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In-Vivo Science International, Inc.

今月の企業関連ニュース/他

7/2　国内最古級のイグアノドン類化石　徳島で発見、約 1 億 3,000 万年前

福井県立恐竜博物館などは 2 日、徳島県勝浦町の約 1 億 3,000 万年前（前期白亜紀）の地層から、草食恐竜イグアノドン類のしっぽの骨「尾椎（びつい）」などの化石を見つけたと発表した。国内最古級とみられ、オンラインで同日開かれた日本古生物学会で発表された。

7/2　コロナが再拡大のきざし　32 都府県で感染増加、広がる「BA.5」

新型コロナウイルスの感染が、全国各地で再び増えつつある。新規感染者数は 5 月中旬から減少傾向が続いていたが、1 週間平均を見ると、32 都府県で前週より増加（6 月 30 日時点）。医療機関では猛暑による熱中症患者とあわせて対応に追われている。感染がより広がりやすいとされるオミクロン株のひとつ「BA.5（ビーエーファイブ）」への置き換わりが進んでおり、専門家は「自粛ムードがゆるむ中、いっきに感染者が増える恐れがある」と警告する。

7/2　米国 Kendall Square に武田薬品が R&D 拠点を確保し、Bayer は癌治療研究所を開設

生命科学/製薬研究の取り組みの中心地・米国マサチューセッツ州ケンブリッジ Kendall Square（ケンドール・スクエア）に武田薬品が研究開発（R&D）センターを新設することを先月下旬の初めに発表したことに続き、Bayer（バイエル）は先月末に同地に癌研究拠点を開設した。
武田薬品が入居するビルの建設は来年 2023 年に始まり、同社が入居できるようになるのは 2026 年になる見込み。
ボストン-ケンブリッジ地区にはおよそ 1,000 ものバイオテクノロジー企業が居を構えており、その中でもケンドール・スクエアは米国東海岸の製薬発明の中心地となっている。

7/2　Novartis が後発品事業 Sandoz を上場させる公算が大きくなっている/Bloomberg

Novartis が価値 250 億ドルの後発品事業 Sandoz を投資会社に売るのではなく上場会社に仕立てる公算がより大きくなっていると事情通が Bloomberg に話している。

7/3　日本人のゲノム 5 万人分の解読完了　創薬研究など期待、東北大の機構

東北大の「東北メディカル・メガバンク機構」が 6 月 30 日、日本の一般住民約 5 万人分のゲノム（DNA の全配列）の解析を完了したと発表した。創薬研究などに活用できるという。今後、10 万人分を目標にして解析を続ける。

7/3　肥満で歯周病悪化、微小物質 2 種が関与　岡山大助教らのグループ確認、タンパク質の生成を阻害

7/3　英国のサル痘の症状が先立つ流行とは異なっている

英国のサル痘といえば西アフリカ帰りの人に限られていたが蔓延国帰りではない人のサル痘が今や同国や他の幾つかの国の性保健（sexual health）診察で確認されることが急に増えている。

7/4　皮膚に貼るだけの COVID-19 抗体検査を開発 -東京大学

7/5　塩野義コロナ飲み薬、20 日にも再審議　国産初、緊急承認も初で注目

7/5　エボラなど危険ウイルス侵入に備え、治療体制充実へ…関西万博で入国増見据え

致死性の高いエボラウイルスなど「特定一種病原体」の国内侵入に備え、厚生労働省は国立感染症研究所（感染研）などで作る研究班を近く設置し、感染者の治療体制を充実させる方針を固めた。動物実験などで治療薬の効果を調べるほか、患者発生時の治療手順も策定する。入国者の増加が予想される 2025 年の大阪・関西万博を見据え、感染症の危機管理を強化することが狙い。

7/5　上海で再びロックダウンか、くすぶる不安－大規模コロナ検査を開始

中国・上海市は 5 日、市内全 16 区のうち 9 区で新型コロナウイルスの大規模検査を始めた。過去 2 日間で複数の感染者が見つかったことを受けたもので、中国の金融ハブである同市が「ゼロコロナ政策」追求の中で再度ロックダウン（都市封鎖）に入るとの懸念が強まっている。
上海市政府が 5 日、対話アプリ「微信（ウィーチャット）」の公式アカウントに掲載した発表文によると、9 地区の全域以外に 3 地区の一部で検査を実施する。「リスクを可能な限り早期に特定し感染拡大を防ぐ」目的で、今週 5-7 日の 3 日間に 2 回にわたって行う。
人口 2,500 万人の同市は、住民と経済に多大な犠牲を強いた 2 カ月間のロックダウンを先月解除したばかり。制限措置を緩和して間もなく感染者数の増加が報告されていることは、より感染力の強い変異株根絶の難しさを示している。

7/6　凍結乾燥細胞からクローン　マウスで成功　山梨大

マウスの尻尾などから採取した細胞（体細胞）をフリーズドライ（真空凍結乾燥）させ、最長で 9 カ月間保管後にクローンマウスを生み出すことに、山梨大の研究チームが成功した。遺伝資源の長期保管技術として期待できるという。論文は 6 日、英科学誌「ネイチャー・コミュニケーションズ」に掲載された。

7/6　オミクロン株の BA.4 と BA.5 系統が米国で急拡大

米国では現在、新型コロナウイルスの新規感染例のうちオミクロン株の 2 つの系統「BA.4」と「BA.5」による感染が半数以上を占めている。どちらの系統も、過去に新型コロナに感染したことのある人だけでなく、3 回目のワクチン接種（ブースター接種）を受けた人においても抗体をすり抜ける能力が高い。
BA.4 は 2022 年 1 月に、BA.5 は 2 月に南アフリカで最初に特定された。米疾病対策センター（CDC）によれば、それから 2 カ月も経たないうちに米国でも優勢になったと推定される。米国では 6 月 19～25 日の 1 週間に、BA.4 は新規症例の 15.7%を占め、BA.5 は 36.6%に上った。

7/6　Eisai/Biogen のアルツハイマー病薬 lecanemab の承認申請を米国 FDA が優先審査中

7/6　心血管やその指標・体重、血圧、糖、脂質がまともな米国成人は今や僅か 7%ほど

7/6　新型コロナの「子ども向けワクチン」 KM バイオが 9 月末申請へ

国内で新型コロナワクチンを開発している KM バイオロジクスは、子ども向けのワクチンについても 9 月末に承認申請する方針を明らかにした。 熊本市の KM バイオロジクスは、感染力をなくしたウイルスから作る「不活化ワクチン」を開発し、9 月末の承認申請を目指している。

7/7　8 種類の感染症選定　国産ワクチン開発支援　新型コロナやサル痘など -厚労省

厚生労働省の専門部会は 7 日までに、国産ワクチン開発を重点的に支援する対象の感染症について、新型コロナウイルスやデング熱、サル痘など 8 種類を選んだ。
将来のパンデミック（世界的大流行）に備え、ワクチン開発を進める企業などを支援する。
他に選ばれたのは、季節性インフルエンザウイルスや蚊が媒介するジカウイルス（ジカ熱）、乳幼児に肺炎を引き起こす RS ウイルス、手足口病の原因となるエンテロウイルス、急性脳炎となるニパウイルスによる感染症。

選定に当たっては、有効なワクチンの有無やヒトからヒトへの感染のしやすさを考慮。日本国内で患者が確保できない状況を想定し、海外で臨床試験（治験）が期待できるかどうかなども検討した。
新型コロナワクチンをめぐっては、欧米や中国と比べ開発が遅れた経緯がある。政府は 3 月、日本医療研究開発機構（AMED）内に、国産ワクチン開発の司令塔機能を担う「先進的研究開発戦略センター（SCARDA）」を設立。国内での開発加速を目指している。

7/7　潰瘍性大腸炎治療で「オルガノイド」を患部に移植…東京医歯大、世界初の試み

東京医科歯科大などの研究チームは7日、大腸の粘膜に炎症が起きる難病「潰瘍性大腸炎」の治療を目指し、腸の粘膜から採取した幹細胞を培養した「オルガノイド」を患部に移植する臨床研究を実施したと発表した。オルガノイドの移植は世界初の試みという。成功すれば粘膜が再生して根治につながる可能性がある。

7/7　世界のサル痘が 6,000 人超え～WHO は専門家を再度集めて事態の緊急さを検討

7/8　大腸がん再発の仕組み解明　化学療法「しがみついて」回避　慶応大

慶応大の研究チームは、大腸がんの元になる「がん幹細胞」が、化学療法の後も生き残り、再増殖する仕組みを明らかにした。日本人が罹患（りかん）するがんの中で、最も患者数の多い大腸がんの再発予防や根治療法開発につながると期待される。論文は 8 日、英科学誌「ネイチャー」に掲載された。

7/8　Boehringer Ingelheim、Evotec、bioMerieux の 3 社が抗菌薬を開発する合弁会社設立

7/8　銅合金+不織布マスク　オミクロン株を不活化　奈良県立医大が確認

奈良県立医科大学（奈良県橿原市）の微生物感染症学講座は、香芝市の企業と共同開発した銅合金を使った不織布マスクについて、銅合金に付着した新型コロナウイルスのオミクロン株を 2 分間で不活化させることを示したと発表した。デルタ株を不活化させることもすでにわかっている。同講座は「高い抗ウイルス性がより確かなものになった」と評価している。

7/9　南アフリカケープタウンの Afrigen が米国政府と mRNA ワクチン製造で提携

7/9　12～15 歳の小児への Pfizer の COVID-19 ワクチン使用を米国 FDA が承認

米国の 12-15 歳の小児への Pfizer/BioNTech の新型コロナウイルス感染症（COVID-19）予防 mRNA ワクチン Comirnaty（コミルナティ；BNT162b2）の使用がこれまでは取り急ぎの認可だったのが承認に。

7/10　葉の直径 3 メートル超、世界最大種巨大スイレンの新種発見

これまで 2 種類だけだと思われていた巨大スイレンに 3 種めが存在することを国際色豊かな研究チームが突き止めた。しかもこの新種は世界最大種で、野生だと葉が直径 10.5 フィート（約 3.2m）に達することも分かった。
新種 V. boliviana の原産地はボリビアで、世界最大の湿地の 1 つであるベニ県リャノス・デ・モホスに自生している。毎年たくさんの花をつけるが、花が開くのはたった 2 日のみで白からピンクへと変わっていくそう。研究の余地がまだあるようで、論文にはさらなる研究と調査の必要性が綴られていた。

7/12　Novavax の COVID-19 ワクチンが認可されたら米国が 320 万回投与分購入

7/13　SIGA Technologies（本社：ニューヨーク州）が 2,800 万ドル分のサル痘薬 TPOXX の注文を受注

7/13　最も心配な将来のウイルス変異体を同定する AI 技術を開発する Apriori Bio が発足（マサチューセッツ州ケンブリッジ）

https://www.prnewswire.com/news-releases/flagship-pioneering-launches-apriori-bio-to-provide-variant-proof-protection-from-the-greatest-viral-threats-301583415.html

7/13　Moderna のオミクロン株込みワクチンが BA.4/5 型への中和抗体をより生み出した

7/14　新型コロナ最悪バージョン「ケンタウルス」が韓国上陸…初の患者発生

新型コロナウイルスのうち最悪バージョンと呼ばれる「BA.2.75（ケンタウルス）」に感染した感染者が韓国でも初めて登場した。近く韓国内で優勢株になるとみられる BA.5 に加えてケンタウルスまで勢力を広げることになれば、これまでの予測よりもはるかに流行規模が大きくなる可能性があるとの懸念が出ている。
BA.2 の別の下位系統であるケンタウルスは今年 5 月にインドで初めて見つかった後、米国・オーストラリア・カナダ・ドイツ・英国など 15 カ国で報告された。専門家は以前の変異株とは違うという意味で BA.2.75 にギリシャ神話に出てくる半人半獣「ケンタウルス（Centaurus）」という別称を命名した。
BA.2.75 系統は以前の下位系統と比較してスパイク（突起）タンパク質に突然変異が多く、ウイルスがより効果的細胞と結合し、ワクチンや感染によって形成された抗体を回避することができ、ブレイクスルー（突破感染）や再感染の危険が高いといわれている。米国医学研究機関スクリプス研究所のエリック・トポル所長は BA.2.75 について「BA.5 より突然変異がさらに 8 カ所多く、相当数が（スパイクタンパク質の）N－ターミナルに位置していて、私たちが今見ているものより免疫回避がさらに深刻な可能性がある」と分析した。

7/14　Pfizer が 4 歳以下のコロナワクチン申請、厚労省に

7/14　Novavax の COVID-19 ワクチン NVX-CoV2373 を米国が取り急ぎ認可

https://www.reuters.com/world/us/us-fda-authorizes-novavax-covid-vaccine-adults-2022-07-13/

7/14　国内のコロナ感染者　累計 1,000 万人超え　初確認から 2 年半　日本で 12 人に 1 人「感染経験」

7/14　サル痘患者、1 万人超に　アフリカ以外で、拡大止まらず

動物由来のウイルス感染症「サル痘」の患者が、これまで継続的に確認されてこなかった欧米など 59 の国と地域で今年に入って計 1 万 845 人に達したことが 13 日、米疾病対策センター（CDC）の集計で分かった。従来の流行地だったアフリカの 6 カ国を合わせると 1 万 1,068 人となり、拡大が止まらない。

7/15　アフリカで「人獣共通感染症」63%増 WHO

世界保健機関（WHO）は 14 日、アフリカでサル痘のような動物からヒトへ、ヒトから動物へ伝播（でんぱ）可能な「人獣共通感染症」の脅威が高まっており、2012～22 年の流行回数は 01～11 年と比べて 63%増加したと明らかにした。
WHO の分析によると、アフリカでは 01～22 年、病気の流行などの「公衆衛生上の事象」が 1,843 件確認された。うち 30%がエボラ出血熱やデング熱、炭疽（たんそ）菌、ペスト、サル痘などの人獣共通感染症の流行だった。

7/15　Amazon が Fred Hutchinson Cancer Research Center と協力して癌ワクチン開発

7/15　Sanofi が 17 製品をドイツの Neuraxpharm に譲渡

7/18　国内感染最多、初の 11 万人超え　新型コロナ、今年 2 月を上回る

7/19　塩野義製薬、開発中コロナワクチンで 5～11 歳対象の治験開始

7/20　塩野義の新型コロナ飲み薬　承認見送り “継続審議に”

国産初の承認を目指した塩野義製薬が開発した新型コロナウイルスの飲み薬にかかわる厚労省の専門部会が行われ、専門部会は期限付きで迅速に審査する「緊急承認」の現時点での適用を見送り、継続審議とした。
この薬は、塩野義製薬が開発した「ゾコーバ（一般名・エンシトレルビル）」と呼ばれる薬で、塩野義製薬によると、これまで行われた臨床試験では喉の痛みや咳、息切れなどの呼吸器症状に特に効果が見られ、「BA4」や「BA5」などの変異株にも効果がある。
今年 5 月に新設された「緊急承認制度」で塩野義製薬は国産初の新型コロナの「飲み薬」の承認を目指していた。
経口薬の承認をめぐっては、6 月の部会で「有効性や安全性を示すデータが不十分」として議論が先送りとされていた。また、7 月 20 日に行われた厚生労働省の専門部会では、「有効性判断できないという意見が多く示されている」として、緊急承認を了承するかについての判断を見送り、継続審議となった。

7/21　Biogen が Aduhelm の教訓を生かして次のアルツハイマー病薬に取り組む

何十年か振りの米国承認アルツハイマー病薬となった Aduhelm（アデュヘルム）の今年 2Q の 3 か月間（4-6 月）の売り上げは昨年同期の 16 分の 1 の 10 万ドル（$100,000）で、Biogen はこれから得た教訓を生かして次のアルツハイマー病薬 lecanemab（レカネマブ）に取り組んでいる。
Biogen と Eisai（エーザイ）が協力して lecanemab を開発しているが、Ph2b 試験結果に基づいて同剤はすでに FDA に承認申請されており、その審査結果は来年 2023 年 1 月 6 日までに判明する。
因みに、Aduhelm が去年 6 月に承認されて爆騰した Biogen の株価はその後半分近くまで下落している。

7/21　第一三共の Enhertu が Seagen の特許を侵害しているとの米国陪審判断は覆らず

Daiichi Sankyo（第一三共）の申し立てが裁判所判事に聞き入れられず、Enhertu（エンハーツ）が Seagen の特許を侵害しているとの米国地裁陪審の判断は覆らなかった。

7/21　唾液中のタンパク質にコロナ感染防止効果 大阪公立大が解明

唾液の中に含まれる特定のタンパク質に新型コロナウイルスの感染を妨げる働きがあることが分かった、と大阪公立大学の研究グループが発表した。年を取って唾液の分泌量が減ることが、高齢者の重症化しやすさに関係している可能性があるという。研究グループは感染予防薬や治療薬の開発につなげたいとしている。

7/21　BA・5 の割合は 96%と国立感染研

国立感染症研究所は 21 日、国内の新型コロナウイルスの感染状況について、オミクロン株の派生型「BA・5」の割合が今週時点で 96%に達したとの推計を厚生労働省の専門家組織会合で示した。

7/22　Amazon が米国のプライマリーケア提供会社 One Medical を 39 億ドルで買収

7/22　日東製薬、飲むコロナ薬を日本より韓国で先行承認推進

日東製薬が、飲む新型コロナウイルス感染症治療剤候補物質「ジョコバ(S-217622)」の市販承認を日本より韓国で先に受ける案を検討している。日本政府が、使用承認を先送りし続けたからだ。

当初、日東製薬は、共同開発会社である日本の塩野義製薬が自国でこの薬の市販承認を受ければ、以後、韓国内の許可手続きに入る計画だった。日東製薬のチェ·ソング社長は 21 日、「日本政府がジョコバ緊急使用承認を保留した後、いくつかの代案について悩んでいる」として「日本より韓国で先に承認を受けるのはその中の一つ」と話した。

7/23　「サル痘」WHO が緊急事態宣言　75 の国と地域で 1.6 万件以上の感染確認

7/24　欧米で急拡大のサル痘感染、98.8%が男性　7 割超が 18～44 歳

欧米を中心に「サル痘」の感染者が増え続けている。世界保健機関（WHO）は 23 日、「国際的に懸念される公衆衛生上の緊急事態」を宣言した。現在の流行は欧米が中心だが、日本でも海外からの観光客の受け入れが増えている。国内で感染者が出ることを想定した備えが重要になる。WHO が約 1 万人の患者を分析したところ、98・8%は男性で、とくに 18～44 歳の男性が症例の 77%を占める。今回の感染者の多くは男性との性的接触のある男性という。

7/24　米国で小児 2 人がサル痘ウイルスに感染

https://www.washingtonpost.com/health/2022/07/22/first-monkeypox-cases-children-united-states/

7/25　サル痘検査態勢準備へ　政府、WHO 緊急事態宣言受け対策会議

7/26　サル痘予防にデンマークの Bavarian Nordic のワクチン Imvanex を使うことを欧州が承認

7/26　WHO 緊急事態宣言下のサル痘、国内初確認 欧州渡航歴ある都内 30 代男性

7/26　豪でコロナ感染・死者が記録的水準に、変異株が猛威

7/27　世界サル痘感染 1.8 万人、WHO は天然痘ワクチン共有呼びかけ

7/28　「ガイア理論」の英科学者ラブロック氏死去 103 歳

地球をひとつの生命体と考える「ガイア理論」や、気候変動に関する先駆的な研究で知られる英国の著名科学者ジェームズ・ラブロック（James Lovelock）氏が、転倒による合併症のため、103 歳の誕生日である 26 日に死去した。遺族が 27 日、明らかにした。

7/28　サル痘、国内で 2 例目　1 例目と無関係　北中米から一時入国の男性

7/28　サル痘に天然痘ワクチンを承認へ

厚生労働省は国内で生産・備蓄している天然痘ワクチンについて、「サル痘」の予防用で近く薬事承認することが、関係者への取材で判明した。医療従事者への使用が念頭にあり、29 日の専門部会の審議結果を踏まえて最終決定する。

7/28　新型コロナ新規感染者数、日本が世界最多　WHO 発表

世界保健機関（WHO）は 27 日、日本の新型コロナウイルスの新規感染者が 24 日までの 1 週間で 96 万 9 千人超に上り、世界最多だったと発表した。日本ではオミクロン株の新たな派生型「BA・5」による「第 7 波」の勢いが続いている。
世界全体の感染者数は 660 万人超で、国別の感染者は米国が約 86 万人、ドイツが約 57 万人、イタリアが約 53 万人、フランスが約 51 万人と続いた。一方、死者は米国が最多で約 2,600 人、ブラジル

が約 1,400 人だった。日本の死者は 272 人。
WHO のテドロス事務局長は 27 日「パンデミックは終わりには程遠い」と強調。

7/29　平均寿命 10 年ぶりに男女ともに縮む　女性 87.57 歳　厚労省

2021 年の日本人の平均寿命は女性は 87・57 歳、男性は 81・47 歳で、いずれも過去最高だった前年を下回った。平均寿命が短くなるのは東日本大震災が起きた 11 年以来、10 年ぶり。厚生労働省が 29 日に公表した「簡易生命表」で明らかになった。

7/29　高齢者の筋力衰え、脳で制御？　特定のたんぱく質増やし、マウス実験

高齢で全身の筋肉が弱る「サルコペニア」の症状を、脳で働く特定のたんぱく質を増やして改善する動物実験に国立長寿医療研究センターなどのグループが成功した。筋肉の老化に脳の働きがかかわることを示した。米専門誌に 29 日に発表する。

7/30　Moderna のオミクロン株ワクチン 6,600 万回投与分をこの秋冬用に米国が購入

オミクロン株 BA.4 型と BA.5 型への Moderna 社の新型コロナウイルス感染（COVID-19）予防ワクチン mRNA-1273.222 を米国政府がこの秋冬の上乗せ接種用に少なくとも 6,600 万回投与分購入する。

7/30　老化でコロナ感染 800 倍に、京都府立医大が「血管内皮細胞」侵入解明

京都府立医科大学の池田宏二教授、的場聖明教授らは、若い血管内皮細胞と比較して老化した血管内皮細胞に新型コロナウイルスが感染しやすいことを明らかにした。実験では、感染早期の段階で老化した血管内皮細胞は、若い内皮細胞に比べて 800 倍も多いウイルスが細胞内に侵入していることが分かった。今後このメカニズムを詳細に明らかにできれば、高齢者の重症化を効率的に予防する方法や治療薬の開発につながる可能性がある。

7/30　バイデン氏「症状ないが隔離」 新型コロナ再陽性

米ホワイトハウスは 30 日、バイデン大統領（79）が新型コロナウイルスの検査で再び陽性になったと発表した。27 日に陰性が確認され、隔離を解除して対面の執務に復帰していたが、30 日午前の検査で再び陽性となった。

7/31　中国ロケット残骸、無制御で落下　最大級の宇宙ごみ、米が批判

米軍は 30 日、中国が自国の宇宙ステーション関連施設の打ち上げに使った運搬ロケット「長征 5 号 B」の残骸が、インド洋上空で大気圏に突入したと発表。中国当局は 31 日、落下地点はフィリピン近海だと発表。EU の監視ネットワークによると、人口密集地から離れた場所に落下するよう制御されていなかった。
残骸は長さ 30 メートル、重さ 17～23 トンとみられ、近年落下した宇宙ごみとしては最大級という。米航空宇宙局のネルソン局長は「中国が具体的な軌道情報を共有しなかった」と批判した。

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. ストレスによって引き起こされる睡眠が後にマウスが不安に対処するのに役立つ

2. 細胞の持つ掃除機能が、毒性を示すタンパク質凝集体から脳神経細胞を守ることを発見
   ー認知症の発症や進行の抑制に重要な手がかりー

3. リズミカルな小腸微生物叢が肥満と 2 型糖尿病を予防 -マウス実験

4. 脂肪燃焼を促進する分子 -マウス実験

5. 音がマウスの痛みをどのように軽減するか
   新たに特定された脳回路が、より効果的な疼痛治療を示している可能性

6. 癌に対する免疫応答強化

7. コロナの起源に関する論文 2 本

8. サル痘：富裕国は COVID-19 の時と同じ間違いを犯すな（Nature Editorial）

1. ストレスによって引き起こされる睡眠が後にマウスが不安に対処するのに役立つ

日付：2022 年 6 月 30 日
ソース：インペリアルカレッジロンドン
概要：

我々は、夜よく眠れないのはストレスが原因だと思っているが、特定の種類のストレスは実際には睡眠を誘発する。今回、ロンドンのインペリアルカレッジと中国の研究機関の研究者らが主導した研究により、これがマウスの脳でどのように起こるかが明らかにされた。彼らは、睡眠がどのように誘発されるかを発見しただけでなく、マウスが経験した睡眠が翌日不安レベルを低下させるとも報告している。調査結果は、「Science」誌で本日報告されている。
我々および全ての哺乳類が経験する睡眠には、主に 2 つのタイプ、レム（REM：夢を見る傾向がある急速な眼球運動）とノンレム（NREM：より深く夢のない睡眠）がある。PTSD に苦しむ人々は、レム睡眠が少なくなるため、レム睡眠は困難な感情やストレスを処理するのに役立つとされている。この研究で研究者らは、レム睡眠とノンレム睡眠の両方で高い睡眠を誘発する特定のニューロンのセットを特定した。
このストレス誘発性の睡眠の新しいメカニズムを発見した研究チームは、責任のあるニューロンを選択的に標的にして、これから睡眠を介してそれらのプラスの効果を高める方法、すなわち睡眠のストレス解消力を高める薬物あるいはその介入への道を見つけたいとしている。

研究関連ニュース/他のトップページに戻る

＜英文＞Sleep triggered by stress can help mice cope with later anxiety -- ScienceDaily

Sleep triggered by stress can help mice cope with later anxiety

Date:

June 30, 2022

Source:

Imperial College London

Summary:

Stress boosts a kind of sleep in mice that subsequently relieves anxiety, according to new research that also pinpoints the mechanism responsible.

FULL STORY

Stress boosts a kind of sleep in mice that subsequently relieves anxiety, according to new research that also pinpoints the mechanism responsible.

Since sleep is similar across mammals, it is likely the same mechanism is triggered in human brains. Uncovering the mechanism could lead to artificial ways to boost its effects, helping to treat persistent stress disorders such as PTSD.

We often think of stress keeping us awake at night, but certain kinds of stress actually appear to induce sleep. Now, a study led by researchers at Imperial College London and institutions in China has uncovered how this happens in the brains of mice.

As well as discovering how sleep is induced, they reported that the sleep experienced by the mice appears to lower their anxiety levels the next day. The findings are reported today in the journal *Science*.

There are two main types of sleep that we, and all mammals experience: REM (rapid eye movement, where we tend to dream), and non-REM (NREM; deeper, dreamless sleep). People who suffer from PTSD experience less REM sleep, contributing to the theory that REM sleep helps us process difficult emotions and stress.

Lead researcher Professor Bill Wisden, from the Department of Life Sciences at Imperial, said: "Our results add weight to the idea that REM sleep helps us cope with stress. However, we previously only knew about ways REM sleep is reduced, such as some drugs that suppress it.

"Now, our study has revealed a mechanism by which REM sleep is induced, paving the way for drugs or other interventions that target the right neurons and boost the stress-busting power of sleep."

The researchers caused a type of psycho-social stress in mice called 'social defeat', which is used as an analogue for human bullying. Mice were exposed to particularly aggressive mice (without physical harm), after which researchers noted that 'flight or fight' hormones rose in their blood, indicating stress.

When the mice then slept, researchers tracked the activity of their neurons (brain cells). This revealed a specific set of neurons that detected and responded to the stress hormone levels and induced sleep high in both NREM and REM.

The activity of these neurons, and levels of NREM and REM sleep, stayed high for around five hours of sleep, during which they also sent signals to other neurons that regulate stress hormones, blocking them from releasing more.

The newly discovered neurons thus not only detected stress and induced sleep as a result, they also triggered the lowering of stress hormones.

Once the mice awoke, the researchers tested their anxiety response, to see how the sleep had affected their stress behaviours. They did this by measuring how long the mice spent in the light, rather than seeking out darkness, as they tend to do more when they are anxious.

Their responses were compared to stressed mice that were either sleep deprived (stimulated with objects) or had their newly identified neurons impaired, meaning they didn't get the restorative sleep normal mice did.

The mice that didn't get their stress-induced sleep spent much more time in the dark, indicating they were more anxious, and their stress hormone levels remained high.

Having found this new mechanism, the team now hope to find ways to selectively target the responsible neurons to boost their positive effects via sleep.

The team were funded by the Wellcome Trust and the UK Dementia Research Institute.
Dementia diagnosis can cause significant psychological stress, and the team hope that if their research can lead to a way to boost the effects of sleep, this will also help people cope with a new diagnosis. People living with dementia also suffer from more emotional disturbances, and boosting REM sleep may also help reduce this distress.

Story Source:

Materials provided by **Imperial College London**. Original written by Hayley Dunning. *Note: Content may be edited for style and length.*

Journal Reference:

1. Xiao Yu et al. **A specific circuit in the midbrain detects stress and induces restorative sleep**. *Science*, 2022 DOI: 10.1126/science.abn0853

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2. 細胞の持つ掃除機能が、毒性を示すタンパク質凝集体から脳神経細胞を守ることを発見

ー認知症の発症や進行の抑制に重要な手がかりー

日付：2022 年 7 月 1 日
ソース：国立量子科学技術研究開発機構
概要：

タウタンパク質は、脳内のニューロンの内部組織を安定化および維持する上で重要な役割を果たすが、認知症やアルツハイマー病などの状態では、ニューロン内に異常に蓄積する。この高リン酸化タウタンパク質（またはタウオリゴマー）の蓄積は、神経原線維変化（NFT）の形成と、認知症の人の脳内のニューロンの最終的な細胞死を引き起こし、疾患の進行性神経変性症状の一因となる。現在、タウタンパク質は選択的オートファジーによって分解される可能性があるとされているが、この正確なメカニズムは謎のままである。しかし、最近の画期的な進歩では、日本の量子科学技術研究開発研究所の科学者らが行った研究により、認知症モデルマウスで、細胞内のタンパク質凝集体をオートファジーによる分解に導くタンパク質 p62 を欠損させると神経細胞に対する毒性が高いタウオリゴマーが脳に蓄積し、脳萎縮と脳内炎症が亢進することを発見した。また、p62 を介したオートファジーがタウオリゴマーを分解し、認知症で生じる神経細胞死や脳内炎症を抑制することを初めて明らかにした。研究者らは、この研究成果は p62 とオートファジーを標的とした認知症の発症や進行を抑制する方法の開発に寄与すると期待している。
チームには、研究者の小野麻衣子とグループリーダーの佐原成彦が含まれていて、どちらも日本の量子科学技術研究開発機構の機能的脳イメージング部門の出身である。
「Aging Cell」誌に掲載された彼らの論文は、2022 年 6 月 5 日にオンラインで利用可能になっている。

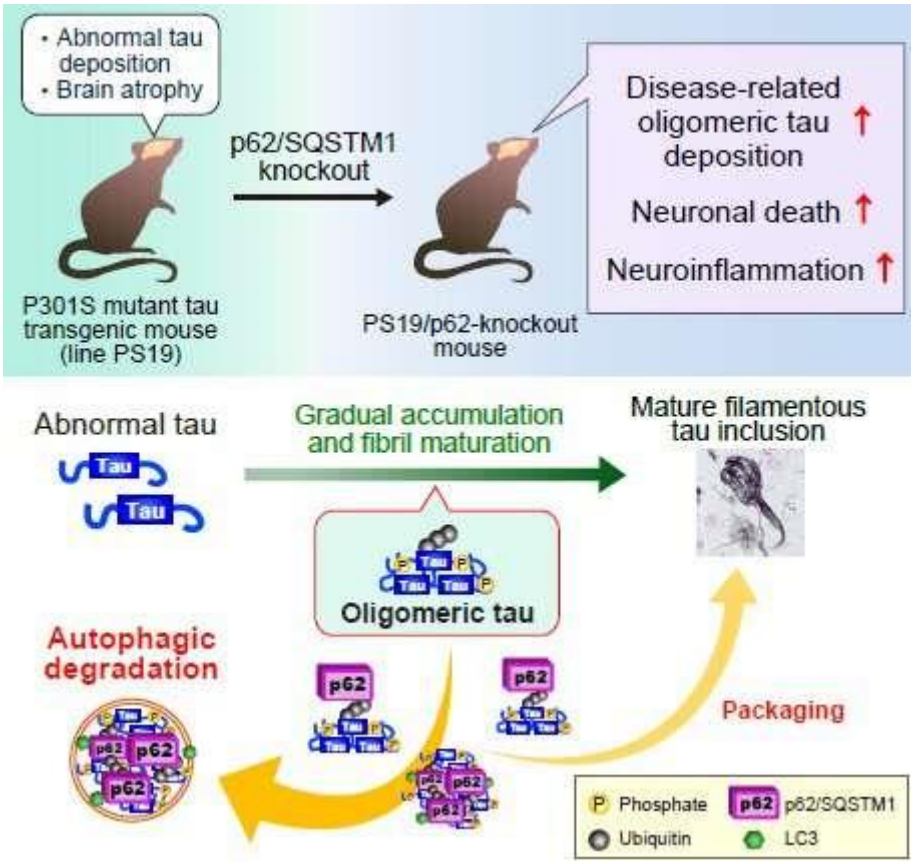
研究関連ニュース/他のトップページに戻る

＜英文＞Protecting the brain from dementia-inducing abnormal protein aggregates (medicalxpress.com)

JULY 1, 2022

Protecting the brain from dementia-inducing abnormal protein aggregates

by The National Institutes for Quantum Science and Technology



Researchers from the National Institutes for Quantum Science and Technology prove that the protein p62 eliminates and prevents the formation of toxic tau protein aggregates and inflammation and degeneration of neurons. Credit: Maiko Ono from National Institutes for Quantum Science and Technology, Japan

In order to maintain cellular homeostasis (i.e., a state of equilibrium), cells undergo selective autophagy or self-degradation of unwanted proteins. Autophagy receptors control this process, by mediating the selection of a target protein that is then "cleared."

Tau proteins—which otherwise play an important role in stabilizing and maintaining the internal organization of neurons in the brain—abnormally accumulate inside neurons in conditions like dementia and Alzheimer's disease. This build-up of hyper-phosphorylated tau proteins (or tau oligomers) causes the formation of neurofibrillary tangles (NFTs) and eventual cell death of neurons in the brains of people with dementia, contributing to the disease's progressive neurodegenerative symptoms. Now, while tau proteins can be degraded by selective autophagy, the exact mechanism of how this occurs remains a mystery.

In a recent breakthrough, however, a study done by scientists at the National Institutes for Quantum Science and Technology in Japan proved the critical role played by a certain gene—the p62 gene—in the selective autophagy of tau oligomers. The team included researcher Maiko Ono, and group leader Naruhiko Sahara—both from the Department of Functional Brain Imaging at the National Institutes for

Quantum Science and Technology in Japan. Their paper, published in *Aging Cell*, was made available online on 5 June 2022.

Previous studies have reported that the abnormal accumulation of the tau proteins may be selectively suppressed by autophagy pathways, through the p62 receptor protein (which is a selective autophagy receptor protein). Says Maiko Ono, "This protein's ubiquitin-binding ability helps in the identification of toxic protein aggregates (like tau oligomers), which can then be degraded by cellular processes and organelles."

This study's novelty, however, lay in the demonstration of p62's "neuroprotective" role in a living model, which had never been done before. So, how did the researchers achieve this? They used mouse models of dementia. The p62 gene had been deleted (or knocked out) in one group of these mice, so they did not express p62 receptor proteins.

On studying the brains of these mice using immunostaining and comparative biochemical analyses, an interesting picture was revealed. Neurotoxic tau protein aggregates were found in the hippocampus—the area of the brain associated with memory—and brainstem—the center that coordinates the body's breathing, heartbeat, blood pressure, and other voluntary processes—of p62 knockout (KO) mice. When we consider this along with the symptoms of dementia, which include memory loss, confusion, and mood changes, these findings make a lot of sense.

MRI scans revealed that the hippocampus of p62 KO mice was degenerated (atrophied) and inflamed. A postmortem assessment of their brains revealed a greater loss of neurons in their hippocampus. Further immunofluorescent studies showed that the abnormal tau species aggregates can cause cytotoxicity leading to inflammation and cell death of neurons in p62 KO mice. Oligomeric tau, specifically, accumulated more in the brains of p62 KO mice.

Overall, the findings of this study prove that by eliminating and, hence, preventing the aggregation of oligomeric tau species in the brain, p62 played a neuroprotective role in models of dementia.

At a time when researchers across the word are trying to develop drugs for dementia and other related neurodegenerative disorders, the findings of this study will be of great importance in providing evidence for the accurate targeting of tau oligomers. The global population of aging humans is increasing each year; hence, the need to develop methods to slow down the onset and progression of various neurodegenerative diseases is also expanding. This study provides a positive step towards addressing that need.

Explore further

Research explores why certain brain neurons are vulnerable to degeneration

More information: Maiko Ono et al, Central role for p62/SQSTM1 in the elimination of toxic tau species in a mouse model of tauopathy, *Aging Cell* (2022). DOI: 10.1111/acel.13615

Journal information: Aging Cell

3. リズミカルな小腸微生物叢が肥満と 2 型糖尿病を予防 –マウス実験

日付：2022 年 7 月 5 日
ソース：カリフォルニア大学サンディエゴ校
概要：

ヒトの腸には、推定 500 から 1,000 の細菌種が存在し、これはおそらく数にして 100,000 兆の微生物となる。2022 年 7 月 5 日に「Cell Reports」誌で公開された新しい論文で、カリフォルニア大学サンディエゴ校医学部の研究者らはマウスモデルを使用して、食事と摂食パターンがこれらの腸内微生物にどのように影響するか、特に肥満と 2 型糖尿病の宿主の健康にどのように影響するかを調査した。
研究者らは最新の研究で、特に回腸とその消化と吸収に関連する独特の機能の観点から、様々な要因の影響と相互作用を解明している。具体的には、食事誘発性肥満（DIO）と時間制限摂食（TRF）が、マウスモデルの回腸微生物叢の組成とトランスクリプトーム（生物のゲノムのタンパク質コード部分）をどのように変化させるかを調べた。研究者らは、マウスモデルでは、DIO と TRF の欠如（マウスは好きなときに好きなだけ食べることができる）が腸内細菌叢のリズムと腸内時計の調節に役立つシグナル伝達経路の混乱をもたらすことを発見、言い換えれば、マウスは太って不健康になった。
これらの発見は、健康な腸内微生物叢を維持する上での食事内容と時間制限のある摂食パターンの影響を強調し、それが代謝の健康を支配する概日リズムを調節するものだ、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＞A rhythmic small intestinal microbiome prevents obesity and type 2 diabetes (medicalxpress.com)

JULY 5, 2022

A rhythmic small intestinal microbiome prevents obesity and type 2 diabetes

by Scott LaFee, University of California - San Diego

In mouse models, researchers found that how much animals ate and when altered their gut microbiome, sometimes for the worse. Credit: Public domain (original work of U.S. Federal Government)

An estimated 500 to 1,000 bacterial species reside in each person's gut, perhaps numbering 100,000 trillion microorganisms. In a new paper, published July 5, 2022 in *Cell Reports*, researchers at University of California San Diego School of Medicine used mouse models to explore how diet and feeding patterns affect these intestinal microbes—and the health of the hosts, particularly with obesity and type 2 diabetes.

In both mice and men, the ileum is the final stretch of the small intestine, connecting to the cecum, the first part of the large intestine. In the ileum, nutrients are drawn out of liquefied food; in the cecum, which also marks the beginning of the colon, the process of extracting water begins.

Both processes are complex, dynamic and profoundly influenced by factors ranging from the types of foods consumed and when, to the microbial residents of the gut, whose presence and behaviors help dictate digestion, absorption of nutrients, vitamin synthesis and development of the immune system.

"It's important to realize that the gut microbiome is constantly changing, not only based on what we're eating, but also based on the time of day," said senior study author Amir Zarrinpar, MD, Ph.D., assistant professor of medicine at UC San Diego School of Medicine and a gastroenterologist at UC San Diego Health.

"Most researchers are getting snapshots of this constantly shifting environment, which makes it hard to understand what is going on in the gut. With this study, we are trying to get multiple snapshots throughout the day, almost like a movie, to better

understand how food and the microbiome interact to affect weight gain and diabetes.

"And what we've learned is that cyclical changes in the gut microbiome are quite important for health since they help with the circadian clock, and with that the regulation and control of glucose, cholesterol and fatty acids—and overall metabolic health."

In their latest work, Zarrinpar and colleagues further elucidate the impact and interplay of these factors, particularly in terms of the ileum and its unique functions related to digestion and absorption. Specifically, they looked at how diet-induced obesity (DIO) and time-restricted feeding (TRF) alter ileal microbiome composition and transcriptome (the protein-coding part of an organism's genome) in mouse models.

The researchers found that in mouse models, DIO and the absence of TRF (mice could eat as much as they wanted whenever they wanted) resulted in disruptions to gut microbiome rhythms and the signaling pathways that help modulate intestinal clocks. In other words, the mice became fat and unhealthy.

"It is interesting that restricting food access with TRF acts not only through restoration of patterns affected under the unhealthy state, but also through new pathways," said first author Ana Carolina Dantas Machado, Ph.D., a postdoctoral scholar in Zarrinpar's lab.

"These findings underscore the influence of diet and time restricted feeding patterns in maintaining a healthy gut microbiome, which in turn modulates circadian rhythms that govern metabolic health," said Zarrinpar. "It's a very complicated relationship between the microbiome and the host, with the former helping determine the latter's gastrointestinal functioning and health."

Their work, said the authors, can inform future studies, in particular investigations of how the gut works or how drugs act upon the gut function depending upon the state of the microbiome at a particular time or time of day.

Explore further

Microbiome links diet to health

More information: Ana Carolina Dantas Machado et al, Diet and feeding pattern modulate diurnal dynamics of the ileal microbiome and transcriptome, *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111008

Journal information: Cell Reports

4. 脂肪燃焼を促進する分子 –マウス実験

日付：2022 年 7 月 5 日
ソース：ボン大学
概要：

通常、脂肪細胞はエネルギーを蓄える。ただし、褐色脂肪細胞ではエネルギーは熱として放散されるため、生物学的ヒーターとして機能する。ほとんどの哺乳類はこのメカニズムを持っており、ヒトの成人では、褐色脂肪の活性化は心臓代謝の健康と正の相関がある。しかし、今日、我々は冬でも我々の身体的ヒーターをほとんど必要としない暖かく快適な暮らしをしている。同時に、ますますエネルギー密度の高い食事をしており、動きとしての運動量は先祖よりもはるかに少なくなっている。これらの 3 つの要因は褐色脂肪細胞にとっては毒であり、それらは徐々に機能を停止し、最終的には死ぬことさえある。その一方で、世界中でひどく太り過ぎの人の数は増え続けている。したがって、世界中の研究グループは、褐色脂肪を刺激して脂肪燃焼を増加させる物質を探している。
そこで、今回ボン大学の研究グループは、死にかけている細胞は、隣人の機能に影響を与えるメッセンジャー分子の混合物を放出する、というメカニズムが褐色脂肪にも存在するかどうかを調査した。彼らは、脂肪を燃焼させることができるイノシンという名前の重要な分子を特定していたが、褐色脂肪細胞に、細胞を事実上死にかけるように厳しいストレスにさらすと、それらがプリンイノシンを大量に分泌すること、また無傷の褐色脂肪細胞がイノシンによって（または単にその近くの死にかけている細胞によって）活性化されること、またその周りの白色脂肪細胞を褐色に変換することを実証した。
実際に、高エネルギー食を与えられ、同時にイノシンで治療されたマウスは、対照動物と比較して痩せたままであり、糖尿病から保護されていた。
研究者らは、このメカニズムの薬理学的可能性を明らかにするには、ヒトでのさらなる研究が必要だとしている。この研究は「Nature」誌に掲載されている。

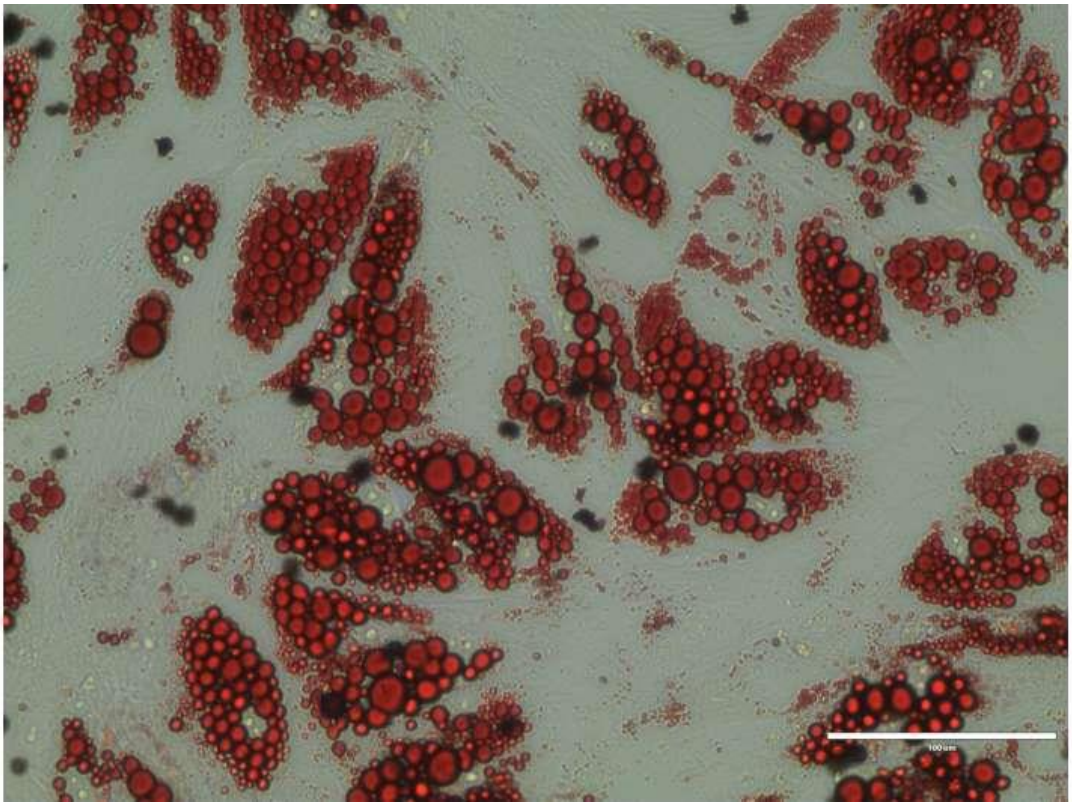
研究関連ニュース/他のトップページに戻る

＜英文＞Molecule boosts fat burning (medicalxpress.com)

JULY 5, 2022

Molecule boosts fat burning

by University of Bonn



Human brown adipocytes, lipid stained red (RedO oil stain). Credit: Laia Reverte Salisa / University of Bonn

Normally, fat cells store energy. In brown fat cells, however, energy is dissipated as heat—brown fat thus serves as a biological heater. Most mammals therefore have this mechanism. In humans it keeps newborns warm; in human adults, brown fat activation positively correlates with cardio-metabolic health.

"Nowadays, however, we're toasty warm even in winter," explains Prof. Dr. Alexander Pfeifer from the Institute of Pharmacology and Toxicology at the University of Bonn. "So our body's own furnaces are hardly needed anymore."

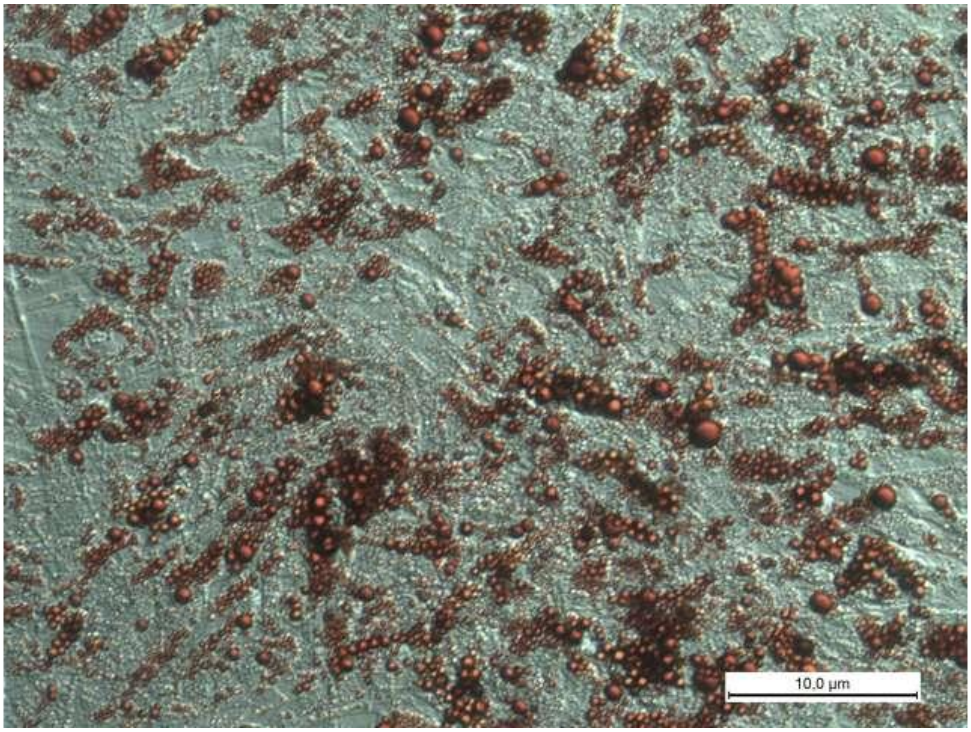
At the same time, we are eating an increasingly energy-dense diet and are also moving far less than our ancestors. These three factors are poison for brown fat cells: They gradually cease to function and eventually even die. On the other hand, the number of severely overweight people worldwide continues to increase. "Research groups around the world are therefore looking for substances that stimulate brown fat and thus increase fat burning," says Pfeifer.

Dying fat cells boost energy combustion of their neighbors

Together with a group of colleagues, the team at the University of Bonn has now identified a key molecule named inosine that is capable of burning fat. "It is known that dying cells release a mix of messenger molecules that influence the function of their neighbors," explains Dr. Birte Niemann from Pfeifer's research group. Together with her colleague Dr. Saskia Haufs-Brusberg, she planned and conducted the central experiments of the study. "We wanted to know if this mechanism also exists in brown fat."

The researchers therefore studied brown fat cells subjected to severe stress, so that the cells were virtually dying. "We found that they secrete the purine inosine in large quantities," Niemann says. More interesting, however, was how intact brown fat cells responded to the molecular call for help: They were activated by inosine (or simply by dying cells in their vicinity). Inosine thus fanned the furnace inside them. White fat cells also converted to their brown siblings. Mice fed a high-energy diet and treated with inosine at the same time remained leaner compared to control animals and were protected from diabetes.

The inosine transporter seems to play an important role in this context: This protein in the cell membrane transports inosine into the cell, thus lowering the extracellular concentration. Therefore, inosine can no longer exert its combustion-promoting effect.



Human brown adipocytes, lipid stained red (RedO oil stain). Credit: Thorsten Gnad / University of Bonn

Drug inhibits the inosine transporter

"There is a drug that was actually developed for coagulation disorders, but also inhibits the inosine transporter," says Pfeifer, who is also a member of the Transdisciplinary Research Areas "Life and Health" and "Sustainable Futures" at the University of Bonn. "We gave this drug to mice, and as a result they burned more energy." Humans also have an inosine transporter. In two to four percent of all people, it is less active due to a genetic variation. "Our colleagues at the University of Leipzig have genetically analyzed 900 individuals," Pfeifer explains. "Those subjects with the less active transporter were significantly leaner on average."

These results suggest that inosine also regulates thermogenesis in human brown fat cells. Substances that interfere with the activity of the transporter could therefore potentially be suitable for the treatment of obesity. The drug already approved for coagulation disorders could serve as a starting point. "However, further studies in humans are needed to clarify the pharmacological potential of this mechanism," Pfeifer says. Neither does he believe that a pill alone will be the solution to the world's rampant obesity pandemic. "But the available therapies are not effective enough at the moment," he stresses. "We therefore desperately need medications to normalize energy balance in obese patients."

The key role played by the body's own heating system is also demonstrated by a major new joined research consortium: The German Research Foundation (DFG) recently approved a Transregional Collaborative Research Center in which the Universities of Bonn, Hamburg and Munich conduct targeted research on brown adipose tissue.

The research was published in *Nature*.

Explore further

Researchers boost fat-burning

More information: Birte Niemann et al, Apoptotic brown adipocytes enhance energy expenditure via extracellular inosine, *Nature* (2022). DOI: 10.1038/s41586-022-05041-0

Journal information: Nature

5. 音がマウスの痛みをどのように軽減するか

新たに特定された脳回路が、より効果的な疼痛治療を示している可能性

日付：2022 年 7 月 7 日
ソース：NIH/国立歯科頭蓋顔面研究所
概要：

NIH を始めとする研究機関の国際チームは、音がマウスの痛みを鈍らせる神経メカニズムを特定し、痛みを治療するためのより安全な方法の開発に情報を与えることができるこの調査結果を、「Science」誌で発表している。
1960 年にさかのぼる人間の研究で、音楽やその他の種類の音が、歯科および医療手術、労働と出産、癌などの急性および慢性の痛みを和らげるのに役立つことが示されている。しかし、脳がこの痛みの軽減または鎮痛をどのように生み出すかは、あまり明確にされてこなかった。
そこで、研究者らはまず、炎症を起こした足のあるマウスを、心地よいクラシック音楽、同じ曲を不快に編曲したもの、ホワイトノイズの 3 種類の音にさらした。驚いたことに、3 種類の音はすべて、バックグラウンドノイズとしては低い強度（ささやき声レベル程度）で再生すると、マウスの痛みに対する感受性が低下した。同じ音のより高い強度は、動物の痛みの反応に影響を与えなかった。
この効果の根底にある脳回路を調査するために、研究者らは、蛍光タンパク質と結合した非感染性ウイルスを使用して、脳領域間の接続を追跡した。彼らは、音に関する情報を受信して処理する聴覚野から、痛みを含む感覚信号の中継局として機能する視床までの経路を特定した。自由に動くマウスでは、低強度のホワイトノイズが視床の経路の受信端にあるニューロンの活動を低下させた。音がない場合、光および小分子ベースの技術で経路を抑制することは、低強度のノイズの痛みを鈍らせる効果を模倣し、経路をオンにすると、動物の痛みに対する感受性が回復した。
この結果は、動物の所見がヒトに当てはまるかどうかを判断するための研究の出発点を科学者らに与えるものであり、最終的には、痛みを治療するためのオピオイドのより安全な代替品の開発に役立つ可能性がある、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＞How sound reduces pain in mice: Newly identified brain circuits may point to more effective pain therapies -- ScienceDaily

How sound reduces pain in mice

Newly identified brain circuits may point to more effective pain therapies

Date:

July 7, 2022

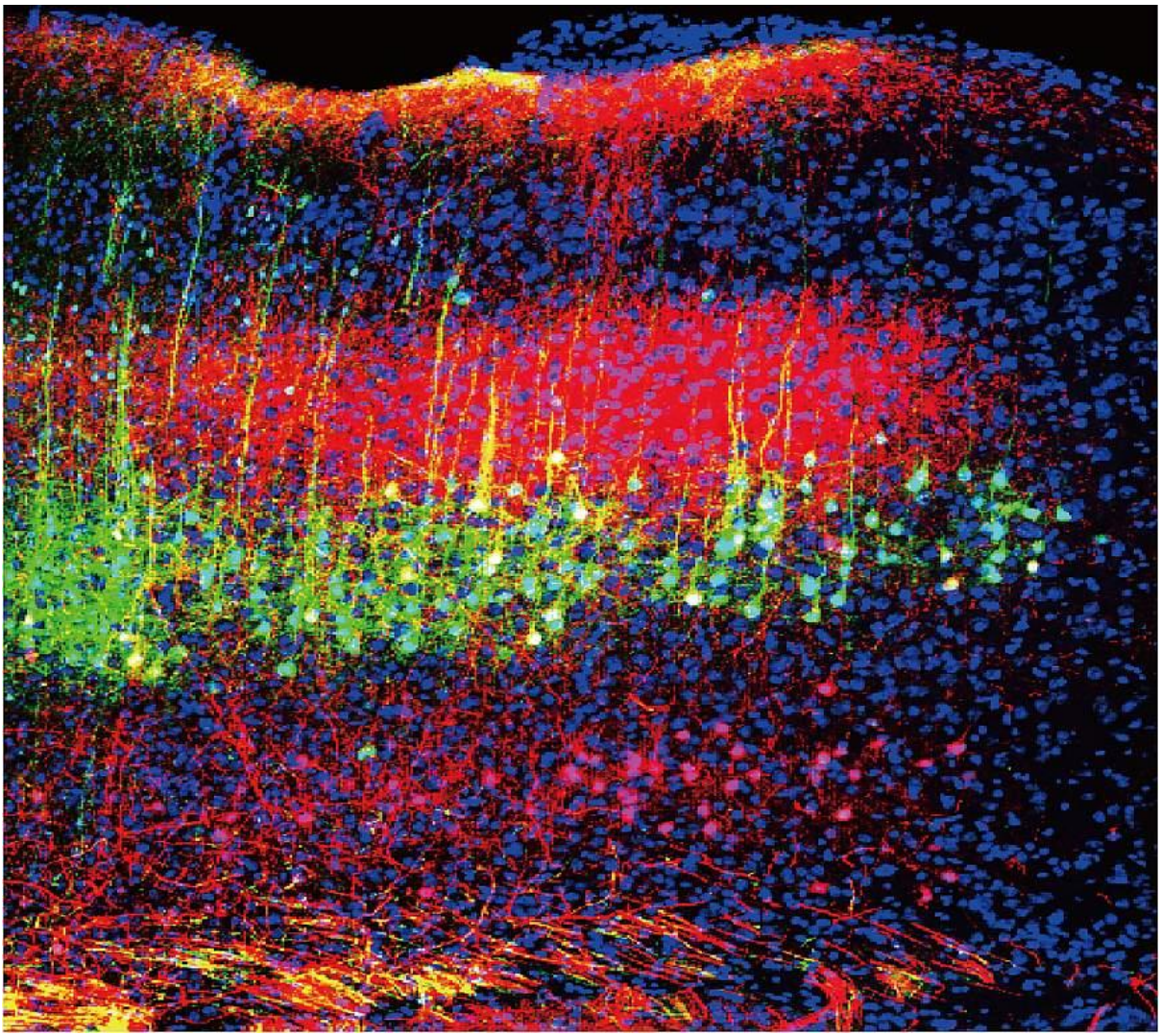
Source:

NIH/National Institute of Dental and Craniofacial Research

Summary:

Scientists have identified the neural mechanisms through which sound blunts pain in mice. The findings could inform development of safer methods to treat pain.

FULL STORY



Sound reduces pain in mice by lowering the activity of neurons in the brain's auditory cortex (green and magenta) that project to the thalamus. *Wenjie Zhou*

An international team of scientists has identified the neural mechanisms through which sound blunts pain in mice. The findings, which could inform development of safer methods to treat pain, were published in *Science*. The study was led by researchers at the National Institute of Dental and Craniofacial Research (NIDCR); the University of Science and Technology

of China, Hefei; and Anhui Medical University, Hefei, China. NIDCR is part of the National Institutes of Health.

"We need more effective methods of managing acute and chronic pain, and that starts with gaining a better understanding of the basic neural processes that regulate pain," said NIDCR Director Rena D'Souza, D.D.S., Ph.D. "By uncovering the circuitry that mediates the pain-reducing effects of sound in mice, this study adds critical knowledge that could ultimately inform new approaches for pain therapy."

Dating back to 1960, studies in humans have shown that music and other kinds of sound can help alleviate acute and chronic pain, including pain from dental and medical surgery, labor and delivery, and cancer. However, how the brain produces this pain reduction, or analgesia, was less clear.

"Human brain imaging studies have implicated certain areas of the brain in music-induced analgesia, but these are only associations," said co-senior author Yuanyuan (Kevin) Liu, Ph.D., a Stadtman tenure-track investigator at NIDCR. "In animals, we can more fully explore and manipulate the circuitry to identify the neural substrates involved."

The researchers first exposed mice with inflamed paws to three types of sound: a pleasant piece of classical music, an unpleasant rearrangement of the same piece, and white noise. Surprisingly, all three types of sound, when played at a low intensity relative to background noise (about the level of a whisper) reduced pain sensitivity in the mice. Higher intensities of the same sounds had no effect on animals' pain responses.

"We were really surprised that the intensity of sound, and not the category or perceived pleasantness of sound would matter," Liu said.

To explore the brain circuitry underlying this effect, the researchers used non-infectious viruses coupled with fluorescent proteins to trace connections between brain regions. They identified a route from the auditory cortex, which receives and processes information about sound, to the thalamus, which acts as a relay station for sensory signals, including pain, from the body. In freely moving mice, low-intensity white noise reduced the activity of neurons at the receiving end of the pathway in the thalamus.

In the absence of sound, suppressing the pathway with light- and small molecule-based techniques mimicked the pain-blunting effects of low-intensity noise, while turning on the pathway restored animals' sensitivity to pain.

Liu said it is unclear if similar brain processes are involved in humans, or whether other aspects of sound, such as its perceived harmony or pleasantness, are important for human pain relief.

"We don't know if human music means anything to rodents, but it has many different meanings to humans -- you have a lot of emotional components," he said.

The results could give scientists a starting point for studies to determine whether the animal findings apply to humans, and ultimately could inform development of safer alternatives to opioids for treating pain.

This research was supported by the NIDCR Division of Intramural Research. Support also came from the National Key Research and Development Program of China Brain Science and Brain-Like Intelligence Technology, National Natural Science Foundation of China, Science Fund for Creative Research Groups of the National Natural Science Foundation of China, CAS Project for Young Scientists in Basic Research, Natural Science Foundation of Anhui Province, and the University of Science and Technology of China Research Funds of the Double First-Class Initiative.

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. Wenjie Zhou, Chonghuan Ye, Haitao Wang, Yu Mao, Weijia Zhang, An Liu, Chen-Ling Yang, Tianming Li, Lauren Hayashi, Wan Zhao, Lin Chen, Yuanyuan Liu, Wenjuan Tao, Zhi Zhang. **Sound induces analgesia through corticothalamic circuits**. *Science*, 2022; 377 (6602): 198 DOI: 10.1126/science.abn4663

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6. 癌に対する免疫応答強化

日付：2022 年 7 月 22 日
ソース：マックス・デルブリュック分子医学センター
概要：

ドイツの医学研究チームは、癌に対する免疫防御を改善したいとの考えから、最近、以前はマウスモデルでのみ可能であったことをヒト細胞で示すことに成功した。彼らの研究成果は、血液癌に対して非常に効果的な免疫療法が開発される可能性を高める、としている。
リンパ腫、多発性骨髄腫、または特定の種類の白血病の患者にとって、キメラ抗原受容体 T 細胞（CAR T 細胞）による治療が癌を克服する最後のチャンスである場合がある。この治療では、患者の血液から T 細胞を採取し、実験室で人工受容体（CAR）を追加する。CAR を装備した T 細胞は、癌細胞の非常に特異的な表面構造を検出することもでき、CAR T 細胞の注入によって、それらは非常に特定の腫瘍細胞に結合して破壊することができる一種の生きた薬として体内を循環する。遺伝子操作された免疫細胞は体内に永久に残り増殖し、癌が再び燃え上がると、それらも行動に戻る。しかし実際には、多くの患者が再発する。これは、腫瘍細胞がタンパク質 EBAG9 をより多く産生することにより、CAR T 細胞を凌駕する可能性があるためである。T 細胞では、EBAG9 は細胞毒性酵素の放出を阻害し、これにより目的の免疫応答が遅くなる。
1 ヶ月前、ヘルムホルツ協会（MDC）のマックス・デルブリュック分子医学センターの研究者らが率いるチームは、「JCI Insight」誌で、マウスの EBAG9 遺伝子をシャットダウンすると癌に対する免疫応答の持続的な増加を導くことを示していた。また、マウスはより多くの T メモリー細胞を発達させた。今回、研究者らは、ヒト CART 細胞においてこれらの重要な発見を invitro で示すことに成功。研究チームは、これが治療的使用への決定的なステップであるとしている。

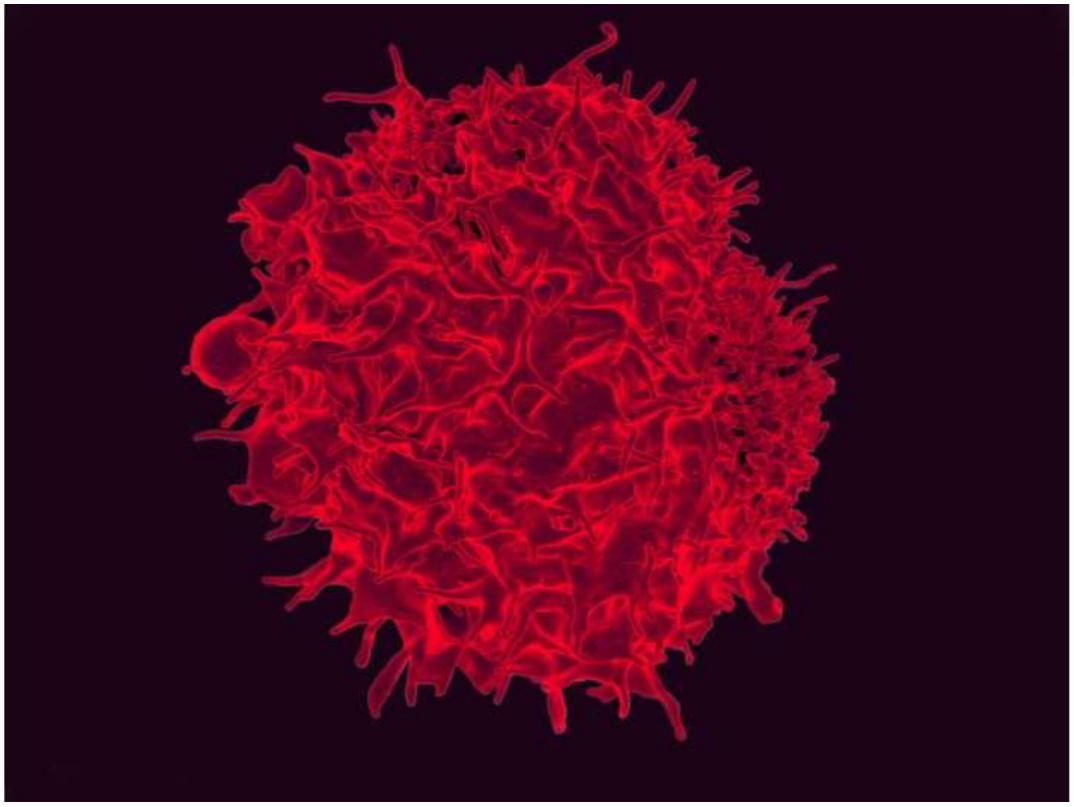
研究関連ニュース/他のトップページに戻る

＜英文＞Strengthening the immune response to cancer (medicalxpress.com)

JULY 22, 2022

Strengthening the immune response to cancer

by Max Delbrück Center for Molecular Medicine



Colorized scanning electron micrograph of a T lymphocyte. Credit: NIAID

For patients with lymphoma, multiple myeloma, or certain types of leukemia, treatment with chimeric antigen receptor T cells (CAR T cells) is sometimes the last chance of overcoming the cancer. The treatment involves taking T cells from the patient's blood and adding artificial receptors—the CARs—to them in the lab. As the guards of our immune system, T cells are on permanent patrol in our blood vessels and tissues, where they hunt down foreign structures. Equipped with CARs, T cells can also detect very specific surface structures on cancer cells. Once the CAR T cells are returned to the patient by infusion, they circulate in the body as a kind of living drug that can bind to very specific tumor cells and destroy them.

The engineered immune cells remain in the body permanently and multiply. If the cancer flares up again, they'll go back into action. That's the theory, at least. But in practice, many patients still relapse. This is because the tumor cells can outwit the CAR T cells by producing more of the protein EBAG9—and by causing the T cells to produce more of it, too. In T cells, EBAG9 inhibits the release of cytotoxic enzymes, which slows the desired immune response.

A month earlier, a team led by last authors Dr. Armin Rehm and Dr. Uta Höpken from the Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) showed in the journal JCI Insight that shutting down the EBAG9 gene in mice led to a sustained increase in the immune response to cancer. The mice also developed more T memory cells. These cells are part of our immunological memory, which allows our immune system to respond better to a cancer antigen after encountering it previously.

Now the researchers have also shown these key findings in vitro, in human CAR T cells. Writing in *Molecular Therapy*, the team says that this is the decisive step on the road to therapeutic use. "Shutting down EBAG9 allows the body to eradicate tumor cells earlier and more radically. As well as achieving longer-lasting therapeutic success, this could also create a real chance of cure," says Rehm.

Releasing the brake for immunotherapy

As soon as the EBAG9 gene was discovered, researchers recognized that it played an important role in cancer. But it took a long time to identify what that role actually was. When the MDC team started working on it in 2009, they found that mice without the gene dealt with bacterial and viral infections much better than mice with the gene, and that they formed more T memory cells, which are of particular interest in tumor biology.

Then in 2015, lead author Dr. Anthea Wirges succeeded in curbing synthesis of the EBAG9 protein using microRNA. For the latest study, she used microRNA to cultivate "EBAG9-silenced" CAR T cells with different human leukemia or lymphoma cells. Just like in the mouse model, the silencing reduced tumor growth much more. Relapses also only developed much later.

"Releasing the EBAG9 brake allows the genetically engineered T cells to release more cytotoxic substances. However, they don't cause the strong cytokine storm that is typically a side effect of CAR therapy," says Wirges. In fact, the risk is minimized because fewer cells are used. "Switching off the immune brake works across the board. We can do it with every CAR T cell that we produce—regardless of which type of blood cancer it targets.

Clinical studies are the next step

However, the first-line therapy for blood cancer will remain chemotherapy combined with conventional antibody therapy, as many patients respond very well to this. "CAR therapy only comes into play if the cancer returns. It's very expensive because it's an individual cellular product for a single person," says Höpken. And a single treatment with that product can save a life.

The EBAG9 work shows how important perseverance and patience are for researchers. Wirges was motivated by the prospect of her work having a real chance of clinical application. Rehm adds that "projects like this allow you to get to grips with a technique in basic research and then apply everything in translational research—right up to toxicological screening for the regulatory processes." Their project has now reached this last stage: The researchers will present their concept to the Paul Ehrlich Institute, Germany's biologics approval agency, in November.

Thanks to their findings from animal models and the in vitro experiments using human cells, the team now knows that releasing the EBAG9 brake is highly effective and doesn't cause any more side effects than conventional CAR T therapy. "We now need bold clinicians and a partner for financing the clinical studies," says Rehm. If

everything goes well, the therapy using EBAG9-silenced CAR T cells could be available to patients in as little as two years' time.

Explore further

Boosting the immune response against cancer

More information: Anthea Wirges et al, EBAG9-silencing exerts an immune checkpoint function without aggravating adverse effects, *Molecular Therapy* (2022). DOI: 10.1016/j.ymthe.2022.07.009

Journal information: Molecular Therapy

7. コロナの起源に関する論文 2 本

日付：2022 年 7 月 26 日
ソース：国際研究チーム（アリゾナ大学、カリフォルニア大学サンディエゴ校など）
概要：

新型コロナウイルスの「起源」として有力とされる、動物から人間への種を越えた感染は、少なくとも 2 回、最大で 20 回あまり起こっていたかもしれない。
米国などの国際研究チームが 7 月 26 日付の米科学誌「サイエンス」に、そんな内容の研究論文を発表した。
主要なメンバーが同じな別の研究チームが、同時に発表したもう 1 本の論文では、流行の初期のデータを分析した結果、中国・武漢市の海鮮市場が、種を越えた感染の「発生地」と考えられるとしている。
新型コロナの「起源」は、動物から人へ、種を越えて感染したウイルスだとする説が有力だ。しかし、いつ、どのように種を越えた感染が起きたのかは、直接的な証拠がなく、よく分かっていない。世界でも最初の流行は中国・武漢市で起こった。武漢市の複数の患者の検体を分析した結果から、初期の新型コロナウイルスは二つの系統に大別できることがわかっている。野生のコウモリから見つかったコロナウイルスに進化的により近い「A 系統」と、A 系統より早く感染拡大を起こし、その後の世界の流行の中心になった「B 系統」だ。B 系統は、いわゆる「武漢株」とも呼ばれ、いまも世界中で拡大するオミクロン株などの変異株の「親」にあたり、ワクチン開発の最初のターゲットにもなった。
研究チームは今回、種を越えた感染がどのように起これば、A と B、二つの系統が生まれ、実際の感染拡大を再現できるかシミュレーションした。まず、種を越えて感染した単一の「起源」から、A と B、二つの系統が派生したと仮定して検討すると、実際の感染拡大パターンと整合しなかった。一方、二つの系統にそれぞれの「起源」があると仮定すると、A 系統が動物のコロナウイルスにより近く、B 系統による感染拡大がより早く起きたことをうまく再現できた。
種を越えた感染の時期は、B 系統が 2019 年 11 月中旬、A 系統は同月下旬と推計された。また分析では、種を越えた感染が起こっても、多くの場合でそのウイルスは次の人に感染できず、自然に消滅すると予測された。現実に起こったように、最終的に、A と B、二つの系統が生き残るには、少なくとも 2 回、最大 23 回の種を越えた感染が起きた可能性があるとされた。

研究関連ニュース/他のトップページに戻る

＜英文＞Studies link COVID-19 to wildlife sales at Chinese market, find alternative scenarios extremely unlikely -- ScienceDaily

Coronavirus jumped to humans at least twice at market in Wuhan, China, studies find -- ScienceDaily

Studies link COVID-19 to wildlife sales at Chinese market, find alternative scenarios extremely unlikely

Date:

July 26, 2022

Source:

University of Arizona

Summary:

Analyses based on locations and viral sequencing of early COVID-19 cases indicate the pandemic started in Huanan market in Wuhan, China, with live animals being sold at the market as the likely source. Genomic studies revealed that the SARS-Cov-2 virus jumped into humans on at two separate occasions.

FULL STORY

A worker in protective clothing disinfects surfaces in a market where meat is sold as a prevention against COVID-19.

An international team of researchers has confirmed that live animals sold at the Huanan Seafood Wholesale Market were the likely source of the

COVID-19 pandemic that has claimed 6.4 million lives since it began nearly three years ago.

Led by University of Arizona virus evolution expert Michael Worobey, international teams of researchers have traced the start of the pandemic to the market in Wuhan, China, where foxes, raccoon dogs and other live mammals susceptible to the virus were sold live immediately before the pandemic began. Their findings were published Tuesday in two papers in the journal *Science*, after being previously released in pre-print versions in February.

The publications, which have since gone through peer review and include additional analyses and conclusions, virtually eliminate alternative scenarios that have been suggested as origins of the pandemic. Moreover, the authors conclude that the first spread to humans from animals likely occurred in two separate transmission events in the Huanan market in late November 2019.

One study scrutinized the locations of the first known COVID-19 cases, as well as swab samples taken from surfaces at various locations at the market. The other focused on genomic sequences of SARS-CoV-2 from samples collected from COVID-19 patients during the first weeks of the pandemic in China.

The first paper, led by Worobey and Kristian Andersen at Scripps Research Institute in San Diego, California, examined the geographic pattern of COVID-19 cases in the first month of the outbreak, December 2019. The team was able to determine the locations of almost all of the 174 COVID-19 cases identified by the World Health Organization that month, 155 of which were in Wuhan.

Analyses showed that these cases were clustered tightly around the Huanan market, whereas later cases were dispersed widely throughout Wuhan -- a city of 11 million people. Notably, the researchers found that a striking percentage of early COVID patients with no known connection to the market -- meaning they neither worked there nor shopped there -- turned out to live near the market. This supports the idea that the market was the epicenter of the epidemic, Worobey said, with vendors getting infected first and setting off a chain of infections among community members in the surrounding area.

"In a city covering more than 3,000 square miles, the area with the highest probability of containing the home of someone who had one of the earliest COVID-19 cases in the world was an area of a few city blocks, with the Huanan market smack dab inside it," said Worobey, who heads UArizona Department of Ecology and Evolutionary Biology.

This conclusion was supported by another finding: When the authors looked at the geographical distribution of later COVID cases, from January and February 2020, they found a "polar opposite" pattern, Worobey said. While the cases from December 2019 mapped "like a bullseye" on the market, the later cases coincided with areas of the highest population density in Wuhan.

"This tells us the virus was not circulating cryptically," Worobey said. "It really originated at that market and spread out from there."

In an important addition to their earlier findings, Worobey and his collaborators addressed the question of whether health authorities found cases around the market simply because that's where they looked.

"It is important to realize that all these cases were people who were identified because they were hospitalized," Worobey said. "None were mild cases that might have been identified by knocking on doors of people who lived near the market and asking if they felt ill. In other words, these patients were recorded because they were in the hospital, not because of where they lived."

To rule out any potentially lingering possibility of bias, Worobey's team took one further step: Starting at the market, they began removing cases from their analyses, going farther in distance from the market as they went, and ran the stats again. The result: Even when two-thirds of cases were removed, the findings were the same.

"Even in that scenario, with the majority of cases, removed, we found that the remaining ones lived closer to the market than what would be expected if there was no geographical correlation between these earliest COVID cases and the market," Worobey said.

The study also looked at swab samples taken from market surfaces like floors and cages after Huanan market was shuttered. Samples that tested positive for SARS-CoV-2 were significantly associated with stalls selling live wildlife.

The researchers determined that mammals now known to be susceptible to SARS-CoV-2, including red foxes, hog badgers and raccoon dogs, were sold live at the Huanan market in the weeks preceding the first recorded COVID-19 cases. The scientists developed a detailed map of the market and showed that SARS-CoV-2-positive samples reported by Chinese researchers in early 2020 showed a clear association with the western portion of the market, where live or freshly butchered animals were sold in late 2019.

"Upstream events are still obscure, but our analyses of available evidence clearly suggest that the pandemic arose from initial human infections from animals for sale at the Huanan Seafood Wholesale Market in late November 2019," said Andersen, who was a co-senior author of both studies and is a professor in the Department of Immunology and Microbiology at Scripps Research.

Virus likely jumped from animals to humans more than once

The second study, an analysis of SARS-CoV-2 genomic data from early cases, was co-led by Jonathan Pekar and Joel Wertheim at the University of California, San Diego and Marc Suchard of the University of California Los Angeles, as well as Andersen and Worobey.

The researchers combined epidemic modeling with analyses of the virus's early evolution based on the earliest sampled genomes. They determined that the pandemic, which initially involved two subtly distinct lineages of SARS-CoV-2, likely arose from at least two separate infections of humans from animals at the Huanan market in November 2019 and perhaps in December 2019. The analyses also suggested that, in this period, there were many other animal-to-human transmissions of the virus at the market that failed to manifest in recorded COVID-19 cases.

The authors used a technique known as molecular clock analysis, which relies on the natural pace with which genetic mutations occur over time, to establish a framework for the evolution of the SARS-CoV-2 virus lineages. They found that a scenario of a singular introduction of the virus into humans rather than multiple introductions would be inconsistent with molecular clock data. Earlier studies had suggested that one lineage of the virus -- named A and closely related to viral relatives in bats -- gave rise to a second lineage, named B. More likely, according to the new data, is a scenario in which the two lineages jumped from animals into humans on separate occasions, both at the Huanan market, Worobey said.

"Otherwise, lineage A would have had to have been evolving in slow motion compared to the lineage B virus, which just doesn't make biological sense," said Worobey.

The two studies provide evidence that COVID-19 originated via jumps from animals to humans at the Huanan market, likely following transmission to those animals from coronavirus-carrying bats in the wild or on farms in China. Moving forward, the researchers say scientists and public officials should seek better understanding of the wildlife trade in China and elsewhere and promote more comprehensive testing of live animals sold in markets to lower the risk of future pandemics.

Funding for the research was provided by the National Institutes of Health and the National Science Foundation.

Story Source:

Materials provided by **University of Arizona**. Original written by Daniel Stolte. *Note: Content may be edited for style and length.*

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Coronavirus jumped to humans at least twice at market in Wuhan, China, studies find

Date:

July 26, 2022

Source:

University of California - San Diego

Summary:

In a pair of related studies, researchers show that the origin of the COVID-19 pandemic was at a Chinese market and resulted from at least two instances of the SARS-CoV-2 virus jumping from live animal hosts to humans working or shopping there.

FULL STORY

In a pair of related studies, published July 26, 2022 online via First Release in *Science*, researchers at University of California San Diego, with colleagues on four continents, show that the origin of the COVID-19 pandemic in 2019 was at the Huanan Seafood Wholesale Market in Wuhan, China, and resulted from at least two instances of the SARS-CoV-

2 virus jumping from live animal hosts to humans working or shopping there.

The findings, first reported in February after the papers were posted online as preprints awaiting peer review, garnered international attention, primarily focusing on identifying the market as the early epicenter of the COVID-19 pandemic. The World Health Organization estimates that there have been more than 566 million confirmed cases of COVID-19 worldwide and 6.3 million deaths since the pandemic was declared in early 2020.

"It's vital that we know as much about the origin of COVID-19 as possible because only by understanding how pandemics get started can we hope to prevent them in the future," said Joel O. Wertheim, PhD, associate professor in the Division of Infectious Diseases and Global Public Health at UC San Diego School of Medicine, and a co-author on both papers.

But elemental to understanding pandemic origins is pinpointing not just where, but how, a pathogen successfully jumps from a non-human animal host to human, known as a zoonotic event.

"I think there's been consensus that this virus did in fact come from the Huanan Market, but a strong case for multiple introductions hasn't been made by anyone else yet," said Wertheim, senior author of the study that posits the SARS-CoV-2 virus, which causes COVID-19, jumped from animals to humans at least twice and perhaps as many as two dozen times.

According to researchers, two evolutionary branches of the virus were present early in the pandemic, differentiated only by two differences in nucleotides -- the basic building blocks of DNA and RNA.

Lineage B, which included samples from people who worked at and visited the market, became globally dominant. Lineage A spread within China, and included samples from people pinpointed only to the vicinity the market. If the viruses in lineage A evolved from those in lineage B, or vice versa, Wertheim said this would suggest SARS-CoV-2 jumped only once from animals to humans.

But work by Wertheim and collaborators found that the earliest SARS-CoV-2 genomes were inconsistent with a single zoonotic jump into humans. Rather, the first zoonotic transmission likely occurred with lineage B viruses in late-November 2019 while the introduction of lineage A into humans likely occurred within weeks of the first event. Both strains were present at the market simultaneously.

Researchers arrived at this conclusion by deciphering the evolutionary rate of viral genomes to deduce whether or not the two lineages diverged from a single common ancestor in humans. They used a technique called molecular clock analysis and an epidemic simulation tool called FAVITES, invented by Wertheim team member Niema Moshiri, PhD, an assistant professor of computer science at Jacobs School of Engineering at UC San Diego and study co-author.

"None of this could have been done without FAVITES," said Wertheim.

Validation

In February 2022, researchers at the Chinese Center for Disease Control and Prevention published a long-delayed analysis of genetic traces of the earliest environmental samples collected at the market two years earlier.

The samples were obtained after the first reports of a new, mysterious illness and after the market had already been shut down. The Huanan Seafood Wholesale Market in Wuhan is a so-called "wet market" where live animals are often slaughtered and sold for human consumption, including in some cases, wildlife.

However, no live wild mammals were left at the market after it was shut down. Instead, Chinese researchers swabbed walls, floors and other surfaces, tested meat still in freezers, sampled sewers and caught mice and stray cats and dogs around the market.

Their findings confirmed the not-yet-published predictions of Wertheim's team that Lineage A was also at the market.

"We felt validated, but what we felt more was immense pressure because they beat our preprint to the punch by about 12 hours, and we could only discuss their findings in light of ours," Wertheim said. "We were also shocked that they had been sitting on evidence for lineage A at the market for over a year without realizing its importance."

The newly published data, said study authors, are powerful evidence that the two viral lineages evolved separately and that multiple spillover events occurred. The Wuhan market reportedly contained a robust live wild animal business, with snakes, badgers, muskrats, birds and raccoon dogs (a canid indigenous to Asia) and other species sold for food. Wertheim said he believes there were likely many viral introductions. At least two successfully made the animal-human leap; other viral strains went extinct.

"While I'm hesitant to call it proof, what we presented is the most comprehensive explanation for the SARS-CoV-2 genomic diversity at the outset of the pandemic," Wertheim said. "There are really no other good explanations for both of these strains being at the market except for multiple jumps into humans."

(The findings undercut a circulating and persistent theory that the SARS-CoV-2 virus escaped from the Wuhan Institute of Virology, located a few miles from the market.)

Jonathan E. Pekar, a doctoral student in Bioinformatics and Systems Biology who co-led the project with Wertheim and is lead author, said the pandemic was likely looming for years, awaiting only for the opportunity when humans would come into contact with an animal host capable of transmitting the virus.

"Everything complicated happened before that introduction," Pekar said. "The last step is just extended contact and transmission from hosts to humans. At that point, it would actually be unusual to only have one introduction. We've seen this before with MERS-CoV (a similar zoonotic virus). We've seen it with humans giving SARS-CoV-2 to minks on farms and then minks giving it back to humans.

"This has happened before, and it's going to keep happening. Nature is a better lab than humans will ever be."

The latest study continues a series of published papers by Wertheim and colleagues investigating and chronicling the origin and spread of COVID-19.

In September 2020, they published data explaining how the first, few cases of novel coronavirus in North America and Europe quickly spread due to insufficient testing and contact tracing. In March 2021, Wertheim, Pekar and colleagues characterized the brief time-period during which SARS-CoV-2 could have circulated undetected before the first human cases in Wuhan.

Co-authors of "The molecular epidemiology of multiple zoonotic origins of SARS-CoV-2" include: Andrew Magee, Karthik Gangavarapu and Marc A. Suchard, all at UCLA; Edyth Parker, Nathaniel L. Matteson, Mark Zeller, Joshua I. Levy and Kristian G. Andersen, all at The Scripps Research Institute; Katherine Izhikevich, Jennifer L. Havens and Tetyana I.Vasylyeva, all at UC San Diego; Lorena Mariana Malpica Serrano and Michael Worobey, both at University of Arizona; Alexander Crits-Christoph, Johns Hopkins Bloomberg School of Public Health; Jade C. Wang and Scott Hughes, both at New York City Department of Health; Jungmin Lee, Heedo Park, Man-Seong Park, Korea University; Katherine Ching Zi Yan and Raymond Tzer Pin Lin, all at National Centre for Infectious Diseases, Singapore; Mohd Noor Mat Isa and Yusuf Muhammad Noor, both at Malaysia Genome and Vaccine Institute; Robert F. Garry, Tulane University; Edward C. Holmes, University of Sydney, Australia; and Andrew Rambaut, University of Edinburgh.

Story Source:

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

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8. サル痘：富裕国は COVID-19 の時と同じ間違いを犯すな

日付：2022 年 7 月 26 日
ソース：Nature Editorial
概要：

サル痘の症例が増え続けている。1 か月前、世界保健機関（WHO）がウイルス性疾患の世界的な発生を国際的に懸念される公衆衛生上の緊急事態（PHEIC）と宣言することに反対したが、既に 5 月の初めから 50 か国以上で約 3,000 件の症例が確認されていた。WHO によると、7 月 23 日までに、その数は 75 の国と地域で 16,000 件を超えた。
WHO の専門家顧問は先週の終わりに再び会合し、大多数は PHEIC の宣言を支持しなかったものの、7 月 23 日に組織は先に進むことを決定した。宣言がなされた今、各国は、病気が歴史的に最も蔓延している低中所得国（LMIC）に十分な資源が提供されることを確実にするために協力しなければならない。
COVID-19 で犯された間違いが繰り返されてはならない。たとえば、緊急時にワクチンをめぐる競争があれば、誰も利益を得られない。これは、多くの国の COVID-19 対応で広まっている問題だ。天然痘ワクチンはサル痘に対して効果的だが、LMIC ではワクチンの供給と診断能力の両方に問題がある。ワクチン提供者は、研究者や保健当局と協力して、この感染症に対応する能力を拡大するために各国が何を必要としているかを判断する必要がある。
サル痘が蔓延していることは、疫学者が数年前から警告しており、「世界は直ぐに適切に対応しなかった代償を払っている」とも言われている。PHEIC 宣言は、これを正す機会を提供するものであり、特に高所得国は、COVID-19 で犯された過ちから学ぶ必要がある。緊急時には、ワクチンの投与量と治療法を競うことは無意味であり、代わりに、診断とワクチンを共有し、それらが最も必要とされる場所をターゲットにする必要がある。

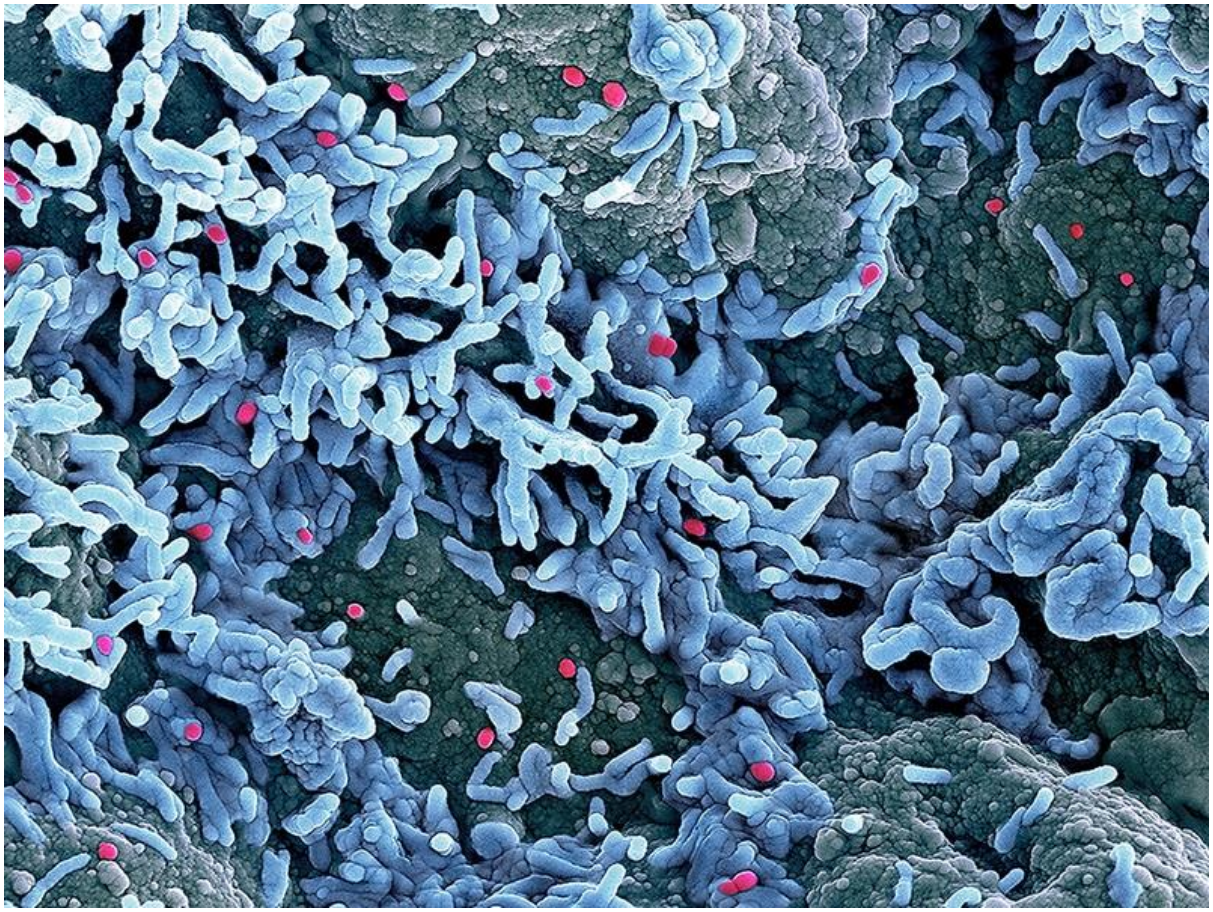
研究関連ニュース/他のトップページに戻る

＜英文＞Monkeypox: wealthy countries must avoid their COVID-19 mistakes (nature.com)

EDITORIAL 26 July 2022

Monkeypox: wealthy countries must avoid their COVID-19 mistakes

Having ignored the disease for decades, high-income countries must share vaccines and treatments quickly with other nations.



Monkeypox particles (red) on the surface of infected cells.Credit: NIH/SPL

Cases of monkeypox continue to rise. A month ago, when the World Health Organization (WHO) decided against declaring the global outbreak of the viral disease a public health emergency of international concern (PHEIC), some 3,000 cases had been confirmed in more than 50 countries since the start of May. By 23 July, that number stood at more than 16,000 cases across 75 countries and territories, according to the WHO.

The WHO's expert advisers met again at the end of last week, and although the majority didn't support declaring a PHEIC, on 23 July the organization decided to go ahead. Now that a declaration has been made, nations must work together to tackle the outbreak and ensure that sufficient resources are provided to low- and middle-income countries (LMICs), where the disease has historically been most prevalent. Mistakes made over COVID-19 must not be repeated.

For example, no one benefits when there is competition for vaccines during an emergency — a widespread problem in many nations' COVID-19 responses. Smallpox vaccines are effective against monkeypox, but in LMICs both vaccine supply and diagnostic capacity are patchy. Vaccine donors need to collaborate with researchers and health officials to determine what each country requires to scale up its ability to respond to this infectious disease.

Monkeypox declared a global emergency: will it help contain the outbreaks?

When a PHEIC is declared, the WHO recommends that nations commit to ramping up the manufacture and supply of diagnostic testing, medicines and vaccines. Research also tends to get a boost from governments, universities and industry — as happened with COVID-19.

The advisers opposed to declaring a PHEIC argued that the disease is treatable through targeted interventions. At present, the burden of disease is overwhelmingly being felt among men who have sex with men, in Europe and North America, and interventions could focus on vaccination in that community. But those supporting declaring a PHEIC argued that the necessary criteria have been met: the outbreak is an extraordinary event and the disease is a global public-health risk that requires a coordinated response.

Until this year, most cases of monkeypox were seen in people in Central and West Africa. In the current outbreak, all of the known fatalities (at least 70

suspected deaths so far) have been in African countries, where studies have shown that young children, older people and those with low immunity have a higher risk of developing severe disease.

The Democratic Republic of the Congo has experienced thousands of suspected cases during the past decade, and in that time hundreds of people have died from a virulent strain that has a mortality rate of around 10% (Z. Jezek *et al. Trop. Geogr. Med.* **40**, 73–83; 1988). But the true figures are not known — and could be higher than estimates suggest.

Monkeypox in Africa: the science the world ignored

In an all-too-common scenario, it has taken a health emergency in Europe and North America for the world to take notice of a disease. As Emmanuel Alakunle and Malachy Okeke at the American University of Nigeria in Yola write in a comment article in *Nature Reviews Microbiology*, the monkeypox outbreak should serve as "a wake-up call" that "highlights how little-to-no attention has been paid to the spread of the virus within endemic areas" (E. F. Alakunle and M. I. Okeke *Nature Rev. Microbiol.* https://doi.org/h5v8; 2022).

Last month, Adesola Yinka-Ogunleye, an epidemiologist at the Nigeria Centre for Disease Control in Abuja, told *Nature* that epidemiologists have been warning for some years that monkeypox is spreading. "The world is paying the price for not having responded adequately," she said.

The PHEIC declaration presents an opportunity to right this wrong. High-income countries in particular must learn from mistakes made over COVID-19. In an emergency it is senseless to compete for vaccine doses and treatments. Instead, diagnostics and vaccines should be shared and targeted to where they are most needed.

In an interview with US National Public Radio earlier this month, Atul Gawande, the official responsible for global health at the US Agency for International Development (USAID) in Washington DC, said that the lowest-income countries tend to be the last to get vaccines. This is an important acknowledgement coming from a senior official at USAID, a major source of vaccines and treatments. There is little doubt that the world's poorest and most vulnerable were failed during the response to COVID-19. Vaccines that offer protection against monkeypox exist and they need to be used for the benefit of all. Wealthy countries must not make the same mistake twice.

Nature **607**, 635-636 (2022)

doi: https://doi.org/10.1038/d41586-022-02036-9