Bio News – July, 2024

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

5/31　肥満薬の全世界年間売り上げが 1,500 億ドルに達しうる

5/31　Biogen の筋萎縮性側索硬化症薬 Qalsody を欧州も承認

Biogen : EU Approves Qalsody To Treat Rare, Genetic Form Of Amyotrophic Lateral Sclerosis | Markets Insider (businessinsider.com)

5/31　Summit の PD-1 と VEGF の両取り抗体の肺癌治療が Merck の王者 Keytruda に勝利

Summit Therapeutics' Lung Cancer Therapy Ivonescimab Shows Improved Progression-Free Survival Versus Merck's Multi-Billion Keytruda In China Study (msn.com)

5/31　iPS 網膜特許利用巡り和解　初の臨床応用、元研究者と理研

人工多能性幹細胞（iPS 細胞）から作った網膜細胞の特許を巡り、元理化学研究所の高橋政代さんが代表を務めるベンチャー企業「ビジョンケア」（神戸市）は 31 日までに、特許を保有する理研やバイオベンチャー「ヘリオス」（東京都）などとの間で、一定の条件のもと特許権を利用できる内容で和解が成立したと発表した。
高橋さんは理研在籍時、iPS 細胞から作った網膜細胞を目の難病患者に移植する世界初の臨床応用に成功。退職して創業したビジョンケアでも治療などのために特許技術の利用を求めたが、協議が折り合わずに経済産業相への「裁定」を申し立てていた。
発表によると、和解成立は 30 日付。ビジョンケア側は裁定請求を取り下げたという。

6/1　BMS の年間 25 万ドルもかかる Krazati が肺癌進行を遅らせる期間はわずか 7 週間弱

Bristol's $250,000 Pill Slows Lung Cancer Growth by Seven Weeks - BNN Bloomberg

6/2　玄米の米糠に含まれる“γ-オリザノール”に認知機能改善の効果 -琉球大学の研究

6/3　より初期の転移性乳癌患者の無増悪生存が AstraZeneca/第一三共の Enhertu で 5 か月延長

Astra's Enhertu breast cancer trial shows 'unprecedented' results | Reuters

20240603_J.pdf (daiichisankyo.co.jp)

6/4　ゴキブリの求愛行動にフェロモンが果たす役割を解明 新しい駆除法に活路 -福岡大など

6/5　歯周病と虫歯の原因菌を 90 分で検出 広島国際大などが技術確立

歯周病と虫歯の原因菌を迅速に検出する技術を広島国際大学などのグループが確立した。これまで 4、5 日ほどかかっていたが、90 分で結果が分かるようにした。歯周病や虫歯の菌の中には全身の疾患に関与しているものが見つかっている。新技術を使えば健康診断や口腔検診の待ち時間の間に結果を伝えることができ、患者が口腔内環境のみならず、全身の状態にも気をつけるような行動変容が起きることを期待しているという。

6/6　パーキンソン病の原因物質、脳内の可視化に成功　治療法開発に期待

神経の難病「パーキンソン病」や「レビー小体型認知症」の原因物質が患者の脳内にたまっている様子を画像でとらえることに、量子科学技術研究開発機構（QST）などの研究チームが世界で初めて成

功した。アルツハイマー病のように、原因物質を標的とした治療法の開発につながると期待される。成果が日本時間の 6 日、米科学誌ニューロンに掲載される。

https://doi.org/10.1016/j.neuron.2024.05.006

6/6　BMS 、ローレンスビル拠点で大規模人員削減、1,000 人近くを解雇

ブリストル マイヤーズ スクイブは、今年始めに発表したコスト削減計画に基づき、ニュージャージー州ローレンスビル拠点で 1,000 人近くの人員を削減しており、約 2,200 人の従業員に影響する。
4 月に発表されたこの計画は、2025 年末までに約 15 億ドルの節約を目指しており、その 3 分の 2 は研究開発費によるものである。

Pharma Industry News and Analysis | FirstWord Pharma
BMS cuts to fall heavily on Lawrenceville site, with close to 1K job losses

6/7　GSK がオリゴヌクレオチド薬の Elsie（本社：カリフォルニア州サンディエゴ）を約 5,000 万ドルを払って手に入れる

After 11-month romance, GSK buys oligonucleotide partner Elsie (fiercebiotech.com)

6/7　Nestle が、糞から集めた細菌が中身の Seres（本社：マサチューセッツ州ケンブリッジ）の経口薬 Vowst の世界権利を買い取る

Nestle's health arm to buy first-ever fecal transplant pill | Reuters

6/8　新型コロナウイルス　沖縄で急拡大の兆候

6/8　中国研究チームが米粒より小さい「脳センサー」開発…手術なしで簡単に挿入、数週間で体内に吸収

米粒ほどの大きさのセンサーで脳の状態を診断できる技術が開発された。このセンサーは手術ではなく注射器を利用して簡単に挿入できるというのが特徴だ。この脳センサーはゼリーのような性質のもので、人間の体内に入った後は、一定の時間がたつと溶けてなくなる。
中国・華中科技大学電子科学科の臧剣鋒教授の研究チームは 5 日「脳の条件によって変わる無線ハイドロゲルセンサーを開発した」という研究結果を国際学術誌「ネイチャー」に発表した。

6/10　奥歯失うと認知症になるリスク増加か　九州大の研究グループ

奥歯のかみ合わせが失われるとアルツハイマー型認知症の発症リスクが高まるという研究結果を、九州大の研究グループがまとめた。2040 年に高齢の認知症患者数が 584 万人になるとの推計もある中、研究グループは奥歯のかみ合わせの維持が認知症予防につながると指摘している。

6/10　東大、国際下水疫学講座を開設　パンデミックに備え研究進める

https://www.t.u-tokyo.ac.jp/press/pr2024-06-06-002

6/11　暑さが止まらない…世界平均気温が 12 カ月連続で過去最高更新

EU の気象機関 Copernicus によると、5 月の世界平均気温が同月として過去最高を記録した。また、昨年 6 月から 12 カ月連続で観測史上最高記録を更新している。

6/11　Moderna のインフルとコロナ詰め合わせワクチン mRNA-1083 の Ph3 試験目標達成

Moderna COVID/flu combo vaccine superior to separate shots in trial | Reuters

6/11　FDA が招集した専門家が Eli のアルツハイマー病薬 donanemab を支持

FDA advisers endorse Eli Lilly's early-stage Alzheimer's drug donanemab | CNN

6/11　健康な人の腸内細菌を保管・治療に活用　「バンク」の運用始まる

難病の潰瘍性大腸炎の治療に取り組む順天堂大の医師らが設立したバイオベンチャー企業が今年 4 月、「腸内細菌バンク」の運用を始めた。患者の治療法の開発に役立てるため、健康な人から腸内細菌の提供を受けて保管する、国内では初の取り組みだという。

6/12　塩野義製薬がフランスの Cilcare の難聴薬候補 2 つの選択権利を取得

Cilcare and Shionogi Announce Exclusive Option Agreement for Innovative Hearing Disorder Treatments | European American Chamber of Commerce New York [EACCNY] | Your Partner for Transatlantic Business Resources

6/12　難病 ALS　治験患者の半数以上で進行食い止め　白血病の薬「ボスチニブ」治験結果を発表　『世界初』めざす iPS 研究所などの取り組み

全身の筋肉が次第に衰えていく難病のALS＝筋萎縮性側索硬化症の進行を、白血病の治療薬で食い止める可能性がある。実現すれば『世界初』とされる取り組みの第2相試験の結果を、京都大学iPS細胞研究所などが発表。

6/13　医療や生命科学へ投資する Foresite Capital が 6 回目の集金で 9 億ドル調達

Foresite Capital Closes $900 Million Life Sciences Venture Fund - WSJ

6/13　ギリシャで観測史上最も早い熱波 アクロポリス一時閉鎖

6/13　干ばつ深刻化のメキシコ 湖で魚が大量死

6/14　機能性成分が青カビで変化　紅麹問題「未知の成分」、国の解析で判明

小林製薬の紅麹（こうじ）サプリの問題で、プベルル酸以外に「未知の成分」とされた二つの物質の化学的な構造を、国立医薬品食品衛生研究所（国衛研）が小林製薬と近畿大と共同で解明し、論文に発表した。この 2 物質は、紅麹サプリの効能にも関わる「機能性成分」そのものが、青カビの作用で変化してできたものと見られる。
2 物質の構造がわかったことで、毒性や機能性成分がどの程度変化したのかなどの解析がしやすくなる。論文はジャーナル・オブ・ナチュラル・メディシンズに掲載された（https://doi.org/10.1007/s11418-024-01827-w）。

6/14　AbbVie が中国 FutureGen の前臨床段階の TL1A 標的抗体 FG-M701 の権利取得

AbbVie inks immune disorder drug licensing deal with China's FutureGen | Reuters

6/14　Pfizer が Flagship 傘下の ProFound（本社：マサチューセッツ州ケンブリッジ）と協力して肥満薬を見つける

Pharma Industry News and Analysis | FirstWord Pharma
Pfizer makes obesity its first pick under Flagship partnership

6/14　JPMorgan が肥満薬への投資資金 5 億ドル強を集めた

JPMorgan to wager on GLP-1 boom with $500M fund | Crain's New York Business (crainsnewyork.com)

6/14　国立衛生研究所部長、論文・審査書類の不正で停職 3 カ月　本人は辞職

国立医薬品食品衛生研究所は 14 日、論文捏造などの不正をしたとして前食品衛生管理部長が停職 3 カ月の懲戒処分となったと発表した。前部長は同日付で辞職。研究歴 20 年のベテランだったといい、国衛研は「コンプライアンス教育を徹底し、再発防止策を着実に実施する」とコメントした。
国衛研によると、前部長は 2021 年発表の鶏肉のカンピロバクター食中毒に関する論文で、実際の研究データと異なる内容を記載し捏造した。また、部長として着任した 16 年以降、病原体を扱う施設で取得した品質管理の国際規格「ISO/IEC17025」の審査資料で、内部監査や会議の記録をでっち上げるなどした。

6/14　「未来医療」の産業化拠点 Nakanoshima Qross が完成、現地で内覧会

医療機関と企業、スタートアップ、支援機関などが集う「未来医療」の産業化拠点、「Nakanoshima Qross（中之島クロス）」が大阪市北区中之島に完成。2024 年 6 月 29 日のグランドオープンを前にこのほど内覧会が行われた。入居する企業や医療機関などが連携し、再生医療をベースにゲノム医療や AI（人工知能）、IoT（モノのインターネット：あらゆるものをインターネットに接続する技術）活用など、医療技術の進歩に即応した「未来医療」の産業化を推進し、国内外の患者に提供することを通じて国際貢献を目指す。

6/14　国際卓越大に東北大を正式認定へ　政府ファンドまず約 100 億円支援

世界トップレベルの研究力をめざす「国際卓越研究大学」に、東北大が正式に認定される見通しになった。文部科学省の有識者会議が 14 日、同大の計画が認定の水準を満たすと認めた。政府がつくった 10 兆円規模の大学ファンドから、初年度に約 100 億円の支援を受ける見通し。
卓越大の初の公募には東京大など 10 大学が応じ、昨年 9 月、東北大だけが候補に選ばれていた。その際、条件付きの選定であるとして、有識者会議は「大学全体の研究力向上の道筋」などについて計画の見直しを要求。東北大は「人文社会科学を中心とした価値創造戦略」「ガバナンス進化」などの体制強化を盛り込んだ改訂版を示し、今回妥当と認められた。

6/16　梅毒感染、10 代妊婦の「200 人に 1 人」 胎児感染は近年で最多に

6/17　武田薬品が Ascentage（本社：メリーランド州ロックビル）の BCR-ABL 阻害薬の選択権利を 1 億ドルで取得

Takeda Signs Option Agreement with Ascentage Pharma to Enter into Exclusive Global License for Olverembatinib, a Third-Generation BCR-ABL Tyrosine Kinase Inhibitor (TKI) | Business Wire

6/17　生殖細胞が寿命に影響　短命小魚で遺伝子操作実験　−大阪大

寿命が半年弱しかないアフリカ原産の小型淡水魚を対象に、受精卵が成長した胚の段階で精子や卵子をできなくする遺伝子操作実験を行ったところ、雄は寿命が延び、雌は縮む結果となった。大阪大と九州大、群馬大の研究チームが 16 日までに米科学誌サイエンス・アドバンシズに発表した。
大阪大微生物病研究所の石谷太教授は「寿命に生殖細胞が関与していることが示された。人を含む多くの動物で寿命に雌雄の差があるメカニズムを解明する手掛かりになる」と話している。

6/18　武田薬品が Ovid（本社：ニューヨーク）から手に入れたてんかん薬 Soticlestat の Ph3 試験 2 つとも失敗

Ovid Therapeutics Reports on Takeda's Announcement of Phase 3 Topline Study Results for Soticlestat | BioSpace

武田薬品が Ovid Therapeutics から手に入れたてんかん薬 Soticlestat（ソチクレスタット；TAK-935/OV935）の Ph3 試験 2 つ・SKYLINE と SKYWAY のどちらも目標に至らなかった。

6/18　水分不足は腸内環境を悪化させ、感染症にかかりやすくする 北里大などマウスで解明

水分摂取を制限したマウスは、通常のマウスに比べて便通が悪くなるだけではなく、腸内細菌のバランスが崩れ、病原菌の排出にも時間がかかることを、北里大学などの研究グループが明らかにした。水分量を通常の半分に減らすと、腸の免疫に著しい乱れが生じ、感染症にかかりやすいことが確認できた。今後はヒトでも同様の結果が生じるかどうかを調べるという。

6/18　長寿の秘訣は「卵子」にあり　オスは「精子」で短命に…大阪大研究チームが魚で実験

卵子があると生物の寿命が延び、精子は縮める－。こんな研究結果について、大阪大微生物病研究所の石谷太教授らの研究チームが発表した。ヒトを含む多くの動物ではオスよりもメスの方が寿命が長いことが知られる。チームは「今回精子と卵子が生き物の寿命の長さに影響することが初めて明らかになった。ヒトの寿命の違いにも関係しているのではないかとしており、今後健康寿命延伸につながる研究への応用が期待される。
実験はアフリカ原産の淡水魚「ターコイズキリフィッシュ」（体長約 4 センチ）を使って実施。平均寿命はオスが約 120 日、メスが約 145 日と他の魚に比べても短命で知られ、人間と同じように加齢とともに筋肉が痩せたり、色素が薄くなったりする。実験では、精巣や卵巣を残す一方で、精子や卵子といった生殖細胞を取り除いたオスとメスの稚魚を育てて、通常のキリフィッシュとの寿命を比較。いずれも通常よりも体のサイズが大きくなるとともに、オスは筋肉の再生能力や骨の量が維持されていた上、平均寿命が 13%延びた。また、体内では長寿に関係すると注目を集めるビタミン D の生成も活発になっていた。メスの場合、卵子がないと平均寿命は 6.6%短縮した。
今回は生まれつき生殖細胞がない場合で実験しており、成長過程での生殖細胞の有無が寿命にもたらす影響は不明。石谷氏は「寿命をコントロールするのが成熟した生殖細胞なのか未分化のものかは分かっておらず、解明は今後の課題だ」と話した。また、チームは精子がないオスの体内に生成されていたビタミン D が、老化を防止するのではないかという点に着目。通常のキリフィッシュにビタミン D を投与したところ、オスの平均寿命が 21%、メスは 7%延び、石谷氏は「老化を抑制することが示唆された」と説明した。
研究結果は米科学誌電子版に掲載された。

6/19　京都賞に透明マント考案、全球凍結研究など 3 氏 稲盛財団

稲盛財団（京都市、金澤しのぶ理事長）は 2024 年の京都賞を、自然界の物質にない性質を持つ人工物質「メタマテリアル」の理論を築き、物体を見えなくする透明マントなどを考案した英インペリアル・カレッジ・ロンドン教授のジョン・ペンドリー氏（80）と、全地球表面が凍りついた「全球凍結」を解明し、またプレートテクトニクスが地球史の前半から起きていたことを実証した米ハーバード大学名誉教授（カナダ・ビクトリア大学客員教授）のポール・ホフマン氏（83）ら 3 氏に贈ると発表した。

6/19　英研究所のコスタンザ教授らにブループラネット賞、地球環境に貢献　旭硝子財団が決定

旭硝子財団（島村琢哉理事長）は 19 日、地球環境問題の解決に向けて貢献した個人や組織をたたえる 2024 年（第 33 回）ブループラネット賞に、経済は有限な生物圏の一部と考える「生態経済学」の基礎を築いた英ユニバーシティ・カレッジ・ロンドン、グローバル・プロスペリティ研究所のロバート・コスタ

ンザ教授と、生物多様性および生態系サービスに関する政府間科学―政策プラットフォーム（IPBES）を選んだと発表した。表彰式は 10 月 23 日、東京都千代田区の東京会館で行う予定。

6/20　FDA が潰瘍性大腸炎への AbbVie の Skyrizi 使用を承認

Pharma Industry News and Analysis | FirstWord Pharma
AbbVie bags expanded FDA nod for Skyrizi in ulcerative colitis

6/21　臓器のための簡単な接着材開発 外科手術短縮へ －岡山大など

外科手術時に臓器同士を簡単に接合したり外したりできる接着材を、岡山大学などの研究グループが開発した。これまで臓器を「貼り合わせる」際は主に縫う方法を採っていたが、高度な技術がなくても迅速に接着できて、大量の水を注げば、組織を傷つけることなくはがすことが可能だ。実用化すれば、手術時間の短縮につながるとともに、次世代に向けた体内埋め込み型デバイスの固定や脱着に使うこともできそうだという。

6/21　蚊の吸血止める分子発見　危険避け「腹八分目」で　－理研など

蚊には、人間や動物の皮膚で血を吸う時間が長引くと攻撃される危険があるため、満腹になる前に吸血をやめる習性がある。この習性を巡り、理化学研究所と東京慈恵会医科大の研究チームは、血液中の分子が、蚊に「腹八分目」で吸血を止めさせるシグナルになっていることを突き止めた。
20 日付の米科学誌セル・リポーツ電子版に発表した。蚊の吸血行動を制御する仕組みの解明は、感染症抑制などへの応用が期待できるという。

6/24　武田薬品の大腸癌薬 Fruzaqla を米国に続いて欧州も承認

Pharma Industry News and Analysis | FirstWord Pharma
EU okays Takeda's Fruzaqla as first new targeted mCRC therapy in over a decade

6/25　英国が高齢者や妊婦に Pfizer の呼吸器合胞体ウイルス（RSV）ワクチンを接種

英国の高齢者や妊婦に GSK のではなく Pfizer の呼吸器合胞体ウイルス（RSV）ワクチン Abrysvo（アブリスボ）が接種される。英国の 75～79 歳高齢者と妊婦への Abrysvo の接種が今秋 9 月 1 日から始まる。妊婦への接種は生まれてくる子の感染を防ぐことを目的とする。
英国での出番争いでは敗れたが、GSK の Arexvy の去年の売り上げは 15 億ドルほどで、Pfizer の Abrysvo に勝っている。ちなみに Abrysvo の去年の売り上げは 8 億 9,000 万ドル。

Older people and pregnant women to be offered new NHS respiratory virus jab | Evening Standard

6/26　生きた皮膚を持つ笑うロボット、東大が開発　医療・美容分野での応用期待

人間の皮膚から培養した細胞を使った、生きた皮膚を持つロボットの顔を開発したと、東京大の研究チームが発表した。論文が 26 日、米科学誌に掲載された。笑顔を作る実験にも成功し、医療や美容分野での応用が期待できるという。

6/26　過敏性肺炎の原因カビ菌抑制にナノイーが効果　パナソニックが検証、99%以上殺菌

パナソニックは、大阪公立大学・向本雅郁名誉教授の監修の下、過敏性肺炎の主な原因となるカビ、トリコスポロンなどに対するナノイー(帯電微粒子水)の殺菌効果を確認した。45 リットルの試験空間の中で、ナノイーを照射した結果、99%以上の殺菌効果が判明し、ナノイー技術が夏型過敏性肺炎への対応策の一つの手段として期待が高まる結果となった。

6/27　大腸菌の大規模ゲノム組み換え解明　−東京大など

大腸菌の中で大規模に DNA が組み換わる仕組みを解明したと、東京大と米アーク研究所のチームが発表した。この仕組みを応用すれば、生命の設計図とされるゲノムを桁違いの規模で改変・生成できる次世代のゲノム編集技術につながる可能性がある。

6/28　Merck/第一三共の肺癌薬 patritumab deruxtecan を FDA が承認せず

Merck's ADC Pact With Daiichi Hits Regulatory Setback in FDA Rejection | BioSpace

6/28　AbbVie が炎症性腸疾患治療 TREM1 阻害抗体の Celsius（本社：マサチューセッツ州ケンブリッジ）を 2 億 5,000 万ドルで買収

AbbVie turns up the heat with $250M Celsius buy (fiercebiotech.com)

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. 心不全の原因が女性と男性で異なる可能性
   マウス研究で、拡張性心不全（HFpEF）の細胞レベルでの性差が特定される

2. 新たな予防戦略への道を開く、アレルギー反応の第一歩

3. マウスの損傷した心臓細胞の再生

4. 老齢マウスの腸内細菌で若いマウスが炎症を引き起こす

5. 出生前のリスク要因によって雄マウスの生殖腺機能が損なわれる

6. 抗癌剤がパーキンソン病を引き起こすタンパク質のつながりを標的とするのに使用できる可能性 −マウス実験

7. ADGRF5 の役割を解明: 腎臓の健康と機能に関する洞察 −マウス実験

8. 腸内の特定の細菌が過食と肥満に関係 −マウス実験
   新しい研究で、脳と腸がどのように対話しているかが明らかに

1. 心不全の原因が女性と男性で異なる可能性
マウス研究で、拡張性心不全（HFpEF）の細胞レベルでの性差が特定される

日付：2024 年 5 月 30 日
ソース：カリフォルニア大学デービス校医療センター
概要：

心不全は、心臓が十分な血液と酸素をポンプすることができない状態であり、約 620 万人のアメリカ人が罹患している。心不全の 5 年死亡率は約 50%だが、生存には多くの要因が影響する。心不全の約半数が HFpEF（駆出率が保持された心不全―拡張性心不全）を患っており、HFpEF を患っている女性の割合は男性のほぼ 2 倍である。この心不全のある男性は、心臓不整脈や突然の心臓死のリスクがより高い。
UC デービス医療センターの新しい研究では、HFpEF の雄と雌のマウス間で細胞レベルでの顕著な違いが見付かった。雌の場合、心臓のフィラメントタンパク質の変化により収縮機能不全が引き起こされた。一方、雄の場合は、心臓細胞からのカルシウムの除去が遅れ、収縮が残った。これらの結果は、HFpEF の治療が性別によって異なる可能性があることを示唆しており、これらの発見によって、女性と男性の HFpEF の治療がどのように異なるかを決定する可能性がある、としている。
これらの結果は、『Cardiovascular Research』誌に掲載されている。

研究関連ニュース/他のトップページに戻る

＜英文＞Cause of heart failure may differ for women and men | ScienceDaily

Cause of heart failure may differ for women and men

Mouse study identifies sex differences at the cellular level for heart failure with preserved ejection fraction (HFpEF)

Date:

May 30, 2024

Source:

University of California - Davis Health

Summary:

A mouse study of heart failure with preserved ejection fraction (HFpEF) found male-female differences at the cellular level. The findings could have implications for how HFpEF is treated in women compared to men.

FULL STORY

A new study from the UC Davis School of Medicine found striking differences at the cellular level between male and female mice with heart failure with preserved ejection fraction (HFpEF).

The findings could determine how HFpEF is treated in women compared to men.

With HFpEF, the heart muscle contracts normally but the heart is unable to fully relax and refill properly between beats. This condition is known as diastolic dysfunction. It can occur if the heart is too stiff or if the contraction process doesn't shut off quickly enough between beats.

The study showed that the diastolic dysfunction in female mice resulted from altered heart filament proteins. In male mice, it resulted from the slow removal of calcium from heart cells between heartbeats, causing a slight contraction to remain between beats.

The findings were published in *Cardiovascular Research.*

"This study demonstrates the importance of conducting research on both male and female populations," said Donald M. Bers, a senior author of the study. Bers is the chair of the Department of Pharmacology and the Joseph Silva Endowed Chair for Cardiovascular Research at the UC Davis School of Medicine. "If these same molecular male-female distinctions occur in obese diabetic patients with HFpEF, it may mean that the best therapeutic strategies for HFpEF in women may differ from those for men."

Heart failure is when the heart cannot pump enough blood and oxygen to support the body. Approximately 6.2 million people in the U.S. have heart failure. The five-year mortality rate for heart failure is around 50%, although many factors can influence survival. About half of those with heart failure have HFpEF, and almost twice as many women have HFpEF compared to men. Men with the heart failure may be more at risk of cardiac arrhythmias and sudden cardiac death.

"Two hit" mouse model to study HFpEF

Obesity and diabetes are common in people with HFpEF. To study the disease, the researchers created a unique "two-hit" mouse model combining two factors.

For the first factor, the researchers used mice genetically lacking a leptin receptor. Leptin is a hormone that promotes satiety. Without it, appetite remains high and the animals become obese and diabetic. For the second factor, mice were exposed to an aldosterone infusion. Aldosterone is a hormone made by the adrenal gland. High levels of aldosterone cause fluid retention.

This animal model of heart failure and diabetes develops HFpEF, allowing researchers to analyze the cellular and molecular mechanisms of muscle contraction and relaxation in male and female mice.

The research team (left to right): Christopher Y. Ko, Juliana Mira Hernandez, Donald M. Bers, Erin Y. Shen and Bence Hegyi in in front of their key findings on the screen.

Dysregulation of calcium, titin

Calcium is critical in the activation of contraction and relaxation of heart muscle cells as well as the heart's electrical activity. Calcium entering the heart cell at each beat causes the muscle to contract. It also helps drive the electric signal that synchronizes the contraction of the millions of heart muscle cells required for the heart to function as an efficient pump. Calcium is removed from the cell at each beat. This allows the heart to relax between beats and fill for the next beat.

In the male mice with HFpEF, the calcium removal from the heart muscle cells was slowed, preventing complete relaxation between beats. The male HFpEF mice also exhibited more abnormal heart rhythms, known as arrhythmias.

In contrast, the females with HFpEF exhibited normal calcium movements into and out of the heart cells. Instead, the researchers observed an increase in a shorter and stiffer form of titin (N2B). Titin is a protein in the heart that acts like a supportive spring. Researchers also observed phosphorylation (a molecular reaction) of titin and another heart filament protein, troponin I. Both the titin and troponin changes made the female heart cells functionally stiffer -- making the heart harder to fill -- even though calcium removal was normal.

"This study reveals different drug targets in males and females and will be a stepping-stone for future trials with sex-specific targeted drugs in HFpEF," said Bence Hegyi, an associate project scientist in the Bers Lab and co-senior author of the study. "Potentially, women with this form of HFpEF could benefit from drugs that reduce cardiac stiffness. On the other hand, men with this form of HFpEF might benefit more from drugs that enhance calcium removal."

Limitations

The researchers noted several limitations of the study. Although the mice in this study may be representative of the substantial number of HFpEF patients who have diabetes and are quite obese, many HFpEF patients may not be represented by this model. Multiple animal models will be needed to understand different subpopulations with HFpEF. Additional preclinical and clinical studies are needed to fully realize the potential benefits of this work.

Additional authors include Erin Shen, Christopher Ko, Emily Spencer, Daria Smoliarchuk and Julie Bossuyt from the UC Davis School of Medicine; Juliana Mira Hernandez from the UC Davis School of Medicine and the University of Antioquia, Medellin, Colombia; and Zaynab Hourani and Henk Granzier from the University of Arizona, Tucson.

Story Source:

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

Journal Reference:

1. Juliana Mira Hernandez, Erin Y Shen, Christopher Y Ko, Zaynab Hourani, Emily R Spencer, Daria Smoliarchuk, Julie Bossuyt, Henk Granzier, Donald M Bers, Bence Hegyi. **Differential sex-dependent susceptibility to diastolic dysfunction and arrhythmia in cardiomyocytes from obese diabetic heart failure with preserved ejection fraction model**. *Cardiovascular Research*, 2024; DOI: 10.1093/cvr/cvae070

2. 新たな予防戦略への道を開く、アレルギー反応の第一歩

日付：2024 年 6 月 3 日
ソース：デューク-NUS メディカルスクール
概要：

デューク-NUS メディカル スクールの科学者らは、ピーナッツ、貝類、花粉、ダニなどのアレルゲンに人が遭遇した後、最初のドミノ倒しがどのように起こるかを特定した。『Nature Immunology』誌の 4 月号に掲載されたこの発見は、これらの重篤な反応を防ぐ薬の開発の先駆けとなる可能性がある。
世界保健機関（WHO）によると、世界人口の 10%以上が食物アレルギーに苦しんでいる。また、アレルギー率が上昇し続けるにつれて、食物によって引き起こされるアナフィラキシーや喘息の発生率も増加している。
デューク-NUS のチームが今回発見したのは、これらの生物活性化学物質を含む粒子状マスト細胞顆粒の放出が、インフラマソームと呼ばれる細胞内多タンパク質複合体の 2 つのメンバーによって制御されていることである。これまで、これらのインフラマソームタンパク質については、感染を検知すると免疫細胞内で自発的に集まり、可溶性化学物質を分泌して免疫系の他の部分に警告を発することしか知られていなかった。
研究者らは、肥満細胞の NLRP3 と ASC タンパク質が集まって個々の細胞内顆粒に結合し、顆粒小体と呼ぶ複合体を形成し、肥満細胞内の細胞骨格によって形成された軌道に沿って顆粒が移動しやすくなったときに、アナフィラキシーショックが観察され、肥満細胞に 2 つのインフラマソームタンパク質である NLRP3 または ASC のいずれかが欠けているマウスでは、アレルゲンにさらされてもアナフィラキシーショックを経験することはない、ということを発見した。
NLRP3 と ASC の輸送役割が判明した後、研究チームは既知のインフラマソーム阻害剤に目を向け、この現象を阻止できるかどうかをテストした。慢性炎症性疾患の臨床試験が行われているものと非常によく似たインフラマソーム阻害薬（CY-09 と呼ばれる）を使用して、アレルゲンを導入する前にマウスに治療を施したところ、前臨床モデルでは、この薬でアナフィラキシーショックを効果的に予防できることがわかった。
これは治療法ではないが、重度のアレルギーを持つ人に、潜在的に外傷的な反応の発症を防ぐための新しい手段を提供する可能性がある、としている。

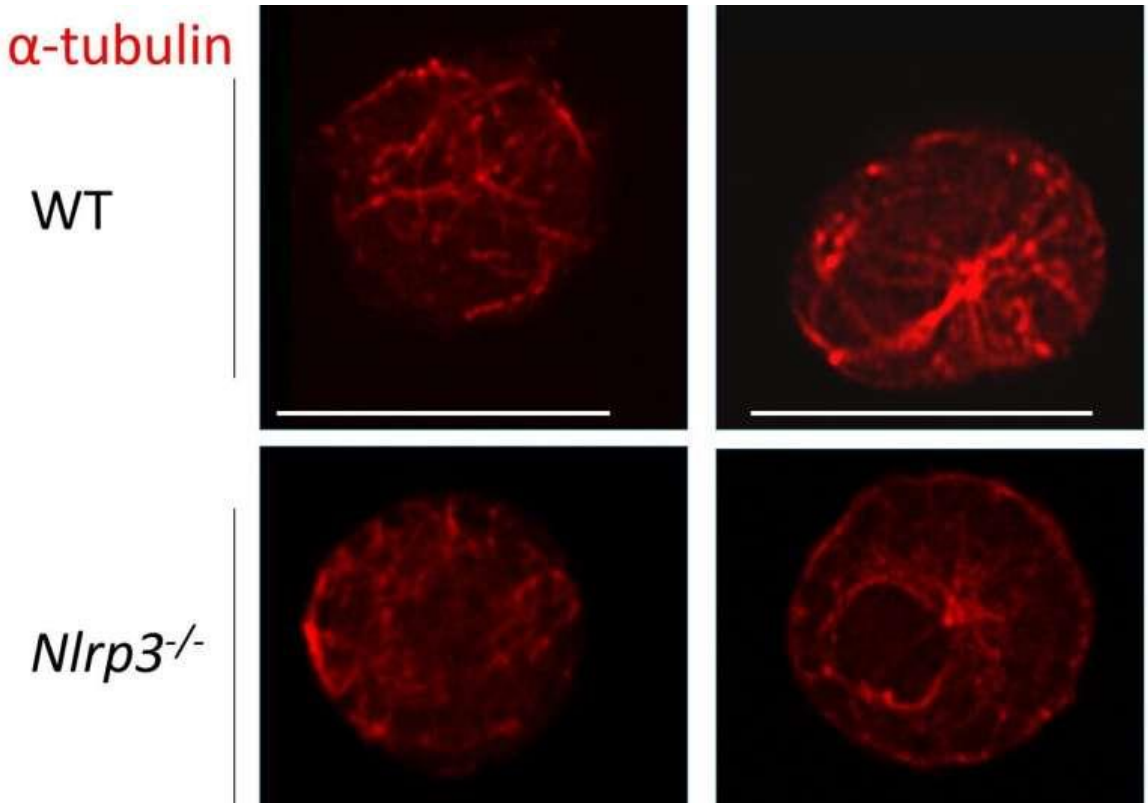
研究関連ニュース/他のトップページに戻る

＜英文＞Researchers identify first step in allergic reactions, paving the way for preventative strategies (medicalxpress.com)

JUNE 3, 2024

Researchers identify first step in allergic reactions, paving the way for preventative strategies

by Duke–NUS Medical School



When NLRP3 and ASC are present in mast cells, the microtubules within the activated mast cells become highly organised within 10 mins of activation with several strands emanating from the microtubule-organizing center and radiating towards the cell surface providing "railtracks" on which granules are conveyed (top row). In contrast, within 10 min of activation, limited organized microtubules were observed in mast cells deficient in either NLRP3 (Nlrp3-/-) (middle row) or ASC (Asc-/-) (bottom row). Credit: Andrea Mencarelli

Scientists at Duke–NUS Medical School have identified how the first domino falls after a person encounters an allergen, such as peanuts, shellfish, pollen or dust mites. Their discovery, published in the journal *Nature Immunology,* could herald the development of drugs to prevent these severe reactions.

It is well established that when mast cells, a type of immune cell, mistake a harmless substance, such as peanuts or dust mites, as a threat, they release an immediate first wave of bioactive chemicals against the perceived threat. When mast cells, which reside under the skin, around blood vessels and in the linings of the airways and the gastrointestinal tract, simultaneously release their pre–stored load of bioactive chemicals

into the blood, instant and systemic shock can result, which can be lethal without quick intervention.

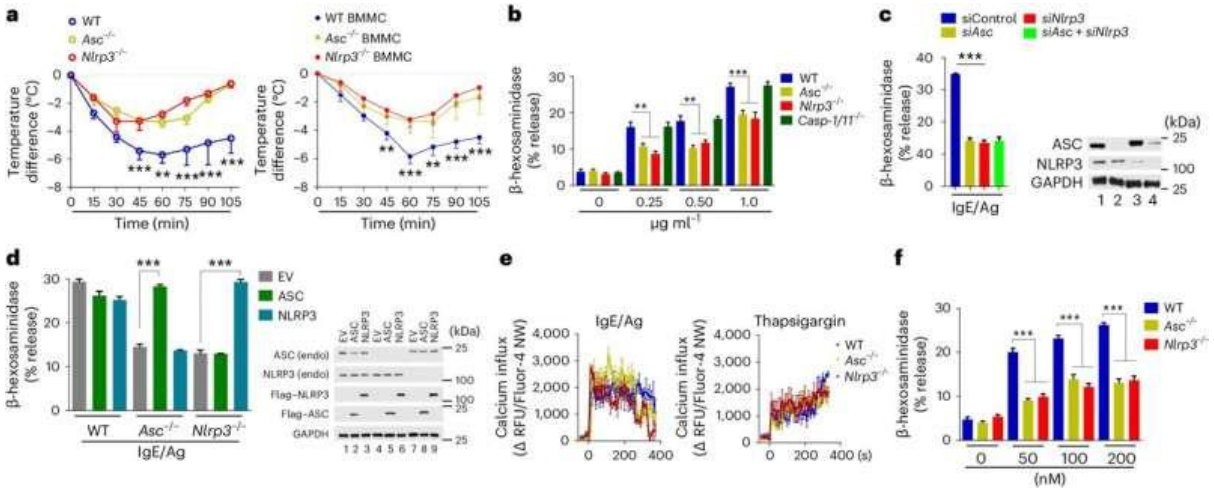
More than 10% of the global population suffers from food allergies, according to the World Health Organization (WHO). As allergy rates continue to climb, so does the incidence of food-triggered anaphylaxis and asthma worldwide. In Singapore, asthma affects one in five children while food allergies are already the leading cause of anaphylactic shock.

What the team at Duke-NUS has now discovered is that the release of particulate mast cell granules, which contain these bioactive chemicals, is controlled by two members of an intracellular multiprotein complex called inflammasome. Until now, these inflammasome proteins were only known to spontaneously assemble within immune cells to secrete soluble chemicals to alert other parts of the immune system upon detection of an infection.

Professor Soman Abraham, Grace Kerby Distinguished Professor of Pathology at Duke University, who led this research when working in Duke-NUS' Emerging Infectious Diseases Programme, said, "We discovered that the inflammasome components played a surprisingly crucial role in transporting particulate mast cell granules which are typically packed in the cell center to the cell surface where they are released. This surprising discovery gives us a precise target where we can intervene to prevent the cascade of events initiated in mast cells that leads to anaphylactic shock."

Prof Abraham and his team's eureka moment came while observing mice whose mast cells lacked either of the two inflammasome proteins, NLRP3 or ASC. When these animals were exposed to allergens, they failed to experience anaphylactic shock.

However, anaphylactic shock was observed when mast cell NLRP3 and ASC proteins assembled and bound to individual intracellular granules, forming a complex the researchers call granulosum, facilitating the granules' movement along tracks formed by the cytoskeleton within the mast cell—akin to hooking them onto a set of "rail tracks."



Inflammasome components mediate MC degranulation following IgE–Ag stimulation.
Credit: *Nature Immunology* (2024). DOI: 10.1038/s41590-024-01788-y

Dr. Pradeep Bist, co–first author of the paper and a principal research scientist with Duke–NUS' Emerging Infectious Diseases Programme, said, "Upon mast cell activation, we observed rapid granule movement on dynamic tracks known as microtubules to the cell membrane, where these granules were promptly released from the cell. However, in mast cells deficient in either NLRP3 or ASC proteins, we found no sign of intracellular granule movement and none of these granules were released."

More information: Andrea Mencarelli et al, Anaphylactic degranulation by mast cells requires the mobilization of inflammasome components, *Nature Immunology* (2024). DOI: 10.1038/s41590-024-01788-y

Journal information: Nature Immunology

Provided by Duke-NUS Medical School

Explore further

Study identifies key role for nervous system in severe allergic shock

3. マウスの損傷した心臓細胞の再生

日付：2024 年 6 月 6 日
ソース：Ann & Robert H. Lurie Children's Hospital of Chicago
概要：

シカゴのアン & ロバート H. ルーリー小児病院のスタンレー・マン小児研究所の科学者らによる研究によって、マウスの心臓の損傷した筋肉細胞を再生する方法が発見された。この研究は、先天性心臓疾患を持つ子供や心筋梗塞で被害を受けた成人の治療に新たな手段を提供する可能性があるとして、『Journal of Clinical Investigation』誌に掲載されている。
胎児期の心筋細胞は出生後に再生できるが、成長とともにこの能力を失う。研究者らは、成体哺乳類の心筋細胞が再びこの再生能力を持つように戻れるかを理解しようとした。胎児心筋細胞はミトコンドリアを通じて細胞エネルギーを生成するのではなく、グルコースで生存するため、研究者らは成体マウスの心臓でミトコンドリア関連遺伝子 UQCRFS1 を削除し、胎児のような状態に戻るようにした。そして成体マウスの心臓組織の損傷部位では、この UQCRFS1 が阻害されると、心臓細胞が再生を開始した。
この発見は、成体の心臓細胞でも細胞分裂と成長が可能になることを示唆しており、このアプローチが、心臓細胞の損傷修復の新しい方向性を提供する可能性がある、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞Regenerating damaged heart cells in mice | ScienceDaily

Regenerating damaged heart cells in mice

Date:

June 6, 2024

Source:

Ann & Robert H. Lurie Children's Hospital of Chicago

Summary:

Scientists have discovered a way to regenerate damaged heart muscle cells in mice, a development which may provide a new avenue for treating congenital heart defects in children and heart attack damage in adults, according to a new study.

FULL STORY

Scientists from Stanley Manne Children's Research Institute at Ann & Robert H. Lurie Children's Hospital of Chicago have discovered a way to regenerate damaged heart muscle cells in mice, a development which may provide a new avenue for treating congenital heart defects in children and heart attack damage in adults, according to a study published in the *Journal of Clinical Investigation*.

Hypoplastic left heart syndrome, or HLHS, is a rare congenital heart defect that occurs when the left side of a baby's heart doesn't develop properly during pregnancy. The condition affects one in 5,000 newborns and is responsible for 23 percent of cardiac deaths in the first week of life.

Cardiomyocytes, the cells responsible for contracting the heart muscle, can regenerate in newborn mammals, but lose this ability with age, said senior author Paul Schumacker, PhD, Patrick M. Magoon Distinguished Professor in Neonatal Research at Lurie Children's and Professor of Pediatrics, Cell and Molecular Biology, and Medicine at Northwestern University Feinberg School of Medicine.

"At the time of birth, the cardiac muscle cells still can undergo mitotic cell division," Dr. Schumacker said. "For example, if the heart of a newborn mouse is damaged when it's a day or two old, and then you wait until the mouse is an adult, if you look at the area of the heart that was damaged previously, you'd never know that there was damage there."

In the current study, Dr. Schumacker and his collaborators sought to understand if adult mammalian cardiomyocytes could revert to that regenerative fetal state.

Because fetal cardiomyocytes survive on glucose, instead of generating cellular energy through their mitochondria, Dr. Schumacker and his collaborators deleted the mitochondria-associated gene UQCRFS1 in the hearts of adult mice, forcing them to return to a fetal-like state.

In adult mice with damaged heart tissue, investigators observed that the heart cells began regenerating once UQCRFS1 was inhibited. The cells also began to take in more glucose, similar to how fetal heart cells function, according to the study.

The findings suggest that causing increased glucose utilization can also restore cell division and growth in adult heart cells and may provide a new direction for treating damaged heart cells, Dr. Schumacker said.

"This is a first step to being able to address one of the most important questions in cardiology: How do we get heart cells to remember how to divide again so that we can repair hearts?" said Dr. Schumacker.

Building off this discovery, Dr. Schumacker and his collaborators will focus on identifying drugs that can trigger this response in heart cells without genetic manipulation.

"If we could find a drug that would turn on this response in the same way the gene manipulation did, we could then withdraw the drug once the heart cells have grown,"

Dr. Schumacker said. "In the case of children with HLHS, this may allow us to restore the normal thickness to the left ventricular wall. That would be lifesaving."

The approach could also be used for adults who have suffered damage due to a heart attack, Dr. Schumacker said.

The study was supported by National Institutes of Health grants HL35440, HL122062, HL118491 and HL109478.

Research at Ann & Robert H. Lurie Children's Hospital of Chicago is conducted through Stanley Manne Children's Research Institute, which is focused on improving child health, transforming pediatric medicine and ensuring healthier futures through the relentless pursuit of knowledge. Lurie Children's is a nonprofit organization committed to providing access to exceptional care for every child. It is ranked as one of the nation's top children's hospitals by *U.S. News & World Report*. Lurie Children's is the pediatric training ground for Northwestern University Feinberg School of Medicine.

Story Source:

Materials provided by **Ann & Robert H. Lurie Children's Hospital of Chicago**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Gregory B. Waypa, Kimberly A. Smith, Paul T. Mungai, Vincent J. Dudley, Kathryn A. Helmin, Benjamin D. Singer, Clara Bien Peek, Joseph Bass, Lauren Beussink-Nelson, Sanjiv J. Shah, Gaston Ofman, J. Andrew Wasserstrom, William A. Muller, Alexander V. Misharin, G.R. Scott Budinger, Hiam Abdala-Valencia, Navdeep S. Chandel, Danijela Dokic, Elizabeth T. Bartom, Shuang Zhang, Yuki Tatekoshi, Amir Mahmoodzadeh, Hossein Ardehali, Edward B. Thorp, Paul T. Schumacker. **Mitochondria regulate proliferation in adult cardiac myocytes**. *Journal of Clinical Investigation*, 2024; DOI: 10.1172/JCI165482

4. 老齢マウスの腸内細菌で若いマウスが炎症を引き起こす

日付：2024 年 6 月 10 日
ソース：イリノイ大学アーバナ・シャンペーン校、ニュース局
概要：

イリノイ大学アーバナ・シャンペーン校を始めとする研究者チームが、老齢マウスの腸内細菌を、腸内細菌を持たないように育てられた若い「無菌」マウスに移植したところ、移植を受けたマウスは、人間の老化に伴う炎症プロセスと類似した炎症の増加を経験した。また、若い無菌マウスに他の若いマウスの細菌を移植した場合には、そのような増加は見られなかった。 研究者らは、この研究結果は、腸内微生物叢の変化が、加齢に伴ってしばしば起こる全身の炎症に関与していることを示唆していると述べている。
多くの研究で、腸内微生物の種類の相対的な豊富さや多様性が比較され、健康や病気に寄与するグループの主要なものについて洞察がもたらされている。しかし、腸内微生物の配列を決定するのは費用がかかり、結果の解釈が難しい場合がある。そのため、研究者らは微生物の機能、具体的には、高齢マウスの腸内微生物叢が免疫反応を刺激する仕組みに注目した。
また、『Aging Cell』誌に報告されたこの研究では、抗生物質が若いマウスよりも高齢マウスの腸内微生物叢に長期間の混乱を引き起こすことも示されている。

研究関連ニュース/他のトップページに戻る

＜英文＞Gut microbes from aged mice induce inflammati | EurekAlert!

NEWS RELEASE 10-JUN-2024

Gut microbes from aged mice induce inflammation in young mice, study finds

Peer-Reviewed Publication

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN, NEWS BUREAU

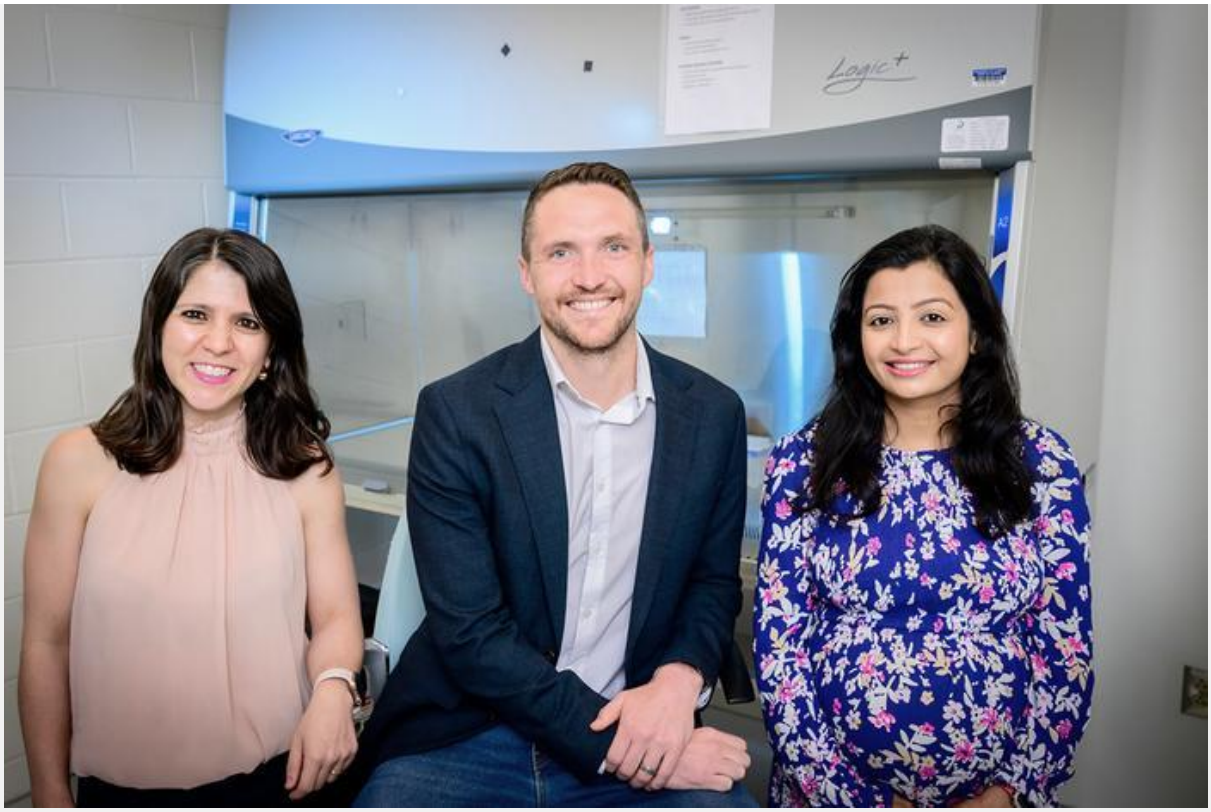


IMAGE:

FROM LEFT, POSTDOCTORAL RESEARCHER ELISA CAETANO-SILVA, KINESIOLOGY AND COMMUNITY HEALTH PROFESSOR JACOB ALLEN, PH.D. STUDENT AKRITI SHRESTHA AND THEIR COLLEAGUES FOUND EVIDENCE LINKING THE GUT MICROBIOMES OF AGED MICE TO AGE-RELATED INFLAMMATION COMMON TO MICE AND HUMANS.

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CREDIT: PHOTO BY FRED ZWICKY

CHAMPAIGN, Ill. — When scientists transplanted the gut microbes of aged mice into young "germ-free" mice — raised to have no gut microbes of their own — the recipient mice experienced an increase in inflammation that parallels inflammatory processes associated with aging in humans. Young germ-free mice transplanted with microbes from other young mice had no such increase.

The findings suggest that changes to the gut microbiome play a role in the systemwide inflammation that often occurs with aging, the researchers said.

Reported in the journal *Aging Cell,* the study also found that antibiotics caused longer-lasting disruptions in the gut microbiomes of aged mice than in young mice.

"There's been a growing consensus that aging is associated with a progressive increase in chronic low-grade inflammation," said Jacob Allen, a professor of kinesiology and

community health at the University of Illinois Urbana-Champaign who led the new research with Thomas Buford, a professor of medicine at the University of Alabama at Birmingham. "And there's a kind of debate as to what drives this, what is the major cause of the aging-induced inflammatory state. We wanted to understand if the functional capacity of the microbiome was changing in a way that might contribute to some of the inflammation that we see with aging."

Previous studies have found associations between age-related changes in the microbial composition of the gut and chronic inflammatory diseases such as Parkinson's disease and Alzheimer's disease. Some studies have linked microbial metabolism to an individual's susceptibility to other health conditions, including obesity, irritable bowel syndrome and heart disease. Age-related changes in the gut microbiome also may contribute to the so-called leaky gut problem, the researchers said.

"Microbiome patterns in aged mice are strongly associated with signs of bacterial-induced barrier disruption and immune infiltration," they wrote.

"The things that are in our gut are supposed to be kept separate from the rest of our system," Buford said. "If they leak out, our immune system is going to recognize them. And so then the question was: 'Is that a source of inflammation?'"

Many studies have compared the relative abundance and diversity of species of microbes in the gut, offering insight into some of the major groups that contribute to health or disease. But sequencing even a portion of the microbes in the gut is expensive and the results can be difficult to interpret, Allen said. That is why he and his colleagues focused on microbial function — specifically, how the gut microbiomes of aging mice might spur an immune response.

The team focused on toll-like receptors, molecules that mediate inflammatory processes throughout the body. TLRs sit in cellular membranes and sample the extracellular environment for signs of tissue damage or infection. If a TLR encounters a molecule associated with a potential pathogen — for example, a lipopolysaccharide component of a gram-negative bacterium — it activates an innate immune response, calling in pro-inflammatory agents and other molecules to fight the infection.

The researchers first evaluated whether the colonic contents of young and aged mice were likely to promote TLR signaling. They found that microbes from aged mice were more likely than those from young mice to activate TLR4, which can sense lipopolysaccharide components of bacterial cell walls. A different receptor, TLR5, was not affected differently in aged or young mice. TLR5 senses a different bacterial component, known as flagellin.

Young germ-free mice transplanted with the microbes of aged mice also experienced higher inflammatory signaling and increased levels of lipopolysaccharides in the blood after the transplants, the team found.

This finding provides "a direct link between aging-induced shifts in microbiota immunogenicity and host inflammation," the researchers wrote.

In other experiments, the team treated mice with broad-spectrum antibiotics and tracked changes in the microbiomes during treatment and for seven days afterward.

"One of the most interesting questions for me was what microbes come back immediately after the treatment with antibiotics ends," Buford said. And in the mice with aged microbiota in their guts, "these opportunistic pathogens were the most quick to come back."

"It appears that as we age our microbiome might be less resilient to antibiotic challenges," Allen said. "This is important because we know that in the U.S. and other Western societies, we're increasingly exposed to more antibiotics as we age."

The study is an important step toward understanding how age-related microbial changes in the gut may affect long-term health and inflammation, the researchers said.

Coauthors of the study also included Illinois postdoctoral researcher Elisa Caetano-Silva; U. of I. Ph.D. student Akriti Shrestha; National Children's Hospital research scientist Michael Bailey; and Jeffrey Woods, the director of the Center on Health, Aging and Disability at Illinois.

Allen also is a professor of nutritional sciences at Illinois and an affiliate of the Carl R. Woese Institute for Genomic Biology at the U. of I.

The National Institutes of Health supported this research.

Editor's notes:

To reach Jacob Allen, email jmallen5@illinois.edu.
To reach Thomas Buford, email twbuford@uabmc.edu.

The paper "Aging amplifies a gut microbiota immunogenic signature linked to heightened inflammation" is available online.

DOI: https://doi.org/10.1111/acel.14190

JOURNAL

Aging Cell

DOI

10.1111/acel.14190

METHOD OF RESEARCH

Experimental study

SUBJECT OF RESEARCH

Animals

ARTICLE TITLE

Aging amplifies a gut microbiota immunogenic signature linked to heightened inflammation

ARTICLE PUBLICATION DATE

9-May-2024

COI STATEMENT

The authors have no conflicts or competing interests to declare.

5. 出生前のリスク要因によって雄マウスの生殖腺機能が損なわれる

日付：2024 年 6 月 14 日
ソース：イリノイ大学アーバナ・シャンペーン校、カール R. ウォース ゲノム生物学研究所
概要：

研究者らは、出生前のジ（2-エチルヘキシル）フタル酸エステルへの曝露が雄マウスの生殖器系に害を及ぼし、生殖能力の障害を引き起こすことを今まで一貫して示してきた。今回、イリノイ大学アーバナ・シャンペーン校の科学者らは、新たな研究で、妊娠したマウスに DEHP と高脂肪食を与えると、それぞれの要因単独よりも子供に多くのダメージを与える可能性があることを明らかにした。
研究者らは、妊娠したマウスで 4 つのグループを使用：1 匹は対照群で、他の 3 匹は DEHP、高脂肪食、その両方を摂取した。その後、平均して雄 6 匹と雌 6 匹の子供が生まれた各一腹を追跡した。
結果は、高脂肪食は DEHP 単独の場合よりも雄の生殖器系にダメージを与え、両方を摂取した母親から生まれた子供の結果が最悪だった。
彼らの研究では、これらのマウスをモデルとして使用、これらの結果を人間で確認する必要があるものの、この研究は、妊娠中の環境と食事に注意する必要があるという警告となるはずだ、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＞Gonadal function in male mice disrupted by prenatal risk factors | ScienceDaily

Gonadal function in male mice disrupted by prenatal risk factors

Date:

June 14, 2024

Source:

Carl R. Woese Institute for Genomic Biology, University of Illinois at Urbana-Champaign

Summary:

Researchers have consistently shown that prenatal exposure to Di (2-ethyhexyl) phthalate harms the reproductive system in male mice and causes fertility defects. In a new study, scientists have shown that the combination of DEHP and a high-fat diet in pregnant mice can cause more damage to pups than each factor alone.

FULL STORY

Researchers have consistently shown that prenatal exposure to Di (2-ethyhexyl) phthalate harms the reproductive system in male mice and causes fertility defects. In a new study, scientists from the University of Illinois Urbana-Champaign have shown that the combination of DEHP and a high-fat diet in pregnant mice can cause more damage to pups than each factor alone.

Male reproductive disorders are a growing issue due to the global decrease in sperm count and quality. Concerningly, chemicals like DEHP, which can be found in food storage containers, pharmaceuticals, and building materials, have been found to be one of the contributing factors. The toxicity of DEHP is due to its ability to mimic the hormones in our bodies, leading to long-term effects on health.

"The scientific community is aware of the fact that the current generation of men produce half as much sperm compared to the previous one," said CheMyong Jay Ko (EIRH), a professor of veterinary medicine. "Although it is shocking, not much attention is paid to understanding the causes."

The researchers used the Barker hypothesis as a guiding principle for their study. Proposed by the British physician and epidemiologist David Barker, the hypothesis argued that the nine months in utero are one of the most critical periods in a person's life and can shape their future health trajectories.

"The Barker hypothesis primarily focuses on nutrition and we wanted to test whether the mother's diet could change the health of the next generation," Ko said. "Additionally, unlike the previous generation, we are constantly exposed to chemicals like DEHP, which can alter how our bodies function. We wanted to ask whether the exposure to both these factors can cause growing babies to have lesser functioning reproductive systems."

In the past, both the Ko lab and other research groups have shown that prenatal exposure to DEHP decreases testosterone levels and causes fertility defects in male mice. Additionally, scientists have shown that maternal high-fat diet can also decrease sperm counts in male offspring. However, the effects of both together had not been studied.

The researchers used four groups of pregnant mice; one was a control and the other three were either exposed to DEHP, or a high-fat diet, or a combination of the two. They then followed each litter, which contained an average of 6 male and 6 female pups.

"Surprisingly, we found that a high-fat diet had a more damaging effect on the male reproductive systems compared to DEHP alone and the pups born from mothers who had been treated with both had the worst outcomes," Ko said.

The researchers measured the weight of the body and different reproductive organs in pups during different stages of growth and puberty. They found that although the body weight of pups born from moms on a high-fat diet alone or in combination with

DEHP was higher than the other pups, the weight of the reproductive organs was lower. They also found that these mice produced less sperm and had lower testosterone levels. By staining the tissues, the researchers found that the reproductive organs had abnormal cells, which were contributing to the gonadal dysfunction.

"In our studies, we used these mice as a model. Although we need to confirm these results in humans, this study should serve as a warning to our generation that we need to be careful about our environment and diet during pregnancy," Ko said.

Story Source:

Materials provided by **Carl R. Woese Institute for Genomic Biology, University of Illinois at Urbana-Champaign**. Original written by Ananya Sen. *Note: Content may be edited for style and length.*

Journal Reference:

1. Radwa Barakat, Po-Ching Patrick Lin, Mary Bunnell, Ji-Eun Oh, Saniya Rattan, Cyrus Arnieri, Jodi A Flaws, CheMyong J Ko. **Prenatal exposure to Di(2-ethylhexyl) phthalate and high-fat diet synergistically disrupts gonadal function in male mice**. *Biology of Reproduction*, 2024; 110 (5): 1025 DOI: 10.1093/biolre/ioae029

6. 抗癌剤がパーキンソン病を引き起こすタンパク質のつながりを標的とするのに使用できる可能性 –マウス実験

日付：2024 年 6 月 17 日
ソース：ジョンズ・ホプキンス大学医学部
概要：

ジョンズ・ホプキンス大学の研究者らが 5 月 31 日に『Nature Communications』誌に発表した新しい研究によると、癌治療薬がパーキンソン病を引き起こす有害なα–シヌクレインを吸収するたんぱく質結合を標的とする可能性があるとしている。
研究者らは、Aplp1 という細胞表面タンパク質が、α–シヌクレインを脳細胞に広げる過程の一部を担うことを、遺伝子組み換えマウスを用いた研究で特定した。この発見は、パーキンソン病の特徴であるα–シヌクレインのタンパク質集積の拡散を助ける過程において、Aplp1 がどのようにして Lag3 と結びつくかを明らかにしている。
Lag3 はすでに米国食品医薬品局（FDA）が承認した複合抗がん剤の標的となっており、研究者らは、FDA によって癌治療薬として承認されているこの Lag3 抗体ニボルマブ/レラトリマブが、細胞がα–シヌクレインの吸収を防ぐ役割を果たす可能性があると述べている。
Aplp1 が実際に有害なα–シヌクレインタンパク質の蔓延に寄与したかどうかを判断するために、研究者らは、Aplp1 または Lag3 のいずれか、または Aplp1 と Lag3 の両方を欠く遺伝子操作マウスの系統を使用した。Aplp1 と Lag3 を持たないマウスでは、有害なα–シヌクレインタンパク質の細胞吸収が 90％減少した。マウスに Lag3 抗体を注射したところ、この薬は Aplp1 と Lag3 の相互作用も阻害し、健康な脳細胞が病気の原因となるα–シヌクレインの塊を吸収できなくなることが分かった。
マウスでの Lag3 抗体の使用が成功したことから、次のステップはパーキンソン病とアルツハイマー病のマウスで抗 Lag3 抗体の試験を行うことだと研究者らは語っている。

研究関連ニュース/他のトップページに戻る

＜英文＞New study suggests cancer drug could be used | EurekAlert!

NEWS RELEASE 17-JUN-2024

New study suggests cancer drug could be used to target protein connection that spurs Parkinson's disease

Peer-Reviewed Publication

JOHNS HOPKINS MEDICINE

In studies with genetically engineered mice, Johns Hopkins Medicine researchers say they have identified a potentially new biological target involving Aplp1, a cell surface protein that drives the spread of Parkinson's disease-causing alpha-synuclein.

The findings, published May 31 in *Nature Communications*, reveal how Aplp1 connects with Lag3, another cell surface receptor, in a key part of a process that helps spread harmful alpha-synuclein proteins to brain cells. Those protein buildups are hallmarks of Parkinson's disease.

Notably, the researchers say, Lag3 is already the target of a combination cancer drug approved by the U.S. Food and Drug Administration (FDA) that uses antibodies to "teach" the human immune system what to seek and destroy.

"Now that we know how Aplp1 and Lag3 interact, we have a new way of understanding how alpha-synuclein contributes to the disease progression of Parkinson's disease," says Xiaobo Mao, Ph.D., associate professor of neurology at the Johns Hopkins University School of Medicine and a member of the Institute for Cell Engineering. "Our findings also suggest that targeting this interaction with drugs could significantly slow the progression of Parkinson's disease and other neurodegenerative diseases."

Mao co-led the research along with Ted Dawson, M.D., Ph.D., Leonard and Madlyn Abramson Professor in Neurodegenerative Diseases at the Johns Hopkins University School of Medicine and director of the Johns Hopkins Institute for Cell Engineering, Valina Dawson, Ph.D. and Hanseok Ko, Ph.D., professors of neurology at the school of medicine and members of the Institute for Cell Engineering.

Long-standing studies have shown that by clumping together and forming protein deposits, misfolded alpha-synuclein proteins journey from brain cell to brain cell, killing those responsible for producing a neurotransmitter called dopamine, and causing Parkinson's disease to progress through a type of "programmed" cell death that Johns Hopkins researchers have identified. The process, parthanatos (from the Greek word for "death"), leads to impairments in movement, emotional regulation and thinking.

Aplp1's bond with Lag3 on the cell's surface enables healthy brain cells to absorb traveling clumps of alpha-synuclein, leading to cell death, the researchers say.

In mouse studies published in 2016 and 2021, Mao and Dawson's team identified Lag3's role in binding with alpha-synuclein proteins, causing Parkinson's disease to spread. However, those studies indicated that another protein was partially responsible for the cell's absorption of misfolded alpha-synuclein.

“Our work previously demonstrated that Lag3 wasn’t the only cell surface protein that helped neurons absorb alpha-synuclein, so we turned to Aplp1 in our most recent experiments,” says Valina Dawson.

To determine whether Aplp1 indeed contributed to the spread of harmful alpha-synuclein proteins, researchers used a line of genetically engineered mice lacking either Aplp1 or Lag3 or both Aplp1 and Lag3. In mice without Aplp1 and Lag3, cell absorption of the harmful alpha-synuclein protein dropped by 90%. After injecting mice with the Lag3 antibody, they found that this drug also blocks the interaction of Aplp1 and Lag3, meaning healthy brain cells could no longer absorb disease-causing alpha-synuclein clumps.

The researchers say the Lag3 antibody nivolumab/relatlimab, a drug FDA approved in 2022 for cancer treatment, could play a role in preventing cells from absorbing alpha-synuclein.

“The anti-Lag3 antibody was successful in preventing further spread of alpha-synuclein seeds in the mouse models and exhibited better efficacy than Lag3-depletion because of Aplp1’s close association with Lag3,” Ted Dawson says.

This research has potential applications in treating other neurodegenerative conditions that have no cures, Mao says. In Alzheimer’s disease, which is associated with symptoms of memory loss, mood instability and muscle problems, tau proteins become misfolded and clump together in neurons at high levels, worsening the condition. In Alzheimer’s research, Mao says scientists could try to target Lag3 — which also binds with the dementia-related tau protein — with the same antibody.

With the success of using the Lag3 antibody in mice, Ted Dawson says the next steps would be to conduct anti-Lag3 antibody trials in mice with Parkinson’s disease and Alzheimer’s disease. The Johns Hopkins researchers are also looking into how they could prevent unhealthy cells from releasing disease-causing alpha-synuclein in the first place.

Other researchers on this study are Hao Gu, Donghoon Kim, Yasuyoshi Kimura, Ning Wang, Enquan Xu, Ramhari Kumbhar, Xiaotian Ming, Haibo Wang, Chan Chen, Shengnan Zhang, Chunyu Jia, Yuqing Liu, Hetao Bian, Senthilkumar Karuppagounder, Fatih Akkentli, Qi Chen, Longgang Jia, Heehong Hwang, Su Hyun Lee, Xiyu Ke, Michael Chang, Amanda Li, Jun Yang, Cyrus Rastegar, Manjari Sriparna, Preston Ge, Saurav Brahmachari, Sangjune Kim, Shu Zhang, Haiqing Liu, Sin Ho Kweon, Mingyao Ying and Han Seok Ko from Johns Hopkins; Yasushi Shimoda from the Nagaoka University of Technology; Martina Saar and Ulrike Muller from Heidelberg University; Creg Workman and Dario Vignali of the University of Pittsburgh School of Medicine and Cong Liu of the Chinese Academy of Sciences.

This work was supported by grants from the National Institutes of Health (R01NS107318, R01AG073291, R01AG071820, 1135 RF1NS125592, K01AG056841, R21NS125559,

R01NS107404, P01AI108545, R01AI144422), the Parkinson's Foundation, the Maryland Stem Cell Research Foundation, the American Parkinson Disease Association, the Uehara Memorial Foundation, the JPB Foundation, the Adrienne Helis Malvin Medical Research Foundation, and the Parkinson's Disease Foundation.

DOI: 10.1038/s41467-024-49016-3

JOURNAL

Nature Communications

7. ADGRF5 の役割を解明: 腎臓の健康と機能に関する洞察 −マウス実験

日付:2024 年 6 月 21 日
ソース:東京工業大学
概要:

東京工業大学生命理工学部の中村信大准教授と杏林大学医学部解剖学教室の長瀬美樹教授が率いる研究チームは、マウスとヒトの一次糸球体内皮細胞(GEnC)で一連の遺伝子ノックアウトおよびノックダウン実験を実施し、糸球体濾過バリア(GFB)維持における接着 G タンパク質共役受容体 F5(ADGRF5)の具体的な役割と基礎となるメカニズムを調査し、ADGRF5 の役割に関する最新の研究成果が発表された。
ADGRF5 は、マウスの GFB の GEnC で発現しており、このバリアの構造と機能の維持に重要な役割を果たしている。研究チームは、ADGRF5 遺伝子をノックアウトしたマウスで実験を行った。その結果、GFB に形態学的な異常が見られ、グロメルルス基底膜の分裂や厚化、GEnC の剥離が観察された。さらに、ADGRF5 の遺伝子をノックダウンしたヒトのプライマリ GEnC でも同様の結果が得られ、GFB の構成要素であるタイプ IV コラーゲンの発現が有意に低下し、GFB の選択透過性に影響を与えることが明らかになった。
ADGRF5 受容体の新しい機能を解明することは、糸球体濾過バリア機能不全、特にタンパク尿の治療における画期的な治療法の発見につながる可能性があり、将来の腎障害治療の開発に向けた貴重な知見を提供する可能性がある。としている。

研究関連ニュース/他のトップページに戻る

＜英文＞Unraveling the role of ADGRF5: Insights into | EurekAlert!

NEWS RELEASE 21-JUN-2024

Unraveling the role of ADGRF5: Insights into kidney health and function

Scientists revealed the role of endothelial cell receptor in maintaining the integrity of the glomerular filtration barrier

Peer-Reviewed Publication

TOKYO INSTITUTE OF TECHNOLOGY

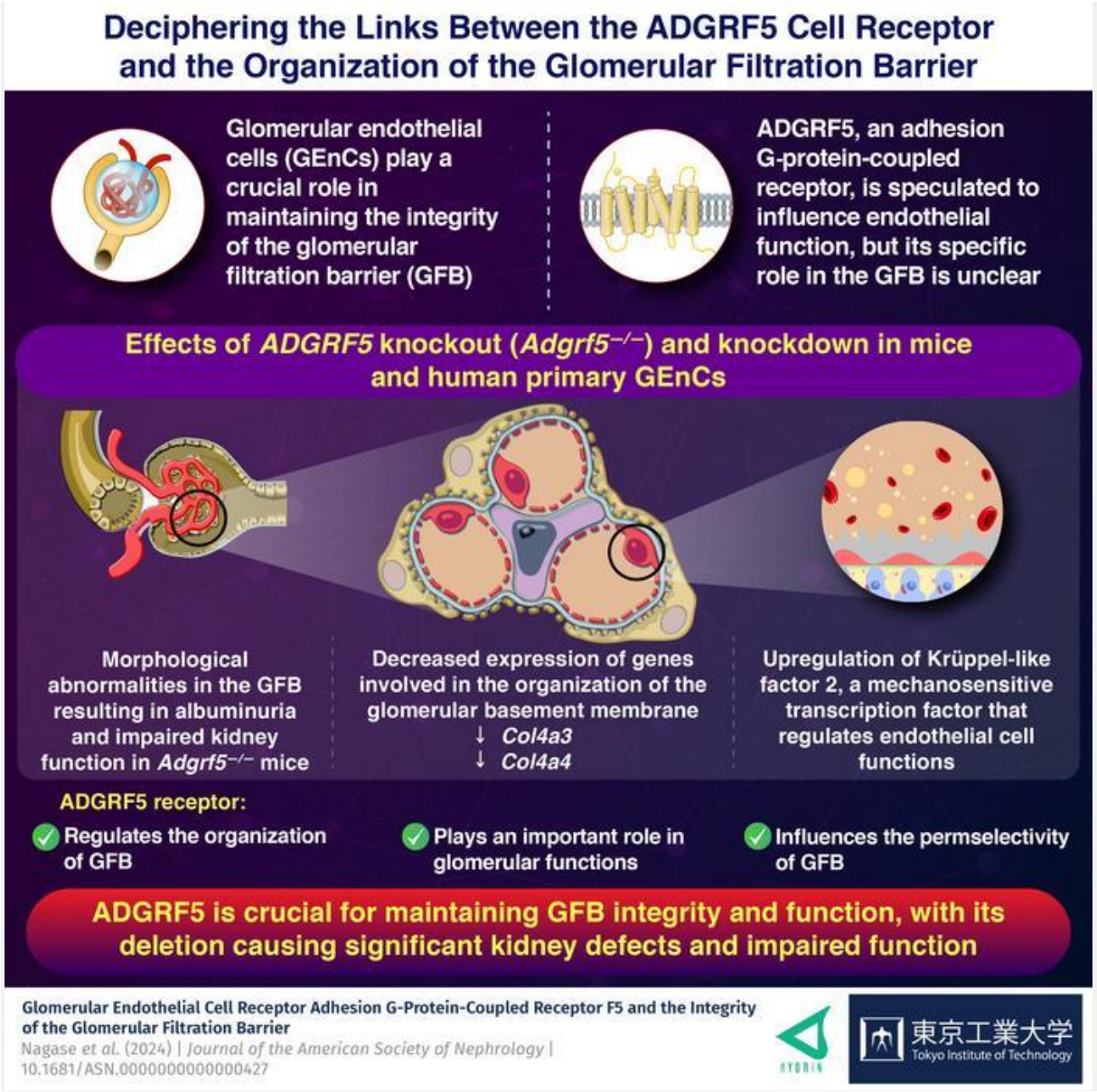

IMAGE:

ADGRF5 IS CRUCIAL FOR MAINTAINING GFB INTEGRITY AND FUNCTION, WITH ITS DELETION CAUSING SIGNIFICANT KIDNEY DEFECTS AND IMPAIRED FUNCTION.

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CREDIT: TOKYO TECH

Glomerulus, the fundamental filtering unit of the kidney, is an intricate network of capillaries — small blood vessels that regulate the movement of ions, water, and metabolites while maintaining impermeability to essential macromolecules such as proteins. The selectively permeable capillary wall, known as the glomerular filtration barrier (GFB), consists of three main components: glomerular endothelial cells (GEnCs), the glomerular basement membrane, and podocytes. GEnCs line the inner

surface of the capillary wall and are covered by a thin layer of glycoproteins and other carbohydrate-based moieties.

Adhesion G-protein-coupled receptor F5 (ADGRF5), a transmembrane cell receptor expressed in GEnCs, is implicated in influencing the integrity of the GFB, potentially playing a role in its structural and functional maintenance. To elucidate the precise role of ADGRF5 in maintaining the integrity of the GFB, a collaborative research study was undertaken by scientists from Tokyo Institute of Technology (Tokyo Tech) and Kyorin University. Their findings were published in the *Journal of the American Society of Nephrology* on June 06, 2024.

The research team led by Associate Professor Nobuhiro Nakamura from the School of Life Science and Technology, Tokyo Tech, Japan, and Professor Miki Nagase from the Department of Anatomy, Kyorin University School of Medicine, Japan, conducted a series of genetic knockout and knockdown experiments in mice and human primary GEnCs to investigate the specific role and underlying mechanisms of ADGRF5 in maintaining the GFB.

Explaining the motivation behind the present research, Dr. Nakamura shares "During our analysis of renal gene expression profiles using the Nephroseq v5 database, we observed a reduced expression of *ADGRF5* mRNA in the glomeruli of patients with diabetic nephropathy. Additionally, there was a positive correlation between glomerular *ADGRF5* expression and the estimated glomerular filtration rate."

Initially, the researchers observed the specific expression of ADGRF5 within endothelial cells that line the glomerular capillary wall. In mice with genetic knockout of *ADGRF5*, the GFB was affected by morphological abnormalities like splitting and thickening of the glomerular basement membrane and GEnC detachment. The overall integrity of GFB was severely impacted leading to albuminuria – presence of albumin proteins in urine.

Furthermore, deletion and knockdown of the *ADGRF5* gene in mice and human primary GEnCs, respectively, revealed alterations in the expression of genes crucial for maintaining the integrity of the GFB. Specifically, knockout/knockdown of *ADGRF5* significantly downregulated type IV collagens (*Col4a3* and *Col4a4*) that comprise the GFB and influence GFB permselectivity. In addition, Krüppel-like factor 2 (*KLF2*), a mechanosensitive transcription factor that regulates endothelial cell functions, was found to be upregulated.

Taken together, their findings highlight the critical functions of ADGRF5 in maintaining the integrity of GFB. Emphasizing the potential impact of the research work, Dr. Nakamura says, "This study reveals a novel mechanism that maintains the GFB. Insights into the role of ADGRF5 aids the understanding of glomerular disorders and significantly contributes to the advancement of future research."

Unlocking the novel functions of the ADGRF5 receptor holds promise for pioneering therapeutic breakthroughs in treating glomerular filtration barrier dysfunctions, notably proteinuria.

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About Tokyo Institute of Technology

Tokyo Tech stands at the forefront of research and higher education as the leading university for science and technology in Japan. Tokyo Tech researchers excel in fields ranging from materials science to biology, computer science, and physics. Founded in 1881, Tokyo Tech hosts over 10,000 undergraduate and graduate students per year, who develop into scientific leaders and some of the most sought-after engineers in industry. Embodying the Japanese philosophy of "monotsukuri," meaning "technical ingenuity and innovation," the Tokyo Tech community strives to contribute to society through high-impact research.

https://www.titech.ac.jp/english/

JOURNAL

Journal of the American Society of Nephrology

DOI

10.1681/ASN.0000000000000427

METHOD OF RESEARCH

Experimental study

SUBJECT OF RESEARCH

Not applicable

ARTICLE TITLE

Glomerular Endothelial Cell Receptor Adhesion G-Protein-Coupled Receptor F5 and the Integrity of the Glomerular Filtration Barrier

ARTICLE PUBLICATION DATE

6-Jun-2024

8. 腸内の特定の細菌が過食と肥満に関係 –マウス実験
新しい研究で、脳と腸がどのように対話しているかが明らかに

日付：2024 年 6 月 26 日
ソース：欧州神経科学協会連合 Federation of European Neuroscience Societies（FENS）
概要：

スペインのバルセロナにある Universitat Pompeu Fabra の Elena Martín-García 教授を中心とする国際研究チームは、特定の腸内細菌が食べ物への中毒性と肥満の発展に関与していることを特定した。彼らはまた、腸と脳がどのようにしてコミュニケーションを取るかについても明らかにした。
研究は 2024 年の Federation of European Neuroscience Societies（FENS）フォーラムで発表され、ジャーナル『Gut』にも同時に掲載された。
この研究では、マウスとヒトで食べ物への中毒性を診断するために Yale Food Addiction Scale（YFAS 2.0）が使用され、特定の腸内細菌が食べ物への中毒を防ぐのに役立つ可能性があることが示された。研究者らが、食物中毒のマウスとそうでないマウスの腸内細菌を調べたところ、食物中毒のマウスではプロテオバクテリア門と呼ばれるグループに属する細菌が増加し、放線菌アクティノバクテリア門に属する細菌が減少していることを発見、これらのマウスでは、バシロタ門のブラウティアと呼ばれる別の種類の細菌の量も減少していた。
さらに、研究は、miRNA（microRNA）の役割にも焦点を当て、特定の miRNA の阻害が食べ物への中毒性の発展を促進することが示されている。
この研究は、食べ物への中毒と関連する食欲障害の新しい治療法の開発に道を開く可能性があ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＞A promising approach to develop a birth control pill for men | ScienceDaily

NEWS RELEASE 26-JUN-2024

Specific bacteria in your gut are involved in compulsive eating and obesity

New research shows how your brain and gut talk to each other

Peer-Reviewed Publication

FEDERATION OF EUROPEAN NEUROSCIENCE SOCIETIES

IMAGE:

PROFESSOR ELENA MARTÍN-GARCÍA

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CREDIT: PROFESSOR ELENA MARTÍN-GARCÍA

Vienna, Austria: An international team of researchers has identified specific bacteria in the gut that are associated with both mice and humans developing an addiction to food that can lead to obesity. They have also identified bacteria that play a beneficial role in preventing food addiction.

The research is presented today (Thursday) at the Federation of European Neuroscience Societies (FENS) Forum 2024 and is published simultaneously in the journal *Gut* [1,2].

Professor Elena Martín-García, from the Laboratory of Neuropharmacology-NeuroPhar in the Department of Medicine and Life Sciences at the Universitat Pompeu Fabra, Barcelona, Spain, told the FENS Forum: “A number of factors contribute to food addiction, which is

characterised by loss of control over food intake and is associated with obesity, other eating disorders and alterations in the composition of bacteria in the gut – the gut microbiome. Until now, the mechanisms underlying this behavioural disorder were largely unknown."

Speaking before the FENS Forum, Professor Rafael Maldonado, who leads the Laboratory, said: "These results from our study may allow us to identify new biomarkers for food addiction and, most importantly, to evaluate whether the beneficial bacteria could be used as potential new treatments for this obesity-related behaviour, which, at present, lacks any effective therapeutic approaches. Potential new treatments could involve using beneficial bacteria and dietary supplementation."

Prof. Martín-García used the Yale Food Addiction Scale (YFAS 2.0) to diagnose food addiction in mice and humans. It contains 35 questions for humans to answer, and these can also be grouped into three criteria for use in mice: persistent food-seeking, high motivation to obtain food, and compulsive behaviour.

She and her colleagues investigated the gut bacteria in mice who were and were not addicted to food and found an increase in bacteria belonging to a group called the Proteobacteria phylum and a decrease in bacteria belonging to the Actinobacteria phylum in the food-addicted mice. These mice also had a decrease in the amount of another type of bacteria called *Blautia* from the Bacillota phylum.

The researchers used the YFAS to classify 88 patients into those who were addicted or not addicted to food. Similar to the findings in mice, decreases in Actinobacteria phylum and *Blautia* were seen in those who were food-addicted and increases in Proteobacteria phylum. Further analyses showed how the findings in humans correlated with those in mice.

Prof. Martín-García said: "The findings in both mice and humans suggested that specific microbiota could be protective in preventing food addiction. In particular, the strong similarities in the amount of *Blautia* underlined the potential beneficial effects of this particular gut bacteria. Therefore, we investigated the protective effects of oral administration of lactulose and rhamnose, which are non-digestible carbohydrates known as 'prebiotics' that can increase the amount of *Blautia* in the gut. We did this in mice and

found that it led to an increase in the abundance of *Blautia* in mice faeces in parallel with dramatic improvements in food addiction. We saw similar improvements when we gave the mice a species of *Blautia* called *Blautia wexlerae* orally as a probiotic.

"The gut microbiota signatures in both mice and humans suggest possible non-beneficial effects of bacteria belonging to the Proteobacteria phylum and potential protective effects of increasing the abundance of Actinobacterial and Bacillota against the development of food addiction."

Prof. Martín-García says the findings show how bacteria in the gut influence brain function and vice versa. "We have demonstrated for the first time a direct interaction between the gut composition and brain gene expression, revealing the complex and multifactorial origin of this important behavioural disorder related to obesity. Understanding the crosstalk between alterations in behaviour and bacteria in the gut constitutes a step forward for future treatments for food addiction and related eating disorders."

She also described work investigating how microRNAs (miRNAs) – small, single-stranded molecules that regulate gene expression and contribute to almost any cellular process – are involved in food addiction [3]. Changes in the expression of miRNAs may be involved in the mechanisms underlying the disorder.

The researchers used a technique called Tough Decoy (TuD) to inhibit specific miRNAs in the medial prefrontal cortex (mPFC) of brains of mice in order to produce mice that were vulnerable to developing food addiction. The mPFC is the part of the brain involved in self-control and decision-making. It was these mice that were also used in the study described above – the food-addicted mice.

They found that inhibition of miRNA-29c-3p promoted persistence of response and enhanced the vulnerability of the mice to develop food addiction. Inhibiting another miRNA called miRNA-665-3p promoted compulsive behaviour and vulnerability to food addiction.

Prof. Maldonado said: “These two miRNAs could act as protective factors against food addiction. This helps us to understand the neurobiology of the loss of eating control, which plays a crucial role in obesity and related disorders. To understand these mechanisms further, we are now exploring how the gut microbiota and miRNA expression in the brain interact in mice.”

Professor Richard Roche, Deputy Head of the Department of Psychology at Maynooth University, Maynooth, County Kildare, Ireland, is chair of the FENS communication committee and was not involved in the research. He said: “Compulsive eating and food addiction is a growing problem worldwide. There are many factors that contribute to it, in particular the environment that people live in and the availability of certain types of food. However, we’ve known for some time that there are probably contributing factors for eating disorders and the research by Professor Martín-García and colleagues shows how the different types of bacteria in the gut have an impact on brain function and vice versa in humans and mice. This understanding opens the way to developing potential new treatments for eating disorders, and we look forward to seeing more research in this area.”

(ends)

Notes

[1] “Neurobiological signatures associated with vulnerability to food addiction in mice and humans”, by Dr Elena Martín-García, Session S21: Mechanistic facets of resilience and vulnerability toward the diversity of challenges, 09.47-10.05 hrs, Thursday 27 June, Hall E: https://fens2024.abstractserver.com/program/#/details/presentations/162

[2] “Gut microbiota signatures of vulnerability to food addiction in mice and humans”, Samulénaite S, García-Blanco A, Mayneris- Perxachs J, *et al*. *Gut,* Epub ahead of print 27 June 2024. doi:10.1136/ gutjnl-2023-331445

[3] “A specific prelimbic-nucleus accumbens pathway controls resilience versus vulnerability to food addiction”, Domingo-Rodriguez et al., *Nature Communications,* (2020)11:782, https://doi.org/10.1038/s41467-020-14458-y
“miRNA signatures associated with vulnerability to food addiction in mice and humans”, Garcia-Blanco et al., *The Journal of Clinical Investigation,* 2022;132(10):e156281. https://doi.org/10.1172/JCI156281

JOURNAL

Gut

DOI

10.1136/gutjnl-2023-331445

METHOD OF RESEARCH

Observational study

SUBJECT OF RESEARCH

People

ARTICLE TITLE

Gut microbiota signatures of vulnerability to food addiction in mice and humans

ARTICLE PUBLICATION DATE

27-Jun-2024