ効果は低くなったと示唆されると述べた。

12/14　Pfizer が Arena Pharmaceuticals（本社：カリフォルニア州サンディエゴ市）買収

Pfizer が Arena Pharmaceuticals をおよそ 67 億ドルで買って第 3 相試験段階の S1P 受容体調節薬 etrasimod（エトラシモド）を手に入れる。

12/14　既存のリウマチ薬「アクテムラ」 コロナによる肺炎に使えるよう厚労省に適用拡大申請

12/15　シベリアで気温 38 度を記録　北極圏の観測史上、最高と認定　国連

12/15　オミクロン株、77 カ国で感染確認

12/15　オミクロン検査の試薬を開発　島津とタカラバイオ

島津製作所は 15 日、新型コロナウイルス新変異株「オミクロン株」の特徴を検出できる PCR 検査試薬を開発したと発表した。「デルタ株」など他の変異株用の試薬と組み合わせて使うことで、迅速かつ効率的な検出につなげる。タカラバイオも同日、同様の試薬の受注を始めたと発表した。

12/16　神経の元になる細胞「60 代から 10 代に」 マウスで若返りに成功

老化とともに衰える神経細胞の「元」を遺伝子操作で若返らせ、マウスの認知機能を改善することに京都大ウイルス・再生医科学研究所のグループが成功した。16 日、米専門誌に発表する。

12/16　温泉入浴で腸内細菌に変化　九州大、別府での研究を中間報告

12/16　中外製薬、コロナ飲み薬の開発断念…厚労省は補助の一部返金求める

中外製薬は16日、新型コロナウイルスの経口薬（飲み薬）として承認を目指していた「AT―527」について、開発を終了すると発表した。厚生労働省への申請も断念する。

12/17　ALS 治療探しで Eli Lilly と提携している Verge Genomics（本社：カリフォルニア州サウスサンフランシスコ市）が 9,800 万ドル調達

12/18　仏、ワクチン事実上義務化へ　追加接種は 4 カ月後から

12/18　欧州が Biogen のアルツハイマー病薬 Aduhelm（アデュヘルム；aducanumab、アデュカヌマブ）を承認すべきでないと判断

12/19　Moderna COVID-19 ワクチンの若い男性の心臓炎症の発生率は Pfizer のより 5 倍高い

デンマークの 12 歳以上の住人およそ 500 万人のうち約 400 万人が Pfizer/BioNTech か Moderna の新型コロナウイルス（SARS-CoV-2）ワクチン BNT162b2 か mRNA-1273 を接種し、どちらのワクチンも女性が心筋炎や心膜炎をより生じ易くなることと関連し、Moderna のワクチン mRNA-1273 は女性に加えて男性がそれらをより生じ易くなることとも関連した。

12/20　Moderna 製ワクチン、ブースター接種でオミクロン株への抗体 37 倍

12/21　Biogen がアルツハイマー病薬 Aduhelm の米国での価格をおよそ半額に

売れ行きが悪い Biogen のアルツハイマー病薬 Aduhelm（アデュヘルム；aducanumab、アデュカヌマブ）の米国での値段が来年 2022 年 1 月 1 日からおよそ半額になり、その販売不振や多発性硬化症（MS）薬後発品の威勢で損なわれる事が予想される売り上げに見合うように同社の経費が削減される。
たとえば平均的な体重 74kg の患者の同剤の 1 年間の値段は 28,200 ドルとなる。

https://www.globenewswire.com/news-release/2021/12/20/2355113/0/en/Biogen-Announces-Reduced-Price-for-ADUHELM-to-Improve-Access-for-Patients-with-Early-Alzheimer-s-Disease.html

12/21　塩野義製薬・開発中の新型コロナ飲み薬は「オミクロン株にも有効性期待できる」と発表

12/21　WHO「接種者も感染の可能性」 オミクロン、デルタ株より速く拡大

12/21　Novavax 製のワクチンを EU が承認　日本でも承認を申請中

	ワクチンのタイプ	供給の見通し	保存方法	生産体制	日本での審査状況
ファイザー(米)、ビオンテック(独)	mRNA	1億9400万回分	零下60～80度で冷凍保存	輸入	特例承認
モデルナ(米)	mRNA	1億回分	零下20度で冷凍保存	輸入	特例承認
アストラゼネカ(英)、オックスフォード大(英)	ウイルスベクター	1億2千万回分	2～8度で冷蔵保存	国内製造が可能	特例承認
ノババックス(米)	組み換えたんぱく	1億5千万回分	2～8度で冷蔵保存	国内製造が可能	未申請

12/21　オミクロン株、新規症例の 73%に　首都やNY市が再び規制強化　米CDC

米疾病対策センター(CDC)は 20 日、新型コロナウイルスの新たな変異株「オミクロン株」が、米国で確認された新規の症例の 73%以上を占めていることを明らかにした。CDCの推計によると、18 日までの1週間に確認された新規の症例のうち、オミクロン株が占める割合は 73.2%、デルタ株は 26.2%だった。

12/21　沖縄米軍クラスター、200 人に　政府、オミクロン検査要請

12/22　Softbank がブラジルの医療会社 Alice への 1 億 2,700 万ドルの投資を率いた

12/23　Pfizer の COVID-19 経口薬 Paxlovid(パクスロビド)を米国 FDA が取り急ぎ認可

12/24　オミクロン株感染者の入院リスクが低いことが英国政府解析でも示された

新型コロナウイルス(SARS-CoV-2)オミクロン株感染者の入院リスクがデルタ株感染者に比べてより低いことが英国政府の保健安全保障庁(UKHSA)の解析でも示された。

12/24　世界でオミクロン株対策強化

イタリアは屋外でのマスク着用を義務付ける措置を復活させ、映画館や劇場、公共交通機関ではより高性能のマスクの着用を義務付けた。さらに来年 1 月末まで祝賀行事を全面的に禁止し、ナイトクラブは閉鎖する。
スペインも屋外でのマスク着用を再び原則義務化する。
南米エクアドルは、国内でオミクロン株感染者が確認されたのを受け、世界で初めて 5 歳以上のワクチン接種を義務化した。
タジキスタン、トルクメニスタン、インドネシア、ミクロネシア、ニューカレドニアはすでに、成人にワクチン接種を義務付けている。
フランスと英国は、1 日当たりの新規感染者数が過去最多を更新したと発表。
「ゼロコロナ」政策を推し進める中国では、「デルタ株」の流行を受けて、人口 1,300 万人の西安(Xi'an)で厳格なロックダウン(都市封鎖)が導入された。

12/25　ASL の治療薬候補、山形大など発見　たんぱく質の凝集抑制に期待

体が徐々に動かなくなる難病「筋萎縮性側索硬化症（ALS）」の新たな治療薬の候補が見つかったと、山形大医学部が 24 日に発表。筋肉が萎縮する原因とされるたんぱく質の異常な凝集を抑制する効果が期待できるという。動物や健常な成人へ試験中で、早ければ 2024 年に患者の臨床試験に入る。

12/25　NY 州で新規感染 4 万 4,000 人超　1 週間で倍増　オミクロン株はすでに 92%超え

12/25　オミクロン株、年末の移動を直撃 世界で 2,300 便欠航

12/28　フランス、週 3 日の在宅勤務義務化へ コロナ対策で

12/28　犬、平均 89 単語を理解　カナダ研究、高い能力判明

12/28　オミクロン株、1 月 11 日前後に大阪で「9 割超え」 北大教授分析

新型コロナウイルスの感染者におけるオミクロン株の割合が、大阪府では 1 月 11 日前後に 90%を超えるとの分析結果を北海道大の伊藤公人教授（生命情報学）らがまとめた。90%に達すると、感染の広がりやすさは 12 月上旬の 2・6 倍ほどになるという。
厚労省によると、27 日までに国内で確認されたオミクロン株の感染者は 316 人。大半は海外からの渡航者やその濃厚接触者だが、感染経路がわからない市中感染も 22 日以降で 36 人確認されている。

12/29　米の新規感染者、過去最多の 1 日 25 万人超　オミクロン株は約 59%

12/29　韓国の Samsung Group が Biogen を買う交渉をしているらしい

12/30　Biogen 買収交渉の噂は正しくないと Samsung BioLogics が発表

12/30　オミクロン、市中感染拡大　デルタ株の最大 4 倍か　専門家「今が勝負」・国内確認 1 カ月

オミクロン株は 11 月 30 日、空港検疫で感染が確認され、今月 22 日には大阪府で市中感染が初めて判明した。厚生労働省によると、28 日時点の感染者は 332 人。同省専門家組織は「感染拡大が急速に進むことを想定すべき状況」と分析した。

12/31　南ア　オミクロン株「ピーク過ぎた」 深夜の外出禁止令を解除

12/31　米、1 日の感染者 50 万人…最悪の冬期パンデミックが現実に

新種のオミクロン変異の拡散により、米国の 1 日あたりのコロナ新規感染者数が 50 万人前後まで急増した。最悪の冬期パンデミックが現実となった。

12/31　中国シノバック製ワクチン、オミクロンに低効果＝査読前論文

中国のシノバック・バイオテック（科興控股生物化学）製の新型コロナウイルスワクチンについて、2 回接種後 Pfizer/BioNTech 製のワクチンでブースター接種（追加接種）を行っても、オミクロン変異株に対する免疫効果が低いとする研究結果が発表された。

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. 大麻が二世代に渡ってマウスの精子数や運動量に影響

2. 特定の神経細胞を刺激して、失われた心筋を再生できる -マウス研究

3. 遺伝子編集技術で単一性のマウス同腹子作成

4. 食事が腸内微生物を介して免疫系機能をどのように変化させるか
   -マウス研究

5. マラソンマウスからの輸血がカウチポテトマウスの脳機能を高める

6. 毎年インフルエンザの予防接種を受ける必要はなくなるかもしれない。
   インフルエンザ共通ワクチンの新たな標的

7. 血液凝固タンパク質の武装解除で、マウスの歯周病を予防
   人間と動物の研究が、歯周病や他の炎症性疾患の治療への洞察を提供

8. “男女の戦い”は父母の遺伝子が栄養をめぐって争う子宮内で始まる

1. 大麻が二世代に渡ってマウスの精子数や運動量に影響

日付：2021 年 12 月 2 日
ソース：ワシントン州立大学
概要：

「Toxicological Sciences」誌に掲載されたワシントン州立大学の研究は、人間と動物の研究に基づいて、大麻が男性の生殖機能を妨げる可能性があることを示している。
人間の研究ではアンケートのような調査に頼らなければならないことも多いが、今回はその人間の研究よりも更に制御された形式でマウスを用いた研究が行われた。
大麻蒸気への猛烈なしかし短期間の曝露は、直接曝露された雄マウスだけでなく、次世代の息子マウスにおいても、その精子数を減らし、その運動性を鈍くした。
研究者らは、30 匹の成体雄マウスを用いて、そのうちの 15 匹を 1 日 3 回 10 日間大麻蒸気にさらした。これは大量だが、大麻を頻繁に使用するヒトの大麻摂取を模倣したものだ。次に、研究者らは、これらのマウスの精子数と運動性を非曝露対照群と比較。すると、曝露期間の直後に、マウスの精子の運動性が低下し、1 か月後に精子数が減少することを発見した。研究者らが、いくつかの雄マウスを暴露されていない雌マウスと交配させたところ、暴露群の雄の子孫も精子数と運動性の低下を示した。大麻にさらされた息子マウスはまた、精子細胞の発達に関連した DNA 損傷と破壊の証拠を示した。
以前のマウス実験では、大麻の主要な精神活性成分であるテトラヒドロカンナビノール（THC）の注射など、他の投与方法を使用しており、今回の研究は気化した大麻を使用した最初の生殖研究だとしている。

研究関連ニュース/他のトップページに戻る

＜英文＞Cannabis impacts sperm counts, motility in tw | EurekAlert!

NEWS RELEASE 2-DEC-2021

Cannabis impacts sperm counts, motility in two generations of mice

Peer-Reviewed Publication

WASHINGTON STATE UNIVERSITY

PULLMAN, Wash. – An intense but short-term exposure to cannabis vapor lowered sperm counts and slowed sperm movement, or motility, not only in the directly exposed male mice but also in their sons.

The Washington State University study, published in the journal *Toxicological Sciences*, builds on other human and animal studies, showing that cannabis can impede male reproductive

function. The current study uses more controlled circumstances than human studies, which often have to rely on surveys, and is the first known reproductive study to use vaporized whole cannabis in mice, which is the more common form humans use. Previous animal studies use other administration methods such as injections of tetrahydrocannabinol (THC), the main psychoactive component of cannabis.

More research needs to be done, but the study's generational findings should give cannabis users pause, said Kanako Hayashi, the paper's corresponding author.

"This is a warning flag. You may take cannabis for some kind of momentary stress, but it could affect your offspring," said Hayashi, who is an associate professor in WSU's School of Molecular Biosciences.

Human sperm counts have declined by as much as 59% in recent decades, according to some estimates. There are likely many reasons for this decline, Hayashi said, but this study adds to the evidence that cannabis use may be detrimental to male reproductive function.

For this study, researchers studied 30 adult male mice. They exposed 15 of them to cannabis vapor three times a day for ten days—an intense amount but one that mimics the cannabis intake of frequent cannabis users. The researchers then compared sperm counts and motility in those mice to the unexposed control group. They found that immediately after the exposure period, the mice's sperm motility decreased, and after one month, sperm counts were lower.

The researchers bred several of the male mice to unexposed female mice. The male progeny of the exposed group also showed lowered sperm count and motility. Cannabis-exposed sons also showed evidence of DNA damage and disruption related to sperm cell development.

"We were not expecting that the sperm would be completely gone or that motility would be completely offset, but the reduction in sperm count and motility of the offspring, the sons, is probably a direct effect of the cannabis exposure to father," said Kanako.

A third-generation, the grandsons of the exposed male mice, did not show the same impacts, however, which suggests that the cannabis exposure impacted the second-generation mice at a developmental stage.

Hayashi and her colleagues are currently testing the theory that cannabis exposure to mice in utero would have deeper generational effects, as the drug would affect the formation of the mice's reproductive system that could be passed down.

The current study was supported in part by funds provided for medical and biological research by the State of Washington Initiative Measure No. 171

JOURNAL

Toxicological Sciences

DOI

10.1093/toxsci/kfab137

METHOD OF RESEARCH

Experimental study

SUBJECT OF RESEARCH

Animals

ARTICLE TITLE

Vapor cannabis exposure generationally affects male reproductive functions in mice

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2. 特定の神経細胞を刺激して、失われた心筋を再生できる -マウス研究

日付:2021 年 12 月 2 日
ソース:ジョンズホプキンス大学医学部
概要:

人間やマウスを含む哺乳類の心筋細胞は出生後に増殖を停止し、後年の心臓の損傷を永続的なものにし、機能を低下させ、心不全を引き起こす。米国疾病予防管理センター(CDC)によると、心血管疾患は依然として米国内で最も一般的な死因であり、4 人に 1 人が死亡している。心臓発作を生き延びた人は最大 10 億個の心筋細胞を失う可能性があり、最初の細胞の総数が多いほど、心臓が発作後より早く回復する傾向があるとされている。
今回、ジョンズホプキンス大学医学部の研究者らは、特定の神経細胞またはそれらを制御する遺伝子を操作することによって、新しい心筋細胞形成が引き起こされ、心臓発作やその他の心臓障害の後に心臓機能を回復する可能性があるとしている。これにはマウス実験からの証拠があるとして、12 月 1 日の「Science Advances」誌でその研究成果を発表している。

研究関連ニュース/他のトップページに戻る

＜英文＞Mouse study suggests manipulation of certain nerve cells can help regenerate lost heart muscle -- ScienceDaily

Mouse study suggests manipulation of certain nerve cells can help regenerate lost heart muscle

Date:

December 2, 2021

Source:

Johns Hopkins Medicine

Summary:

Human heart muscle cells cease to multiply after birth, making any heart injury later in life a permanent one, reducing function and leading to heart failure. Now, however, researchers say they have new evidence from mouse experiments that manipulating

certain nerve cells or the genes that control them might trigger the formation of new heart muscle cells and restore heart function after heart attacks and other cardiac disorders.

FULL STORY

Human heart muscle cells cease to multiply after birth, making any heart injury later in life a permanent one, reducing function and leading to heart failure. Now, however, Johns Hopkins Medicine researchers say they have new evidence from mouse experiments that manipulating certain nerve cells or the genes that control them might trigger the formation of new heart muscle cells and restore heart function after heart attacks and other cardiac disorders.

More specifically, they say, results of their study, published Dec. 1, in *Science Advances*, sheds new light on how some neurons regulate the number of heart muscle cells.

Nerve cells have long been known to regulate heart function, but their role and impact during heart development and their effect on muscle cell growth has been unclear.

"Our study sought to examine the role of so-called sympathetic neurons on heart development after birth, and what we found is that by manipulating them, there could be tremendous potential for regulating the total number of muscle cells in the heart even after birth," says Emmanouil Tampakakis, M.D., assistant professor of medicine at the Johns Hopkins University School of Medicine, and the lead author of the study.

The nerve cells that make up the sympathetic nervous system (SNS) control automatic processes in the body such as digestion, heart rate and respiration. The SNS is typically associated with "fight-or-flight" responses, the body's general response to alarming, stressful or threatening situations.

For the new study, the research team created a genetically modified mouse model by blocking sympathetic heart neurons in developing mouse embryos, and analyzed the drivers of heart muscle cell proliferation through the first two weeks of life after birth.

What they found was a significant decrease in the activity of a pair of genes -- the period 1 and period *2* genes -- already known to control the circadian cycle. Remarkably, removing those two circadian genes in mouse embryos, the researchers saw increased neonatal heart size and an increase in the number of cardiomyocytes, or heart muscle cells, by up to 10%. This suggested that the effect of sympathetic nerves on heart muscle cells is likely mediated through these two circadian or "clock" genes.

Clock genes are components of the circadian rhythm pattern that in mammals regulates bodily functions on a more-or-less 24-hour cycle aligned with hours of daylight and darkness.

"Shortly after birth, mammals, including people and mice, stop producing heart muscle cells. And unlike other organs, like the liver, the heart can't regenerate after it's damaged," says Tampakakis. "We've shown that it may be possible to manipulate nerves and/or circadian genes, either through drugs or gene therapies, to increase the number of heart cells after birth."

People who survive a heart attack can lose up to a billion heart muscle cells, and Tampakakis says there is scientific evidence that hearts tend to recover faster after an attack when the total number of cells to begin with is higher. By manipulating sympathetic nerves and clock genes -- a

technique called neuromodulation -- researchers believe the heart could be made to respond to injury much better.

"Neuromodulation is a pretty new concept in cardiology, and we believe these are the first reports that associate clock genes with new growth of heart muscle cells." says Chulan Kwon, Ph.D., M.S., associate professor of medicine and director of the Cardiovascular Stem Cell Program at the Johns Hopkins University School of Medicine. "Our study, maybe for the first time, shows what's happening if you block the supply of nerves to the heart, and provides new insights for developing neuromodulation strategies for cardiac regeneration."

Tampakakis says his team is working on further experiments to characterize the different groups of neurons that supply the heart and demonstrate how those nerves develop and adjust over time and after heart injury.

According to the U.S. Centers for Disease Control and Prevention, cardiovascular disease remains the most common cause of death in the country causing one in four deaths.

This work was supported by the National Institutes of Health, American Heart Association Maryland Stem Cell Research Fund, W.W. Smith Charitable Trust, the Magic that Matters Fund and The JHU Mirowski Discovery Award.

Other scientists who conducted the research include Harshi Gangrade, Stephanie Glavaris, Myo Htet, Sean Murphy, Brian Leei Lin, Ting Liu, Amir Saberi, Matthew Miyamoto, of Johns Hopkins Medicine; Gabsang Lee of Johns Hopkins University School of Medicine; Liliana Minichiello of Oxford University; William Kowalski and Yoh-Suke Mukouyama of the National Institutes of Health.

None of the authors have disclosures or conflicts of interest in the study to report.

Story Source:

Materials provided by **Johns Hopkins Medicine**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Emmanouil Tampakakis, Harshi Gangrade, Stephanie Glavaris, Myo Htet, Sean Murphy, Brian Leei Lin, Ting Liu, Amir Saberi, Matthew Miyamoto, William Kowalski, Yoh-Suke Mukouyama, Gabsang Lee, Liliana Minichiello, Chulan Kwon. **Heart neurons use clock genes to control myocyte proliferation**. *Science Advances*, 2021; 7 (49) DOI: 10.1126/sciadv.abh4181

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3. 遺伝子編集技術で単一性のマウス同腹子作成

日付：2021 年 12 月 3 日
ソース：英国フランシスクリック研究所
概要：

フランシスクリック研究所の科学者らは、ケント大学と協力して、遺伝子編集技術を使用して、100%の効率でメスのみおよびオスのみのマウス同腹子を作成することに成功した。本日（12 月 3 日金曜日）「Nature Communications」誌で公開されたこの原理実証研究は、科学研究やおそらく農業においても動物福祉を改善するためにこの技術をどのように使用できるかを示している。
科学研究や農業では、オスまたはメスの動物のみが必要になることがよくある。たとえば、オスまたはメスの生殖に関する実験室での研究では、研究対象の性別の動物のみが必要だ。そして農業では、産卵と乳牛群ではメスの動物だけが必要だ。これは、不必要な性別の動物が出生後に淘汰されるのが一般的な慣行であることを意味している。
研究者らの新しい方法では、受精直後に胚を不活性化するために 2 つの部分からなる遺伝子システムを使用し、目的の性別のみを発達させることができる。子孫の性別を制御するためのそのような遺伝に基づく方法は、両方の産業で淘汰を劇的に減らすことができる、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＞Researchers use gene editing to create single-sex mice litters | Alloa and Hillfoots Advertiser (alloaadvertiser.com)

3rd December

Researchers use gene editing to create single-sex mice litters

By Press Association 2021

Mouse

Scientists have used gene-editing technology to create female-only and male-only mice litters with 100% efficiency.

The technology could be used to improve animal welfare in scientific research and also agriculture.

Scientific research can often require either male or female animals, like laboratory research into reproduction

In farming, only female animals are required for egg production and in dairy herds, meaning it is common practice for animals of the unrequired sex to be culled after birth.

The method demonstrated in the new study uses a two-part genetic system to inactivate embryos shortly after fertilisation, allowing only the desired sex to develop.

According to the researchers, such a genetically based method to control the sex of offspring could drastically reduce culling in both industries.

This work could have immediate and valuable impact in scientific laboratories

James Turner

The embryo selection is based on the fact there are two elements of CRISPR-Cas9: the Cas9 enzyme that cuts the DNA, allowing scientists to alter specific regions, and the guide RNA which carries the Cas9 to the right location on the genome.

One element of the system was placed on the father's X or Y chromosome, meaning it would only be inherited by female or male embryos respectively.

The other element is contributed by the mother and is inherited by all embryos.

A specific gene, which is essential to DNA replication and repair, was targeted.

When an embryo was formed from a sperm and an egg, each containing one half of CRISPR-Cas9, the gene editing was triggered in the embryo and it was not able to develop beyond a very early stage of around 16 to 32 cells.

Using this method the Francis Crick Institute and University of Kent researchers were able to control the sex of a litter with 100% effect.

To produce a male-only litter, the researchers edited the father's X chromosome, meaning only females inherited the deleterious mutation, and for a female-only litter, they edited the Y chromosome.

The method did not lead to a 50% decrease in the number of offspring produced - the litter sizes were between 61% and 72% of control litters.

The researchers suggest this is because animals such as mice produce more eggs than required during each ovarian cycle, allowing for a proportion to be lost during early development without reducing litter size.

This suggests that in situations where one sex is needed, fewer breeding animals will be required to produce the same number of the desired offspring.

As the offspring that survive only contain half of the CRISPR-Cas9 elements within their genome, this acts as a control preventing the sex selection being passed down to further generations.

Charlotte Douglas, first author and former PhD student and postdoctoral scientist at the Crick, said: “This method works as we split the genome-editing process in half, between a male and female, and it is only when the two halves meet in an embryo through breeding that it is activated.

“Embryos with both halves cannot develop beyond very early cell stages.

“We’ve also shown this process works successfully in different combinations - introducing either the Cas9 or the guide RNA elements on to the mother’s or father’s chromosomes.”

James Turner, author and group leader of the Sex Chromosome Biology Laboratory at the Crick, said: “This work could have immediate and valuable impact in scientific laboratories, as we’ve shown how it is safe and effective in mice, a common mammal used in medical and scientific research.

“While a lot of research needs both sexes, there are areas of study where only one is needed.

“For example, when studying the reproductive system, sex-specific diseases or certain hormones.”

The researchers suggest the findings may be applicable to other animals, further research is needed, and should be considered at ethical and regulatory levels.

The study is published in Nature Communications.

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4. マラソンマウスからの輸血がカウチポテトマウスの脳機能を高める

日付：2021 年 12 月 8 日
ソース：スタンフォード大学医学部
概要：

運動はマウスの脳にとっても我々の脳にとっても素晴らしいことであるが、今回マウス、人間で行われた多くの研究によって、このことが明らかにされた。
スタンフォード大学の新しい研究では、マラソンを実行しているマウスが享受している脳の利点を、カウチポテトの仲間に移すことが可能であることが示されている。
研究者らは、12 月 8 日に「Nature」誌で発表されたこの研究で、同じ年齢のたくさん運動しているマウスと座りがちなマウスの血液サンプルを比較した。彼らは、運動するマウスからの輸血が座りがちなマウスの神経炎症を減らし、認知能力を改善することを示した。
さらに、研究者らは、抗神経炎症性運動効果に重要な役割を果たしていると思われる血液由来のタンパク質を単離することにも成功した。

研究関連ニュース/他のトップページに戻る

＜英文＞Blood from marathoner mice boosts brain funct | EurekAlert!

NEWS RELEASE 8-DEC-2021

Blood from marathoner mice boosts brain function in their couch-potato counterparts

Peer-Reviewed Publication

STANFORD MEDICINE

Physical exercise is great for a mouse's brain, and for yours. Numerous studies conducted in mice, humans and laboratory glassware have made this clear. Now, a new study shows it's possible to transfer the brain benefits enjoyed by marathon-running mice to their couch-potato peers.

Stanford School of Medicine researchers have shown that blood from young adult mice that are getting lots of exercise benefits the brains of same-aged, sedentary mice. A single protein in the blood of exercising mice seems largely responsible for that benefit.

The discovery could open the door to treatments that — by taming brain inflammation in people who don't get much exercise — lower their risk of neurodegenerative disease or slow its progression.

In the study, to be published Dec. 8 in *Nature*, the Stanford researchers compared blood samples from exercising and sedentary mice of the same age. They showed that transfusions of blood from running mice reduced neuroinflammation in the sedentary mice and improved their cognitive performance. In addition, the researchers isolated a blood-borne protein that appears to play an important role in the anti-neuroinflammatory exercise effect.

Inflammation and cognitive health

Neuroinflammation has been strongly tied to neurodegenerative diseases in humans, said Tony Wyss-Coray, PhD, professor of neurology and neurological sciences. Animal studies have indicated that neuroinflammation precipitates neurodegenerative disorders and that reversing or reducing neuroinflammation can prolong cognitive health, he said.

Anybody who's suffered from influenza can relate to the loss of cognitive function that comes from a fever-inducing viral infection, Wyss-Coray said: "You get lethargic, you feel disconnected, your brain doesn't work so well, you don't remember as clearly."

That's a result, at least in part, of the bodywide inflammation that follows the infection. As your immune system ramps up its fight, the inflammation spills over into your brain. Neuroinflammation also exacerbates the progression of Alzheimer's and other neurodegenerative diseases, said Wyss-Coray, a neuro-immunologist who in a study published earlier this year identified signs of brain inflammation in people who had died of COVID-19.

Wyss-Coray is the new study's senior author. The lead author is Zurine De Miguel, PhD, a former postdoctoral scholar in Wyss-Coray's group who is now an assistant professor of psychology at California State University, Monterey Bay.

It's already known that exercise induces a number of healthy manifestations in the brain, such as more nerve-cell production and less inflammation.

"We've discovered that this exercise effect can be attributed to a large extent to factors in the blood, and we can transfer that effect to a same-aged, non-exercising individual," said Wyss-Coray, the D. H. Chen Professor II.

Nightly mouse marathon

Mice love to run. Give a caged mouse access to a running wheel a few inches in diameter and, with no training or prompting, it will rack up 4 to 6 miles a night (they sleep by day) on legs that are much shorter than ours. If you lock the wheel, the mouse won't log nearly as much exercise, although it's still free to skitter hither and thither about its cage (roughly

equivalent to heading into the kitchen now and then to fetch a beer or a snack from the fridge).

The investigators put either functional or locked running wheels into the cages of 3-month-old lab mice, which are metabolically equivalent to 25-year-old humans. A month of steady running was enough to substantially increase the quantity of neurons and other cells in the brains of marathoner mice when compared with those of sedentary mice.

Next, the researchers collected blood from marathoner and, as controls, sedentary mice. Then, every three days, they injected other sedentary mice with plasma (the cell-free fraction of blood) from either marathoner or couch-potato mice. Each injection equaled 7% to 8% of the recipient mouse's total blood volume. (An equivalent amount in humans would be about ½ to ¾ of a pint.)

"The mice getting runner blood were smarter," Wyss-Coray said. On two different lab tests of memory, sedentary mice injected with marathoner plasma outperformed their equally sedentary peers who received couch-potato plasma.

In addition, sedentary mice receiving plasma from marathoner mice had more cells that give rise to new neurons in the hippocampus (a brain structure associated with memory and navigation) than those given couch-potato plasma transfusions.

The scientists compared activation levels of thousands of genes in the hippocampus of sedentary mice receiving marathoner versus those receiving couch-potato plasma. Of the roughly 2,000 genes whose activation levels changed in response to marathoner plasma, the 250 whose activation levels changed most prominently were known to be most strongly linked to inflammatory processes, and their activation-level changes suggested lower neuroinflammation among mice who received marathoner-blood transfusions.

"The runners' blood was clearly doing something to the brain, even though it had been delivered outside the brain, systemically," said Wyss-Coray.

Turning to an examination of proteins in the marathoner mice's blood, the Stanford team identified 235 distinct proteins, of which 23 were scarcer and 26 more abundant in marathoner compared with couch-potato mice. Several of these differentially expressed proteins were associated with the complement cascade — a set of about 30 blood-borne proteins that interact with one another to kick-start the immune response to pathogens. Chronic inflammation resulting from aberrant activation of the complement system, Wyss-Coray noted, appears to accelerate the progression of many neurodegenerative disorders.

A protein of interest

Removing a single protein, clusterin, from marathoner mice's plasma largely negated its anti-inflammatory effect on sedentary mice's brains. No other protein the scientists similarly tested had the same effect.

Clusterin, an inhibitor of the complement cascade, was significantly more abundant in the marathoners' blood than in the couch potatoes' blood.

Further experiments showed that clusterin binds to receptors that abound on brain endothelial cells, the cells that line the blood vessels of the brain. These cells are inflamed in the majority of Alzheimer's patients, noted Wyss-Coray, whose research has shown that blood endothelial cells are capable of transducing chemical signals from circulating blood, including inflammatory signals, into the brain.

Clusterin by itself, even though administered outside the brain, was able to reduce brain inflammation in two different strains of lab mice in which either acute bodywide inflammation or Alzheimer's-related chronic neuroinflammation had been induced.

Separately, the investigators found that at the conclusion of a six-month aerobic exercise program, 20 military veterans with mild cognitive impairment, a precursor to Alzheimer's disease, had elevated clusterin levels in their blood.

Wyss-Coray speculated that a drug that enhances or mimics clusterin's binding to its receptors on brain endothelial cells might help slow the course of neuroinflammation-associated neurodegenerative diseases such as Alzheimer's.

Wyss-Coray is a member of the Stanford Wu Tsai Neuroscience Institute, Stanford Bio-X, and the Stanford Maternal and Child Health Research Institute; and a faculty fellow of Stanford ChEM-H.

Other Stanford study co-authors are former postdoctoral scholars Nathalie Khoury, PhD, Niclas Olsson, PhD, Ryan Vest, PhD, and Hui Zhang, PhD; former graduate student Michael Betley, DVM, PhD; former neurology instructor Benoit Lehallier, PhD; former undergraduate Drew Willoughby; postdoctoral scholars Andrew Yang, PhD, Oliver Hahn, PhD, and Nannan Lu, PhD; former medical and graduate student Liana Bonanno, MD, PhD; Palo Alto Veterans Institute for Research assistant Lakshmi Yerra; former staff scientist Lichao Zhang, PhD; laboratory manager Nay Lui Saw; former life sciences research associate Davis Lee; Kaci Fairchild, PhD, clinical assistant professor of psychology; former life science research professional Patrick McAlpine; Mehrdad Shamloo, PhD, professor of neurosurgery; Joshua Elias, PhD, assistant professor of chemical and systems biology; and Thomas Rando, MD, PhD, professor of neurology and neurological sciences.

The study was funded by the National Institutes of Health (grants AG0047820 and 1F32AG067652), the Stanford Alzheimer's Disease Research Center (NIH grant P30

AG066515), the U.S. Department of Veterans Affairs, the U.S. Department of Defense, the Alzheimer's Association and the Marie Curie Foundation, the NOMIS Foundation, the Simons Foundation and the Wu Tsai Neurosciences Institutes' Brain Rejuvenation Project with support from the Bertarelli Foundation

Stanford's Department of Neurology and Neurological Sciences also supported the work.

# # #

The Stanford University School of Medicine consistently ranks among the nation's top medical schools, integrating research, medical education, patient care and community service. For more news about the school, please visit http://med.stanford.edu/school.html. The medical school is part of Stanford Medicine, which includes Stanford Health Care and Stanford Children's Health. For information about all three, please visit http://med.stanford.edu.

JOURNAL

Nature

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5. 酵素による実験的治療で、致命的な炭疽菌感染からマウスを保護

日付：2021 年 12 月 8 日
ソース：米陸軍感染症研究所
概要：

炭疽病を引き起こす細菌である炭疽菌は、世界の多くの地域で最も重大なバイオテロの脅威の 1 つであると同時に、元々はヒツジやヤギなどの家畜や野生動物の感染症で、ヒトに感染することもある人獣共通感染症であるため公衆衛生上の課題としても認識されている。
科学者らは、この研究で、炭疽病を引き起こす細菌によって生成される酵素を改変することで、致命的な病気の感染からマウスを保護できることを実証。「Science Translational Medicine」誌の今日のオンライン版で発表されたこの発見は、炭疽菌の多剤耐性菌株を治療するための潜在的な治療戦略を示唆しており、他の細菌感染症の新しい治療法につながる可能性がある、としている。

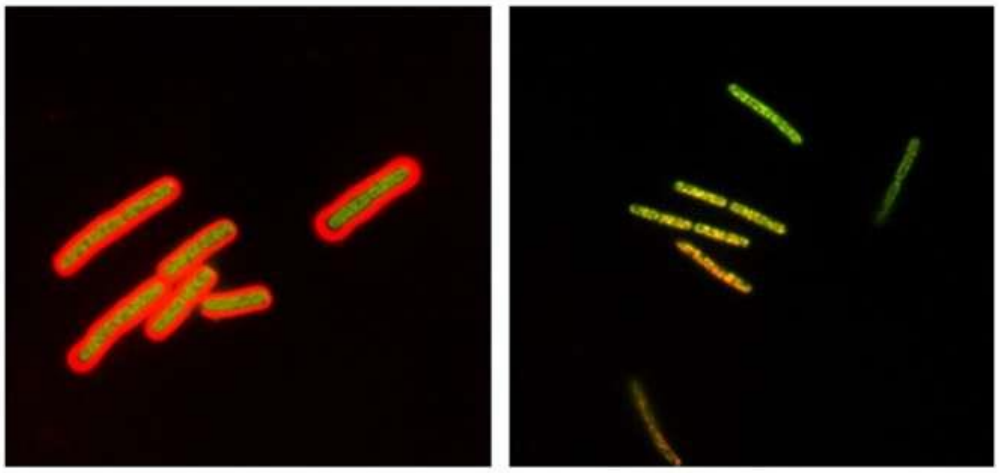
研究関連ニュース/他のトップページに戻る

＜英文＞Experimental treatment with enzyme protects mice from lethal anthrax infection (medicalxpress.com)

DECEMBER 8, 2021

Experimental treatment with enzyme protects mice from lethal anthrax infection

by US Army Medical Research Institute of Infectious Diseases



Capsule removal from Bacillus anthracis by treatment with Capsule Depolymerase

Capsule removal from Bacillus anthracis by treatment with capsule depolymerase (capsule shown in red). Credit: Wilson J. Ribot, USAMRIID

Scientists have demonstrated that modifying an enzyme produced by the bacterium that causes anthrax can protect mice from infection with the deadly disease. Their findings, published in today's online edition of *Science Translational Medicine*, suggest a potential therapeutic strategy for treating multidrug-resistant strains of anthrax, and could lead to new treatments for other bacterial infections.

Bacillus anthracis, the bacterium that causes anthrax, is recognized as one of the most significant bioterrorism threats, as well as a public health challenge in many parts of the world. Three main components allow it to cause disease—lethal toxin, edema toxin, and capsule. In this study, the researchers developed a method to degrade the capsule surrounding the bacterium, allowing it to be ingested and destroyed by the white blood cells—thus reducing virulence.

Public health officials have become increasingly concerned about strains of anthrax that appear to be resistant to treatment with known antibiotics, according to Arthur M. Friedlander, M.D., the paper's senior author. He and his team at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) worked with investigators at the U.S. Naval Research Laboratories, the University of Washington in Seattle, and the University of California at Davis to explore alternative treatment approaches that do not rely on the use of antibiotic drugs.

One promising avenue is to make the bacterium more susceptible to the innate immune system—the human body's first line of defense against a pathogenic "invader." The innate immune response consists of physical, chemical and cellular defenses that work to immediately prevent the spread of foreign pathogens throughout the body. Enzymes known as capsular depolymerases, which are naturally produced by several classes of bacteria, have emerged as a potential new line of antivirulence agents.

"Identification of the capsule depolymerase enzyme within the anthrax bacillus led us to attempt to use that enzyme to remove the capsule," said Friedlander. "When this proved successful, we utilized recombinant DNA technology and protein engineering methods to engineer and reconfigure the enzyme in new ways."

Those "engineering changes" included circular permutation by protein design, to enhance stability and make the enzyme easier to produce, and pegylation, which improves the enzyme's pharmacokinetics—the properties that allow it to be absorbed and properly distributed within the body. The team then tested the pegylated enzyme, known as PEG-CapD-CPS334C, to be sure it had retained its enzymatic activity.

In the study, 10 of 10 mice infected with anthrax spores from a nontoxigenic encapsulated strain were completely protected after treatment with PEG-CapD-CPS334C, while only 1 of 10 mice receiving a control treatment survived. Similarly, treatment of mice infected with a fully virulent encapsulated strain using PEG-CapD-CPS334C protected 8 of 10 animals, while only 2 of 10 control animals survived.

"This strategy renders B. anthracis susceptible to the innate immune responses and does not rely on antibiotics," the authors concluded. "These findings suggest that enzyme-catalyzed removal of the capsule may be a potential therapeutic strategy for the treatment of multidrug-resistant anthrax and other bacterial infections."

It could also allow warfighters exposed to anthrax through natural or other means to be treated at the time of exposure or shortly thereafter, preserving combat power in forward areas where advanced diagnostics and treatments may not be readily available.

Explore further

Anthrax capsule vaccine completely protects monkeys from lethal inhalational anthrax

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More information: Patricia M. Legler et al, Treatment of experimental anthrax with pegylated circularly permuted capsule depolymerase, *Science Translational Medicine* (2021). DOI: 10.1126/scitranslmed.abh1682

Journal information: Science Translational Medicine

Provided by US Army Medical Research Institute of Infectious Diseases

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6. 毎年インフルエンザの予防接種を受ける必要はなくなるかもしれない。インフルエンザ共通ワクチンの新たな標的

日付：2021 年 12 月 23 日
ソース：スクリプス研究所
概要：

シカゴ大学のスクリプス研究所とマウントサイナイ医科大学の科学者らは、インフルエンザウイルスの新しいアキレス腱を特定し、インフルエンザワクチンの探求を進めている。彼らは、チームがアンカーと名付けた、ウイルスの長い間無視されていた部分に対する抗体は、ウイルスが毎年変異している場合でも、多種多様なインフルエンザ株を認識する可能性があると、12 月 23 日に「Nature」誌で報告している。
インフルエンザは米国で毎年大体 2,000 万人以上に影響を及ぼし、2 万人以上の死者を出す。インフルエンザに対するワクチンは、通常、インフルエンザウイルスの表面から外側に伸びるタンパク質であるヘマグルチニン（HA）の頭部を認識する抗体を生成する。頭部は HA の最もアクセスしやすい領域であり良い標的にはなるものの、残念ながら最も変異しやすいものの 1 つでもあるため、毎年新しいワクチンが必要になる。
新しい研究で、研究チームは、季節性インフルエンザワクチンを接種された人、あるいは自然感染した人の血液中に存在する 358 種類の抗体を特徴づけた。参加者の血液中に存在する新しい抗体のコレクションは、各 HA 分子がインフルエンザビリオンの膜に付着している場所の近くで、茎の一番下に結合したため、彼らは HA のこのセクションをアンカーと名付け、さらに研究を始めた。彼らは、結局 HA アンカーに対する 50 の異なる抗体を特定、その抗体は、多くの季節性インフルエンザ株の原因となるさまざまな H1 インフルエンザウイルスを認識した。一部の抗体は、ラボテストでインフルエンザのパンデミック H2 および H5 株を認識することもできた。そしてマウスでは、抗体は 3 つの異なる H1 インフルエンザウイルスによる感染からうまく保護された。
研究者らは、さまざまなインフルエンザ株の HA アンカーを最も直接的に標的とするワクチンを設計する方法について将来の研究を計画している、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＞No more annual flu shot? New target for universal influenza vaccine -- ScienceDaily

No more annual flu shot? New target for universal influenza vaccine

Date:

December 23, 2021

Source:

Scripps Research Institute

Summary:

A new antibody discovered in the blood of some people vaccinated against or infected with influenza can recognize a broad variety of flu viruses.

FULL STORY

Scientists at Scripps Research, University of Chicago and Icahn School of Medicine at Mount Sinai have identified a new Achilles' heel of influenza virus, making progress in the quest for a universal flu vaccine. Antibodies against a long-ignored section of the virus, which the team dubbed the anchor, have the potential to recognize a broad variety of flu strains, even as the virus mutates from year to year, they reported Dec. 23, 2021 in the journal *Nature*.

"It's always very exciting to discover a new site of vulnerability on a virus because it paves the way for rational vaccine design," says co-senior author Andrew Ward, PhD, professor of Integrative Structural and Computational Biology at Scripps Research. "It also demonstrates that despite all the years and effort of influenza vaccine research there are still new things to discover."

"By identifying sites of vulnerability to antibodies that are shared by large numbers of variant influenza strains we can design vaccines that are less affected by viral mutations," says study co-senior author Patrick Wilson, MD, who was previously at the University of Chicago and recently recruited to Weill Cornell Medicine as a professor of pediatrics and a scientist in the institution's Gale and Ira Drukier Institute for Children's Health. "The anchor antibodies we describe bind to such a site. The antibodies themselves can also be developed as drugs with broad therapeutic applications."

In a typical year, influenza affects more than 20 million people in the United States and leads to more than 20,000 deaths. Vaccines against influenza typically coax the immune system to generate antibodies that recognize the head of hemagglutinin (HA), a protein that extends outward from the surface of the flu virus. The head is the most accessible regions of HA, making it a good target for the immune system; unfortunately, it is also one of the most variable. From year to year, the head of HA often mutates, necessitating new vaccines.

Researchers have designed experimental influenza vaccines to be more universal, spurring the body to create antibodies against the less-variable stalk region of HA, which extends like a stem between the influenza virion and the HA head. Some of these universal flu vaccines are currently in early clinical trials.

In the new study, a collaborative team of scientists characterized 358 different antibodies present in the blood of people who had either been given a seasonal influenza vaccine, were in a phase I trial for an experimental, universal influenza vaccine, or had been naturally infected with influenza.

Many of the antibodies present in the blood of participants were antibodies already known to recognize either the HA head or stalk. But a collection of new antibodies stood out; the antibodies bound to the very bottom of the stalk, near where each HA molecule is attached to the membrane of the flu virion.

The co-first authors of the manuscript -- Julianna Han, a staff scientist in the Ward lab, and Jenna Guthmiller, a postdoctoral fellow at the University of Chicago -- named this section of HA the anchor, and began studying it further. In all, the scientists identified 50 different antibodies to the HA anchor, from a total of 21 individuals. The antibodies, they discovered, recognized a variety of H1 influenza viruses, which account for many seasonal flu strains. Some of the antibodies were also able to recognize pandemic H2 and H5 strains of influenza in lab tests. And in mice, the antibodies successfully protected against infection by three different H1 influenza viruses.

"In order to increase our protection to these highly mutating viruses, we need to have as many tools as we can," says Han. "This discovery adds one more highly potent target to our repertoire." Importantly, these antibodies appear to be fairly common in people, and belong to a class of antibodies that any person's body can produce -- an important consideration in designing a vaccine to spur their development.

"The human immune system already has the ability to make antibodies to this epitope, so it's just a matter of applying modern protein engineering methods to make a vaccine that can induce those antibodies in sufficient numbers," adds Guthmiller.

The researchers say that future, improved iterations of a universal vaccine could more purposefully aim to generate anchor antibodies. Until now, scientists designing universal vaccines hadn't paid attention to whether the anchor region of the stem was included as a target. Ideally, a universal influenza vaccine will lead to antibodies against multiple sections of the virus -- such as both the HA anchor and the stalk -- to increase protection to evolving viruses.

The researchers are planning future studies on how to design a vaccine that most directly targets the HA anchor of different influenza strains.

In addition to Han and Ward, authors of the study, "Broadly neutralizing antibodies target a hemagglutinin anchor epitope," include Sara Richey and Alba Torrents de la Pena of Scripps; Jenna Guthmiller, Henry Utset, Lei Li, Linda Yu-Ling Lan, Carole Henry, Christopher Stamper, Olivia Stovicek, Haley Dugan, Nai-Ying Zheng, Micah Tepora, Dalia Bitar, Siriruk Changrob, Min Huang and Patrick Wilson of University of Chicago; Meagan McMahon, George O'Dell, Alec Freyn, Fatima Amanat, Victoria Rosado, Shirin Strohmeier, Adolfo Garcia-Sastre, Raffael Nachbagauer, Peter Palese and Florian Krammer of Icahn School of Medicine at Mount Sinai; Monica Fernandez-Quintero and Klaus Liedl of University of Innsbruck, Lauren Gentles and Jesse Bloom of Fred Hutchinson Cancer Research Center; and Lynda Coughlan of University of Maryland School of Medicine

This work was supported by funding from the National Institute of Allergy and Infectious Diseases (K99AI159136, U19AI082724,U19AI109946, U19AI057266, P01AI097092, R01AI145870-01, R21AI146529, and T32AI007244-36), the NIAID Centers of Excellence for Influenza Research and Surveillance (HHSN272201400005C, HHSN272201400008C), the NIAD Centers of Excellence for Influenza Research and Response (75N93019R00028), the NIAID Collaborative Influenza Vaccine Innovation Centers (75N93019C00051), the Bill and Melinda Gates Foundation (OPP1084518) and the Austrian Science Fund (P34518).

Story Source:

Materials provided by **Scripps Research Institute**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Jenna J. Guthmiller, Julianna Han, Henry A. Utset, Lei Li, Linda Yu-Ling Lan, Carole Henry, Christopher T. Stamper, Meagan McMahon, George O'Dell, Monica L. Fernández-Quintero, Alec W. Freyn, Fatima Amanat, Olivia Stovicek, Lauren Gentles, Sara T. Richey, Alba Torrents de la Peña, Victoria Rosado, Haley L. Dugan, Nai-Ying Zheng, Micah E. Tepora, Dalia J. Bitar, Siriruk Changrob, Shirin Strohmeier, Min Huang, Adolfo García-Sastre, Klaus R. Liedl, Jesse D. Bloom, Raffael Nachbagauer, Peter Palese, Florian Krammer, Lynda Coughlan, Andrew B. Ward, Patrick C. Wilson. **Broadly neutralizing antibodies target a hemagglutinin anchor epitope**. *Nature*, 2021; DOI: 10.1038/s41586-021-04356-8

7. 血液凝固タンパク質の武装解除で、マウスの歯周病を予防
人間と動物の研究が、歯周病や他の炎症性疾患の治療への洞察を提供

日付：2021 年 12 月 23 日
ソース：国立衛生研究所/国立歯科頭蓋顔面研究所（NIDCR）
概要：

歯周病は、30 歳以上のアメリカ人のほぼ半数と 65 歳以上のアメリカ人の 70%に影響を及ぼす。これは、歯を支える組織の細菌感染症で、その初期の段階では、歯周病は歯茎の発赤と腫れ（炎症）を引き起こす。歯周炎と呼ばれる進行した段階では、下にある骨が損傷し、歯の喪失につながる。科学者らは、歯周炎が免疫細胞の反応の誇張によって引き起こされることを知ってはいたが、これまで、何が反応を引き起こしたのか、そしてそれがどのように組織や骨の損傷を引き起こしたのかは不明であった。
国立衛生研究所の一部である国立歯科頭蓋顔面研究所（NIDCR）の科学者が主導した研究によると、血液凝固タンパク質の遮断機能により、マウスの歯周病による骨量減少が防止された。フィブリンと呼ばれるタンパク質の異常な蓄積と歯周炎との関係を調査するために、科学者らは、PLG 欠損マウスを研究し、ヒトの遺伝子データを分析した。
動物と人間のデータを利用して、研究者らは、フィブリンの蓄積が、歯茎と下にある骨に損傷を与える過剰な免疫応答を引き起こすことを発見した。
「Science」誌に発表されたこの研究は、異常なフィブリン活性を抑制することで、歯周病や、関節炎や多発性硬化症などのフィブリンの蓄積を特徴とする他の炎症性疾患の予防または治療に有望である可能性があることを示唆している。

研究関連ニュース/他のトップページに戻る

＜英文＞Disarming a blood-clotting protein prevents gum disease in mice: Human and animal study offers insight into treating periodontal disease and other inflammatory disorders -- ScienceDaily

Disarming a blood-clotting protein prevents gum disease in mice

Human and animal study offers insight into treating periodontal disease and other inflammatory disorders

Date:

December 23, 2021

Source:

NIH/National Institute of Dental and Craniofacial Research

Summary:

Blocking function of a blood-clotting protein, called fibrin, prevented bone loss from periodontal (gum) disease in mice, according to new research. The study suggests that suppressing abnormal fibrin activity could hold promise for preventing or treating periodontal disease, as well as other inflammatory disorders marked by fibrin buildup, including arthritis and multiple sclerosis.

FULL STORY

Blocking function of a blood-clotting protein prevented bone loss from periodontal (gum) disease in mice, according to research led by scientists at the National Institute of Dental and Craniofacial Research (NIDCR), part of the National Institutes of Health. Drawing on animal and human data, the researchers found that buildup of the protein, called fibrin, triggers an overactive immune response that damages the gums and underlying bone. The study, which was published in *Science*, suggests that suppressing abnormal fibrin activity could hold promise for preventing or treating periodontal disease, as well as other inflammatory disorders marked by fibrin buildup, including arthritis and multiple sclerosis.

Periodontal disease affects nearly half of Americans over age 30, and 70% of those 65 and older. It is a bacterial infection of the tissues supporting the teeth. In its early stages, periodontal disease causes redness and swelling (inflammation) of the gums. In advanced stages, called periodontitis, the underlying bone becomes damaged, leading to tooth loss. While scientists have known that periodontitis is driven in part by an exaggerated immune cell response, until now, it was unclear what triggered the response, and how it caused tissue and bone damage.

"Severe periodontal disease can lead to tooth loss and remains a barrier to productivity and quality of life for far too many Americans, especially those lacking adequate access to dental care," said NIDCR Director Rena D'Souza, D.D.S., Ph.D. "By providing the most comprehensive picture yet of the underlying mechanisms of periodontal disease, this study brings us closer to more effective methods for prevention and treatment."

At sites of injury or inflammation, fibrin normally plays a protective role, helping to form blood clots and activating immune cells to fight infection. But too much fibrin has been linked with health problems, including a rare form of periodontitis due to a condition called plasminogen (PLG) deficiency. In affected people, mutations in the *PLG* gene lead to fibrin buildup and disease at various body sites, including the mouth.

To explore the connection between abnormal fibrin buildup and periodontitis, the scientists, led by NIDCR investigators Niki Moutsopoulos, D.D.S., Ph.D., and Thomas Bugge, Ph.D., studied PLG deficiency in mice and analyzed human genetic data.

Like humans with the condition, PLG-deficient mice developed periodontitis, including periodontal bone loss and elevated levels of fibrin in the gums. The mice's gums were crowded with immune cells called neutrophils, which are also found at high levels in common forms of periodontitis.

Neutrophils typically defend the oral cavity from harmful microbes. But an excessive neutrophil response is thought to cause tissue damage.

To find out if fibrin was driving this overactive response, the researchers impaired its ability to interact with (bind to) protein receptors on neutrophils. The weakened binding between fibrin and neutrophils completely prevented periodontal bone loss in PLG-deficient mice. Strikingly, it also reduced bone loss in normal mice with a common, age-related form of periodontitis, suggesting that similar mechanisms were at play in both forms of the disease.

"This study suggests that fibrin can cause neutrophil immunity to shift from protective to damaging in certain circumstances," said Moutsopoulos, who credited postdoctoral fellow and study first author Lakmali Silva, Ph.D., for her research that led to the findings. "This fibrin-neutrophil engagement may be a driver of periodontitis."

A genetic analysis of over 1,000 people seemed to support the animal findings. Even in the absence of PLG deficiency, variations in the *PLG* gene were linked to an increased risk of severe periodontitis, consistent with the idea that similar processes contribute to rare and common forms of the disease.

Taken together, the study suggests that excessive buildup of fibrin in the gums -- whether due to changes in genes like *PLG*, chronic inflammation from a bacterial infection, or some combination of the two -- triggers an elevated and ultimately harmful neutrophil response that causes periodontal disease.

The results are also in line with findings from other research teams, which have found that elevated fibrin may contribute to other inflammatory and autoimmune diseases such as arthritis and multiple sclerosis, and that interfering with fibrin activity could help treat these conditions.

"Our data support the idea that targeting the fibrin-neutrophil interaction could be a promising treatment avenue to explore in both rare and common forms of periodontitis," added Silva.

This research was supported by the NIDCR Division of Intramural Research. Support also came from the intramural programs of the National Institute on Deafness and Other Communication and the National Institute of Allergy and Infectious Diseases, the extramural programs of the National Institute of Diabetes and Digestive and Kidney Diseases, the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National Fund for Scientific and Technological Development, Chile.

Story Source:

Materials provided by **NIH/National Institute of Dental and Craniofacial Research**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Lakmali M. Silva, Andrew D. Doyle, Teresa Greenwell-Wild, Nicolas Dutzan, Collin L. Tran, Loreto Abusleme, Lih Jiin Juang, Jerry Leung, Elizabeth M. Chun, Andrew G. Lum, Cary S. Agler, Carlos E. Zuazo, Megan Sibree, Priyam Jani, Vardit Kram, Daniel Martin, Kevin Moss, Michail S. Lionakis, Francis J. Castellino, Christian J. Kastrup, Matthew J. Flick, Kimon Divaris, Thomas H. Bugge, Niki M. Moutsopoulos. **Fibrin is a critical regulator of neutrophil effector function at the oral mucosal barrier**. *Science*, 2021; 374 (6575) DOI: 10.1126/science.abl5450

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8. “男女の戦い”は父母の遺伝子が栄養をめぐって争う子宮内で始まる

日付:2021 年 12 月 27 日
ソース:ケンブリッジ大学
概要:

ケンブリッジ大学の科学者らは、胎児が胎盤からの栄養素の供給を制御するために使用する重要な信号を特定し、父親と母親から受け継いだ遺伝子間の綱引きを明らかにした。マウスで実施されたこの研究は、一部の赤ちゃんが子宮内で成長しにくい理由を説明するのに役立つ可能性がある。
赤ちゃんの 10%から 15%は子宮内での成長が不十分であり、胎盤の血管の成長が低下していることがよくある。人間の場合、これらの血管は妊娠中期から後期にかけて劇的に拡張し、満期で全長約 320 キロメートルに達する、とされている。父親の遺伝子が胎児のより大きな血管とより多くの栄養素の要求を促進し、母親の遺伝子が彼女の提供する栄養の量を制御しようとし、ゲノムレベルでの性別の戦いが繰り広げられる、としている。
ケンブリッジ大学の科学者が率いるチームが本日「Developmental Cell」誌で発表した研究では、遺伝子操作されたマウスを使用して、胎児が胎盤内の血管の成長を促進する信号を生成する方法を示している。この信号はまた、胎盤の他の細胞に変化を引き起こし、母親からのより多くの栄養素が胎児に到達できるようにする。
彼らの調査結果は、妊娠中に胎児、胎盤、母親がどのように相互にコミュニケーションするかについてのより良い理解を可能にする。

研究関連ニュース/他のトップページに戻る

＜英文＞'Battle of the sexes' begins in womb as father and mother's genes tussle over nutrition -- ScienceDaily

'Battle of the sexes' begins in womb as father and mother's genes tussle over nutrition

Date:

December 27, 2021

Source:

University of Cambridge

Summary:

Scientists have identified a key signal that the fetus uses to control its supply of nutrients from the placenta, revealing a tug-of-war between genes inherited from the father and

from the mother. The study, carried out in mice, could help explain why some babies grow poorly in the womb.

FULL STORY

Cambridge scientists have identified a key signal that the fetus uses to control its supply of nutrients from the placenta, revealing a tug-of-war between genes inherited from the father and from the mother. The study, carried out in mice, could help explain why some babies grow poorly in the womb.

As the fetus grows, it needs to communicate its increasing needs for food to the mother. It receives its nourishment via blood vessels in the placenta, a specialised organ that contains cells from both baby and mother.

Between 10% and 15% of babies grow poorly in the womb, often showing reduced growth of blood vessels in the placenta. In humans, these blood vessels expand dramatically between mid and late gestation, reaching a total length of approximately 320 kilometres at term.

In a study published today in *Developmental Cell*, a team led by scientists at the University of Cambridge used genetically engineered mice to show how the fetus produces a signal to encourage growth of blood vessels within the placenta. This signal also causes modifications to other cells of the placenta to allow for more nutrients from the mother to go through to the fetus.

Dr Ionel Sandovici, the paper's first author, said: "As it grows in the womb, the fetus needs food from its mum, and healthy blood vessels in the placenta are essential to help it get the correct amount of nutrients it needs.

"We've identified one way that the fetus uses to communicate with the placenta to prompt the correct expansion of these blood vessels. When this communication breaks down, the blood vessels don't develop properly and the baby will struggle to get all the food it needs."

The team found that the fetus sends a signal known as IGF2 that reaches the placenta through the umbilical cord. In humans, levels of IGF2 in the umbilical cord progressively increase between 29 weeks of gestation and term: too much IGF2 is associated with too much growth, while not enough IGF2 is associated with too little growth. Babies that are too large or too small are more likely to suffer or even die at birth, and have a higher risk to develop diabetes and heart problems as adults.

Dr Sandovici added: "We've known for some time that IGF2 promotes the growth of the organs where it is produced. In this study, we've shown that IGF2 also acts like a classical hormone -- it's produced by the fetus, goes into the fetal blood, through the umbilical cord and to the placenta, where it acts."

Particularly interesting is what their findings reveal about the tussle taking place in the womb.

In mice, the response to IGF2 in the blood vessels of the placenta is mediated by another protein, called IGF2R. The two genes that produce IGF2 and IGF2R are 'imprinted' -- a process by which molecular switches on the genes identify their parental origin and can turn the genes on or off. In this case, only the copy of the *igf2* gene inherited from the father is active, while only the copy of *igf2r* inherited from the mother is active.

Lead author Dr Miguel Constância, said: "One theory about imprinted genes is that paternally-expressed genes are greedy and selfish. They want to extract the most resources as possible

from the mother. But maternally-expressed genes act as countermeasures to balance these demands."

"In our study, the father's gene drives the fetus's demands for larger blood vessels and more nutrients, while the mother's gene in the placenta tries to control how much nourishment she provides. There's a tug-of-war taking place, a battle of the sexes at the level of the genome."

The team say their findings will allow a better understanding of how the fetus, placenta and mother communicate with each other during pregnancy. This in turn could lead to ways of measuring levels of IGF2 in the fetus and finding ways to use medication to normalise these levels or promote normal development of placental vasculature.

The researchers used mice, as it is possible to manipulate their genes to mimic different developmental conditions. This enables them to study in detail the different mechanisms taking place. The physiology and biology of mice have many similarities with those of humans, allowing researchers to model human pregnancy, in order to understand it better.

The lead researchers are based at the Department of Obstetrics and Gynaecology, the Medical Research Council Metabolic Diseases Unit, part of the Wellcome-MRC Institute of Metabolic Science, and the Centre for Trophoblast Research, all at the University of Cambridge.

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Story Source:

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