Bio News – September, 2020

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

7/31　色で知らせる COVID-19 唾液検査を Sorrento Therapeutics（サンディエゴ）がコロンビア大から取得

8/1　Sanofi/GSK の COVID-19 ワクチン開発を米政府が最大 21 億ドルを払って支援

8/2　コロナにカニクイザルも感染　9 月にワクチン投与実験へ -滋賀医大など

8/3　Merck & Co の COVID-19 ワクチンの臨床試験が今四半期中に始まる

Moderna, Pfizer/BioNTech, AstraZeneca/オックスフォード大学等のワクチンと違って 2 回接種ではなく 1 回接種のワクチン V591 の臨床試験を Merck & Co が間もなく始める。Merck & Co が IAVI と協力して開発している別の COVID-19 ワクチン V590 も今年中に臨床試験が始まる。
V591 も V590 も投与後に体内で増えるため 1 回の投与で効果があると Merck の研究リーダーRoger Perlmutter 氏は言っている。

8/4　新型コロナウイルス中和抗体の感染予防効果を調べる試験を Eli Lilly が開始

8/4　新型ウイルスワクチン、「見つからない可能性も」 WHO が警告

8/4　COVID-19 即座検査を行き渡らせる米国政府取り組みで 7 製品を選抜

自宅や医療現場で即座に正確な結果を出す新型コロナウイルス感染検査が行き渡るようにする米国立衛生研究所（NIH）の取り組み Rapid Acceleration of Diagnostics（RADx）によって 7 品への総額 2 億 4,870 万ドル支援が決定された。

8/6　J&J の COVID-19 ワクチンができたら米国が 1 億回投与分を 10 億ドルで取得

8/7　無症状の新型コロナウイルス感染者もウイルス量は発症者と同様に多い

8/7　ワクチン 1 億 2 千万回分を供給へ　日本と AstraZeneca で合意

8/7　科学論文数、中国が米国を抜き初のトップ　研究費も猛追

8/7　恐竜もがんになる、医学・恐竜の専門家らが共同研究で発見

https://www.jiji.com/jc/article?k=20200807040415a&g=afp

8/8　日本が AstraZeneca の COVID-19 ワクチンを予約～武田薬品が Novavax のワクチンを製造

AstraZeneca の新型コロナウイルス感染（COVID-19）予防ワクチン AZD1222 が成功したら 1 億 2,000 回分を手に入れる約束を日本政府が同社と交わし、JCR Pharma がその製造の一部を担う。
また、武田薬品は Novavax の COVID-19 ワクチン NVX-CoV2373 を製造して日本で売る権利を手に入れ、日本政府は武田薬品によるそのワクチン製造の取り組み支援を約束。

8/8　インドの Serum Institute による COVID-19 ワクチン製造をゲイツ財団が支援

AstraZeneca や Novavax 等からの新型コロナウイルス感染（COVID-19）予防ワクチンを最大 1 億回投与分作って新興国に提供するための資金 1 億 5,000 万ドルをゲイツ財団（Bill & Melinda Gates Foundation）が Serum Institute of India に提供。

Serum Institute は *Gavi の COVAX Advance Market Commitment (AMC) に含まれる 92 か国にそれらのワクチンを 1 回投与分定価 3 ドル以内で販売。

*Gavi – 開発途上国の予防接種率向上を目的とした官民パートナーシップ「Gavi ワクチンアライアンス」

https://www.reuters.com/article/us-health-coronavirus-india-vaccine/indias-serum-institute-to-get-150-million-from-gates-foundation-for-covid-19-vaccine-idUSKCN2531B4?feedType=mktg&feedName=&WT.mc_id=Newsletter-US&utm_source=Sailthru&utm_medium=email&utm_campaign=US%202018%20Health%20Report%202020-08-07&utm_term=2018%20-%20US%20Health%20Report

8/8　Pfizer が Gilead の COVID-19 薬レムデシビルの製造を手伝う

8/9　ウイルス胃がんの仕組み解明　千葉大など　治療法確立に期待

8/10　アビガン成分のロシア製品が無作為化試験で COVID-19 患者ウイルス除去を早めた

8/11　ロシア、新型コロナワクチン認可　世界初　安全性に疑問も

8/12　肺組織で新型コロナウイルス受容体 ACE2 は殆ど発現していない～独立した 2 つの研究から

8/12　中国やその他アジア市場向けの薬を手に入れて開発する LianBio が船出

8/13　ワクチン臨床試験、ウイルス攻撃する「中和抗体」が増加…Phizer など

8/13　Bristol-Myers Squibb が 3 億ドルを投じて医療格差是正や多様性底上げに取り組む

https://www.fiercepharma.com/pharma/bristol-myers-squibb-devotes-300m-to-address-racial-inequality

8/13　エーザイが米国本拠をニュージャージー州 Nutley に移転

8/17　1 型と 2 型糖尿病患者の COVID-19 死亡率は非糖尿病よりそれぞれ 3 倍と 2 倍高い

8/18　「医師が論文 5 本で捏造や改ざん」 阪大と国循が発表

https://www.asahi.com/articles/ASN8L6J5VN8LPLBJ006.html

8/18　米カリフォルニア州デスバレーで 54.4 度観測 史上最高気温の可能性

8/18　母の骨盤と子の頭形が対応　アカゲザル、難産緩和か　京大

母親の骨盤と胎児の頭の形は対応関係にあることが分かったと、京都大の研究チームが発表。アカゲザルのコンピューター断層撮影(CT)のデータを解析し、頭が産道を通りやすくして難産を緩和していると考えられ、ヒトも同様とみられるという。論文は 18 日、米科学アカデミー紀要に掲載される。

8/18　新型コロナウイルス感染者のみならず接した家族にも T 細胞反応が備わりうる -カロリンスカ研究所

8/19　武田薬品が日本の従業員の早期退職を募る

8/19　Merck が約束していた 13 億ドルの英国ロンドン研究拠点の建設が来年始まる

8/19　J&J が、自己免疫疾患パイプラインを強化するため Momenta Pharma を 65 億ドルで買収

8/19　50 年間「消失状態」のハネジネズミ、アフリカの角で発見

https://www.afpbb.com/articles/-/3299917

8/19　FDA が、BioMarin の血友病遺伝子治療を未承認

https://www.statnews.com/2020/08/19/fda-rejects-biomarin-hemophilia-gene-therapy/

8/19　Gilead の大ヒットが予想される炎症性疾患治療薬 filgotinib を FDA がデータ不足で未承認

8/20　Biogen の米国での 1 年間売り上げ約 38 億ドルの Tecfidera の後発品を Mylan が発売

8/20　母乳から複製可能な新型コロナウイルス検出されず～母乳からの感染はなさそう

出産した新型コロナウイルス感染（COVID-19）女性 18 人の母乳を調べた結果によると、母乳を介して赤ちゃんに感染が移ることはなさそう。

8/21　破産したセンサー入り薬剤開発会社 Proteus を大塚製薬が買うことを裁判所が承認

破産したセンサー入り薬剤開発会社 Proteus Digital Health を提携会社・大塚製薬が 1,500 万ドルで買うことを、Novartis を含む投資家の反対を押し切って裁判所が許可。

8/21　軽症の COVID-19 患者の 3 人に 1 人（32%）から発症から 15 日までに抗体を検出 -フランス

8/22　アステラス製薬の遺伝子治療試験で更に 1 人が死亡～高用量投与群 17 人中 3 人目

8/23　中国でワクチンの緊急投与開始　対象は医療関係者ら

8/24　新型コロナ回復者の血漿使う治療法、米が緊急許可

https://www.statnews.com/2020/08/23/fda-under-pressure-from-trump-expected-to-authorize-blood-plasma-as-covid-19-treatment/

8/24　飲料水で約 500 人が体調不良に、赤痢菌に感染 -中国

8/24　世界初のワクチン「接種希望しない」52%…ロシア世論調査、安全性に懸念

8/25　武田薬品が店頭販売品事業を投資会社 Blackstone に約 23 億ドルで売ると発表

8/25　早大が新型コロナの高感度の抗原検査法を開発

http://www.qlifepro.com/news/20200820/covid-19-5.html

8/25　香港男性がコロナ再感染、2 種類のウイルス株確認　世界初の実証

8/26　Biogen の 2 月末の会議を発端にしておよそ 2 万人が新型コロナウイルスに感染したと推定された

8/27　新型コロナウイルスへの女性の T 細胞反応は男性より強力

軽～中等度症状の新型コロナウイルス感染（COVID-19）入院患者 39 人（男性 17 人、女性 22 人）を Yale 大学の Akiko Iwasaki（岩崎明子）氏のチームが調べたところ、女性は男性に比べて T 細胞が多くてより活性化しており、男性では T 細胞反応は高齢であるほど劣り、T 細胞反応が劣ることが病状悪化と関連した。女性では炎症性サイトカインが多いことが病状悪化と関連した。
女性に比べて男性の方が重症化しやすいことに今回の研究で判明した免疫反応の男女差が寄与しているかもしれない。

8/27　ジェネリックの談合で米国司法省が Teva を訴えた

8/27　慶応大の iPS 心臓病治療を了承 -厚労省部会

8/27　コロナ重症化招く「免疫の暴走」、阪大などが端緒を解明

新型コロナウイルス感染症の重症化には、免疫が暴走する「サイトカインストーム」がかかわることが報告されている。大阪大学などの研究チームは「PAI1」というたんぱく質が血液中に増えることが、サイトカインストームの引き金になることをつきとめ、米科学アカデミー紀要に発表。

8/28　Vaccitech の次世代 COVID-19 ワクチンの開発を英国政府が助成

Vaccitech は、AstraZeneca の新型コロナウイルス感染（COVID-19）ワクチン AZD1222（ChAdOx1 nCoV-19）の土台・チンパンジーアデノウイルスベクターChAdOx1 の提供元企業。

8/28　COVID-19 を含む大厄災への備え/対処を支援する J&J と米国政府の取り組みが発足

新型コロナウイルス感染（COVID-19）流行を含む世界規模の厄災への備えや対処を支援する取り組み、Blue Knight を Johnson & Johnson（J&J）と米国政府機関 BARDA が立ち上げた。

8/28　神経回路、再接続する分子　マウスで成功、治療応用期待―慶大など

https://www.jiji.com/jc/article?k=2020082801064&g=soc

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. ハダカデバネズミの細胞は癌化し難いわけではないらしい

2. 新型コロナワクチン、注目の有力候補はこの7つ
   開発が急がれるワクチン、最終治験に進み期待を集める先行組とその現状

3. 土地利用の変化が病気発生のリスクを増加させる可能性

4. 自然発症型糖尿病マウスモデル作製に成功
   膵臓再生医療の新しい移植モデル動物として期待

5. 酸素療法がマウスの肺微生物叢に害を与える
   ～重症患者の酸素レベル低下治療に影響か～

6. 特定の酵素喪失で、マウスの脂肪代謝と運動持久力が増加

7. 癌性腫瘍を攻撃する際の微生物叢の役割

8. ダウン症マウスがこの障害へのより良い理解へと導く

9. ゲノム解析により、多くの動物が新型コロナウイルス感染に対して脆弱である可能性が判明

1. ハダカデバネズミの細胞は癌化し難いわけではないらしい

日付：2020 年 8 月 3 日
ソース：ケンブリッジ大学
概要：

ハダカデバネズミは癌になり難いことで知られており、ハダカデバネズミの細胞は通常のマウス細胞と違って癌誘発遺伝子を導入しても癌化しないという結果を米国のチームが 2013 年に *Nature* 誌に報告した。しかし、先月英国ケンブリッジ大学のチームが同じく *Nature* 誌に報告した実験によると、どうやってもそうはならずハダカデバネズミ細胞は癌誘発遺伝子の導入でマウスやラット細胞と同様に癌化した、と報告している。
英国の研究者らによると、ハダカデバネズミが癌になり難いのは細胞の生来の性質によるのではなく、免疫系などの細胞を取り巻く環境に起因するのではないか、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.theguardian.com/science/2020/jul/01/new-study-of-naked-mole-rats-cancer-resistance-sparks-row

NEW STUDY OF NAKED MOLE RATS' CANCER RESISTANCE SPARKS ROW

Cambridge team say 2013 study was flawed and rarity of tumours in rodents still unexplained

Naked mole rats have been described by one expert as resembling a sabre-toothed sausage.
Photograph: Antonio Zazueta Olmos/Antonio Olmos

With a hairless, wrinkly body, a whopping pair of front teeth and tiny eyes, the naked mole rat might seem an unusual creature to fight over, but a row has erupted among scientists over what might be its most unusual feature: a striking resistance to cancer.

The burrowing rodents, native to east Africa and described by one expert as resembling a sabre-toothed sausage, have long fascinated researchers.

Not only do they have surprisingly long lifespans, with some living for more than 30 years, but they do not feel certain kinds of pain and can survive for lengthy periods without oxygen, thanks to a system previously only found in plants.

They are also one of the only mammals known to live in highly organised, multigenerational colonies – a type of behaviour, known as eusociality, also seen in ants and bees.

But it is the rarity of cancer in naked mole rats that is at the heart of a new row. The dispute has its origins in a 2013 study by a US-led team who found that, unlike in mouse cells, when cancer-causing genes were introduced into naked mole rat cells, the cells did not turn cancerous.

However, researchers in Cambridge say that when they sought to harness the finding, they were shocked to find that the genetically altered naked mole rat cells not only grew on soft agar – a substance that only supports cancerous cells – but caused tumours when injected into mice.

“All of a sudden they were growing, in our hands, perfectly fine,” said Dr Walid Khaled, a cancer researcher at the University of Cambridge.

Writing in the journal Nature, Khaled and colleagues describe how their results held across 79 cell cultures grown from five types of tissue taken from 11 different naked mole rats.

To further check the results, the team carried out a host of tests, including using naked mole rat cells from the original US-led team.

Dr Ewan St John Smith, also from Cambridge University, said the results were “quite a dramatic difference” from the 2013 study. He said he and his colleagues were “paranoid” about checking their findings, but the results held. “These things can grow,” said Khaled.

The Cambridge team say their experiments suggest the 2013 study involved a problematic technique for selecting genetically altered cells, meaning many of the naked mole rat cells tested on soft agar did not contain the cancer-causing genes and hence, unsurprisingly, did not grow.

“It is like not putting [in] the major ingredient. Effectively the set-up is flawed,” said Khaled.

However, the US-led team have hit back, writing in Nature that the Cambridge researchers achieved different results because they introduced additional sections of DNA into the cells, which meant far higher levels of proteins were produced from the cancer-causing genes, overriding the naked mole rat's natural cancer-resistance mechanisms.

"In nature we would not normally see such high levels of this gene expression," said Prof Vera Gorbunova, of the University of Rochester.

Khaled said the Cambridge team's results held even when they used the same DNA sections as the US-led group, and some of the latter's latest experiments confirmed the findings.

Gorbunova agreed that her team's new work showed cancerous naked mole rat cells could be produced in such circumstances, but said the effect was far smaller than for mouse cells. She said her team used naked mole rat cell cultures from the 2013 study in their new experiments, noting that they could have accumulated mutations over the years, explaining why they became cancerous.

The Cambridge team say their work suggests naked mole rat cells are no more intrinsically resistant to becoming cancerous than cells of other animals, and other factors must be behind the rarity of tumours in the rodents..

Smith said that among the possibilities, the neighbourhood around the cells may play an important role, as may the mole rats' immune system.

Ultimately, he said, the new research was important for tackling cancer. "If we understand why mole rats don't get cancer, that opens up doors for us understanding news ways of potentially preventing cancer occurring in humans."

2. 新型コロナワクチン、注目の有力候補はこの7つ

開発が急がれるワクチン、最終治験に進み期待を集める先行組とその現状

日付：2020 年 8 月 5 日
ソース：https://natgeo.nikkeibp.co.jp/atcl/news/20/080400458/?P=2
概要：

モデルナ社

ワクチン名称：mRNA-1273

開発母体：米マサチューセッツ州に本社を置くバイオテクノロジー企業。米国立衛生研究所と共同開発。

どんなワクチンか：ウイルスの遺伝物質（この場合は mRNA）の断片をヒト細胞に注入するタイプのワクチン。この断片がコロナウイルスを模したウイルスタンパク質を作り、コロナウイルスの存在を認識するよう免疫系を訓練する。この技術はこれまで、どの疾患に対しても承認された実績がない。もし成功すれば、ヒトへの使用が承認された初めての mRNA ワクチンとなる。

現状：7 月 27 日、モデルナ社は第 3 相臨床試験を開始したと発表。ただし、第 2 相試験の結果も引き続き観察するとしている。第 1 相試験の予備的な結果は、健康な被験者がコロナウイルス抗体を産生し、またヒト免疫反応のもう一つの武器である T 細胞からの反応も得られたことを示している。第 3 相試験においては、米国で 3 万人の協力者に対してワクチン投与が行われる。モデルナ社は、2021 年以降、少なくとも年間 5 億回分のワクチンを製造できる見込みだと発表している。その理由の一つとして、スイスの製薬会社ロンザ社との契約によって、年間最大 10 億回分のワクチン製造が可能になったことを挙げている。

（参考記事：「モデルナ社のワクチン候補、臨床試験の最終段階へ」）

ファイザー社

ワクチン名称：BNT162b2

開発母体：米ニューヨーク州に本社を置く世界最大級の製薬会社。ドイツのバイオテクノロジー企業ビオンテック社と共同開発。

どんなワクチンか：ファイザー社とビオンテック社の候補ワクチンも同じく mRNA ワクチンであり、ビオンテック社が過去、同技術を実験的ながんワクチンに用いた実績に基づいて開発が進められている。ファイザー社は米国政府と、2020 年 12 月までに 1 億回分のワクチンを提供する契約を約 20 億ドルで結んでいる。この契約は、ワクチンが承認・供給された時点で発効する。

現状：7 月 27 日、ファイザー社とビオンテック社は、新型コロナウイルス（SARS-CoV-2）の伝播が著しい地域の多様な集団を対象とする、第 2 相と第 3 相を兼ねた試験を開始。米国 39 州、ブラジル、アルゼンチン、ドイツにおいて、対象者 3 万人におけるワクチンの効果を検証する。同プロジェクトは、早ければ 2020 年 10 月に規制当局に承認申請し、2021 年末までに 13 億回分の供給を目指している。第 1 および第 2 相試験データの予備的な結果は、このワクチンが新型コロナウイルスのタンパク質に特異的な抗体と T 細胞応答を産生することを示している。

オックスフォード大学

ワクチン名称：ChAdOx1 nCoV-19

開発母体：英国の大学。英バイオ製薬大手アストラゼネカ社と共同開発。

どんなワクチンか：オックスフォード大学のワクチン候補は、ウイルスベクターワクチンとして知られているもので、いわば免疫系に提示される「トロイの木馬」のような働きをする。同大学の研究チームは、コロナウイルスが細胞に侵入するのを助ける新型コロナウイルスのスパイクタンパク質を、風邪の原因となるアデノウイルスを弱毒化させたものに移植。このアデノウイルスをヒトに注射することによって、スパイクタンパク質が免疫反応を引き起こすことを狙う。アストラゼネカ社とオックスフォード大は、10 億回分の生産を予定し、原価で販売することで合意している。

現状：第 1 相、第 2 相臨床試験の予備的な結果は、このワクチンが、抗体の増加や T 細胞からの強い免疫反応を誘発したこと、また副作用は倦怠感や頭痛などの軽度なものであったことを示している。現在は第 3 相臨床試験に進んでおり、ブラジル、英国、米国、南アフリカで、最大 5 万人の志願者を採用することを目指している。

（参考記事：「英オックスフォード大のコロナワクチン候補、最終治験を開始」）

シノバック・バイオテック（科興控股生物技術）社

名称：CoronaVac

開発母体：中国のバイオ製薬企業。ブラジルのブタンタン研究所と共同開発。

どんなワクチンか：CoronaVac は不活化ワクチン、つまり感染力をなくしたコロナウイルスを利用するワクチンだ。不活化された病原体は病気を引き起こすことはないが、年に 1 度接種するインフルエンザワクチンと同じように、免疫反応を引き起こせる。

現状：7 月 3 日、ブラジルの規制当局は CoronaVac に対し、第 2 相試験の結果を引き続き観察しつつ、第 3 相試験に進むことを承認した。シノバック・バイオテック社によると、第 1 相、第 2 相試験ではこれまでのところ、同ワクチンが重篤な副作用を伴わない免疫反応を引き起こすことが示されているという。学術誌「サイエンス」に掲載された、サルを用いた初期試験の予備的な結果では、このワクチンが 10 種類の新型コロナウイルスの株を中和する抗体を産出す

ることが明らかになっている。第 3 相試験では、ブラジルの医療従事者から約 9000 人を採用する予定だ。

シノファーム（中国医薬集団）社

ワクチンの名称：なし

開発母体：中国の国有製薬会社。中国、武漢生物製品研究所と共同開発。

どんなワクチンか：シノファーム社もまた、不活化新型コロナウイルスワクチンを採用し、2020 年末までの一般市民への提供を目指している。同ワクチン候補の初期試験では、参加者に強い中和抗体反応が誘発され、重篤な副作用はみられなかった。

現状：7 月中旬、シノファーム社はアラブ首長国連邦（UAE）において、18～60 歳の、基礎疾患のない志願者 1 万 5000 人を対象に第 3 相試験を開始。シノファーム社が UAE を選んだのは、同国がおよそ 200 カ国から集まった多様な人口を抱えている点が、試験場所として理想的であったためだ。

マードック子供研究所

名称：BCG ワクチン

開発母体：オーストラリア最大の子供の健康に関する研究機関。メルボルン大学と共同研究。

どんなワクチンか：過去 100 年近くにわたり、結核の予防に用いられてきた BCG ワクチンは、弱毒化した生きたウシ型結核菌（カルメット・ゲラン桿菌）だ。長年の間に、この生ワクチンが免疫系を刺激することで、体が結核以外の病気を撃退する際の助けとなる可能性を示す証拠が見つかっている。研究者らは、こうした利点が新型コロナウイルスに対しても有効かどうかを調べており、現在、オーストラリアで第 3 相試験が行われようとしている。ただし WHO は、4 月 12 日の時点で、BCG ワクチンがコロナウイルス感染症から人々を守る証拠はないと述べている。

現状：4 月、マードック子供研究所の研究者らは、BCG がコロナウイルスにも効果を発揮するかどうかを確かめる一連のランダム化比較試験を開始。研究のために 1 万人の医療従事者の採用を目指している。

カンシノ・バイオロジクス（康希諾生物）社

名称：Ad5-nCoV

開発母体：中国の製薬スタートアップ。

どんなワクチンか：カンシノ・バイオロジクス社もまた、弱毒化したアデノウイルスを用いて、新型コロナウイルスのスパイクタンパク質を体内に導入するウイルスベクターワクチンを開発している。医学雑誌「ランセット」に掲載された第 2 相試験の予備的な結果は、このワクチンが「1 回の接種で大多数の患者に有意な免疫反応」を誘発したことを示している。重篤な副作用は報告されていない。

現状：同社は厳密にはまだ第 2 相試験の段階にあるが、6 月 25 日、限定的にヒトへの使用が承認された。中国政府はこのワクチンを軍隊でのみ、1 年間使用することを認めている。

研究関連ニュース/他のトップページに戻る

---

3. 土地利用の変化が病気発生のリスクを増加させる可能性

日付：2020 年 8 月 5 日
ソース：ロンドン大学
概要：

人類は地球上の居住可能な土地の半分以上を開拓して急増する人口にあてがってきた。この地球規模の変化が野生生物のバランスを崩している。森林、草原、砂漠などが都市、住宅地、農地に変わることで多くの生物は減るか消滅するが、逆に繁栄する生物もいる。ロンドン大学（UCL）主導で *Nature* 誌に発表された調査結果によると、痛手を被るのはサイやダチョウなど食べ物や住まいが凝っていて、比較的大きく、寡勢で、より長生きする動物。それに対してネズミやムクドリ等の小さく、大勢で、すばしこくて、短命でこだわりが少ない動物は逆により繁栄する、としている。
そういった繁栄する動物は滅びる動物に比べて病原体を宿していることが多く、従って人が住めるように自然を変えれば動物から人に移りうる病原体による感染症はより広まり易くなる。農地や都市は、今後数十年は拡大し続けることが予想されるため、様変わりした土地では有害な病原体を宿しうる動物とより遭遇しやすくなり、病気の発生には益々注意して対応する必要がある、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/2020-08/ucl-luc080320.php

NEWS RELEASE 5-AUG-2020

LAND USE CHANGES MAY INCREASE DISEASE OUTBREAK RISKS

UNIVERSITY COLLEGE LONDON

Global changes in land use are disrupting the balance of wild animal communities in our environment, and species that carry diseases known to infect humans appear to be benefiting, finds a new UCL-led study.

The findings, published in *Nature*, may have implications for future spillovers of diseases originating in animal hosts.

The research team, led by the UCL Centre for Biodiversity & Environment Research, studied evidence from 6,801 ecological communities from six continents, and found that animals known

to carry pathogens (disease-causing microorganisms) that can infect humans were more common in landscapes intensively used by people.

The evidence was sourced from a dataset of 184 studies incorporating close to 7,000 species, 376 of which are known to carry human-shared pathogens.

The researchers say we may need to alter how we use land across the world to reduce the risk of future spillovers of infectious diseases.

Lead author, PhD candidate Rory Gibb (UCL Centre for Biodiversity & Environment Research) said: "The way humans change landscapes across the world, from natural forest to farmland for example, has consistent impacts on many wild animal species, causing some to decline while some others persist or increase.

"Our findings show that the animals that remain in more human-dominated environments are those that are more likely to carry infectious diseases that can make people sick."

Species that host zoonotic pathogens (which can jump from animals to people) constituted a higher proportion of the animal species found in human-influenced (disturbed) environments compared to the ecological communities in more wild habitats.

The same relationship is seen for animals that tend to carry more pathogens of any kind - whether or not they can affect humans.

In comparison, most other wild animal species are found in lower numbers in disturbed environments compared to natural habitats. The researchers say this suggests that similar factors may be influencing both whether a species can tolerate humans and how likely it is to carry potentially zoonotic diseases.

Co-lead author Dr David Redding (ZSL Institute of Zoology and UCL Centre for Biodiversity & Environment Research) said: "Other studies have found that outbreaks of emerging zoonotic infectious diseases appear to be increasingly common - our findings may help to explain that pattern, by clarifying the underlying ecological change processes that are interacting to drive infection risks."

Senior author Professor Kate Jones (UCL Centre for Biodiversity & Environment Research and ZSL Institute of Zoology) said: "Global land use change is primarily characterised by the conversion of natural landscapes for agriculture, particularly for food production. Our findings underscore the need to manage agricultural landscapes to protect the health of local people while also ensuring their food security."

The researchers say that while there are numerous other factors influencing emergent disease risks, the findings point to strategies that could help mitigate the risk of further infectious disease outbreaks comparable to COVID-19.

Professor Jones said: "As agricultural and urban lands are predicted to continue expanding in the coming decades, we should be strengthening disease surveillance and healthcare provision in those areas that are undergoing a lot of land disturbance, as they are increasingly likely to have animals that could be hosting harmful pathogens."

Dr Redding added: "Our findings provide a context for thinking about how to manage land use changes more sustainably, in ways that take into account potential risks not only to biodiversity, but also to human health."

###

The study, by researchers from UCL, ZSL, University of Oxford and Imperial College London, used data from the Projecting Responses of Ecological Diversity in Changing Terrestrial Systems (PREDICTS) biodiversity database. It was supported by the Natural Environment Research Council, the Medical Research Council, Wellcome and the Royal Society.

---

4. 自然発症型糖尿病マウスモデル作製に成功
膵臓再生医療の新しい移植モデル動物として期待

日付：2020 年 8 月 5 日
ソース：東京工業大学
概要：

https://www.titech.ac.jp/news/2020/047450.html

要点

- インスリン 2 タンパク質の 104 番目のアミノ酸残基を欠失
- 重度免疫不全モデルマウス BRJ マウスに遺伝子変異導入
- インスリン治療により正常な血糖値に回復

概要

東京工業大学 生命理工学院 生命理工学系の粂昭苑教授、坂野大介助教、井上愛里大学院生（博士後期課程 1 年）らの研究グループは、熊本大学 生命資源研究・支援センターの荒木喜美教授、同大 ヒトレトロウイルス学共同研究センターの岡田誠治教授、順天堂大学大学院医学系研究科の小池正人教授らとの共同研究により、マウスのインスリン 2 タンパク質への Q104del 変異導入[用語 1]による自然発症型の糖尿病モデルマウスを作製した（図 1）。作製した糖尿病モデルマウスは遺伝的な変異により発症するため、従来の薬剤投与による糖尿病モデルよりも安定に糖尿病を発症することができる。そして、重度免疫不全モデルマウス[用語 2]の系統に遺伝子変異を導入したため、ヒト iPS 細胞や ES 細胞から作成された膵臓（すいぞう）細胞の糖尿病治療効果を評価するための細胞移植実験への活用が期待される。

この成果は 7 月 22 日付で英国の科学誌「*Scientific Reports*（サイエンティフィック・リポーツ）」にオンライン掲載された。

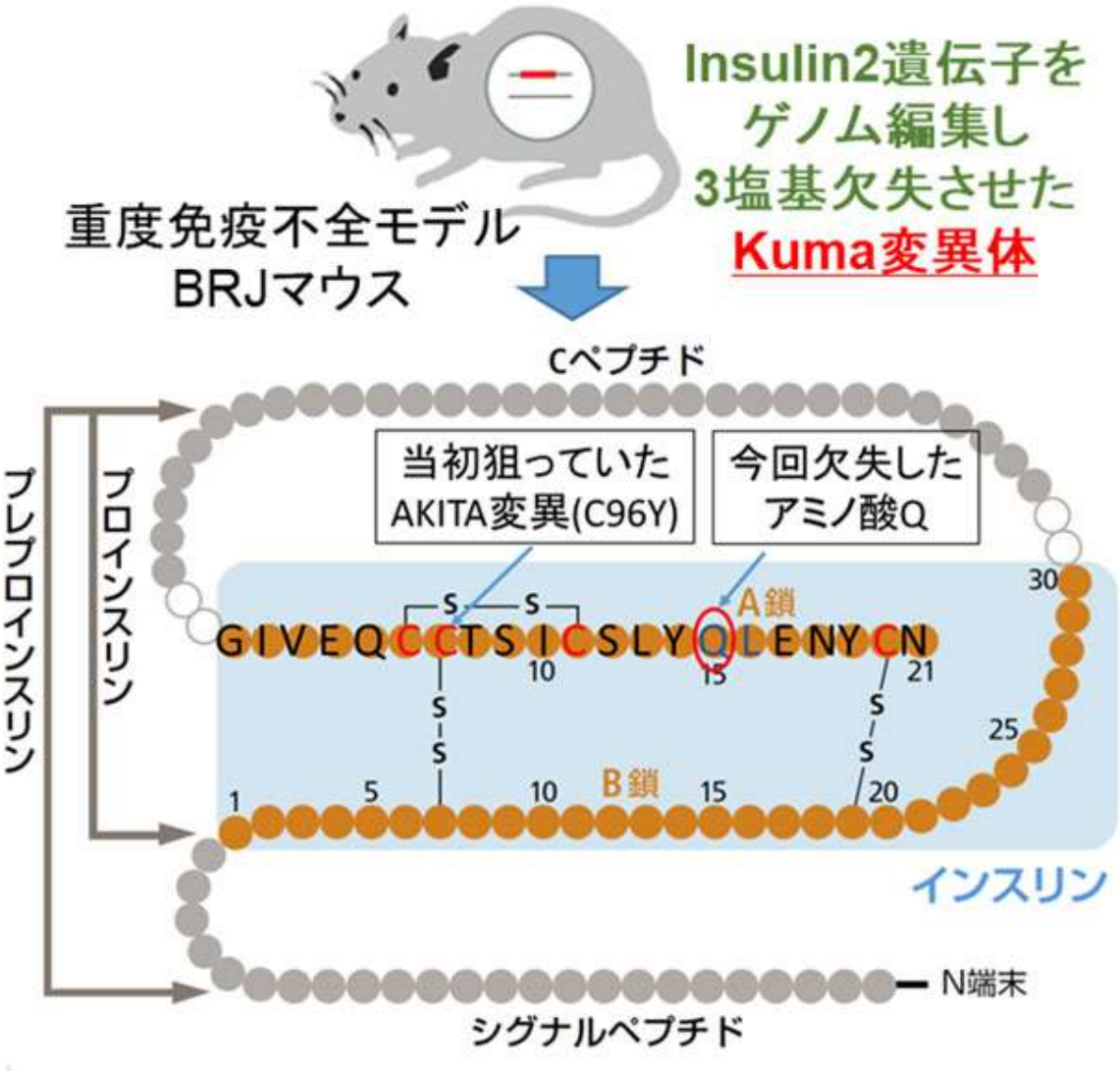


図 1. CRISPR/Cas9 システムを用いた Kuma 変異をもつマウスの樹立
CRISPR/Cas9 システムを用いて重篤な免疫不全 BRJ マウスに、変異の導入を試みた。
当初狙った相同組み換え体は得られなかったが、その代わり、遺伝子修復時に起こった 3 塩基 DNA の欠失を有するマウス系統を得た。このゲノム配列の欠失によりインスリン 2 タンパク質の 104 番目アミノ酸であるグルタミンが失われていた。

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/2020/08/200805133304.htm

MOVE OVER AKITA: INTRODUCING 'KUMA MUTANT' MICE FOR ISLET TRANSPLANTATION RESEARCH

Date:

August 5, 2020

Source:

Tokyo Institute of Technology

Summary:

Scientists have used a gene editing technique to establish a novel mouse model of permanent neonatal diabetes -- the immune-deficient Kuma mutant mice with a specific deletion in the Insulin2 (Ins2) gene. This model is expected to be useful for studying the mechanisms governing insulin-producing cell dysfunctions in the pancreas as well as for evaluating human stem-cell derived or interspecies-derived insulin-producing cell transplantation.

FULL STORY

Scientists have used a gene editing technique to establish a novel mouse model of permanent neonatal diabetes -- the immune-deficient Kuma mutant mice with a specific deletion in the Insulin2 (Ins2) gene. This model is expected to be useful for studying the mechanisms governing insulin-producing cell dysfunctions in the pancreas as well as for evaluating human stem-cell derived or interspecies-derived insulin-producing cell transplantation.

Diabetes seldom occurs in newborns -- a condition known as neonatal diabetes. But when it does, it's mostly due to a mutation in a single gene such as the KCNJ11 or insulin (INS). This early-onset type of diabetes differs from type-1 diabetes in that it occurs within the first six months of life and can be either transient or permanent. Most of the mutations that underly this disease prevent the pancreas from producing sufficient insulin, which leads to high blood glucose levels or hyperglycemia.

To understand what causes permanent neonatal diabetes and to find a cure, scientists often use mouse and pig models having Insulin2 (Ins2)C96Y gene mutations. These models develop permanent early-onset diabetes resembling neonatal diabetes. However, a major limitation of these models is that by using them, inter-species transplantation of pancreatic insulin-producing cells (pancreatic beta cells), called islet transplantation, cannot be evaluated, due to adverse immune system reactions characterizing such interspecies transplantation.

Now, in a paper published in *Scientific Reports*, scientists from Tokyo Tech describe how they established a new mouse model of permanent neonatal diabetes, which exhibits severe insulin-deficiency and beta-cell dysfunction in an immune deficient background. As Professor Shoen Kume, who led the study explains, "We wanted to create a mouse model that would allow us to evaluate the efficacy of transplanting human stem cell-derived or xenogeneic pancreatic beta cells into these mice without having to consider immune responses"

To achieve this goal, the scientists used the CRISPR/Cas9 gene editing technique to introduce a three base pair deletion in the Ins2 gene of a severely-immunodeficient BRJ mouse, that lacked mature T and B lymphocytes and natural killer (NK) cells. This mutation causes a Gln (Q) deletion (p.Q104del), hampering insulin production. The scientists named the mutation 'Kuma mutation'.

Upon examining the Kuma mice as they aged, the scientists discovered that both male and female Kuma mutants developed hyperglycemia three weeks after their birth. They conjectured that this may be due to the low stability of the mutant insulin protein. The scientists also noted that these mice had markedly reduced beta-cell area, size, and mass, as well as a significantly decreased number and size of insulin granules within the beta cells. This meant that the mice could serve as a permanent neonatal diabetes model for islet transplantation.

To corroborate this, their treatment with insulin implants over four weeks successfully reversed their hyperglycemia.

Based on these findings, Prof Kume and his team believe that "the Kuma mutant can not only be used for molecular studies of the Insulin gene and beta cell dysfunction, but its immune-deficient background allows it to be an attractive model for studies examining the functionality of transplanted beta-cells generated from human- or xenogeneic-derived stem cells."

Moreover, as the Kuma mutation is well conserved across different species, the same gene-editing approach can be applied to creating permanent neonatal diabetic models in other animal species, making advancement in the research on this disease condition a little bit easier.

Story Source:

Materials provided by **Tokyo Institute of Technology**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Daisuke Sakano, Airi Inoue, Takayuki Enomoto, Mai Imasaka, Seiji Okada, Mutsumi Yokota, Masato Koike, Kimi Araki, Shoen Kume. **Insulin2Q104del (Kuma) mutant mice develop diabetes with dominant inheritance**. *Scientific Reports*, 2020; 10 (1) DOI: 10.1038/s41598-020-68987-z

---

Cite This Page:

- MLA
- APA
- Chicago

Tokyo Institute of Technology. "Move over Akita: Introducing 'Kuma mutant' mice for islet transplantation research." ScienceDaily. ScienceDaily, 5 August 2020. <www.sciencedaily.com/releases/2020/08/200805133304.htm>.

---

5. 酸素療法がマウスの肺微生物叢に害を与える
～重症患者の酸素レベル低下治療に影響か～

日付:2020 年 8 月 12 日
ソース:ミシガン大学医学部
概要:

重度の COVID-19 の特徴の一つは、息切れと低酸素血症と呼ばれる血中酸素レベルの低下である。入院すると、これらの患者は、レベルを正常に戻すために酸素を投与される。しかしながら、ミシガン大学の研究者らによる新しい研究は、この普遍的な治療が予期しない原因 -微生物叢- を介して意図しない結果をもたらす可能性があることを示唆している。
この研究室では、長年にわたり健康と疾患における肺微生物叢の役割を調査してきた。その結果、比較的清潔で細菌がいないと想定されていた肺でも、腸内と同じように細菌のバランスが重要であることが知られていた。彼らの以前の研究は、酸素がこのバランスを乱し、肺損傷に寄与することを既に発見していた。
今回研究者らは、マウス実験で、マウスの肺の微生物叢が高酸素濃度によってたった一日で変わったこと、それに対して肺の損傷は三日後まで検出されなかったこと、を実証した。更に、遺伝的に同一のマウスに対して2つのグループ、一つは細菌があるもの、もう一つは細菌のないもの、を比較した場合、細菌の無いマウスは酸素による肺損傷から保護された、ことを明らかにした。研究者らは、肺の微生物叢が何らかの形で肺の損傷に関与しており、その微生物叢に害を与える酸素療法に警笛を鳴らしている。

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/2020/08/200812144114.htm

OXYGEN THERAPY HARMS LUNG MICROBIOME IN MICE

STUDY COULD HAVE IMPLICATIONS FOR TREATMENT OF REDUCED OXYGEN LEVELS IN CRITICALLY ILL PATIENTS

Date:

August 12, 2020

Source:

Michigan Medicine - University of Michigan

Summary:

A new mouse study hints that oxygen therapy may have unintended consequences via an unexpected source -- the microbiome.

FULL STORY

One of the hallmarks of severe COVID-19 is shortness of breath and significantly reduced levels of oxygen in the blood, called hypoxemia. Upon hospitalization, these patients are administered oxygen in an attempt to bring their levels back up to normal. However, a new study hints that this universal therapy may have unintended consequences via an unexpected source -- the microbiome.

"It had been assumed that the lungs were relatively clean and free of bacteria," says Shanna Ashley, Ph.D., a former Post-Doctorate Fellow with the Division of Pulmonary and Critical Care Medicine at U-M Medical School. "We now know that the balance of bacteria inside the lungs matters much like it does in the gut." Ashley worked with a team led by Robert Dickson, M.D., Assistant Professor of Pulmonary & Critical Care Medicine and Microbiology and Immunology, whose lab has spent years exploring the role of the lung microbiome in health and disease. Their work has found that oxygen disrupts this balance, contributing to lung injury.

Scientists have long known that oxygen can damage the lungs. "Oxygen is actually a potent lung toxin," says Dickson. "If I put healthy mice in 100% oxygen, they will die in five days, and they'll have the same kind of severe lung injury that patients with COVID-19 or other lung damage have."

Patients in intensive care are often treated with high concentrations of oxygen for long periods of time. Their team began to explore how therapeutic oxygen was affecting the lung microbiome. They looked at critically ill patients who were on a ventilator for more than 24 hours and studied bacteria detected in specimens from their lungs. They found marked differences in the bacteria species present in samples from patients depending on whether they received low, intermediate, or high concentrations of oxygen. Specifically, patients who received high oxygen concentrations were much more likely to grow Staphylococcus aureus, bacteria that are very oxygen-tolerant and a common cause of lung infections in the ICU.

"Different types of bacteria vary quite a bit from each other in how well they can handle oxygen," Dickson says, "So we wondered if the oxygen we give our patients might be influencing the bacterial communities in their respiratory tract."

To better understand the relationship between oxygen and lung bacteria, the team designed a series of experiments in mice. They first exposed healthy mice to high concentrations of oxygen to determine the effects of oxygen on the lung bacteria of healthy mice.

"When we gave high concentrations of oxygen to healthy mice, their lung communities changed quickly, and just like we predicted," said Ashley. "The oxygen-intolerant bacteria went down, and the oxygen-tolerant bacteria went up." After three days of oxygen therapy, oxygen-tolerant Staphylococcus was by far the most commonly detected bacteria in mouse lungs.

The team next designed experiments to answer a key "chicken or the egg" question: do these altered bacterial communities contribute to lung injury? Or are bacterial communities altered

because the lung is injured? They first addressed this by comparing the relative timing of changes in lung bacteria as compared to the onset of lung injury.

Using mice, they were able to demonstrate that while the lung microbiome was changed by high oxygen concentrations after only a day, lung injury wasn't detectable until after 3 days, proving that damage to the lung followed the disruption of the microbiome, and not the other way around. Furthermore, they showed that natural variation in lung bacteria was strongly correlated with variation in the severity of inflammation in oxygen-exposed mice.

To further strengthen the causal link, they turned to germ-free mice, which completely lack a microbiome. "We wanted to see whether there was a selective advantage or disadvantage to having bacteria-free lungs when exposed to therapeutic oxygen," says Ashley. When comparing two groups of genetically identical mice -- one with bacteria and one without -- the mice without bacteria were protected from oxygen-induced lung injury.

"That was an extraordinary finding for us," said Dickson. "Compared to conventional mice, these germ-free mice have the same genetics and receive the same oxygen dosing, but their lungs are protected from injury. Nothing in our current understanding of oxygen-induced lung injury can explain that finding."

"It really makes the case that the microbiome is somehow playing a role in lung injury," said Ashley.

Targeting the microbiome

Critically ill patients receiving oxygen are typically administered antibiotics as well. The team wondered: Could antibiotics alter the severity of oxygen-induced lung injury in mice? "The short answer is yes, we can affect the severity, but it wasn't in the direction we predicted," says Dickson. Vancomycin, an antibiotic that targets gram-positive bacteria like Staphylococcus, had no effect on lung injury, while ceftriaxone, a gram-negative antibiotic, made things worse.

"The microbiome is not all good and not all bad," comments Dickson. "That's why it's important for us to figure out the mechanisms here. We're currently using very non-specific interventions, when what we need is targeted manipulation of the microbiome."

Ashley agrees. "We need to think about using the microbiome as a therapeutic target to prevent doing further damage to patients' lungs while they are on a ventilator or receiving oxygen."

Dickson cautions against changing clinical practice prematurely based on these findings. "The question of how much oxygen to give critically ill patients is a complex one, and a topic of intense study," says Dickson. "Our findings are exciting, but I still look to randomized controlled trials to inform my decisions about how to dose oxygen in sick patients."

James Kiley, director of the Division of Lung Diseases at the National Heart, Lung, and Blood Institute, part of the National Institutes of Health, agrees. "This study provides important insights into the contributions of the microbiome toward inflammation and damage in lungs exposed to varying levels of oxygen, and supports the continued importance of understanding how the microbiome and related factors impact lung disease and clinical outcomes."

Funding for this study was provided by the National Institutes of Health/National Heart, Lung, and Blood Institute.

Story Source:

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

Journal Reference:

1. Shanna L. Ashley, Michael W. Sjoding, Antonia P. Popova, Tracy X. Cui, Matthew J. Hoostal, Thomas M. Schmidt, William R. Branton, Michael G. Dieterle, Nicole R. Falkowski, Jennifer M. Baker, Kevin J. Hinkle, Kristine E. Konopka, John R. Erb-Downward, Gary B. Huffnagle, Robert P. Dickson. **Lung and gut microbiota are altered by hyperoxia and contribute to oxygen-induced lung injury in mice**. *Science Translational Medicine*, 2020; 12 (556): eaau9959 DOI: 10.1126/scitranslmed.aau9959

Cite This Page:

- MLA
- APA
- Chicago

Michigan Medicine - University of Michigan. "Oxygen therapy harms lung microbiome in mice: Study could have implications for treatment of reduced oxygen levels in critically ill patients." ScienceDaily. ScienceDaily, 12 August 2020. <www.sciencedaily.com/releases/2020/08/200812144114.htm>.

---

6. 特定の酵素喪失で、マウスの脂肪代謝と運動持久力が増加

日付：2020 年 8 月 13 日
ソース：ハーバード大学医学部
概要：

ハーバードメディカルスクールの研究者らは、8 月 4 日号の *Cell Metabolism* 誌で発表した研究で、栄養素の利用可能性の感知と脂肪を分解する筋細胞の能力の調節において、酵素 –プロリルヒドロキシラーゼ 3（PHD3）– の重要な役割を特定した。
栄養素が豊富な場合、PHD3 は不必要な脂肪代謝を抑制するブレーキとして機能。そしてこのブレーキは、燃料が少なく、運動中などにより多くのエネルギーが必要なときに解放される。
驚くべきことに、マウスで PHD3 産生をブロックすると、特定のフィットネス指標が劇的に改善されることが研究で示された。通常の同腹子マウスと比較して、PHD3 酵素を欠くマウスは、トレッドミルで 40%長く、50%遠くまで走り、運動中の最大酸素摂取量を測定する有酸素持久力のマーカーである VO2 max が高かった、としている。
調査結果は、細胞がどのように燃料を代謝するかについての主要なメカニズムに光を当て、筋肉機能とフィットネスのより良い理解への手がかりを提供すると、している。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/08/200813155827.htm

LOSS OF A SPECIFIC ENZYME BOOSTS FAT METABOLISM AND EXERCISE ENDURANCE IN MICE

Date:

August 13, 2020

Source:

Harvard Medical School

Summary:

Blocking the activity of a fat-regulating enzyme in the muscles of mice leads to an increased capacity for endurance exercise, according to the results of a new study.

FULL STORY

Mouse on exercise wheel (stock image).

Credit: © Emilia Stasiak / stock.adobe.com

Sugars and fats are the primary fuels that power every cell, tissue and organ. For most cells, sugar is the energy source of choice, but when nutrients are scarce, such as during starvation or extreme exertion, cells will switch to breaking down fats instead.

The mechanisms for how cells rewire their metabolism in response to changes in resource availability are not yet fully understood, but new research reveals a surprising consequence when one such mechanism is turned off: an increased capacity for endurance exercise.

In a study published in the Aug. 4 issue of *Cell Metabolism*, Harvard Medical School researchers identified a critical role of the enzyme, prolyl hydroxylase 3 (PHD3), in sensing nutrient availability and regulating the ability of muscle cells to break down fats. When nutrients are abundant, PHD3 acts as a brake that inhibits unnecessary fat metabolism. This brake is released when fuel is low and more energy is needed, such as during exercise.

Remarkably, blocking PHD3 production in mice leads to dramatic improvements in certain measures of fitness, the research showed. Compared with their normal littermates, mice lacking the PHD3 enzyme ran 40 percent longer and 50 percent farther on treadmills and had higher VO2 max, a marker of aerobic endurance that measures the maximum oxygen uptake during exercise.

The findings shed light on a key mechanism for how cells metabolize fuels and offer clues toward a better understanding of muscle function and fitness, the authors said.

"Our results suggest that PHD3 inhibition in whole body or skeletal muscle is beneficial for fitness in terms of endurance exercise capacity, running time and running distance," said senior study author Marcia Haigis, professor of cell biology in the Blavatnik Institute at HMS. "Understanding this pathway and how our cells metabolize energy and fuels potentially has broad applications in biology, ranging from cancer control to exercise physiology."

However, further studies are needed to elucidate whether this pathway can be manipulated in humans to improve muscle function in disease settings, the authors said.

Haigis and colleagues set out to investigate the function of PHD3, an enzyme that they had found to play a role regulating fat metabolism in certain cancers in previous studies. Their work showed that, under normal conditions, PHD3 chemically modifies another enzyme, ACC2, which in turn prevents fatty acids from entering mitochondria to be broken down into energy.

In the current study, the researchers' experiments revealed that PHD3 and another enzyme called AMPK simultaneously control the activity of ACC2 to regulate fat metabolism, depending on energy availability.

In isolated mouse cells grown in sugar-rich conditions, the team found that PHD3 chemically modifies ACC2 to inhibit fat metabolism. Under low-sugar conditions, however, AMPK activates and places a different, opposing chemical modification on ACC2, which represses PHD3 activity and allows fatty acids to enter the mitochondria to be broken down for energy.

These observations were confirmed in live mice that were fasted to induce energy-deficient conditions. In fasted mice, the PHD3-dependent chemical modification to ACC2 was significantly reduced in skeletal and heart muscle, compared to fed mice. By contrast, the AMPK-dependent modification to ACC2 increased.

Longer and further

Next, the researchers explored the consequences when PHD3 activity was inhibited, using genetically modified mice that do not express PHD3. Because PHD3 is most highly expressed in skeletal muscle cells and AMPK has previously been shown to increase energy expenditure and exercise tolerance, the team carried out a series of endurance exercise experiments.

"The question we asked was if we knock out PHD3," Haigis said, "would that increase fat burning capacity and energy production and have a beneficial effect in skeletal muscle, which relies on energy for muscle function and exercise capacity?"

To investigate, the team trained young, PHD3-deficient mice to run on an inclined treadmill. They found that these mice ran significantly longer and further before reaching the point of exhaustion, compared to mice with normal PHD3. These PHD3-deficient mice also had higher oxygen consumption rates, as reflected by increased VO2 and VO2 max.

After the endurance exercise, the muscles of PHD3-deficient mice had increased rates of fat metabolism and an altered fatty acid composition and metabolic profile. The PHD3-dependent modification to ACC2 was nearly undetectable, but the AMPK-dependent modification increased, suggesting that changes to fat metabolism play a role in improving exercise capacity.

These observations held true in mice genetically modified to specifically prevent PHD3 production in skeletal muscle, demonstrating that PHD3 loss in muscle tissues is sufficient to boost exercise capacity, according to the authors.

"It was exciting to see this big, dramatic effect on exercise capacity, which could be recapitulated with a muscle-specific PHD3 knockout," Haigis said. "The effect of PHD3 loss was very robust and reproducible."

The research team also performed a series of molecular analyses to detail the precise molecular interactions that allow PHD3 to modify ACC2, as well as how its activity is repressed by AMPK.

The study results suggest a new potential approach for enhancing exercise performance by inhibiting PHD3. While the findings are intriguing, the authors note that further studies are needed to better understand precisely how blocking PHD3 causes a beneficial effect on exercise capacity.

In addition, Haigis and colleagues found in previous studies that in certain cancers, such as some forms of leukemia, mutated cells express significantly lower levels of PHD3 and consume fats to fuel aberrant growth and proliferation. Efforts to control this pathway as a potential strategy for treating such cancers may help inform research in other areas, such as muscle disorders.

It remains unclear whether there are any negative effects of PHD3 loss. To know whether PHD3 can be manipulated in humans -- for performance enhancement in athletic activities or as a treatment for certain diseases -- will require additional studies in a variety of contexts, the authors said.

It also remains unclear if PHD3 loss triggers other changes, such as weight loss, blood sugar and other metabolic markers, which are now being explored by the team.

"A better understanding of these processes and the mechanisms underlying PHD3 function could someday help unlock new applications in humans, such as novel strategies for treating muscle disorders," Haigis said.

Additional authors on the study include Haejin Yoon, Jessica Spinelli, Elma Zaganjor, Samantha Wong, Natalie German, Elizabeth Randall, Afsah Dean, Allen Clermont, Joao Paulo, Daniel Garcia, Hao Li, Olivia Rombold, Nathalie Agar, Laurie Goodyear, Reuben Shaw, Steven Gygi and Johan Auwerx.

The study was supported by the National Institutes of Health (grants R01CA213062, P30DK036836, R25 CA-89017 and P41 EB015898), Ludwig Center at Harvard Medical School, Glenn Foundation for Medical Research, Ecole Polytechnique Fédérale de Lausanne and the Fondation Suisse de Recherche sur les Maladies Musculaires.

Story Source:

Materials provided by **Harvard Medical School**. Original written by Kevin Jiang. *Note: Content may be edited for style and length.*

Journal Reference:

1. Haejin Yoon, Jessica B. Spinelli, Elma Zaganjor, Samantha J. Wong, Natalie J. German, Elizabeth C. Randall, Afsah Dean, Allen Clermont, Joao A. Paulo, Daniel Garcia, Hao Li, Olivia Rombold, Nathalie Y.R. Agar, Laurie J. Goodyear, Reuben J. Shaw, Steven P. Gygi, Johan Auwerx, Marcia C. Haigis. **PHD3 Loss Promotes Exercise Capacity and Fat Oxidation in Skeletal Muscle**. *Cell Metabolism*, 2020; 32 (2): 215 DOI: 10.1016/j.cmet.2020.06.017

Cite This Page:

- MLA
- APA
- Chicago

Harvard Medical School. "Loss of a specific enzyme boosts fat metabolism and exercise endurance in mice." ScienceDaily. ScienceDaily, 13 August 2020. <www.sciencedaily.com/releases/2020/08/200813155827.htm>.

---

7. 癌性腫瘍を攻撃する際の微生物叢の役割

日付:2020 年 8 月 13 日
ソース:カルガリー大学
概要:

カルガリー大学 Cumming School of Medicine (CSM) のスナイダー慢性疾患研究所の研究者らは、我々の免疫系が癌性腫瘍と闘う時にどの腸内細菌が役立ち、どのようにそれを行うのかを発見し、*Science* 誌に発表した。この発見により、身体の免疫応答を増幅するのに役立つ癌治療法である免疫療法が機能する理由と、機能しない理由が新たに理解される可能性がある、としている。
まず、研究者らは、免疫療法で治療する際、結腸直腸癌の腫瘍と関係がある細菌種を特定。無菌マウスを使ってこれらの細菌を導入した。これらのマウスでは腫瘍は劇的に縮小したが、有益な細菌を受け取らなかったマウスには、免疫療法は効果がなかった。
調査結果は、免疫療法を特定の微生物療法と組み合わせると、結腸直腸がんの場合と同様に、免疫系がメラノーマ、膀胱癌の癌細胞を認識して攻撃する能力を高めることを示している。

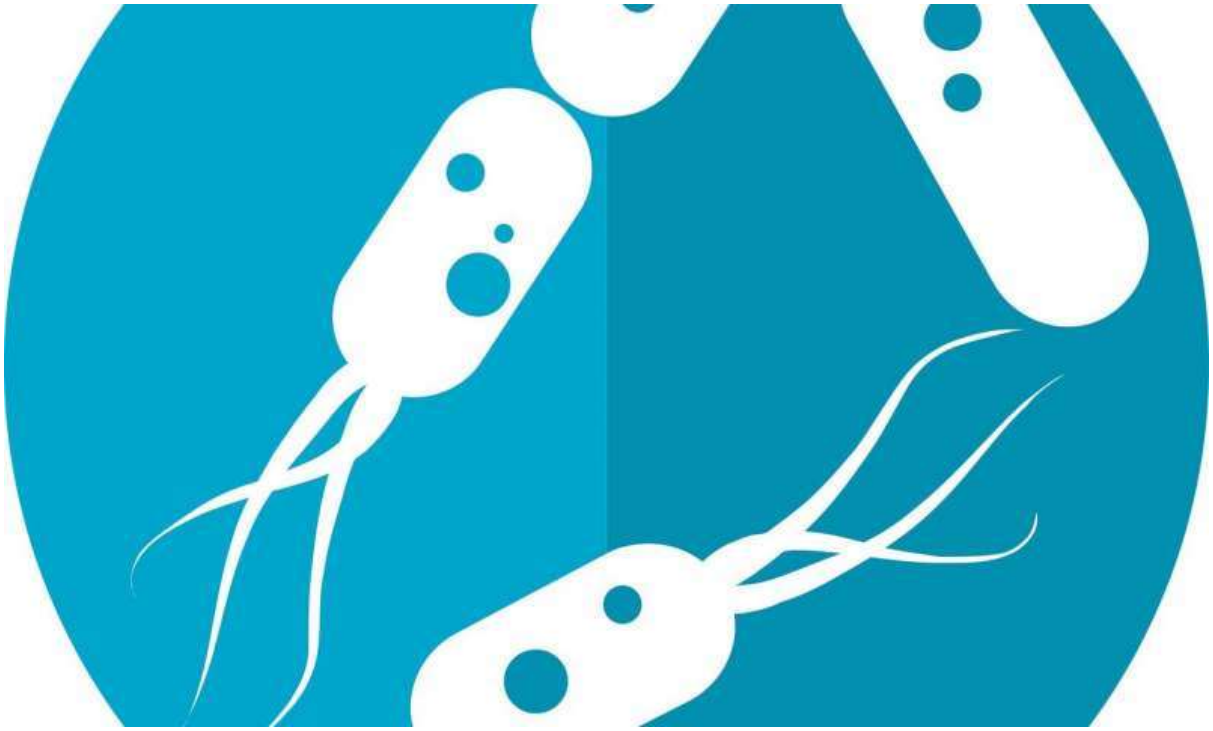
研究関連ニュース/他のトップページに戻る

＜英文＞https://medicalxpress.com/news/2020-08-microbiome-role-cancerous-tumours.html

AUGUST 13, 2020

RESEARCHERS DISCOVER THE MICROBIOME'S ROLE IN ATTACKING CANCEROUS TUMOURS

By University of Calgary



Credit: CCo Public Domain

Researchers with the Snyder Institute for Chronic Diseases at the Cumming School of Medicine (CSM) have discovered which gut bacteria help our immune system battle cancerous tumors and how they do it. The discovery may provide a new understanding of why immunotherapy, a treatment for cancer that helps amplify the body's immune response, works in some cases, but not others. The findings, published in *Science*, show combining immunotherapy with specific microbial therapy boosts the ability of the immune system to recognize and attack cancer cells in some melanoma, bladder and colorectal cancers.

Dr. Kathy McCoy, Ph.D., is a leading expert on the body's relationship with the microbiome. She and her team are focused on harnessing the power of the microbiome to improve health and treat diseases. McCoy says to harness and direct that power scientists need to better understand the role bacteria play in regulating the immune system.

"Recent studies have provided strong evidence that gut microbiota can positively affect anti-tumor immunity and improve the effectiveness of immunotherapy in treating certain cancers, yet, how the bacteria were able to do this remained elusive, " says McCoy, director of the International Microbiome Centre at the University of Calgary and principal investigator on the study. "We've been able to build on that work by showing how certain bacteria enhance the ability of T-cells, the body's immunity soldiers that attack and destroy cancerous cells."

First, the researchers identified bacterial species that were associated with colorectal cancer tumors when treated with immunotherapy. Working with germ-free mice, they then introduced these specific bacteria along with immune checkpoint blockade, a

type of cancer immunotherapy. Research revealed that specific bacteria were essential to the immunotherapy working. The tumors shrank, drastically. For those subjects that did not receive the beneficial bacteria, the immunotherapy had no effect.

"We found that these bacteria produce a small molecule, called inosine," says Dr. Lukas Mager, MD, Ph.D., senior postdoctoral researcher in the McCoy lab and first author on the study. "Inosine interacts directly with T-cells and together with immunotherapy, it improves the effectiveness of that treatment, in some cases destroying all the colorectal cancer cells."

The researchers then validated the findings in both bladder cancer and melanoma. The next step in this work will be to study the finding in humans. The three beneficial bacteria associated with the tumors in mice have also been found in cancers in humans.

"Identifying how microbes improve immunotherapy is crucial to designing therapies with anti-cancer properties, which may include microbials," says McCoy. "The microbiome is an amazing collection of billions of bacteria that live within and around us everyday. We are in the early stage of fully understanding how we can use this new knowledge to improve efficacy and safety of anti-cancer therapy and improve cancer patient survival and well-being."

Explore further

Could cancer immunotherapy success depend on gut bacteria?

More information: "Microbiome-derived inosine modulates response to checkpoint inhibitor immunotherapy" *Science* (2020). science.sciencemag.org/lookup/ ... 1126/science.abc3421

Journal information: Science

Provided by University of Calgary

---

8. ダウン症マウスがこの障害へのより良い理解へと導く

日付：2020 年 8 月 18 日
ソース：ジョンズホプキンズ大学医学部
概要：

ジョンズホプキンズ大学医学部の研究者らは、実験動物でシミュレートすることが最も困難な障害の 1 つと長い間考えられてきた、ダウン症候群の新しいマウスレプリカの作成に成功した。この研究結果は、6 月 29 日の *eLife Sciences* 誌に掲載されている。
TcMAC21 と名付けられたこれらのマウスは、それと分かる顔の構造、先天性心疾患の有病率の高さ、通常よりも小さい小脳、学習の困難など、人間のダウン症候群が示す多くの特性を示す。
研究者らは、単一の動物モデルが人間の状態を完全に再現することはできないと警告しているものの、この研究で開発された TcMAC21 マウスモデルは、ダウン症候群の人々を助けるための新しくより良い戦略を作成する良い出発点である、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＞https://www.eurekalert.org/pub_releases/2020-08/jhm-rsto81820.php

NEWS RELEASE 18-AUG-2020

RESEARCH STORY TIP: DOWN SYNDROME MICE OPEN DOOR TO BETTER UNDERSTANDING OF THE DISORDER

JOHNS HOPKINS MEDICINE

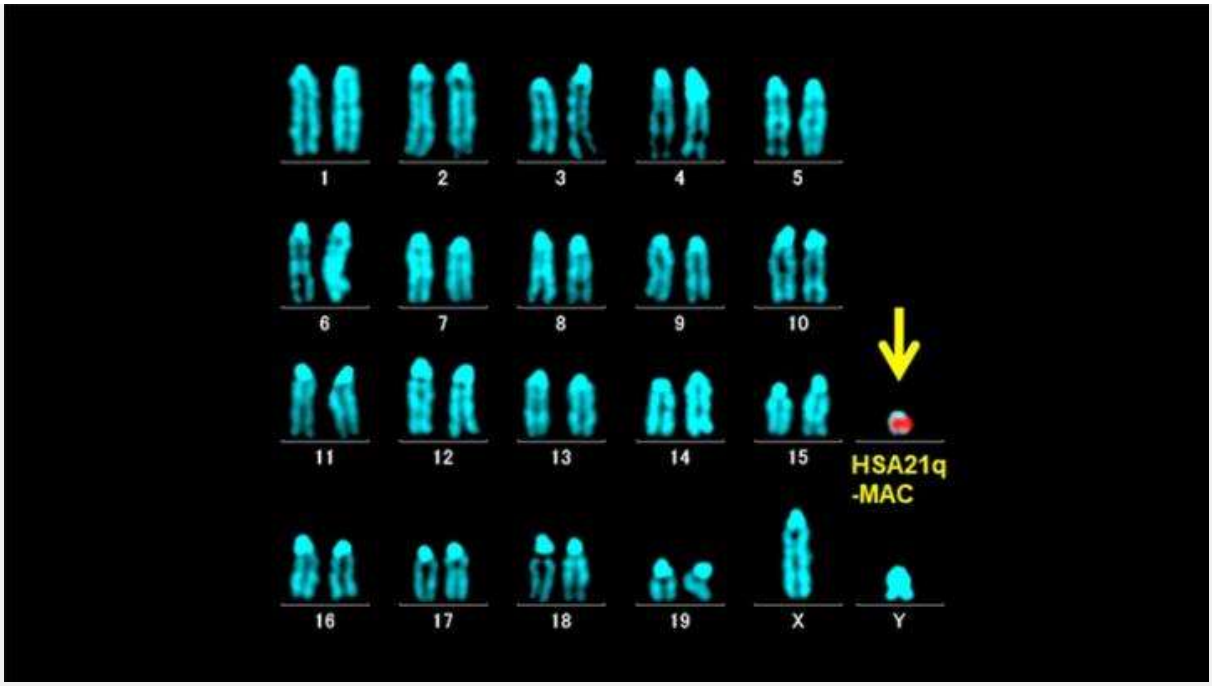


IMAGE: PHOTOGRAPH OF A KARYOTYPE - THE COLLECTION OF CHROMOSOMES WITHIN EACH CELL OF AN ORGANISM - FROM A MALE MOUSE ENGINEERED BY JOHNS HOPKINS MEDICINE RESEARCHERS TO MODEL DOWN SYNDROME... **view more**

CREDIT: JOHNS HOPKINS MEDICINE

Scientists across the globe often use mouse models in the study of human conditions to advance the pursuit of medicines and treatments. Now, Johns Hopkins Medicine researchers and their collaborators have created and characterized a new mouse replica of Down syndrome, long considered one of the most challenging disorders to simulate in laboratory animals.

A report of their research appeared June 29, 2020, in the journal *eLife* Sciences.

The new model may help researchers better understand how people with Down syndrome learn and develop, and eventually, lead to new therapies for potentially deadly complications of the condition, such as heart disease and thyroid problems.

Down syndrome, caused by trisomy 21, occurs when a person is born with an extra partial or entire copy of the 21st chromosome. Typically associated with distinct facial features and developmental delays, people with Down syndrome also experience difficulties with learning and memory, as well as higher rates of thyroid disease, blood and immune disorders and heart disease. Treating these conditions in people with Down syndrome is complicated by their genetics.

"There are more than 500 genes on chromosome 21 that can be overexpressed," says Roger Reeves, Ph.D., professor of physiology at the Johns Hopkins University School of Medicine. "So, in comparison to many other genetic conditions, Down syndrome is vastly more complex."

Further complicating the development of successful treatments is the lack of an accurate animal model to study the biology of Down syndrome and test potential therapies for conditions associated with it.

Reeves and his team endeavored to improve research efforts by creating a more precise replica of the condition in mice. They did this by inserting a human copy of chromosome 21 into mice using the rodent's own cellular structures that organize DNA. This enables the mouse cells to reliably copy and sort the extra human chromosome into new cells as they divide. It also lets the mice pass the additional genetic material on to their offspring.

This means that these mice, named TcMAC21 by the researchers, can be used relatively easily and at low cost in long-term experiments.

The resulting TcMAC21 mice have many characteristics indicative of Down syndrome in humans, including a distinct facial structure, a greater prevalence for congenital heart defects, a smaller-than-usual cerebellum and learning difficulties.

The researchers caution that no single animal model can perfectly replicate a human condition. However, they believe that the TcMAC21 mouse model developed in this study is a good starting point to create new and better strategies for helping people with Down syndrome.

"Our goal is to improve the health of people with Down syndrome to give them the best chance at achieving their full potential," says Reeves.

###

9. ゲノム解析により、多くの動物が新型コロナウイルス感染に対して脆弱である可能性が判明

日付：2020 年 8 月 21 日
ソース：カリフォルニア大学デービス校
概要：

カリフォルニア大学デービス校を中心とした国際チームの新しい研究によると、SARS-CoV-2、COVID-19 を引き起こす新型コロナウイルスの潜在的な脅威に直面している種は人間だけではない。SARS-CoV-2 が細胞に結合して細胞に侵入するために使用する主な受容体である ACE2（アンジオテンシン変換酵素 2）の分析は、鳥、魚、両生類、爬虫類、哺乳類を含む 410 の脊椎動物種にわたり、多くが新規コロナウイルスによる感染に感受性がある可能性があることを明らかにしている。その中には、絶滅危惧種や特に類人猿や霊長類も含まれる。
SARS-CoV-2 に感染する可能性のある種の約 40%は、国際自然保護連合によって「絶滅危惧種」と分類されており、特に人から動物への感染に対して脆弱である、としている。この研究は 8 月 21 日に全米科学アカデミー紀要に掲載された。
この発表の中で、ハイリスクのフラグが付けられた動物には、ゴリラ、スマトラオランウータン、テナガザル、コククジラやバンドウイルカなどの海洋哺乳類、およびチャイニーズハムスターなどが含まれる。猫、牛、羊などの家畜のリスクは中程度で、犬、馬、豚は ACE2 結合のリスクが低いことが判明した。ミンク、猫、犬、ハムスター、ライオン、トラにおいては、ウイルスは ACE2 受容体を使用している場合と、ACE2 以外の受容体を使用して宿主細胞にアクセスしている場合がある。
又、SARS-CoV-2 の直接の祖先はコウモリの種に由来している可能性があるとされているが、コウモリは、ACE2 受容体を介して新型コロナウイルスに感染するリスクが非常に低いことが判明している。

研究関連/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/08/200821161423.htm

GENOMIC ANALYSIS REVEALS MANY ANIMAL SPECIES MAY BE VULNERABLE TO SARS-COV-2 INFECTION

Date:

August 21, 2020

Source:

University of California - Davis

Summary:

Analysis of ACE2, the main receptor that SARS-CoV-2 uses to bind and enter cells, across 410 vertebrate species reveals that many are potentially susceptible to infection by the novel coronavirus. They include a number of endangered and threatened species, notably apes and old world primates. The study could also reveal potential intermediate hosts and animal models for the virus.

FULL STORY

Sumatran orangutan (stock image).

Credit: © Anton Petrus / stock.adobe.com

Humans are not the only species facing a potential threat from SARS-CoV-2, the novel coronavirus that causes COVID-19, according to a new study from the University of California, Davis.

An international team of scientists used genomic analysis to compare the main cellular receptor for the virus in humans -- angiotensin converting enzyme-2, or ACE2 -- in 410 different species of vertebrates, including birds, fish, amphibians, reptiles and mammals.

ACE2 is normally found on many different types of cells and tissues, including epithelial cells in the nose, mouth and lungs. In humans, 25 amino acids of the ACE2 protein are important for the virus to bind and gain entry into cells.

The researchers used these 25 amino acid sequences of the ACE2 protein, and modeling of its predicted protein structure together with the SARS-CoV-2 spike protein, to evaluate how many of these amino acids are found in the ACE2 protein of the different species.

"Animals with all 25 amino acid residues matching the human protein are predicted to be at the highest risk for contracting SARS-CoV-2 via ACE2," said Joana Damas, first author for the paper and a postdoctoral research associate at UC Davis. "The risk is predicted to decrease the more the species' ACE2 binding residues differ from humans."

About 40 percent of the species potentially susceptible to SARS-CoV-2 are classified as "threatened" by the International Union for Conservation of Nature and may be especially vulnerable to human-to-animal transmission. The study was published Aug. 21 in the *Proceedings of the National Academy of Sciences*.

"The data provide an important starting point for identifying vulnerable and threatened animal populations at risk of SARS-CoV-2 infection," said Harris Lewin, lead author for the study and a distinguished professor of evolution and ecology at UC Davis. "We hope it inspires practices that protect both animal and human health during the pandemic."

Endangered species predicted to be at risk

Several critically endangered primate species, such as the Western lowland gorilla, Sumatran orangutan and Northern white-cheeked gibbon, are predicted to be at very high risk of infection by SARS-CoV-2 via their ACE2 receptor.

Other animals flagged as high risk include marine mammals such as gray whales and bottlenose dolphins, as well as Chinese hamsters.

Domestic animals such as cats, cattle and sheep were found to have a medium risk, and dogs, horses and pigs were found to have low risk for ACE2 binding. How this relates to infection and disease risk needs to be determined by future studies, but for those species that have known infectivity data, the correlation is high.

In documented cases of SARS-COV-2 infection in mink, cats, dogs, hamsters, lions and tigers, the virus may be using ACE2 receptors or they may use receptors other than ACE2 to gain access to host cells. Lower propensity for binding could translate to lower propensity for infection, or lower ability for the infection to spread in an animal or between animals once established.

Because of the potential for animals to contract the novel coronavirus from humans, and vice versa, institutions including the National Zoo and the San Diego Zoo, which both contributed genomic material to the study, have strengthened programs to protect both animals and humans.

"Zoonotic diseases and how to prevent human to animal transmission is not a new challenge to zoos and animal care professionals," said co-author Klaus-Peter Koepfli, senior research scientist at Smithsonian-Mason School of Conservation and former conservation biologist with the Smithsonian Conservation Biology Institute's Center for Species Survival and Center for Conservation Genomics. "This new information allows us to focus our efforts and plan accordingly to keep animals and humans safe."

The authors urge caution against overinterpreting the predicted animal risks based on the computational results, noting the actual risks can only be confirmed with additional experimental data. The list of animals can be found here.

Research has shown that the immediate ancestor of SARS-CoV-2 likely originated in a species of bat. Bats were found to be at very low risk of contracting the novel coronavirus via their ACE2 receptor, which is consistent with actual experimental data.

Whether bats directly transmitted the novel coronavirus directly to humans, or whether it went through an intermediate host, is not yet known, but the study supports the idea that one or more

intermediate hosts was involved. The data allow researchers to zero in on which species might have served as an intermediate host in the wild, assisting efforts to control a future outbreak of SARS-CoV-2 infection in human and animal populations.

Additional authors on the study include: Marco Corbo, UC Davis Genome Center; Graham M. Hughes and Emma C. Teeling, University College Dublin, Ireland; Kathleen C. Keough and Katherine S. Pollard, UC San Francisco; Corrie A. Painter, Nicole S. Persky, Diane P. Genereux, Ross Swofford, Kerstin Lindblad-Toh and Elinor K. Karlsson, Broad Institute of MIT and Harvard, Cambridge, Massachussetts; Michael Hiller, Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany; Andreas R. Pfenning, Carnegie Mellon University, Pittsburgh; Huabin Zhao, Wuhan University, Wuhan, China; Oliver A. Ryder, San Diego Zoo Institute for Conservation Research, Escondido, and UC San Diego; Martin T. Nweeia, Harvard School of Dental Medicine, Boston, and Smithsonian Institution, Washington D.C.

The research in this study was coordinated as part of the Genome 10K Organization, which includes the Bat1K, Zoonomia, the Vertebrate Genomes Project and the Earth BioGenome Project. Genomic information for the study was also provided the National Center for Biotechnology Information's GenBank, the San Diego Zoo's Frozen Zoo and the Smithsonian's Global Genome Initiative. This work was supported by the Robert and Rosabel Osborne Endowment.

Story Source:

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

Journal Reference:

1. Joana Damas, Graham M. Hughes, Kathleen C. Keough, Corrie A. Painter, Nicole S. Persky, Marco Corbo, Michael Hiller, Klaus-Peter Koepfli, Andreas R. Pfenning, Huabin Zhao, Diane P. Genereux, Ross Swofford, Katherine S. Pollard, Oliver A. Ryder, Martin T. Nweeia, Kerstin Lindblad-Toh, Emma C. Teeling, Elinor K. Karlsson, Harris A. Lewin. **Broad host range of SARS-CoV-2 predicted by comparative and structural analysis of ACE2 in vertebrates**. *Proceedings of the National Academy of Sciences*, Aug. 21, 2020; DOI: 10.1073/pnas.2010146117

Cite This Page:

- MLA
- APA
- Chicago

University of California - Davis. "Genomic analysis reveals many animal species may be vulnerable to SARS-CoV-2 infection." ScienceDaily. ScienceDaily, 21 August 2020. <www.sciencedaily.com/releases/2020/08/200821161423.htm>.
