Bio News – June, 2020

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

4/29　オックスフォード大学の COVID-19 ワクチンがサルの感染を予防～NYT 紙

4/30　COVID-19 流行中のイタリア北部で院外心停止が去年同時期より 6 割近く多く発生

4/30　Ph1 入りのオックスフォード大学 COVID-19 ワクチンを AstraZeneca が引き受ける

5/1　Gilead のレムデシビルは重症 COVID-19 患者に早めに投与した方がより有効/Ph3 試験

5/1　阪大の研究グループ・受精の際に精子側に必須な3遺伝子を特定

http://www.biken.osaka-u.ac.jp/achievement/research/2020/141

5/1　新型コロナウイルス感染者の半数近い 43%が一切無症状、しかも感染を移しうる/ベトナム

5/1　新型コロナウイルス感染を一度脱した人の 3%ほどが再度陽性になっている/韓国

5/1　コロナ禍の収束日を AI が予測　シンガポールのラボが情報公開

人工知能（AI）の開発に注力するシンガポール工科設計大学（SUTD）データドリブンイノベーションラボが、世界各国から公開されているデータを元に、新型コロナウイルスの「収束日」を予測し、その結果を公開。
研究チームは、各国から取得可能な統計データと AI 技術を駆使し、新型コロナウイルスがそれぞれ 97%、99%、100%の割合（収束度）で収束する日をそれぞれ予測。公開されたページには、世界全体および各国の「収束予測日」が細かに掲載されている。
それによれば、世界全体で感染が収束に向かう“ターニングポイント”とされたのは 4 月 11 日。完全（100%）に収束する日は、2020 年の 12 月 19 日と見込まれている。なお、ほぼ収束に近づく収束度 97%の日時予測としては 5 月 30 日、99%は 6 月 17 日とされている。
日本の場合、ターニングポイントとされているは 4 月 14 日。安倍首相の緊急事態宣言から 1 週間後の時点だ。次いで、完全な収束日は 9 月 26 日（97%が 5 月 20 日、99%が 6 月 5 日）とされている。
早急な感染症対策を講じ着実に収束に向かっていると各国から評価されている韓国の予測収束日は、5 月 12 日。同じく拡大を食い止めることに成功したベトナムも、5 月 20 日と割と早い段階での収束が見込まれた。欧米諸国は、米国（8 月 22 日）、ドイツ（8 月 1 日）、英国（8 月 14 日）、フランス（8 月 5 日）、イタリア（8 月 25 日）、スペイン（8 月 7 日）など、いずれも 8 月中と予測されている。
なお、この AI による予測は、各国から公式に発表された統計資料をベースにしているため、どの程度にわたり正確性を担保できるかは、データの正確性および透明性に寄るところが大きい。

5/2　WHO 一度解除しても必要あれば外出制限など再び

5/2　米国 FDA「レムデシビル」緊急使用認める

重症の新型コロナウイルス感染（COVID-19）入院患者に Gilead Sciences の抗ウイルス薬 Remdesivir（レムデシビル）を使うことを緊急事態下の特例として米国 FDA が許可。
今回の認可は正式な承認ではなく、一時的な措置であり、Remdesivir は依然として非承認薬であると Gilead は言っている。

5/2　レムデシビル、承認手続き開始　米認可受け特別適用　厚労相「申請から 1 週間で」

5/3　COVID-19 への取り組みが他の原因による死亡を増やした可能性/英国

2020 年 4 月 10 日までの 1 週間のイングランドとウェールズの全死亡数は過去 5 年間のその週の死亡数の平均を 7,996 人上回った。その増加分は同週に COVID-19 で死亡した 6,213 人を 1,783 人上回っており、COVID-19 封じ込めの対策は COVID-19 以外の死亡を増やしたかもしれないと英国のシンクタンク Nuffield Trust の John Appleby 氏は懸念している。
ED に足を運ばなかった人達に何があったのかは少なくとも現時点では不明だが、それらの人々が治療に出向いていれば防げたものもあったかもしれない、としている。又、COVID-19 による死亡は報告より実際には多いかもしれず、もしそうなら報告にあがっていないそれらの COVID-19 死亡が紛れ込んで他の原因による死亡を水増ししたことも考えられる、ともしている。

5/4　Roche の血中 COVID-19 抗体検出検査を FDA が承認～感度 99.8%

5/4　COVID-19 流行は 1 年半～2 年ほど続く～米大学の感染症研究センターCIDRAP 予想

5/5　米国の 1 日の COVID-19 死亡が来月には約 3,000 人に増えると政府が予想/NYT 紙報道

5/5　フランスで昨年末に新型コロナ患者　医師らが検出

https://www.cnn.co.jp/world/35153330.html

5/5　レムデシビル、重症患者向けに優先配分　厚労省が方針

5/6　米国の COVID-19 対応の要職 BARDA（生物医学先端研究開発機構）長を解任された Rick Bright 氏が告発書を提出

早くから COVID-19 について警告していたことをトランプ政権は無視し、政治的な圧力を加えたなどと Bright 氏は主張。

5/6　COVID-19 による医療途絶で 3 か月間に米国の 8 万人が一般的な癌 5 つの診断を逃す

基準の 2 月に比べて 4 月の初めには乳癌、前立腺癌、大腸癌、子宮頸癌、肺癌の検診/検査数が 4 割～9 割も減っている。

5/6　米国人の約 6%が脂肪肝

5/6　コロナ感染歴ある子どもに「川崎病」症状　欧米で相次ぐ

5/6　Roche が COVID-19 抗体検査増産のためにドイツ工場に 5 億ドル近くを投じる

5/6　40 年前に開発の薬「イベルメクチン」 コロナに有効か　2015 年にノーベル医学生理学賞を受賞した北里大学の大村教授が開発

5/7　新型コロナの治療薬に光明　感染抑制能を有する VHH 抗体を取得　北里大学・EME・花王の研究で

https://www.kitasato-u.ac.jp/jp/albums/abm.php?f=abm00026718.pdf&n=20200507_%E6%96%B0%E5%9E%8B%E3%82%B3%E3%83%AD%E3%83%8A%E3%82%A6%E3%82%A4%E3%83%AB%E3%82%B9%EF%BC%88SARS-CoV-2%EF%BC%89%E3%81%AB%E5%AF%BE%E3%81%97%E3%81%A6%E6%84%9F%E6%9F%93%E6%8A%91%E5%88%B6%E8%83%BD%EF%BC%88%E4%B8%AD%E5%92%8C%E8%83%BD%EF%BC%89%E3%82%92%E6%9C%89%E3%81%99%E3%82%8BVHH%E6%8A%

97%E4%BD%93%E3%81%AE%E5%8F%96%E5%BE%97%E3%81%AB%E6%88%90%E5%8A%9F.pdf

5/7　新型コロナ、人への感染は 19 年終盤から　英大学が遺伝子分析

5/7　コロナ治療薬「レムデシビル」を特例承認　申請から3日

5/7　レムデシビル、患者への投与は無償に　対象は重症の患者

5/8　糖尿病によるがん発症リスク　ハエで仕組み解明 -京大

5/8　COVID-19 男性の精液からウイルス検出～性行為で感染がうつるかどうかは不明

中国の新型コロナウイルス感染（COVID-19）男性 38 人を調べたところ 6 人（16%）の精液から新型コロナウイルス（SARS-CoV-2）が検出された。

5/9　スペインの 1 日の新型コロナウイルス感染（COVID-19）死亡数が再び増加

5/9　1,000 を超える臨床試験が新型コロナウイルス感染流行のせいで中止されている

5/9　武田や CSL 等が取り組む回復者血漿から作る COVID-19 治療の試験が今夏に始まる

新型コロナウイルス感染（COVID-19）回復者から集めた血漿から作る抗 COVID-19 ポリクローナルを協力して開発する武田薬品と CSL Behring の発起による提携・CoVIg-19 Plasma Alliance に新たに 4 社が加わり、更に米国立衛生研究所（NIH）の助けを借りて今夏にその製品の効果や安全性を調べる臨床試験が始まる。

5/9　COVID-19 流行に伴う屋内待機を背景に米国の脳卒中検査が 4 割近く減少

5/11　研究力ランキング、日本勢初のトップ10陥落…中国勢が躍進

英科学誌ネイチャーは、主要科学誌に2019年に掲載された論文数などにもとづく研究機関の研究力ランキングをまとめた。日本勢は東京大の11位が最高で、ランク付けを始めた16年以降、初めてトップ10から陥落した。
ランキングは、自然科学系の82雑誌で発表された論文への貢献度を、研究機関別に調べた。その結果、50位以内に入った日本勢は11位の東京大（前年8位）、37位の京都大（同29位）だけだった。1位は5年連続で中国科学院だった。中国勢は今回、新たに2機関がトップ10にランク入りするなど、躍進が目立った。
また、国別のランキングでは、日本は米国、中国、ドイツ、英国に続く5位。16年以降、上位7か国の順位に変動はないが、論文貢献度は今回、中国が前年比で15・4%増と急上昇した一方、日本は5.1%減だった。

https://www.yomiuri.co.jp/science/20200511-OYT1T50080/

5/11　コルジセピンは体内時計を 12 時間ずらす作用あり～時差ボケ治療薬となりうる

5/11　遺伝子薬、1 回 1 億 6,707 万円で保険適用へ　国内史上最高額、難病治療

難病の脊髄（せきずい）性筋萎縮症の遺伝子治療薬「ゾルゲンスマ」について厚生労働省は 1 回 1 億 6,707 万 7,222 円で公的医療保険を適用する方針を固めた。脊髄性筋萎縮症は、運動神経を維持して筋肉を動かすのに不可欠なたんぱく質が不足する神経疾患。特定の遺伝子の機能が欠けるのが原因で、生後 6 カ月くらいまでに発症する最重症のタイプでは、症状が進むと筋力が低下し、人工呼

吸器が必要となる。薬は 2 歳未満の患者に、正常な遺伝子を点滴で 1 回投与する。国内では 3 月に承認され、スイスの製薬大手ノバルティスファーマが保険適用を申請していた。

5/12　Merck & Co の本拠地が現在のニュージャージー州ケニルワースから近所のローウェーに移転

5/12　Moderna の COVID-19 ワクチン開発が米国 FDA の Fast Track 優遇の対象になった

5/13　国内メーカー「富士レビオ」の抗原検査キット承認　30分で結果

5/13　下水中のウイルス分析　新たな“コロナ感染指標”

5/14　新型コロナ、遠紫外線ランプでウイルス死滅 -コロンビア大実験結果

https://www.afpbb.com/articles/-/3283035

5/14　COVID-19 流行下のイタリア北部で川崎病様小児疾患がいつもより 30 倍多く発生

5/14　新型コロナウイルス感染は猫から猫に移る～人→猫→人の感染連鎖の調査が必要

3 匹の猫（ネコ）にあえて新型コロナウイルス（SARS-CoV-2）を投与したところ最大 6 日後までウイルスが検出され、一緒に過ごさせた SARS-CoV-2 非投与ネコに感染が移った。
どの猫にも症状は認めらず、飼い主が気づかないままの SARS-CoV-2 感染源となる恐れがある、としている。この研究はウィスコンシン大学マジソン校、国立感染症研究所、国立国際医療研究センター、および東京大学の共同研究として行われた。

https://www.nejm.org/doi/full/10.1056/NEJMc2013400

5/14　トランプ氏が褒めたコロナ検査システム（Abbott 社製の「ID NOW」）、半数近くが偽陰性 - NYU など研究チーム

5/15　新型コロナ対応「WHO を支持」 日中韓保健相が声明

5/15　新型コロナウイルスを被ってすぐの RT-PCR 検査は当てにならないらしい

https://www.jwatch.org/fw116641/2020/05/14/covid-19-false-negatives-projections-africa-predictive

5/15　妊婦の COVID-19 入院/重症化率は高くない～経過は概ね良好で新生児の感染率 5% -オックスフォード大

http://www.ox.ac.uk/news/2020-05-11-pregnant-women-are-not-greater-risk-severe-covid-19-other-women

5/17　仏と中国での無作為化試験 2 つのどちらも COVID-19 にヒドロキシクロロキン無効

5/18　スイスの ADC Therapeutics が 2 億 3,270 万ドル IPO 調達

5/18　Moderna（マサチューセッツ州）の COVID-19 ワクチンの Ph1 途中解析で全員に中和抗体が備わっていた

https://www.nytimes.com/2020/05/18/health/coronavirus-vaccine-moderna.html

5/18　断酒薬ジスルフィラム（ノックビン）で肥満マウスの体重減少～脂肪肝も解消

今月の研究関連ニュース/他　5 参照

5/19　新型コロナウイルス感染（COVID-19）検出犬の育成に英国政府が 50 万ポンド提供

犬に新型コロナウイルス（SARS-CoV-2）感染者を見つけさせる取り組みを英国政府が 50 万ポンド（61 万ドル）超を出して支援。
癌の幾つか、パーキンソン病、マラリアを識別するように訓練された生物指標検出犬はすでに存在する。
London School of Hygiene and Tropical Medicine, Durham University, 慈善団体 Medical Detection Dogs による今回の取り組みが成功すれば、空港などの公共の場で一匹の COVID-19 識別犬に 1 時間あたり最大 250 人の検査を任せることができる、としている。同様の取り組みが米国やフランスでも始まっている。

https://www.lshtm.ac.uk/newsevents/news/2020/uk-government-supports-covid-19-detection-dogs-trial

5/19　SARS 感染患者から見つけた新型コロナウイルス中和抗体を Vir が Nature に報告

2003 年に SARS-CoV（または SARS）感染した患者のメモリーB 細胞から見つけた抗体 S309 が新型コロナウイルス（SARS-CoV-2）の細胞感染を防ぐことを Biogen 元 CEO・George Scangos 氏が率いる Vir Biotechnology が発見して Nature 誌に報告。

https://www.afpbb.com/articles/-/3283712

5/19　iPS 心臓治療、慶応大が厚労省に申請　年内にも移植へ

5/19　WHO 拠出「恒久停止も」トランプ大統領が警告、脱退も示唆

https://www.afpbb.com/articles/-/3283762?cx_part=latest

5/19　トランプ大統領、抗マラリア薬の服用明かす　FDAは使用に警告

5/20　COVID-19 肺炎患者の回復がアビガンと別のインフルエンザ薬で有意差なし

5/21　世界初、重病赤ちゃんに移植　ES から作った肝細胞　成育センター

5/21　新型コロナ、自然感染とワクチンで免疫獲得 サル実験で確認 -ベス・イスラエル・ディーコネス医療センター（BIDMC）

5/21　新型コロナウイルスの体内侵入の足場となる ACE2 発現が小児の鼻では少なく、年齢が上がるにつれて多くなる

5/22　AstraZeneca の COVID-19 ワクチン 3 億回投与分の実現に米国政府が 12 億ドル捻出

5/23　抗マラリア薬のコロナ治療利用、死亡リスク増と関連か

5/24　米国 2 州（カルフォルニア州、ワシントン州）での COVID-19 入院男性の約半数が集中治療に陥った～女性は約 3 人に 1 人

5/24　感染母親の母乳から新型コロナウイルス（SARS-CoV-2）が検出された

新型コロナウイルス感染（COVID-19）女性 2 人の母乳を調べたところ 1 人からその原因ウイルス SARS-CoV-2 が検出され、その女性の赤ちゃんも感染していた。赤ちゃんの感染が母乳経由かその他の経路によるのかは不明。

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31181-8/fulltext

5/25　Roche がシークエンス会社 Stratos Genomics を取得

https://www.reuters.com/article/us-roche-hldg-m-a-stratos/roche-buys-u-s-gene-sequencing-tech-company-stratos-genomics-idUSKBN22Y0MX

5/26　ミンクから人に新型コロナウイルス感染～動物から人への恐らく初めての伝播例 -オランダ

https://www.reuters.com/article/us-health-coronavirus-netherlands-mink/dutch-government-second-case-of-mink-transmitting-coronavirus-to-human-idUSKBN23112K

5/26　アビガンの 5 月承認を断念　加藤厚労相「治験を継続」

5/26　COVID-19 妊婦 15 人の生児出産後の胎盤を調べたところ血流障害がより認められた -ノースウエスタン大

新型コロナウイルス感染（COVID-19）妊婦 15 人の生児出産後の胎盤をすぐに調べたところ、母親から胎児への血流不足をもたらす血管異常・母体血流障害指標や絨毛間腔血栓がより認められた。凝固異常や血管損傷が COVID-19 患者の病態と認識されるようになっており、どうやら胎盤でも新型コロナウイルス（SARS-CoV-2）絡みの血栓形成が発生していると著者は言っている。

5/26　アルツハイマー病遺伝子 APOE4 と重度 COVID-19 が生じ易さが関連

5/27　COVID-19 患者のほぼ 9 割（87%）に嗅覚消失あり～欧州での約 2,000 人調査

5/27　塩野義製薬が Tetra を完全買収

アルツハイマー病 Ph2 目標非達成にもかかわらず、3 月に所有分を半分に増やした Tetra Therapeutics を塩野義製薬が完全に買収。

5/27　Merck & Co が満を持して新型コロナウイルス感染治療の取り組みに着手

https://www.marketwatch.com/story/merck-does-deals-to-develop-coronavirus-vaccines-drug-2020-05-26-71032439

5/27　回復者 3 割に後遺症の恐れと指摘　イタリア呼吸器学会、肺にリスク

5/27　イタリア、新型コロナ死者の 96%に基礎疾患－保健当局調査

5/27　成人T細胞白血病に新薬　遺伝子の「さび」取り除く -佐賀大など

5/28　心臓神経網の 3 次元モデル　ラットで構築 -米トマス・ジェファソン大など

hhttps://www.slashgear.com/researchers-create-the-first-3d-map-of-heart-neurons-28622562/

5/28　人工知能（AI）創薬の insitro が 1 億 4,300 万ドル調達

5/28　中国武漢の新型コロナウイルス感染者 76 人の検査で半数近い 42%が無症状

中国武漢の一つの病院に去年 12 月末から今年 2 月末までに入院した新型コロナウイルス（SARS-CoV-2）感染（COVID-19）患者 26 人の接触者検査で見つかった感染者 78 人のうち半数近い 33 人（42.3%）は無症状だった。無症状の人は発症者に比べてより若く（年齢中央値 37 歳 vs 56 歳）、女性が大半（22 人；67%）を占めた。
無症状の人の鼻喉液からは 8 日間（中央値）ウイルスが検出された。

5/29　がん細胞標的のカプセル　治療遺伝子を効率運搬 -東芝・信州大

https://www.jiji.com/jc/article?k=20200529000006&g=soc

5/29　ヒドロキシクロロキンの Lancet 誌掲載 COVID-19 試験の懸念を専門家 120 人超が表明

抗マラリア薬ヒドロキシクロロキン（hydroxychloroquine）で新型コロナウイルス感染（COVID-19）患者がより死んでいるとした先週金曜日発表の Lancet 誌掲載観察試験の懸念を問い、同剤の扱いは無作為化試験のデータに基づく必要があるとの研究者や医療専門家 120 人以上連名の手紙が同試験の著者 Mandeep Mehra 氏等や Lancet 編集者 Richard Horton 氏に送られた。

https://www.theguardian.com/world/2020/may/29/covid-19-surgisphere-hydroxychloroquine-study-lancet-coronavirus-who-questioned-by-researchers-medical-professionals

5/29　Massachusetts Eye and Ear が開発した COVID-19 ワクチンを Novartis が製造

5/29　米、WHO との関係解消 トランプ氏が表明

https://www.statnews.com/2020/05/29/trump-us-terminate-who-relationship/

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. 免疫調節薬がマウスの歯周病を改善

2. マウスとヒトのリンパ管：類似点と相違点

3. 呼吸器感染症に対する免疫応答に重要な役割を果たす細胞型が新たに発見された

4. 断食とビタミン C の組み合わせが治療の難しい癌に効果的

5. 断酒薬で肥満マウスの体重減少、代謝機能も改善

6. 「深く」痛みを止める脳中枢の発見 −マウス実験

7. 体重増加を妨げる可能性がある“痩せ”に関連する遺伝子

8. ヒトの SARS-CoV-2 感染を模倣するマウスモデル

9. 免疫疾患のサイトカインストームをモデル化したマウスが COVID-19 パンデミックの解決策を指摘

1. 免疫調節薬がマウスの歯周病を改善

日付：2020 年 4 月 28 日
ソース：eLife ワシントン大学
概要：

ラパマイシンは、現在移植患者の臓器拒否反応を防ぐために使用されている免疫抑制剤である。以前のマウス研究では、延命効果をもたらす可能性があることも示唆されていることから、多くの加齢関連疾患に対するこの薬物の効果を研究する関心につながっている。*eLife* 誌において今日発表されたワシントン大学の新しい研究によると、この薬物がマウスの加齢に伴う歯周病の問題も解決することを示している。マウスも人間と同様に加齢と共に骨の損失、炎症、口腔細菌の変化を経験することが分かっている。
研究者らは、マイクロコンピュータ断層撮影と呼ばれる 3D イメージング技術を使用して、ラパマイシン処理マウスと未処理マウスを比較したところ、処理されたマウスは未処理マウスよりも骨が多く、投与されている期間に実際に新しい骨を成長させることが分かった。また、処理されたマウスは、歯茎の炎症が少なく、歯周病に関連する細菌が少なく、健康な若いマウスで見られるものに類似した口腔細菌の混合物があったことが明らかになった。
研究者らは、ラパマイシンが特定の状態の治療に既に使用されている一方で、ヒトが感染症に罹り易くなる可能性があり、少なくとも臓器移植患者が通常摂るより高い慢性用量で糖尿病を発症するリスクが高まる可能性がある、と付け加えている。
ラパマイシンの利点がそのリスクにどの程度上回るのか、ヒトでの臨床試験でテストする必要がある、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-04/e-idi042820.php

NEWS RELEASE 28-APR-2020

IMMUNE-REGULATING DRUG IMPROVES GUM DISEASE IN MICE

Short-term treatment with rapamycin, a drug used to treat transplant patients, reduces bone loss, inflammation and changes to oral bacteria in older mice with gum disease

ELIFE

A drug that has life-extending effects on mice also reverses age-related dental problems in the animals, according to a new study published today in *eLife*.

Periodontal disease, also known as gum disease, is a common problem in older adults that causes painful inflammation, bone loss and changes in the good bacteria that live in the mouth. Yet there are no treatments available beyond tooth removal and/or having good oral hygiene. The findings suggest that treatments targeting the aging process in the mouth might help.

Rapamycin is an immune-suppressing drug currently used to prevent organ rejection in transplant recipients. Previous studies in mice have also suggested that it may have life-extending effects, which has led to interest in studying the drug's effects in many age-related diseases.

"We hypothesised that biological aging contributes to periodontal disease, and that interventions that delay aging should also delay the progress of this disease," says lead author Jonathan An, Acting Assistant Professor at the Department of Oral Health Sciences, University of Washington, Seattle, US.

To find out if rapamycin might slow periodontal disease, An and his colleagues added the drug to the food of middle-aged mice for eight weeks and compared their oral health with untreated mice of the same age. Similar to humans, mice also experience bone loss, inflammation and shifts in oral bacteria as they age.

Using a 3D-imaging technique called micro-computed tomography, the team measured the periodontal bone, or bone around the tooth, of the rapamycin-treated and untreated mice. They showed that the treated mice had more bone than the untreated mice, and had actually grown new bone during the period they were receiving rapamycin.

The work also showed that rapamycin-treated mice had less gum inflammation. Genetic sequencing of the bacteria in their mouths also revealed that the animals had fewer bacteria associated with gum disease and a mix of oral bacteria more similar to that found in healthy young mice.

"By targeting this aging process through rapamycin treatment, our work suggests that we can delay the progress of gum disease and actually reverse its clinical features," explains senior author Matt Kaeberlein, Professor of Pathology and Adjunct Professor of Oral Health Sciences at the University of Washington.

However, Kaeberlein adds that while rapamycin is already used to treat certain conditions, it can make people more susceptible to infections and may increase their risk of developing diabetes, at least at the higher chronic doses typically taken by organ transplant patients. "Clinical trials in humans are needed to test whether rapamycin's potential oral health and other benefits outweigh its risks," he concludes.

###

Reference

The paper 'Rapamycin rejuvenates oral health in aging mice' can be freely accessed online at https://doi.org/10.7554/eLife.54318. Contents, including text, figures and data, are free to reuse under a CC BY 4.0 license.

Media contact

Emily Packer, Senior Press Officer
eLife
e.packer@elifesciences.org
01223 855373

About *eLife*

eLife is a non-profit organisation created by funders and led by researchers. Our mission is to accelerate discovery by operating a platform for research communication that encourages and recognises the most responsible behaviours. We work across three major areas: publishing, technology and research culture. We aim to publish work of the highest standards and importance in all areas of biology and medicine, including Cell Biology, and Immunology and Inflammation, while exploring creative new ways to improve how research is assessed and published. We also invest in open-source technology innovation to modernise the infrastructure for science publishing and improve online tools for sharing, using and interacting with new results. *eLife* receives financial support and strategic guidance from the Howard Hughes Medical Institute, the Knut and Alice Wallenberg Foundation, the Max Planck Society and Wellcome. Learn more at https://elifesciences.org/about.

To read the latest Cell Biology research published in *eLife*,
visit https://elifesciences.org/subjects/cell-biology.

And for the latest in Immunology and Inflammation,
see https://elifesciences.org/subjects/immunology-inflammation.

---

2. マウスとヒトのリンパ管：類似点と相違点

日付：2020 年 5 月 5 日
ソース：ウプサラ大学（スウェーデン）
概要：

ウプサラ大学の研究者らは、国際的共同研究で、マウスとヒトのリンパ節リンパ管を細胞レベルまでマッピングすることに成功した。この結果は、最終的には、科学者らがウイルスと癌に対する免疫システムを強化する新しい方法を発見するのに役立つ可能性があるとして、*Frontiers of Cardiovascular Research* 誌に発表している。
我々の免疫システムは、乾癬、アテローム性動脈硬化症、癌などの慢性炎症性疾患を含むさまざまな疾患に関与しており、病気のメカニズムにおける免疫系の役割を研究するために、多くの科学者はマウスを含む動物モデルを使用している。
動物モデルを使用することで、研究者らはさまざまな遺伝子の機能をテストし、治療戦略を評価でき、これらはすべて貴重な知識を提供する。しかし、マウスモデルの結果を人間に翻訳するには、さまざまな種類の細胞機能を制御するシグナル伝達経路をもっと深く理解する必要がある、とこの研究を主導したウプサラ大学の免疫学、遺伝学および病理学部門研究者、マリア・ウルブマー氏は説明している。
研究チームは、マウスとヒトの個々の細胞の遺伝子の活動を分析した。遺伝子活性プロファイルに基づいて、彼らは両方の種がリンパ節にリンパ管内皮細胞の 5 つの異なるグループおよび類似したグループを持っていること、またそのうちの 2 つは以前には知られていなかったものである、ということを証明することができた。この発見は、リンパ節内のリンパ管の以前に発表された分析を補足し、免疫細胞がどのようにリンパ節に出入りするか、およびそれらの活動がどのように調節されるかについての科学的理解に役立つ。
結果として、基本的な血管の機能はマウスとヒトで同じではあるが、同時に、2 種間の遺伝子活性に決定的な違いがあることを指摘しており、この発見が将来の研究にとって大変重要だ、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-05/uu-lvi050520.php

NEWS RELEASE 5-MAY-2020

LYMPHATIC VESSELS IN MICE AND HUMANS: ALIKE YET DIFFERENT

UPPSALA UNIVERSITY

In an international collaboration, researchers from Uppsala University have mapped the lymph node lymphatic vessels in mice and humans down to the level of individual cells. The results may

eventually help scientists to discover new methods for strengthening the immune system against viruses and cancer. Their work has been published in the journal Frontiers of Cardiovascular Research.

The unique microenvironment of the lymph nodes plays an important role in maintaining an efficient immune system. When we have an infection, the lymph nodes swell and release activated white blood cells into the body through the lymphatic vessels. It is important to understand how these vessels work if we are to develop new drugs to improve the immune system; for example, new vaccines.

Previous research has shown that the specialised cells that make the lymphatic vessels, known as lymphatic endothelial cells, both communicate with white blood cells and actively assist in regulating the immune system. Until now, however, researchers have only understood the importance of a few of the genes that control the versatility of these cells.

Our immune system is involved in a range of different diseases, including chronic inflammatory diseases such as psoriasis, atherosclerosis and cancer. In order to study the role of the immune system in disease mechanisms, many scientists use model systems, including mice.

"By using model systems, we researchers can test the function of various genes and evaluate treatment strategies, all of which provides us with valuable knowledge. However, in order to translate findings from mouse models to humans we need a better understanding of the similarities and differences between the signalling pathways and genes that control cell function in the different species," explains Maria Ulvmar, a researcher who led the study at Uppsala University's Department of Immunology, Genetics and Pathology.

The research teams that conducted the study analysed the activity of genes in individual cells in mice and humans. Based on the gene activity profiles, they were able to demonstrate that both species have five distinct and similar groups of lymphatic endothelial cells in the lymph nodes, two of which were previously unknown. This discovery, complements previous published analysis of the lymphatic vessels in the lymph nodes and will help the scientific understanding of how immune cells enter and leave the lymph nodes and how their activity is regulated.

The results support the proposition that basic vessel functionality is the same in mice and humans. At the same time, researchers noted crucial differences in gene activity between the two species. This discovery is important for future research.

"This new knowledge will make it possible for my team and other researchers to focus our research on the genes expressed in humans and eventually identify new ways to strengthen the immune system against viral diseases and cancer for example. My team is currently looking at how the lymph node endothelium changes in cancer and contributes to metastases in breast cancer. This an exciting new area of research and we are looking forward to new advances in

our understanding of organ-specific and immune-regulating functions of the lymphatic endothelial cells over the next few years," says Maria Ulvmar.

###

The study has been conducted in collaboration with researchers from Karolinska Institutet/AstraZeneca Integrated Cardio Metabolic Centre in Stockholm and research teams in Finland and the United States.

Xiang M., Adrián Grosso R, Takeda A., Pan J., Bekkhus T., Brulois K., Dermadi D., Nordling S., Vanlandewijck M., Jalkanen S., Maria H. Ulvmar* and Eugene C. Butcher* (2020) A single-cell transcriptional roadmap of the mouse and human lymph node lymphatic vasculature. *Frontiers in Cardiovascular Medicine* 30 April 2020. DOI:10.3389/fcvm.2020.00052

*equal contribution

---

3. 呼吸器感染症に対する免疫応答に重要な役割を果たす細胞型が新たに発見された

日付：2020 年 5 月 8 日
ソース：VIB（フランダース バイオテクノロジー研究所）
概要：

VIB の免疫研究センターのチームを中心とする国際的科学者グループは、ウイルス性呼吸器感染症のマウスを使用して、新しいタイプの抗原提示性免疫細胞を特定した。この発見は免疫学の教科書を書き直すほどの発見だとして、*Immunity* 誌に発表されている。
樹状細胞（DC）ファミリーの一部であるこれらの細胞は、呼吸器系ウイルス感染時に他の免疫細胞に抗原を提示する重要な役割を果たし、回復期の血漿がウイルス感染患者の免疫応答を高めるのにどのように役立つかを説明できる。
この調査結果は、呼吸器系ウイルスによって引き起こされる今の COVID-19 パンデミックにも直接関連している。現在検討されている緊急治療は、回復期の血漿、または回復した患者の血漿の使用であり、回復期の血漿とウイルス特異の抗体が機能するメカニズムの 1 つが、inflammatory type 2 conventional DC (inf-cDC2) のブーストによることを示した最初の研究である。ブーストされた DC ははるかに強力な免疫応答を誘発するため、この研究はウイルス感染症およびその他の炎症性疾患に対する治療的介入の新たなターゲットを明らかにするものだ、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＞https://www.sciencedaily.com/releases/2020/05/200508155915.htm

NEWLY DISCOVERED CELL TYPE PLAYS CRUCIAL ROLE IN IMMUNE RESPONSE TO RESPIRATORY INFECTIONS

Date:

May 8, 2020

Source:

VIB (the Flanders Institute for Biotechnology)

Summary:

With a discovery that could rewrite the immunology textbooks, an international group of scientists have identified a new type of antigen-presenting immune cell.

With a discovery that could rewrite the immunology textbooks, an international group of scientists, including the teams of Bart Lambrecht, Martin Guilliams, Hamida Hammad, and Charlotte Scott (all from the VIB-UGent Center for Inflammation Research) identified a new type of antigen-presenting immune cell. These cells, that are part of an expanding family of dendritic cells, play a crucial role presenting antigens to other immune cells during respiratory virus infections, and could explain how convalescent plasma helps to boost immune responses in virus-infected patients.

Inflammation and immunity

When our body faces an infection, it responds with inflammation and fever. This is a sign that the immune system does its work, and leads to the activation of many cells, like soldiers in an army. Dendritic cells (DCs) are the generals of that army. They can precisely activate and instruct the soldiers to kill infected cells by presenting antigens derived from the 'invaders' to cells of the immune system.

Mistaken identity

There are several types of DCs that perform antigen-presenting functions in the body. A first type of conventional DCs continuously scan the body for dangerous invaders, even when there is no infection. When there is inflammation triggered by infection, another subset of DCs emerges from inflammatory monocytes. Because monocyte-derived DCs are easily prepared in vitro from monocytes isolated form human blood, it was always assumed these cells were very important antigen-presenting cells. Clinical trials using monocyte-derived DCs in cancer therapy have however been disappointing.

A study by the teams of Bart Lambrecht, Martin Guilliams, Hamida Hammad, and Charlotte Scott (all from the VIB-UGent Center for Inflammation Research) and international colleagues, shows that monocyte-derived DCs are poor antigen-presenting cells, but have wrongly been assumed to have these functions because of a case of mistaken identity.

The scientists studied mice with a viral respiratory infection (pneumonia virus of mice and influenza virus) with single-cell technologies. This single-cell resolution allowed them to finely separate the monocyte-derived cells from other DCs during their response to the infection. They found that monocyte-derived DCs do exist, but actually do not present antigens. The reason for all the confusion in the past is that a look-alike new DC emerges -- called inflammatory type 2 conventional DC, or inf-cDC2 -- that combines some of the best characteristics of monocytes, macrophages, and conventional DCs, to induce the best form of immunity.

Bart Lambrecht: "This was a big surprise for us. We've all been taught that monocyte-derived cells are excellent antigen presenting cells, certainly when there's inflammation. Now, we show that it's actually a new hybrid DC type that's doing all the work. This really changes what we know about the immune system and is very important knowledge for understanding respiratory viral infections and other inflammatory diseases."

Martin Guilliams: "It took a massive team effort but the strength of single-cell sequencing has finally cracked the complex DC code. Many contradicting findings from the last two decades now make much more sense. This also opens tremendous therapeutic opportunities, since vaccination strategies can now be designed to trigger formation of inf-cDC2s and thus generate a stronger antiviral immune response."

Charlotte Scott: "Through the use of single cell technologies we have been able to align all the findings from the past few years and identify the distinct cell types involved. Moving forward it will be very interesting to see under what other inflammatory conditions these inf-cDC2s are generated and how they can potentially be targeted therapeutically."

Convalescent plasma and COVID-19

The findings of the researchers also have a direct relevance for the current COVID-19 pandemic, caused by another respiratory virus. An emergency treatment that is currently being explored is the use of convalescent plasma, or the blood plasma of recovered patients.

Cedric Bosteels, lead author of the new paper: "One of the unique features of the new DCs is that they express functional Fc receptors for antibodies that are found in the plasma of patients who have recovered from COVID-19"

This study is the first to show that one of the mechanisms through which convalescent plasma and the virus-specific antibodies in it work, is via boosting of inf-cDC2. Since boosted DCs induce a much stronger immune response, this study reveals a new target for therapeutic intervention for viral infections and other inflammatory diseases.

Funding

This study was funded by the European Research Council, University Ghent, Research Foundation Flanders (FWO), and the Health Research Council New Zealand.

Story Source:

Materials provided by **VIB (the Flanders Institute for Biotechnology)**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Bosteels, Neyt, et al. **nflammatory Type 2 cDCsAcquire Features of cDC1s and Macrophages to Orchestrate Immunity to Respiratory Virus Infection**. *Immunity*, 2020

Cite This Page:

- MLA
- APA
- Chicago

VIB (the Flanders Institute for Biotechnology). "Newly discovered cell type plays crucial role in immune response to respiratory infections." ScienceDaily. ScienceDaily, 8 May 2020. <www.sciencedaily.com/releases/2020/05/200508155915.htm>.

---

4. 断食とビタミン C の組み合わせが治療の難しい癌に効果的

日付：2020 年 5 月 12 日
ソース：南カリフォルニア大学
概要：

南カリフォルニア大学（USC）とミラノの IFOM 癌研究所の科学者らは、ビタミン C と組み合わせると断食模倣ダイエット（Fasting Mimicking Diet -FDM）がある種のタイプの癌の治療により効果的である可能性があることを発見した。
研究者らは、断食は依然として癌患者にとっては挑戦的な選択肢であるが、より安全で実行可能な選択肢としては、身体が断食しているように細胞を反応させる低カロリーの植物ベースの食事である、と述べている。
彼らの調査結果は、空腹を模倣した食事とビタミン C の低毒性治療が、より毒性の高い治療に取って代わる可能性があることを示唆している。
ビタミン C の癌と戦う可能性に関しては、以前の研究の結果はまちまちであるが、最近の研究では、特に化学療法との併用で、ある程度の有効性を示し始めている。彼らの最初の in vitro 実験は顕著な効果を示した、としており、断食模倣ダイエットまたはビタミン C のみを単独で使用すると、がん細胞の増殖が減少し、がん細胞死がわずかに増加したが、併用すると劇的な効果があり、ほとんどすべての癌細胞が殺された。また、マウスを用いた研究では、この組み合わせが結腸直腸癌の複数のマウスモデルで腫瘍の進行を遅らせたし、一部のマウスでは、疾患の退行を引き起こした、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-05/uosc-ac0051220.php

NEWS RELEASE 12-MAY-2020

A COMBO OF FASTING PLUS VITAMIN C IS EFFECTIVE FOR HARD-TO-TREAT CANCERS, STUDY SHOWS

UNIVERSITY OF SOUTHERN CALIFORNIA

Scientists from USC and the IFOM Cancer Institute in Milan have found that a fasting-mimicking diet could be more effective at treating some types of cancer when combined with vitamin C.

In studies on mice, researchers found that the combination delayed tumor progression in multiple mouse models of colorectal cancer; in some mice, it caused disease regression. The results were published in the journal *Nature Communications*.

"For the first time, we have demonstrated how a completely non-toxic intervention can effectively treat an aggressive cancer," said Valter Longo, the study senior author and the director of the USC Longevity Institute at the USC Leonard Davis School of Gerontology and professor of biological sciences at the USC Dornsife College of Letters, Arts and Sciences. "We have taken two treatments that are studied extensively as interventions to delay aging-- a fasting-mimicking diet and vitamin C -- and combined them as a powerful treatment for cancer."

The researchers said that while fasting remains a challenging option for cancer patients, a safer, more feasible option is a low-calorie, plant-based diet that causes cells to respond as if the body were fasting. Their findings suggest that a low-toxicity treatment of fasting-mimicking diet plus vitamin C has the potential to replace more toxic treatments.

Results of prior research on the cancer-fighting potential of vitamin C have been mixed. Recent studies, though, are beginning to show some efficacy, especially in combination with chemotherapy. In this new study, the research team wanted to find out whether a fasting-mimicking diet could enhance the high-dose vitamin C tumor-fighting action by creating an environment that would be unsustainable for cancer cells but still safe for normal cells.

"Our first in vitro experiment showed remarkable effects," said Longo. "When used alone, fasting-mimicking diet or vitamin C alone reduced cancer cell growth and caused a minor increase in cancer cell death. But when used together, they had a dramatic effect, killing almost all cancerous cells."

Longo and his colleagues detected this strong effect only in cancer cells that had a mutation that is regarded as one of the most challenging targets in cancer research. These mutations in the KRAS gene signal the body is resisting most cancer-fighting treatments, and they reduce a patient's survival rate. KRAS mutations occur in approximately a quarter of all human cancers and are estimated to occur in up to half of all colorectal cancers.

The study also provided clues about why previous studies of vitamin C as a potential anticancer therapy showed limited efficacy. By itself, a vitamin C treatment appears to trigger the KRAS-mutated cells to protect cancer cells by increasing levels of ferritin, a protein that binds iron. But by reducing levels of ferritin, the scientists managed to increase vitamin C's toxicity for the cancer cells. Amid this finding, the scientists also discovered that colorectal cancer patients with high levels of the iron-binding protein have a lower chance of survival.

"In this study, we observed how fasting-mimicking diet cycles are able to increase the effect of pharmacological doses of vitamin C against KRAS-mutated cancers," said Maira Di Tano, a study co-author at the IFOM, FIRC Institute of Molecular Oncology in Milan, Italy. "This occurs through the regulation of the levels of iron and of the molecular mechanisms involved in oxidative stress. The results particularly pointed to a gene that regulates iron levels: heme-oxygenase-1."

The research team's prior studies showed that fasting and a fasting-mimicking diet slow cancer's progression and make chemotherapy more effective in tumor cells, while protecting normal cells from chemotherapy-associated side effects. The combination enhances the immune system's anti-tumor response in breast cancer and melanoma mouse models.

The scientists believe cancer will eventually be treated with low-toxicity drugs in a manner similar to how antibiotics are used to treat infections that kill particular bacteria, but which can be substituted by other drugs if the first is not effective.

To move toward that goal, they say they needed to first test two hypotheses: that their non-toxic combination interventions would work in mice, and that it would look promising for human clinical trials. In this new study, they said that they've demonstrated both. At least five clinical trials, including one at USC on breast cancer and prostate cancer patients, are now investigating the effects of the fasting-mimicking diets in combination with different cancer-fighting drugs.

###

Additional authors include Franca Raucci and Claudio Vernieri of IFOM, FIRC Institute of Molecular Oncology, Milan, Italy; Irene Caffa and Alessio Nencioni of the Department of Internal Medicine, University of Genoa and IRCCS Ospedale Policlinico San Martino, Genoa, Italy; Roberta Buono, Maura Fanti and Sebastian Brandhorst of the Longevity Institute, USC Leonard Davis School of Gerontology and Department of Biological Sciences; Giuseppe Curigliano of the University of Milan, Department of Oncology and Hemato-Oncology and Division of Early Drug Development, European Institute of Oncology, IRCCS, Milan; Filippo De Braud of the University of Milan, Department of Oncology and Hemato-Oncology, and Medical Oncology Department, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy.

The study was funded by Associazione Italiana Ricerca sul Cancro grant number 21820 and by NIA/NIH Grant # PO1 AG055369.

Longo is the founder of and has an ownership interest in L-Nutra; the company's food products are used in studies of the fasting-mimicking diet. Longo's interest in L-Nutra was disclosed and managed per USC's conflicts-of-interest policies. USC has an ownership interest in L-Nutra and the potential to receive royalty payments from L-Nutra. USC's financial interest in the company has been disclosed and managed under USC's institutional conflict of interest policies.

5. 断酒薬で肥満マウスの体重減少、代謝機能も改善

日付：2020 年 5 月 14 日
ソース：National Institutes of Health
概要：

アルコール使用障害の治療に 50 年以上使用されてきたジスルフィラムを使用したマウスの適応外実験では、両性の肥満の中年マウスは一貫して体重を正常化し、代謝損傷を逆転させた。この国際研究は、国立衛生研究所の一部である国立老化研究所（NIA）の研究者らによって主導された。結果は、5 月 14 日に *Cell Metabolism* 誌のオンライン版で公開された。
研究チームによると、ポジティブな結果の鍵は、ジスルフィラムの抗炎症特性に由来すると思われる。肥満マウスの両方のグループ（コントロールとジスルフィラム）には、いかなる形の運動も行われなかったし、また、顕著な自発的な行動変化も見られなかった、としている。彼らが観察した証拠に基づいて、研究者らはジスルフィラムの有益な結果は単に薬物に由来すると考えている。また、マウスのジスルフィラムからの負の副作用は観察されなかった。
研究チームは、これらの結果は動物実験に基づくものであり、現時点では人間にとっての潜在的な利益を推定することはできないと強調している。つまり、現時点でジスルフィラムを臨床試験以外の体重管理には適応外使用しないことを勧めている。それでも、調査結果を踏まえて、彼らはジスルフィラムの可能性を研究するための将来のステップを計画している、としている。

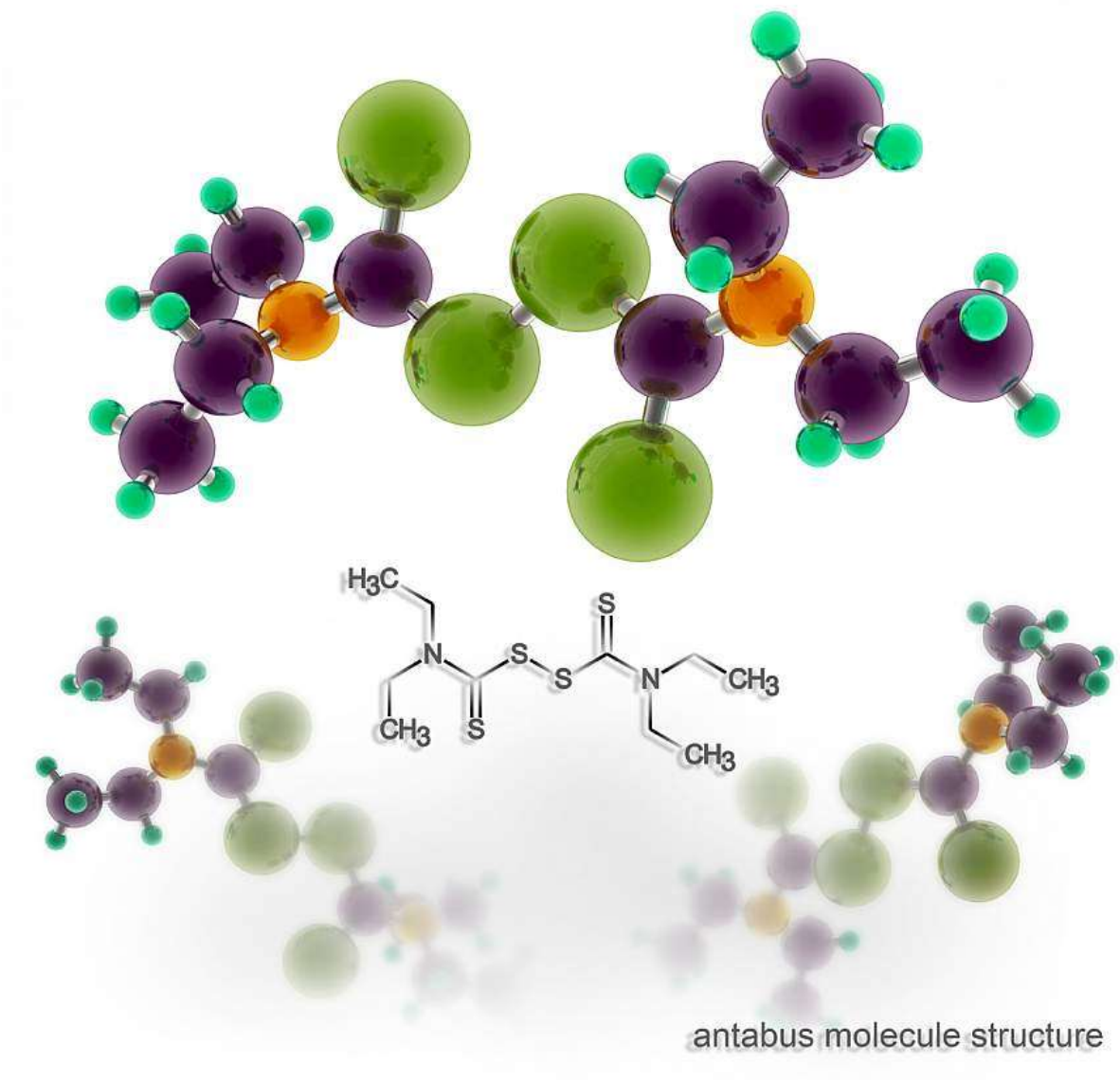
研究関連ニュース/他のトップページに戻る

＜英文＞https://www.nih.gov/news-events/news-releases/repurposed-drug-helps-obese-mice-lose-weight-improve-metabolic-function

Thursday, May 14, 2020

REPURPOSED DRUG HELPS OBESE MICE LOSE WEIGHT, IMPROVE METABOLIC FUNCTION

Treatment with disulfiram, normally prescribed to treat alcohol use disorder, shows health benefits in animal study.



Mice made obese from a high fat diet were switched to a diet dosed with disulfiram, which helped them lose weight and improve their metabolic health.*iStockPhoto*

An off-label experiment in mice using disulfiram, which has been used to treat alcohol use disorder for more than 50 years, consistently normalized body weight and reversed metabolic damage in obese middle-aged mice of both sexes. The international study was led by researchers at the National Institute on Aging (NIA), part of the National Institutes of Health . The results were published online in the journal *Cell Metabolism* on May 14.

The scientific team studied groups of 9-month-old lab mice who had been fed a high-fat diet for 12 weeks. As expected, this diet made the mice overweight and they started to show signs of pre-diabetes-like metabolic problems, such as insulin resistance and elevated fasting blood sugar levels. Next, the scientists divided these mice into four groups to be fed four different diets for an additional 12 weeks: a standard diet alone, a high-fat diet alone, a high-fat diet with a low amount of disulfiram, or a high-fat diet with a higher amount of disulfiram. As expected, the mice who stayed on the high-fat diet alone continued to gain weight and show metabolic problems. Mice who switched to

standard diet alone gradually saw their body weight, fat composition and blood sugar levels return to normal.

The mice in the remaining two groups, with either a low or high dose of disulfiram added to their still-fatty food, showed a dramatic decrease in their weight and related metabolic damage. Mice on the high disulfiram dose lost as much as 40% of their body weight in just four weeks, effectively normalizing their weight to that of obese mice who were switched back to standard diet. Mice in either disulfiram dose diet group became leaner and showed significant improvement in blood glucose levels on par with the mice who were returned to standard diet. Disulfiram treatment, which has few harmful side effects in humans, also appeared to protect the pancreas and liver from damage caused by pre-diabetic type metabolic changes and fat build up usually caused by eating a high-fat diet.

The NIA scientists, Michel Bernier, Ph.D., and Rafael de Cabo, Ph.D., collaborate frequently with researchers at NIH and beyond on studies into how changes in dietary patterns like intermittent fasting could lead to cognitive and physical health benefits. They first became interested in disulfiram after reading about the benefits this class of drug has shown in treating type 2 diabetes in rats, coupled with the growing interest in repurposing drugs that may also improve healthy aging.

“When we first went down this path, we did not know what to expect, but once we started to see data showing dramatic weight loss and leaner body mass in the mice, we turned to each other and couldn’t quite believe our eyes,” Bernier said.

According to study’s research team, the key to the positive results seem to stem from disulfiram’s anti-inflammatory properties, which helped the mice avoid imbalances in fasting glucose and protected them from the damage of fatty diet and weight gain while improving metabolic efficiency. Both groups of obese mice (control and disulfiram) were not subjected to any form of exercise, nor did they demonstrate noticeable spontaneous behavioral changes. Based on the evidence they observed, the researchers believe the beneficial results of disulfiram stem solely from the drug. They did not observe any negative side effects from disulfiram in the mice.

The research team stresses that these results are based on animal studies, and they cannot be extrapolated to any potential benefits for human at this point. It is recommended that disulfiram not be used off-label for weight management outside of the context of clinical trials. Still, given the findings, they are planning future steps for studying disulfiram’s potential, including a controlled clinical study to test if it could help individuals with morbid obesity lose weight, as well as deeper investigation into the drug’s molecular mechanisms and potential for combining with other therapeutic interventions.

The research was supported by NIA through its intramural research program, NIA grants AG031782 and AG038072, in collaboration with colleagues from the National Institute of Alcohol Abuse and Alcoholism, Yale University, Albert Einstein College of Medicine, Korea Research Institute of Bioscience and Biotechnology, and University of Sydney, Australia.

This press release describes a basic research finding. Basic research increases our understanding of human behavior and biology, which is foundational to advancing new and better ways to prevent, diagnose and treat disease. Science is an unpredictable and incremental process— each research advance builds on past discoveries, often in unexpected ways. Most clinical advances would not be possible without the knowledge of fundamental basic research.

About the National Institute on Aging (NIA): NIA leads the U.S. federal government effort to conduct and support research on aging and the health and well-being of older people. Learn more about age-related cognitive change and neurodegenerative diseases via NIA's Alzheimer's and related Dementias Education and Referral (ADEAR) Center website. For information about a broad range of aging topics, visit the main NIA website and stay connected.

About the National Institute on Alcohol Abuse and Alcoholism (NIAAA): The National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health, is the primary U.S. agency for conducting and supporting research on the causes, consequences, diagnosis, prevention, and treatment of alcohol use disorder. NIAAA also disseminates research findings to general, professional, and academic audiences. Additional alcohol research information and publications are available at https://www.niaaa.nih.gov/.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

NIH…Turning Discovery Into Health®

REFERENCE:

Bernier et al. Disulfiram prevents and treats diet-induced obesity and related co-morbidities in mice. *Cell Metabolism*. 2020 May 14. doi:TBD

###

6. 「深く」痛みを止める脳中枢の発見 –マウス実験

日付:2020 年 5 月 18 日
ソース:デューク大学
概要:

デューク大学の研究チームは、動物の痛みの感覚を大幅に制御できるマウスの脳の小さな領域を発見した。このブレインセンターは痛みをオンにするのではなく、オフにする。また、対苦痛センターを探す場所としてはあまり思いつかないような場所、すなわち、攻撃・逃避反応といったストレスのかかる事態に対処するための自律神経系の働きや一般的な不安といったようなネガティブな感情や反応の本拠地である扁桃体にある。
これまでの研究のほとんどは、痛みによってオンになっている領域に焦点を当てていた。しかし痛みを処理している場所は非常に多く、痛みを止めるにはそれらを全てオフにする必要があるのだが、今回発見されたブレインセンターは、この一つだけで痛みをオフにすることができる、としている。
研究者らはマウスの活性化されたニューロンの経路を追跡するために先駆者が開発した技術を使用して、CeAga ニューロン(CeA は中央扁桃体を表し、ga は全身麻酔による活性化を示す)が脳の多くの異なる領域に接続されていることを発見。マウスに穏やかな痛みの刺激を与えることにより、研究者らはすべての痛みによって活性化される脳の領域をマッピングすることができた。研究者らがこれらの CeAga ニューロンの活動を弱めると、マウスは、一時的な発作が再び激しくなったり痛んだりしたかのように反応した。
研究者らは、これらの細胞のみを活性化して痛みを抑制する可能性のある薬剤を将来の鎮痛剤として探すつもりだ、としている。この研究成果は、5 月 18 日に *Nature Neuroscience* 誌のオンライン版に掲載されている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/05/200518145008.htm

SCIENTISTS FIND BRAIN CENTER THAT 'PROFOUNDLY' SHUTS DOWN PAIN

Date:

May 18, 2020

Source:

Duke University

Summary:

A research team has found a small area of the brain in mice that can profoundly control the animals' sense of pain. Somewhat unexpectedly, this brain center turns pain off, not on. It's located in an area where few people would have thought to look for an anti-pain center, the amygdala, which is often considered the home of negative emotions and responses, like the fight or flight response and general anxiety.

FULL STORY

Neurons illustration (stock image).

Credit: © peterschreiber.media / stock.adobe.com

A Duke University research team has found a small area of the brain in mice that can profoundly control the animals' sense of pain.

Somewhat unexpectedly, this brain center turns pain off, not on. It's also located in an area where few people would have thought to look for an anti-pain center, the amygdala, which is often considered the home of negative emotions and responses, like the fight or flight response and general anxiety.

"People do believe there is a central place to relieve pain, that's why placebos work," said senior author Fan Wang, the Morris N. Broad Distinguished Professor of neurobiology in the School of Medicine. "The question is where in the brain is the center that can turn off pain."

"Most of the previous studies have focused on which regions are turned ON by pain," Wang said. "But there are so many regions processing pain, you'd have to turn them all off to stop pain. Whereas this one center can turn off the pain by itself."

The work is a follow-up to earlier research in Wang's lab looking at neurons that are activated, rather than suppressed, by general anesthetics. In a 2019 study, they found that general anesthesia promotes slow-wave sleep by activating the supraoptic nucleus of the brain. But sleep and pain are separate, an important clue that led to the new finding, which appears online May 18 in *Nature Neuroscience*.

The researchers found that general anesthesia also activates a specific subset of inhibitory neurons in the central amygdala, which they have called the CeAga neurons (CeA stands for central amygdala; ga indicates activation by general anesthesia). Mice have a relatively larger central amygdala than humans, but Wang said she had no reason to think we have a different system for controlling pain.

Using technologies that Wang's lab has pioneered to track the paths of activated neurons in mice, the team found the CeAga was connected to many different areas of the brain, "which was a surprise," Wang said.

By giving mice a mild pain stimulus, the researchers could map all of the pain-activated brain regions. They discovered that at least 16 brain centers known to process the sensory or emotional aspects of pain were receiving inhibitory input from the CeAga.

"Pain is a complicated brain response," Wang said. "It involves sensory discrimination, emotion, and autonomic (involuntary nervous system) responses. Treating pain by dampening all of these brain processes in many areas is very difficult to achieve. But activating a key node that naturally sends inhibitory signals to these pain-processing regions would be more robust."

Using a technology called optogenetics, which uses light to activate a small population of cells in the brain, the researchers found they could turn off the self-caring behaviors a mouse exhibits when it feels uncomfortable by activating the CeAga neurons. Paw-licking or face-wiping behaviors were "completely abolished" the moment the light was switched on to activate the anti-pain center.

"It's so drastic," Wang said. "They just instantaneously stop licking and rubbing."

When the scientists dampened the activity of these CeAga neurons, the mice responded as if a temporary insult had become intense or painful again. They also found that low-dose ketamine, an anesthetic drug that allows sensation but blocks pain, activated the CeAga center and wouldn't work without it.

Now the researchers are going to look for drugs that can activate only these cells to suppress pain as potential future pain killers, Wang said.

"The other thing we're trying to do is to (transcriptome) sequence the hell out of these cells," she said. The researchers are hoping to find the gene for a rare or unique cell surface receptor among these specialized cells that would enable a very specific drug to activate these neurons and relieve pain.

This research was supported by the National Institutes of Health (DP1MH103908, R01 DE029342, R01 NS109947, R01 DE027454), the Holland-Trice Scholar Award, the W.M. Keck Foundation, and a predoctoral fellowship from the National Science Foundation.

Story Source:

Materials provided by **Duke University**. Original written by Karl Leif Bates. *Note: Content may be edited for style and length.*

Journal Reference:

1. Thuy Hua, Bin Chen, Dongye Lu, Katsuyasu Sakurai, Shengli Zhao, Bao-Xia Han, Jiwoo Kim, Luping Yin, Yong Chen, Jinghao Lu, Fan Wang. **General anesthetics activate a potent central pain-suppression circuit in the amygdala**. *Nature Neuroscience*, 2020; DOI: 10.1038/s41593-020-0632-8

---

7. 体重増加を妨げる可能性がある“痩せ”に関連する遺伝子

日付：2020 年 5 月 21 日
ソース：Cell Press　ブリティッシュ・コロンビア大学
概要：

5 月 21 日に *Cell* 誌で発表されたブリティッシュ・コロンビア大学の研究者らによる研究では、エストニアの 47,000 人を超える人々の遺伝子データベースを使用して、代謝が健康な痩せた人の体重増加を妨げる役割を果たしている可能性がある“痩せ”に関連する遺伝子、ALK 遺伝子、を特定している。
彼らは、この遺伝子を削除するとハエやマウスが痩せることを示し、脳でのその発現がエネルギー消費の調節に関与している可能性があることを発見した。
その遺伝子はさまざまな種類の癌で頻繁に変異することが知られており、腫瘍の発生を促進する癌遺伝子である。が、癌以外での ALK の役割は不明のままであった。
ALK が削除されたマウスは、通常のマウスと同じ食事量と活動レベルがあるにもかかわらず、体重と体脂肪は低くなった、つまり、食餌による肥満に耐性があることが分かった。
また、研究チームのマウス研究では、脳で高発現している ALK が脂肪組織に食物からより多くの脂肪を燃焼させるように指示することによりその役割を果たすことを示唆した。
研究者たちは、ALK を発現するニューロンがどのように脳を分子レベルで調節して代謝のバランスを取り、“痩せ”を促進するかをさらに研究する予定だ、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/05/200521112617.htm

SCIENTISTS IDENTIFY GENE LINKED TO THINNESS THAT MAY HELP RESIST WEIGHT GAIN

Date:

May 21, 2020

Source:

Cell Press

Summary:

Researchers used a genetic database of more than 47,000 people in Estonia to identify a gene linked to thinness that may play a role in resisting weight gain in metabolically healthy thin people. They show that knocking out this gene results in thinner flies and

mice and find that expression of it in the brain may be involved in regulating energy expenditure.

FULL STORY

While others may be dieting and hitting the gym hard to stay in shape, some people stay slim effortlessly no matter what they eat. In a study publishing May 21 in the journal *Cell*, researchers use a genetic database of more than 47,000 people in Estonia to identify a gene linked to thinness that may play a role in resisting weight gain in these metabolically healthy thin people. They show that deleting this gene results in thinner flies and mice and find that expression of it in the brain may be involved in regulating energy expenditure.

"We all know these people: it's around one percent of the population," says senior author Josef Penninger, the director of the Life Sciences Institute and professor of the department of medical genetics at the University of British Columbia. "They can eat whatever they want and be metabolically healthy. They eat a lot, they don't do squats all the time, but they just don't gain weight.

"Everybody studies obesity and the genetics of obesity," he says. "We thought, 'Let's just turn it around and start a new research field.' Let's study thinness."

Penninger's team looked at data from the Estonian Biobank, which includes 47,102 people aged 20 to 44 years old. The team compared the DNA samples and clinical data of healthy thin individuals with normal-weight individuals and discovered genetic variants unique to thin individuals in the ALK gene.

Scientists have known that the ALK gene frequently mutates in various types of cancer, and it gained a reputation as an oncogene, a gene that drives the development of tumors. The role of ALK outside of cancer has remained unclear. But this new finding suggested that the gene may play a role as a novel thinness gene involved in weight-gain resistance.

The researchers also found that flies and mice without ALK remained thin and were resistant to diet-induced obesity. Furthermore, despite having the same diet and activity levels as normal mice, mice with deleted ALK have lower body weight and body fat. The team's mouse studies also suggested that ALK, which is highly expressed in the brain, plays a part there by instructing the fat tissues to burn more fat from food.

The researchers say that therapeutics targeting the gene might help scientists fight obesity in the future. "If you think about it, it's realistic that we could shut down ALK and reduce ALK function to see if we did stay skinny," says Penninger. "ALK inhibitors are used in cancer treatments already. It's targetable. We could possibly inhibit ALK, and we actually will try to do this in the future." Further research will be required to see if these inhibitors are effective for this purpose. The team also plans to further study how neurons that express ALK regulate the brain at a molecular level to balance metabolism and promote thinness.

The Estonian Biobank that the team studied was ideal because of its wide age range and its strong phenotype data. But one limitation for replicating these findings is that biobanks that collect biological or medical data and tissue samples don't have a universal standard in data collection, which makes comparability a challenge. The researchers say they will need to confirm their findings with other data banks through meta-analysis. "You learn a lot from biobanks," says

Penninger. "But, like everything, it's not the ultimate answer to life, but they're the starting points and very good points for confirmation, very important links and associations to human health."

The team says that its work is unique because of how it combines exploration of the genetic basis of thinness on a population- and genome-wide scale with in vivo analyses in mice and flies of the gene's function. "It's great to bring together different groups, from nutrition to biobanking, to hardcore mouse and fly genetics," says Penninger. "Together, this is one story including evolutionary trees in metabolism, the evolutionary role of ALK, human evidence, and hardcore biochemistry and genetics to provide causal evidence."

Story Source:

Materials provided by **Cell Press**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Michael Orthofer, Armand Valsesia, Reedik Mägi, Qiao-Ping Wang, Joanna Kaczanowska, Ivona Kozieradzki, Alexandra Leopoldi, Domagoj Cikes, Lydia M. Zopf, Evgenii O. Tretiakov, Egon Demetz, Richard Hilbe, Anna Boehm, Melita Ticevic, Margit Nõukas, Alexander Jais, Katrin Spirk, Teleri Clark, Sabine Amann, Maarja Lepamets, Christoph Neumayr, Cosmas Arnold, Zhengchao Dou, Volker Kuhn, Maria Novatchkova, Shane J.F. Cronin, Uwe J.F. Tietge, Simone Müller, J. Andrew Pospisilik, Vanja Nagy, Chi-Chung Hui, Jelena Lazovic, Harald Esterbauer, Astrid Hagelkruys, Ivan Tancevski, Florian W. Kiefer, Tibor Harkany, Wulf Haubensak, G. Gregory Neely, Andres Metspalu, Jorg Hager, Nele Gheldof, Josef M. Penninger. **Identification of ALK in Thinness**. *Cell*, 2020; DOI: 10.1016/j.cell.2020.04.034

Cite This Page:

- MLA
- APA
- Chicago

Cell Press. "Scientists identify gene linked to thinness that may help resist weight gain." ScienceDaily. ScienceDaily, 21 May 2020. <www.sciencedaily.com/releases/2020/05/200521112617.htm>.

Cite This Page:

- MLA
- APA
- Chicago

Washington University School of Medicine. "Diabetes reversed in mice with genetically edited stem cells derived from patients: CRISPR corrects genetic defect so cells can normalize blood sugar." ScienceDaily. ScienceDaily, 22 April 2020. <www.sciencedaily.com/releases/2020/04/200422214036.htm>.

---

8. ヒトの SARS-CoV-2 感染を模倣するマウスモデル

日付：2020 年 5 月 27 日
ソース：Cell Press
概要：

中国北京の国立食品医薬品管理研究所（NIFDC）の研究者らは、CRISPR/Cas9 遺伝子編集技術を使用して、ヒトアンジオテンシン変換酵素 II（hACE2）（SARS-CoV-2 が結合し、ヒト細胞に侵入するために使用する受容体）を生成するマウスを作った。そしてこのマウスモデルが、重篤な急性呼吸器症候群コロナウイルス 2（SARS-CoV-2）による感染に関して、人間の患者で観察された特徴を再現すると、5 月 26 日に *Cell Host & Microbe* 誌で報告している。
研究者の話によると、これらのマウスモデルは遺伝的に安定しており、個人差はほとんどない。さらに、肺のウイルス RNA 負荷は SARS-CoV-2 感染のモデリングに hACE2 を発現する他の遺伝子組み換えマウスと比較してはるかに高く、さまざまな組織での hACE2 の分布は、人間で観察されたものとよく一致している。
このマウスモデルを使用した今後の研究により、SARS-CoV-2 がどのように脳に侵入し、ウイルスがどのように胃腸環境を生き残り、気道に侵入するかが明らかになる可能性があり、このモデルが、SARS-CoV-2 と戦うためのワクチンや治療法のテストにも役立つはずだ、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/05/200527123332.htm

MOUSE MODEL MIMICS SARS-COV-2 INFECTION IN HUMANS

Date:

May 27, 2020

Source:

Cell Press

Summary:

A mouse model of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reproduces features observed in human patients, researchers report.

FULL STORY

A mouse model of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reproduces features observed in human patients, researchers report May 26 in the journal *Cell Host & Microbe*. Using CRISPR/Cas9 gene editing technology, the researchers generated mice that produce human angiotensin-converting enzyme II (hACE2) -- the receptor that SARS-CoV-2 binds to and uses to enter human cells.

"A small animal model that reproduces the clinical course and pathology observed in COVID-19 patients is highly needed," says co-senior study author You-Chun Wang of the National Institutes for Food and Drug Control (NIFDC) in Beijing, China. "The animal model described here provides a useful tool for studying SARS-CoV-2 infection and transmission."

Wang and his collaborators used CRIPSR/Cas9 to generate a mouse model that could express hACE2. According to the authors, their mouse model has several advantages compared with other genetically engineered mice that express hACE2 for modeling SARS-CoV-2 infection. Instead of being randomly inserted, hACE2 is inserted precisely into a specific site on the X chromosome, and it completely replaces the mouse version of the protein. In addition, this is a genetically stable model, with few differences among individuals. Moreover, the viral RNA loads in the lung are much higher, and the resulting distribution of hACE2 in various tissues better matches that observed in humans.

After being infected with SARS-CoV-2 through the nose, the genetically engineered mice showed evidence of robust viral RNA replication in the lung, trachea, and brain. "The presence of viral RNAs in brain was somewhat unexpected, as only a few COVID-19 patients have developed neurological symptoms," says co-senior study author Cheng-Feng Qin of the Academy of Military Medical Sciences (AMMS) in Beijing, China.

SARS-CoV-2 S protein, which binds to hACE2 to enter host cells, was also present in the lung tissue and brain cells. Moreover, the researchers identified the major airway cells targeted by SARS-CoV-2 as Clara cells that produce the protein CC10. "Our result provides the first line of evidence showing the major target cells of SARS-CoV-2 in the lung," says co-senior study author Yu-Sen Zhou of AMMS.

In addition, the mice developed interstitial pneumonia, which affects the tissue and space around the air sacs of the lungs, causing the infiltration of inflammatory cells, the thickening of the structure that separates air sacs, and blood vessel damage. Compared with young mice, older mice showed more severe lung damage and increased production of signaling molecules called cytokines. Taken together, these features recapitulate those observed in COVID-19 patients.

When the researchers administered SARS-CoV-2 into the stomach, two of the three mice showed high levels of viral RNA in the trachea and lung. The S protein was also present in lung tissue, which showed signs of inflammation. According to the authors, these findings are consistent with the observation that patients with COVID-19 sometimes experience gastrointestinal symptoms such as diarrhea, abdominal pain, and vomiting. But 10 times the dose of SARS-CoV-2 was required to establish infection through the stomach than through the nose.

Future studies using this mouse model may shed light on how SARS-CoV-2 invades the brain and how the virus survives the gastrointestinal environment and invades the respiratory tract. "The hACE2 mice described in our manuscript provide a small animal model for understanding unexpected clinical manifestations of SARS-CoV-2 infection in humans," says co-senior study author Chang-Fa Fan of NIFDC. "This model will also be valuable for testing vaccines and therapeutics to combat SARS-CoV-2."

This work was primarily supported by the National Key Research and Development Project of China, the National Science and Technology Major Project of China, the National Natural Science Foundation of China, and the Guangdong Pearl River talent plan.

Story Source:

Materials provided by **Cell Press**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Shi-Hui Sun, Qi Chen, Hong-Jing Gu, Guan Yang, Yan-Xiao Wang, Xing-Yao Huang, Su-Su Liu, Na-Na Zhang, Xiao-Feng Li, Rui Xiong, Yan Guo, Yong-Qiang Deng, Wei-Jin Huang, Quan Liu, Quan-Ming Liu, Yue-Lei Shen, Yong Zhou, Xiao Yang, Tong-Yan Zhao, Chang-Fa Fan, Yu-Sen Zhou, Cheng-Feng Qin, You-Chun Wang. **A mouse model of SARS-CoV-2 infection and pathogenesis**. *Cell Host & Microbe*, 2020; DOI: 10.1016/j.chom.2020.05.020

Cite This Page:

9. 免疫疾患のサイトカインストームをモデル化したマウスが COVID-19 パンデミックの解決策を指摘

日付:2020 年 5 月 28 日
ソース:シンシナティー小児病院医療センター
概要:

シンシナティー小児病院医療センターの癌の病理学者の Gang Huang 博士は、トランスジェニックマウス系統の発明者の一人だが、重症の COVID-19 患者において、致命的な小児免疫疾患 HLH(血球貪食性リンパ組織球症)の治療に使用される薬物テストに成功し、呼吸器系と複数のシステムの炎症を劇的に逆転させた臨床試験の共同研究者である。
今回、この研究の第 2 フェーズの臨床試験のデータが *Journal of Allergy and Clinical Immunology* 誌に掲載されており、このデータによると、シンシナティー小児病院で開発された HLH をモデル化するトランスジェニックマウスが、COVID-19 ウイルスのパンデミック時に、人々の命を救う重要な役割を果たす可能性がある。
重篤な COVID-19 患者の身体に免疫系によって産生された炎症細胞が浸水する、いわゆるサイトカインストームは、二次 HLH と闘う子供達の一般的な特徴であり、Huang 博士は、実験室でヒトの二次 HLH を忠実に模倣するように作成されたトランスジェニックマウスで見られる症状とも非常に似ていることに気づいた。また、中国の武漢の研究者と共同で行ったその前臨床研究の一部が、二次 HLH を治療するための薬物ルキソリチニブを特定するのに役立った、とも言っている。

研究関連/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/05/200528092132.htm

HLH RESEARCH POINTS TO TREATMENT FOR COVID-19 CYTOKINE STORMS

HOW MICE THAT MODEL IMMUNE DISEASE'S CYTOKINE STORMS MAY POINT TO SOLUTION FOR GLOBAL PANDEMIC

Date:

May 28, 2020

Source:

Cincinnati Children's Hospital Medical Center

Summary:

A transgenic mouse developed to model the deadly childhood immune disease HLH (hemophagocytic lymphohistiocytosis) may play a key role in saving lives during the COVID-19 virus pandemic.

FULL STORY

A transgenic mouse developed at Cincinnati Children's to model the deadly childhood immune disease HLH (hemophagocytic lymphohistiocytosis) may play a key role in saving lives during the COVID-19 virus pandemic.

One of the genetically engineered mouse strain's inventors -- Cincinnati Children's cancer pathologist Gang Huang, PhD -- is co-investigator on a small clinical trial that successfully tested a drug used to treat to HLH (ruxolitinib) to dramatically reverse respiratory and multi-system inflammation in severely ill COVID-19 patients. Data from the Phase II clinical study is published in the *Journal of Allergy and Clinical Immunology*.

The study involved 43 hospitalized patients diagnosed with severe COVID-19 between February 9 and February 28 in Wuhan, China, believed to be ground zero for the pandemic. The multi-center study was led by Jianfeng Zhou, MD, PhD, Department of Hematology at Tongji Hospital, Tongji Medical College and Huazhong University of Science in Wuhan.

Zhou is a longtime collaborator of Huang and colleagues at the Cincinnati Children's HLH Center of Excellence, part of the Cancer and Blood Diseases Institute.

Ruxolitinib Shows Signs of Benefit

Patients taking ruxolitinib were randomly selected to receive two daily 5mg oral doses of the anti-inflammatory drug, plus the standard of care treatment for COVID-19. A randomly selected control group of 21 patients received a placebo along with the standard of care treatment.

"Ruxolitinib recipients had a numerically faster clinical improvement," study authors write in their report. "Significant chest CT improvement, a faster recovery from lymphopenia and favorable side-effect profile in ruxolitinib group were encouraging and informative to future trials to test efficacy of ruxolitinib in a larger population."

Patients treated with ruxolitinib saw a shorter median time to clinical improvement compared to the control group. Researchers reported that 90 percent% of ruxolitinib patients showed CT scan improvement within 14 days, compared with 9 percent of patients from the control group. Three patients in the control group eventually died of respiratory failure. All the severely ill patients who received ruxolitinib survived.

More clinical testing of the drug is needed. A larger Phase III clinical trial RUXCOVID by Incyte and Novartis is now testing up to 400 severely ill COVID-19 patients with the drug, according to Huang. Preliminary clinical data from the study is expected during the summer, he added.

"This is the first therapy we know of that appears to work effectively to quiet the cytokine storm and inflammation in severe COVID-19 disease, and there are no significant toxicities to patients who take the drug by two pills a day," Huang said. "This is critical until we can develop and distribute enough effective vaccine to help prevent people from becoming infected."

Calming the 'Cytokine Storm'

The so-called cytokine storm that inundates the bodies of severely ill COVID-19 patients with inflammatory cells produced by the immune system is a common feature of children battling secondary HLH, which happens in patients where initial HLH treatment has not worked. Huang, who along with a large portion of the world's scientific community was busy trying to study and find solutions to COVID-19, noticed this common clinical feature of both illnesses.

He also noticed that severe COVID-19 disease clinical manifestations are very similar to those seen in transgenic laboratory mice created to faithfully mimic human secondary HLH in the lab. That preclinical laboratory research, some of it in collaboration with the researchers in Wuhan, China, helped identify the drug ruxolitinib for treating secondary HLH. The anti-inflammatory drug is also used to treat other blood diseases including leukemia.

"I approached our research colleagues in Wuhan and explained our observations and recommended this drug be tested to quiet the cytokine storm in the multi-system inflammation in patients with severe COVID-19 disease," Huang said. "The disease was spreading very rapidly and many people were dying. We believed the existing clinical drug would help save lives. So, we worked to push it forward before there is an effective vaccine for everyone."

Huang said the work with colleagues in China was completed on a compressed timeframe as scientists around the world went on high alert to battle the pandemic in January. During their work, Huang and researchers in China found other clinical studies involving other diseases where ruxolitinib also had worked well at quieting inflammation, and testing on COVID-19 patients proceeded.

Funding support for the JACI study came as part of an Emergency Research Project of Tongji Hospital, Huazhong University of Science and Technology (2020kfyXGYJ045), an Emergency Research Project of Hubei province (2020FCA006).

Story Source:

Materials provided by **Cincinnati Children's Hospital Medical Center**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Yang Cao, Jia Wei, Liang Zou, Tiebin Jiang, Gaoxiang Wang, Liting Chen, Liang Huang, Fankai Meng, Lifang Huang, Na Wang, Xiaoxi Zhou, Hui Luo, Zekai Mao, Xing Chen, Jungang Xie, Jing Liu, Hui Cheng, Jianping Zhao, Gang Huang, Wei Wang, Jianfeng Zhou. **Ruxolitinib in treatment of severe coronavirus disease 2019 (COVID-19): A multicenter, single-blind, randomized controlled trial**. *Journal of Allergy and Clinical Immunology*, 2020; DOI: 10.1016/j.jaci.2020.05.019

Cite This Page:

- MLA
- APA
- Chicago

Cincinnati Children's Hospital Medical Center. "HLH research points to treatment for COVID-19 cytokine storms: How mice that model immune disease's cytokine storms may point to solution for global pandemic." ScienceDaily. ScienceDaily, 28 May 2020. <www.sciencedaily.com/releases/2020/05/200528092132.htm>.
