Bio News – October, 2024

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

9/2　1型糖尿病患者に iPS 細胞から作る膵島細胞を移植、京大病院が来年にも治験実施…インスリン注射不要に

膵臓の細胞が正常に働かない重症の1型糖尿病について、京都大病院が iPS 細胞（人工多能性幹細胞）から作った細胞のシートを患者に移植する治験を、来年にも実施する計画であることが、京大関係者らへの取材でわかった。有効性が確認されれば、注射治療が継続的に必要な患者の負担を軽減する効果が期待できるという。企業による大規模な治験を経て、2030 年以降の実用化を目指す。

9/2　運動の神経伝達「左脳→右手足」「右脳→左手足」とは限らない　-京大

脳の右側が傷つけられると、左の手足がまひし、左側の脳が傷つくと右の手足が動きにくくなる。運動神経の指令が、左右の脳から延髄で交差して体の左右逆側に伝達されるためだ。ところが、けがからの回復時には、ふだんは機能していない左右の脳をつなぐ神経経路が働き、左脳→右脳→右手足、右脳→左脳→左手足と、運動にかかわらない側の脳が活性化されていると、京都大などの研究チームが動物実験で確かめた。
研究成果が科学誌「ネイチャーコミュニケーションズ」に発表された。脊髄損傷や脳梗塞でまひした患者の効果的なリハビリへの応用が期待される。

9/3　フィンランドの北極圏ラップランド、観測史上最も暑い夏

フィンランドの北極圏、ラップランド（Lapland）地方の今年の夏の気温は、観測史上最も高かったとする調査結果をフィンランド気象研究所の専門家が 2 日、AFP に明らかにした。

9/4　中高生が内視鏡で模擬手術 ～消化器内科の体験セミナー―東京医科大～

9/4　Moderna のエムポックスワクチン mRNA-1769 がサルの感染病変をより抑制

Moderna’s experimental mpox vaccine reduces severity of disease, early study finds　- MarketWatch

Mpox Protection: Moderna's New mRNA Vaccine May Beat Today's MVA Shot (genengnews.com)

9/5　世界中で猛暑の夏、2年連続で記録更新

9/6　Eli Lilly の週 1 回投与インスリンが Novo Nordiks との競争を激化

Eli Lilly の週 1 回投与インスリン efsitora alfa（エフシトラ アルファ）の第 3 相試験がさらに 2 つ成功した。これにより、より長時間作用するインスリンの開発をめぐるノボノルディスクとの競争が激化する。

Eli Lilly's weekly insulin intensifies race with Novo Nordisk (msn.com)

9/6　科研費、倍増求め文科相に申し入れ　主要学会のべ 220 万人超所属

日本の研究力の低下に歯止めをかけようと、全国の研究者の研究資金となる国の科学研究費助成事業（科研費）を現状の 2 倍に増やすよう、主要学会連合の代表者が 6 日、盛山正仁文部科学相に要望書を提出した。

9/6　今夏の熱中症警戒アラート過去最多 -環境省

環境省は 6 日、熱中症対策についての専門家会議を開き、市民に予防を呼びかける熱中症警戒アラートの今夏の発表数が約 1,500 回で過去最多だったと明らかにした。

9/7　Lilly が再び乗った投資で肥満薬開発の OrsoBio（本社：カリフォルニア州パロアルト）が 6,700 万ドル調達

Obesity drug startup raises $67M; Vor's 'shielded transplant' shows promise | BioPharma Dive

9/10　第一三共/Merck の荷付き抗体 B7-H3 抗体の小細胞肺癌治療効果が引き続き有望

Pharma Industry News and Analysis | FirstWord Pharma
WCLC24: Expectations rise as Merck & Co., Daiichi's ADC continues to impress in SCLC

9/11　手術ができない…抗菌薬の原料・原薬 100%中国依存の恐怖　製薬各社が国産急ぐ深刻理由

https://www.sankei.com/article/20240911-W4YEPXKC6JKFZNNSX73WIRCCFE/

9/11　Lilly が週 1 回投与インスリン efsitora の Ph3 試験の良好な結果について 2 つの論文報告

Lilly posts more positive data on once-weekly insulin prospect (fiercebiotech.com)

9/11　塗ると肌が一時的に透明になる「黄色い液体」 生きたマウスの皮膚を透過、内臓や脳内の観察に成功

スタンフォード大学などに所属する研究者らが発表した論文「Achieving optical transparency in live animals with absorbing molecules」は、体内の臓器などの生体内部を、その上にある組織を可視光に対して透明にすることで非侵襲的に観察する手法を提案した研究報告である。この方法を用いると、生きている動物の皮膚を一時的に透明にし、内部組織を観察することができる。
マウスの皮膚の約 10 倍の厚さがある人間でこの方法をテストしていない。研究チームは、人間の組織に最適な染料の用量や投薬方法はまだ分かっていないため、今後の課題としている。

9/12　Gilead 社の年 2 回注射薬 lenacapavir が Ph3 試験第二弾で HIV 感染を 96%完封

Gilead's (GILD) Twice-Yearly Shot Prevents 96% of HIV Cases in Study - Bloomberg

9/13　iPS から小腸の多層再現　創薬に期待、京大

京都大などの研究グループは、人工多能性幹細胞（iPS 細胞）や胚性幹細胞（ES 細胞）から体内で実際にある形に似た多層構造を持つ小腸組織の再現に成功したと、13 日までに米科学誌「セル・ステム・セル」電子版に発表した。小腸の多層構造を生体外で作ることができたのは初めて。

9/13　哺乳類がおしりで呼吸できるのを発見　今年も日本にイグ・ノーベル賞

人々を笑わせ、考えさせた研究に贈られる「イグ・ノーベル賞」の受賞者が 12 日（日本時間 13 日）に発表された。哺乳類が肛門（こうもん）から呼吸できることを発見した東京医科歯科大・大阪大の武部貴則教授（再生医学）らのチームが、生理学賞に輝いた。日本人の受賞は 18 年連続。イグ・ノーベル賞はノーベル賞をパロディーにした賞で米科学雑誌が主催する。

9/13　アステラス製薬の閉経薬 Veozah の肝障害について FDA が一層の注意を求めている

FDA warns that Veozah can cause serious liver injury | Pharmaceutical | The Pharmaletter | The Pharmaletter

9/13　自己増幅型の新型コロナワクチン承認へ、少量接種で効果が持続…厚労省部会が了承

厚生労働省の専門家部会は 12 日、製薬会社「Meiji Seika ファルマ」（東京都）が開発した、新型コロナウイルスのオミクロン株の新系統「JN. 1」に対応したワクチン「コスタイベ」（商品名）について、製造販売の承認を了承した。遺伝物質「メッセンジャーRNA（mRNA）」ワクチンを改良した新しいタイプで、少量の接種で効果が長く続く特性がある。

Note: このワクチンに関しては今月 9 日に看護倫理学会によって緊急声明が出されている

新型コロナ「レプリコンワクチン」に看護倫理学会が緊急声明を出し注意喚起の異例事態へ

https://pinzuba.news/articles/-/8o68?utm_source=yahoo&utm_medium=referral&utm_campaign=rellink&page=3

9/14　Moderna の開発品いくつかが失速

Moderna forecasts lower sales next year, shares near four-year low | Reuters

9/14　コロナ重症度の目印、順天堂大などが明らかにした遺伝的特徴

順天堂大学の服部浩一特任先任准教授らは、新型コロナウイルス感染症の重症度の目印となる遺伝的特徴を明らかにした。コロナ患者の検体組織を解析。血液や血管に関わる遺伝子の個体差を比べたところ、日本人に最も多い遺伝子の個性を持つ患者は他の遺伝子の個体差に比べ重症度が低くなることが分かった。新型コロナの重症化の予想や早期診断などに役立つ可能性があると期待される。東京大学との共同研究。成果は国際科学誌電子版に掲載された。

9/15　「常緑」の仕組み解明　冬に栄養蓄積　京都大

温帯で生育する常緑植物の葉が冬になっても枯れない仕組みを、京都大生態学研究センターの研究グループが解明した。日の短い秋や冬は葉に栄養をため、春になって花や実に移した後に枯れるという。論文は英科学誌「ネイチャー・コミュニケーションズ」に掲載された。

9/15　甘いカフェイン飲料は体内時計が乱れやすい？　マウス実験で「昼夜逆転」 広島大の研究グループ発表

ブラックコーヒーよりも砂糖入りコーヒーの方が体内時計が乱れやすい―。広島大の研究グループがそんな可能性を示す研究成果を発表した。マウスを使った実験で、甘みを加えたカフェイン水を与えると生活リズムが乱れ、本来の夜行性から昼行性になった。
成果は、英ネイチャー系の学術誌「npj　Science　of　Food」に掲載された。

9/16　アスリート遺伝子の研究を停止　国立スポーツ科学センター

日本スポーツ振興センター（JSC）国立スポーツ科学センターが、トップアスリートらの遺伝子と、競技の成績やけがのリスクとの関連を調べる研究に着手したものの、その後、停止していたことが 16 日分かった。2017 年度から始まったが、アスリートの選別や差別につながることを懸念する声が内部で上がり、外部有識者の意見も踏まえて 22 年度に分析を停止。協力した 2 千人以上にはまだ経緯を伝えていない。

9/17　明治傘下製薬社、Meiji Seika ファルマ、豪製コロナワクチン供給へ

オーストラリアの製薬大手 CSL と米新興バイオ企業アークトゥルス・セラピューティクスが製造する、新型コロナウイルスの変異株「オミクロン株」の亜種「JN. 1」系統対応ワクチン「コスタイベ（KOSTAIVE）

筋注用」について、日本の独占販売権を保有する明治ホールディングスの製薬子会社 Meiji Seika ファルマ（東京都中央区）が、来月にも供給を開始することが分かった。

9/17　Merck の Keytruda とエーザイの Lenvima の併用が肝癌 Ph3 試験でとうとう効果あり

Merck's Keytruda-Lenvima pair wins one in liver cancer subtype (fiercepharma.com)

9/18　「ネオセルフ」への攻撃で症状　自己免疫病の仕組み解明　−大阪大

ウイルスをやっつける免疫細胞が、自分の組織を攻撃して自己免疫病を起こすのはなぜか。大阪大の荒瀬尚教授らのグループが、自己と非自己のほか、「異物をもつ自己」を認識して攻撃する仕組みがあることを見つけ、米専門誌に発表した。新たな治療法開発につながる可能性がある。
グループは、ペプチドではなく自己の異常なたんぱく質が提示されているケースを見つけて「ネオセルフ」と名づけて研究を続けてきた。
ネオセルフの細胞をもつマウスを作って解析すると臓器のはれ、発熱など、全身エリテマトーデス（SLE）という自己免疫病の症状が出た。この症状はネオセルフ自体ではなく、ネオセルフを異物として認識し攻撃する T 細胞があることで引き起こされることもわかった。

9/18　Athira（本社：ワシントン州ボセル）がアルツハイマー病の失敗後、従業員の 70%を解雇、ALS 薬に賭ける

Athira Pharma は、今月初めのアルツハイマー病候補薬の失敗を受けて、火曜日、筋萎縮性側索硬化症（ALS）やその他の神経変性疾患の経口薬候補薬 ATH-1105 の開発に再び注力するため、従業員を 70%削減する再編を発表。

Pharma Industry News and Analysis | FirstWord Pharma
Athira lays off 70% of staff, bets on ALS drug after Alzheimer's bust

9/18　慶応医学賞に斎藤通紀さんら　iPS 細胞から精子や卵子をつくる研究

医学・生命科学の分野で優れた業績をあげた研究者に贈る今年の慶応医学賞に、京都大高等研究院の斎藤通紀教授（54）と、英グーグル・ディープマインド社のデミス・ハサビス最高経営責任者（48）が選ばれた。慶応義塾大学が発表した。授賞式は 11 月 20 日。賞状とメダル、賞金1千万円が両氏に贈られる。

9/19　性同一性障害から「性別不合」に　政府、WHO の最新版和訳で

心と体の性が一致しないトランスジェンダーが障害ではないとの考えの広がりを巡り、政府が 2027 年の施行を目指す世界保健機関（WHO）の「国際疾病分類」最新版の和訳で、性同一性障害ではなく「性別不合」を採用したことが 19 日分かった。ゲーム障害として知られる症状は「ゲーム行動症」と訳した。同日の厚生労働省の専門部会で和訳案がおおむね了承された。

9/19　コロナ定期接種、新タイプ含む 5 製品了承

厚生労働省のワクチン分科会は 19 日、今シーズンの定期接種で使う新型コロナウイルスワクチンについて、メッセンジャーRNA が細胞内で複製される「レプリコン」という新しいタイプのワクチンを含む 5 製品の使用を了承した。

9/19　ノーベル賞有力候補に日本ゆかりの 2 氏　光触媒と脳科学の研究者

英学術情報会社クラリベイトは 19 日、ノーベル賞の自然科学 3 賞と経済学賞の新たな有力候補 22 人を発表した。日本からは信州大アクア・リジェネレーション機構特別特任教授で東京大特別教授の堂免一成氏（70）と、米国国立眼病研究所の彦坂興秀氏を挙げた。

9/20　ネコ iPS 細胞、作製成功　阪公大、病気の解明に期待

細胞の情報を初期化し、さまざまな臓器や組織になれる能力（多能性）を持たせた人工多能性幹細胞（iPS 細胞）を巡り、ネコでも高品質の細胞作製に成功したと、20 日までに大阪公立大などのチームが発表した。病気のネコから細胞を作ることで、疾患を再現して調べたり、薬の効きを確かめたりすることに応用できるという。
チームによると、さまざまな細胞に分化する能力など iPS 細胞の特徴がすべて確かめられたものをネコで作製したのは世界初という。世界的に動物実験を避ける流れがある中で、鳩谷晋吾・大阪公立大教授（獣医学）は「iPS 細胞が代わりを果たせるのではないか。難しい病気の解明に期待したい」と話した。
チームは昨年、イヌの iPS 細胞作製に成功。その際に活用した遺伝子と同様のものがネコにもあり、それらをネコの線維芽細胞に入れたところ、作り出すことができた。ただ、初期化しなかった線維芽細胞が多く増殖し、iPS 細胞がうまく増えないという問題があった。
チームは初期化する際、薬剤に耐性を持たせる遺伝子を導入。初期化していない細胞だけが死ぬように薬剤で処理したところ、iPS 細胞だけを効率よく増やすことができた。

9/20　ブタからの「異種移植」厚労省が審査委を新設へ　特有の論点を議論

ブタの臓器をヒトへ移植する「異種移植」について、厚生労働省は、異種移植に特化した審査委員会を新設する方向で検討に入った。国内でヒトに移植される前に、その計画に問題がないか、この委員会が審査する。同省が 20 日、再生医療に関する専門家部会の会合で提案し、了承された。

9/20　新型コロナウイルス、中国の市場起源説に新たな証拠 新研究

新型コロナウイルス、中国の市場起源説に新たな証拠 新研究　写真 3 枚　国際ニュース：AFPBB News

9/21　パンダの iPS 細胞を初作製　将来は繁殖に応用　中国チーム

ジャイアントパンダの人工多能性幹細胞（iPS 細胞）を初めて作ったと、中国四川省成都市の「成都ジャイアントパンダ繁殖研究基地」などの研究チームが 20 日付の米科学誌サイエンス・アドバンシズに発表した。マウスでは iPS 細胞を精子や卵子に変える技術が実現しており、将来はパンダの iPS 細胞からの精子や卵子を使った体外受精により繁殖させることを目指すという。

9/21　AstraZeneca の点鼻インフルエンザワクチン FluMist の自己投与を FDA が承認

US FDA approves AstraZeneca's self-administered nasal spray flu vaccine | Reuters

9/23　重い腎臓病の胎児にブタの腎臓移植、東京慈恵医大が学内審査へ…世界的に注目の「異種移植」

重い腎臓病の胎児にブタの腎臓を一時的に移植する臨床研究について、東京慈恵医大などのチームが近く、学内の委員会に実施の審査を申請することがわかった。委員会の議論が順調に進めば、年度内にも移植計画を国に申請する。

9/24　アルツハイマー病新薬 Lilly の「ドナネマブ」を厚労省が 24 日承認

厚生労働省は 24 日、米製薬大手イーライリリーが開発したアルツハイマー病新薬「ドナネマブ」の製造販売を承認した。原因物質を除去して進行抑制を狙う新しいタイプの薬で、昨年実用化したエーザイなどの「レカネマブ」に続き 2 例目。

9/24　第一三共/AstraZeneca の Dato-DXd が乳癌 Ph3 試験でも生存改善示せず

Datopotamab deruxtecan final overall survival results reported in patients with metastatic HR-positive, HER2-low or negative breast cancer in TROPION-Breast01 Phase III trial | Business Wire

9/24　徳島大学開発の筋萎縮性側索硬化症（ALS）の新薬「ロゼバラミン」発表　早ければ年内に製造・販売か【徳島】

徳島大学は 2001 年から開発し治験を進めていた ALS = 筋萎縮性側索硬化症の新薬が、早ければ年内にも製造、販売が始まる見込みだと、9 月 24 日の会見で発表した。

ＡＬＳ新薬、厚労省が承認＝治験で生存期間５００日超延長―既存薬上回る、患者ら期待：iJAMP ポータル (jiji.com)

9/24　東京大、10 万円値上げ正式決定　授業料、来年度入学から　20 年ぶり改定

東京大は 24 日、来年度入学から年間の授業料を約 10 万円引き上げ、約 64 万円とすることを正式決定した。
改定案が役員会議で了承された。同大の授業料値上げは 20 年ぶりで、他大学も追随する可能性がある。

9/24　胃癌を治療するアステラス製薬の抗 CLDN18.2 抗体 Vyloy を欧州承認

Astellas' Vyloy Approved in Europe as First-Line Treatment for CLDN18.2-Positive Gastric Cancer | Precision Medicine Online

9/24　大学発の医療系スタートアップ支援、文科省が 4 拠点を選定…150 億円で新薬実用化や販路拡大

文部科学省は、大学発の医療系スタートアップ（新興企業）を財政面や人材面などでサポートする国内4か所の支援拠点を選定した。優れた医薬品や医療機器の実用化を支援したり、海外に販路を拡大するノウハウを伝えたりしてビジネスにつなげられるようにする。

9/25　遺伝子治療の売れ行き不振で苦しい bluebird bio（本社：マサチューセッツ州ケンブリッジ）が従業員を 25%削減

Bluebird bio lays off 25% of workforce as gene therapy pioneer struggles to stay afloat | Fierce Pharma

9/25　みんなに届け iPS　山中さん理事長の財団、毎月の寄付を募集

京都大学 iPS 細胞研究財団（理事長=山中伸弥・京大教授）が、毎月 1 千円以上の定額を寄付してくれる人を募るキャンペーン「みんなに届け iPS」を始めた。2022 年度から今年で 3 回目。寄付は iPS 細胞技術による新しい治療法確立を支援する取り組みなどに活用される。

9/25　Novartis、Flagship の Generate と 10 億ドル以上のバイオバックス契約を締結

Novartis は、Flagship が設立した Generate:Biomedicines（本社：マサチューセッツ州ソマービル）と、複数の適応症にわたるタンパク質治療薬の開発に向けて、10 億ドル以上の価値がある可能性がある契約を締結した。

両社は潜在的な疾患領域について詳細を明らかにしておらず、9 月 24 日のリリースでは、この契約を「マルチターゲットコラボレーション」とのみ言及した。

Generate gains another $1B-plus Big Pharma partnership (fiercebiotech.com)

AI firm Generate signs $1bn discovery deal with Novartis | pharmaphorum

9/25　Sanofi が Mike Quigley 氏を国際研究を指揮する新たな研究リーダーに任命

Sanofi が今週、新たな最高科学責任者（CSO）を任命。これは、同社がこれまで以上に研究開発に注力する姿勢を確立する一連の措置の一環であると同社は主張している。
STAT が入手した社内メモによると、Sanofi は月曜日、スタートアップ企業のデュアリタス・セラピューティクスやテリニ・バイオの元 CEO で、Gilead の研究生物学担当上級副社長である Mike Quigley 氏を最高科学責任者兼グローバル研究責任者に任命したと発表した。

Sanofi hires Mike Quigley as next chief scientist, internal memo says – Endpoints News (endpts.com)

Sanofi names new chief scientific officer amid push to redefine itself (statnews.com)

9/26　経口中絶薬、外来でも使用可能に　無床診療所への拡大は再審議

人工妊娠中絶のための飲み薬について、厚生労働省の薬事審議会は 25 日、一定の条件を満たせば外来での使用を可能とする方針を了承した。入院ベッドのない無床診療所での使用については、「準備が整っていない」とし、専門家部会で再度審議する。

9/26　Emergent（本社：カリフォルニア州レッドウッドシティー）が天然痘/エムポックスに備えたワクチンなどの製品 4 億ドル分を受注

Emergent BioSolutions racks up $400M in mpox preparedness orders as outbreak continues its spread | Fierce Pharma

9/26　血液がん遺伝子検査が実用化　網羅的に解析、診断に有用

国立がん研究センターと大塚製薬などは 26 日、白血病やリンパ腫などの血液のがんを対象に開発した、400 以上の遺伝子異常を網羅的に調べる「がん遺伝子パネル検査」が製造販売承認を受けたと発表した。血液がんでの承認は国内で初めて。今後保険適用される見通し。
がんに関わる遺伝子の異常をまとめて調べる遺伝子検査は、固形がんを対象とした複数がすでに保険適用となっている。一方血液がんは原因となる遺伝子が固形がんと異なり、種類も多いため、検査の開発が遅れていた。

9/26　ウンチをしないオタマジャクシを新発見　−名古屋大の研究チーム

名古屋大学の研究チームは 9 月 25 日、オタマジャクシの姿でいる間はフンをしないカエルがいることを発見したと発表した。石垣島や西表島、台湾に生息する「アイフィンガーガエル」で、このような特殊な適応戦略は、カエルで初めて確認したとう。

9/27　BMS の統合失調症薬 Cobenfy（コベンフィ）を米国承認

数十年ぶりの統合失調症の新薬、BMS の Cobenfy として知られる KarXT に対する FDA の承認は、BMS の取引の手腕を示すものであり、新世代の治療薬の転換点となるだろう、と PharmaVoice に書かれている。

Behind the rise BMS' Cobenfy, the first new schizophrenia drug in decades | PharmaVoice

9/27　麻酔薬が不足 「供給を制限」メーカー通達　製造所の移転が原因

9/27　デンマークの Novo Nordisk がドイツの Evotec と組んで細胞治療用の技術を開発

Novo, Evotec Ink Stem Cell Partnership as Drugmaker Looks to Expand Pipeline - BioSpace

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. インスリンを生成するベータ細胞は他の膵臓内分泌細胞と連携する必要がない –マウス実験

2. アルツハイマー病マウスモデルにおける記憶喪失を回復させる新薬の発見

3. 「減量の奇跡の薬」GLP-1R 作動薬の新たな中枢作用標的がマウス研究で明らかに

4. マウスのセロトニン放出が逆境からの回復力を支える重要な媒介に

5. 棘ネズミが社会神経科学の新たな道を示す

6. 高齢マウスにおける卵巣機能を延ばす新たな治療法

7. マウスの腸内細菌叢と攻撃性との関連性に関する研究

8. 豚がラット肝炎ウイルスの人間への感染経路となる可能性

9. パーキンソン病治療が意思決定に与える悪影響 –マウス研究

1. インスリンを生成するベータ細胞は他の膵臓内分泌細胞と連携する必要がない –マウス実験

日付：2024 年 9 月 3 日
出典：ジュネーブ大学

概要：
血糖値の調節は膵臓の β 細胞がグルコースを検出し、インスリンを分泌する能力に依存している。β 細胞が機能しなくなると糖尿病が発症する。これまでの科学的見解では、β 細胞は他のホルモンを生成する膵臓内分泌細胞と協力する必要があるとされていた。しかし、ジュネーブ大学の研究チームが行った最新の研究では、成人マウスの膵臓に β 細胞のみが存在する状態でも血糖調節やインスリン感受性が向上することが示された。この研究結果は『Nature Metabolism』誌に掲載されている。
研究チームは、膵臓の非 β 細胞を選択的に除去したマウスを用い、β 細胞だけで血糖調節がどのように行われるかを調べた。その結果、β 細胞のみで構成された膵臓でも血糖値の管理が非常に効果的で、標準のマウスよりも健康であることが分かった。特に高脂肪食を摂取した場合やインスリン抵抗性のテストを行った際にも、インスリン感受性が改善されていた。
この研究は、膵臓の非 β 細胞が血糖調節において必須でないことを示しており、これまでの認識を覆す結果となっている。今後の研究では、インスリン細胞に焦点を当てた治療法の開発が期待されており、特に細胞の機能転換を促進する分子の同定や、幹細胞を用いた新たな β 細胞の生成が進められる予定である。

研究関連ニュース/他のトップページに戻る

＜英文＞Insulin cells don't need to team up | ScienceDaily

Insulin cells don't need to team up

Scientists show that insulin-producing beta cells don't need other pancreatic endocrine cells to stabilize blood sugar levels

Date: September 3, 2024

Source: Université de Genève

Summary:

Our glycaemic balance is based on the ability of the pancreatic beta cells to detect glucose and secrete insulin to maintain our blood sugar levels. If these cells malfunction, the balance is broken, and diabetes develops. Until now, the scientific community agreed that beta cells needed the other hormone-producing cells of the

pancreas to function properly. A team has now demonstrated the opposite: in adult mice whose pancreas contains only beta cells, glycaemia regulation and insulin sensitivity are even better than in standard animals.

FULL STORY

Our glycaemic balance is based on the ability of the pancreatic beta cells to detect glucose and secrete insulin to maintain our blood sugar levels. If these cells malfunction, the balance is broken, and diabetes develops. Until now, the scientific community agreed that beta cells needed the other hormone-producing cells of the pancreas to function properly. A team from the University of Geneva (UNIGE) has demonstrated the opposite: in adult mice whose pancreas contains only beta cells, glycaemia regulation and insulin sensitivity are even better than in standard animals. These results, which open major clinical prospects, can be read in the journal *Nature Metabolism*.

In 2010, the team led by Pedro Herrera, a professor in the Department of Genetic Medicine and Development and in the Diabetes Centre at the UNIGE Faculty of Medicine, discovered the remarkable ability of pancreatic cells to change function.

If beta cells die prematurely, the endocrine cells normally responsible for producing other hormones, such as glucagon or somatostatin, can start producing insulin.

"Until now, it was thought that the differentiated adult cells of an organism could not regenerate and reorientate themselves functionally.

Pharmacologically triggering this cellular plasticity could therefore form the basis of an entirely new therapy for diabetes.

But what happens if all the cells of the endocrine pancreas abandon their original function to start producing insulin?

It is what we wanted to find out in our new study," explains Pedro Herrera.

Non-beta cells are not essential

It was accepted that beta cells could only function correctly in the presence of the other hormone-producing cells -- alpha, delta and gamma cells -- grouped together in islets within the pancreas.

"To verify this, we produced mice in which, when they reach adulthood, all the non-beta cells in the pancreas can be selectively eliminated to observe how the beta cells manage to regulate glycaemia," explains Marta Perez Frances, a researcher in Pedro Herrera's laboratory and first author of this work.

"Surprisingly, not only were our mice perfectly capable of managing their blood sugar levels effectively, but they were even healthier than the control mice!"

Even when fed a high-fat diet or tested for resistance to insulin -- one of the main markers of diabetes -- these mice showed improved sensitivity to insulin in all the target tissues, and particularly in adipose tissue.

Why? "There is an adaptation process in which the body recruits other hormonal cells from outside the pancreas to cope with the sudden reduction in glucagon and other pancreatic hormones," notes Pedro Herrera. "But this clearly shows that non-beta cells of the pancreatic islets are not essential for maintaining glycaemic balance." These results are surprising and challenge the prevailing conception up until now.

Emerging new therapies

Naturally, around 2% of pancreatic cells change their function in the event of insulin deficiency. The challenge is now to identify a molecule capable of inducing and amplifying this conversion. Another strategy would be to differentiate stem cells in vitro to produce new beta cells before transplanting them into the patients. "Our results are proof that strategies focusing on insulin cells could really pay off," enthuses Pedro Herrera. "The next stage of our work will therefore involve establishing the molecular and epigenetic profile of non-beta cells from diabetic and non-diabetic individuals in the hope of identifying the elements which could make it possible to induce the conversion of these cells in the pathological context of diabetes."

Story Source:

Materials provided by Université de Genève. *Note: Content may be edited for style and length.*

Journal Reference:

1. Marta Perez-Frances, Eva Bru-Tari, Christian Cohrs, Maria Valentina Abate, Léon van Gurp, Kenichiro Furuyama, Stephan Speier, Fabrizio Thorel, Pedro L. Herrera. Regulated and adaptive in vivo insulin secretion from islets only containing β-cells. *Nature Metabolism*, 2024; DOI: 10.1038/s42255-024-01114-8

2. アルツハイマー病マウスモデルにおける記憶喪失を回復させる新薬の発見

日付：2024 年 9 月 3 日
出典：オーバーン大学物理学部

概要：
オーバーン大学の科学者たちは、新薬「トロリルゾール（troriluzole）」がアルツハイマー病マウスモデルの記憶喪失と認知機能の低下を逆転させる可能性を示す研究を発表した。この研究は『Journal of Neurochemistry』誌に掲載され、トロリルゾールがアルツハイマーの初期段階の変化にどのように作用するかが初めて示されている。
研究の主導者であるミランダ・リード教授は、薬剤が病気の初期段階に介入することで、アルツハイマー病を予防または治癒する療法を開発することを目指していると述べている。この研究では、トロリルゾールが早期のアルツハイマーを模倣する遺伝子改変マウスにおいて正常な脳機能を維持できることが示された。結果として、トロリルゾールは有害なグルタミン酸のレベルを低下させ、マウスの記憶と学習能力を改善することが確認された。トロリルゾールを投与したマウスは、シナプスのグルタミン酸レベルが有意に減少し、脳の過活動が低下した。この分子的変化は具体的な改善につながり、迷路のナビゲーションなどの記憶テストでのパフォーマンス向上が見られた。
今後は、トロリルゾールが病気の進行の異なる段階でどのように作用するかを解明するためのさらなる研究が必要とされている。

研究関連ニュース/他のトップページに戻る

＜英文＞Auburn researchers show novel drug rescues me | EurekAlert!

NEWS RELEASE 3-SEP-2024

Auburn researchers show novel drug rescues memory loss in Alzheimer's mouse model

New research from Auburn University reveals a potential breakthrough in Alzheimer's treatment, showing that the drug troriluzole can reverse memory loss and cognitive decline in mice.

Peer-Reviewed Publication

AUBURN UNIVERSITY DEPARTMENT OF PHYSICS

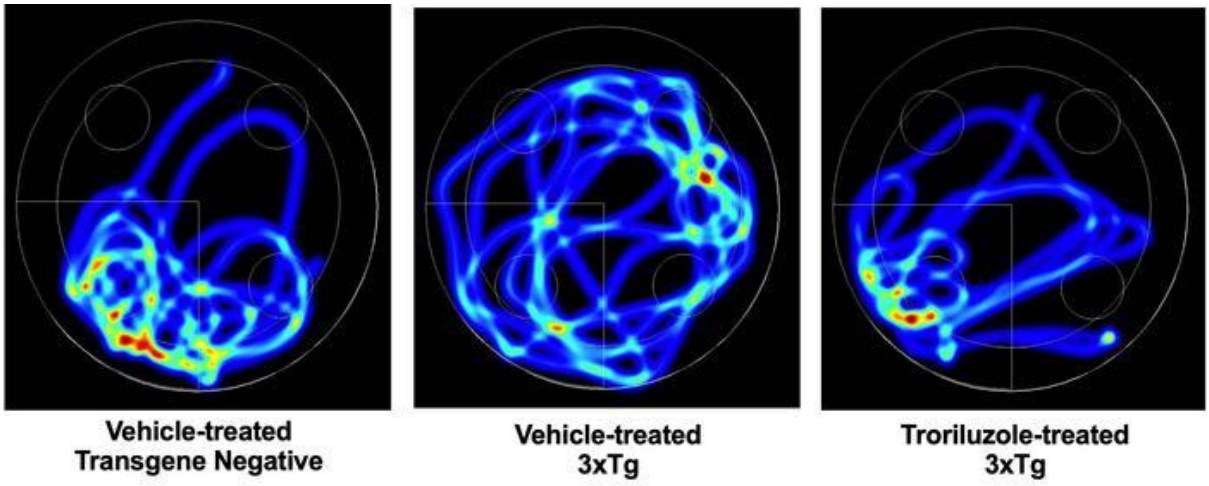


image:

Shown are representative heatmap visualization of spatial occupancy during probe trials of the Morris water maze. The warmer the colors correlate with an increased time spent in that

view more

Credit: Dr. Michael Gramlich & Dr. Miranda Reed

AUBURN, AL — In a recent development in Alzheimer's disease research, Auburn University scientists have studied a new drug, troriluzole, that can prevent brain changes leading to memory loss and cognitive decline in a mouse model of the disease. This study, recently published in the *Journal of Neurochemistry*, is the first to show how troriluzole can target early-stage alterations associated with Alzheimer's, providing new hope for potential treatments.

Dr. Miranda Reed, a Professor in the department of Drug Discovery at Auburn University and Delivery and the studies main researcher, noted that "by examining how drug treatments can intervene early in the disease process, we aim to develop therapies that might prevent or even cure Alzheimer's." "This study also highlights how scientific advancements can transform our understanding of complex diseases like Alzheimer's," said Dr. Michael Gramlich, an Assistant Professor of Biophysics and the study's other main researcher.

Breaking New Ground in Alzheimer's Research

Alzheimer's disease affects millions of people worldwide, causing progressive memory loss, confusion, and eventually the inability to perform basic tasks. Despite decades of research, a cure remains elusive. Alzheimer's is characterized by the accumulation of amyloid plaques and tau tangles in the brain, which disrupt neural communication. In the early stages, excessive levels of the neurotransmitter glutamate cause damaging overactivity in synapses, the connections between nerve cells.

The study conducted by Auburn University researchers, led by Drs. Miranda Reed and Michael Gramlich, investigated how troriluzole, a novel drug, can maintain normal brain function in mice genetically modified to replicate early Alzheimer's stages. The results are compelling: troriluzole not only reduced harmful glutamate levels but also improved memory and learning in the mice, suggesting a maintenance of healthy brain function.

"Our research demonstrates that by targeting synaptic activity early, we may be able to prevent or slow the progression of Alzheimer's. This could revolutionize the way we approach treatment for this disease," noted both researchers.

How Troriluzole Works

In the Auburn study, mice treated with troriluzole showed a significant reduction in synaptic glutamate levels and decreased brain hyperactivity. These molecular changes led to tangible improvements: the treated mice performed better in memory tests, such as navigating mazes, indicating that their cognitive functions were restored.

"These findings are promising because they suggest that troriluzole can protect the brain at a fundamental level, starting with molecular changes and resulting in improved cognitive abilities," said Dr. Reed. "It's like repairing an engine before it fails completely."

A Collaborative Effort with Wide Implications

This research was a collaborative effort involving Auburn University's College of Science and Mathematics, the Harrison College of Pharmacy, and the Center for Neuroscience Initiative, along with private researchers and students. The team's combined expertise in neuroscience and pharmacology was crucial to the study's success.

"This collaboration blends basic science and pharmaceutical research to tackle one of the most challenging neurological issues of our time," Dr. Gramlich emphasized. "Our work not only enhances scientific understanding of Alzheimer's disease but also offers a potential new treatment that could improve the lives of millions worldwide."

What's Next?

While the results in mice are encouraging, the researchers emphasize the need for further studies to determine how troriluzole works at different stages of disease progression.

JOURNAL:

Journal of Neurochemistry

DOI:

10.1111/jnc.16215

METHOD OF RESEARCH:

Experimental study

SUBJECT OF RESEARCH:

Animals

ARTICLE TITLE:

Troriluzole rescues glutamatergic deficits, amyloid and tau pathology, and synaptic and memory impairments in 3xTg-AD mice

ARTICLE PUBLICATION DATE:

30-Aug-2024

COI STATEMENT:

Vladimir Coric and Irfan A. Qureshi, authors of the manuscript, are employees and shareholders of Biohaven Pharmaceuticals.

3. 「減量の奇跡の薬」GLP-1R 作動薬の新たな中枢作用標的がマウス研究で明らかに

日付：2024 年 9 月 5 日
出典：中国科学院深圳先進技術研究院

概要：
中国科学院深圳先進技術研究院の研究グループは、抗肥満薬リラグルチドの食欲抑制と体重減少効果をマウスを用いて明らかにし、『Journal of Clinical Investigation』誌で発表している。
肥満は世界的に重要な慢性疾患であり、健康問題や医療負担を引き起こしている。抗肥満薬は生活習慣や食事療法よりも高い効果を示し、手術に比べてリスクや副作用が少ない。GLP-1 受容体作動薬は 2014 年以降、特に糖尿病治療や体重減少において注目されている。
GLP-1 は、腸の L 細胞や脳幹の一部の神経細胞から分泌されるホルモンで、その作用は GLP-1 受容体を介している。リラグルチドは最初の GLP-1 ベースの抗肥満薬で、食欲を抑え、胃の排出を遅らせる。研究者たちは、腹側側坐核（LS）に GLP-1 受容体が豊富に存在し、リラグルチドがこの領域の GLP-1R 陽性神経細胞を強く活性化することを発見。LS 内で GLP-1 受容体の機能を低下させると、リラグルチドの食欲抑制効果と体重減少効果が弱まることがわかった。
また、自由に動き回るマウスを用いて、食事中の LSGLP-1R 神経細胞の活動を調査したところ、食事開始時に Ca2+信号が有意に減少し、その後も食事中は低いままで、食事終了後に元のレベルに戻ることが観察された。これにより、これらの神経細胞の活性化が食欲を抑制し、体重を減少させることが示された。
この研究は、食行動の神経メカニズムに関する貴重な知見を提供し、摂食障害や肥満治療の新たな戦略を模索するための基盤を築くものである。

研究関連ニュース/他のトップページに戻る

＜英文＞Researchers reveal new central action target | EurekAlert!

NEWS RELEASE 5-SEP-2024

Researchers reveal new central action target of the “weight loss miracle drug” GLP-1R agonists in mice

Peer-Reviewed Publication

SHENZHEN INSTITUTE OF ADVANCED TECHNOLOGY, CHINESE ACADEMY OF SCIENCES

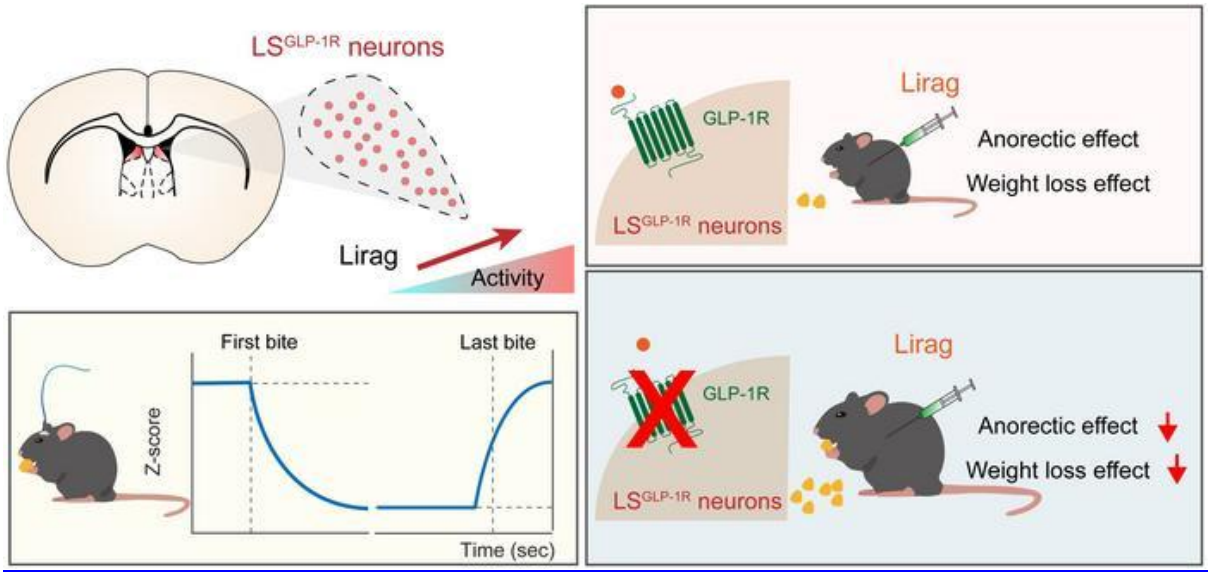


image:

Summary of the role of LSGLP-1R neurons in mediating the anorectic and weight-lowering effects of liraglutide in mice.

view more

Credit: ZHU Yingjie

A research group led by Prof. ZHU Yingjie from the Shenzhen Institute of Advanced Technology (SIAT) of the Chinese Academy of Sciences (CAS), has revealed the essential role of lateral septum (LS) neurons in mediating anorectic and weight-lowering effects of the anti-obesity drug— liraglutide in mice.

The study was published in the *Journal of Clinical Investigation* on Sep. 03.

Obesity is now among the top ten chronic diseases worldwide, causing a range of health issues and increasing the medical burden. Anti-obesity medications have shown greater efficacy than lifestyle changes and diet, with lower risks and fewer side effects than surgery. Since 2014, GLP-1 receptor agonists have emerged as a groundbreaking class of medications, significantly outperforming other weight loss drugs in both effectiveness and safety. They have been showing a trend toward becoming the next generation of "blockbuster" drugs, particularly in diabetes management and weight loss.

Glucagon-like peptide-1 (GLP-1) is an incretin hormone encoded by the *proglucagon* gene (GCG), primarily secreted by intestinal L cells and a subset of neurons in the brainstem. Its effects are mediated through the GLP-1 receptor (GLP-1R), a class B G protein-coupled receptor widely expressed in both the peripheral and central nervous systems. Liraglutide, a short-acting GLP-1R agonist, reduces appetite and slows gastric emptying, making it the first GLP-1-based anti-obesity drug on the market. Despite the widespread expression of GLP-1R in the brain, the precise neural mechanisms through which its agonists regulate food intake and body weight remain poorly understood.

In this study, researchers discovered that GLP-1 receptors (GLP-1Rs) are abundantly expressed in the dorsal LS, and they found that liraglutide strongly activated GLP-1R-positive ($LS^{GLP\text{-}1R}$) neurons in this region. Knockdown of GLP-1Rs in the LS attenuates liraglutide's effects on feeding suppression and weight-lowering, whereas targeted knockdown in the hypothalamic regions, such as the paraventricular nucleus of the

hypothalamus (PVN) and arcuate nucleus of the hypothalamus (Arc), fails to replicate the effect. This suggests that GLP-1Rs in LS mediated the anorectic effect of liraglutide.

Furthermore, researchers investigated the intrinsic activity of $LS^{GLP\text{-}1R}$ neurons during natural feeding by using fiber photometry in freely moving mice. They observed a significant decrease in Ca^{2+} signals at the start of food consumption, which continued throughout the eating period and returned to baseline after feeding ended. The activation of these neurons suppresses feeding and reduces body weight, mimicking the effects of liraglutide. Conversely, the inactivation of these neurons substantially attenuates liraglutide's anorectic and weight-reducing efficacy.

This study provides valuable insights into the neural mechanisms underlying feeding behavior, paving the way for new strategies to treat eating disorders and obesity, as well as further exploration of the GLP-1 signaling pathway.

JOURNAL:

Journal of Clinical Investigation

DOI:

10.1172/JCI178239

METHOD OF RESEARCH:

Commentary/editorial

SUBJECT OF RESEARCH:

Animals

ARTICLE TITLE:

GLP-1R–positive neurons in the lateral septum mediate the anorectic and weight-lowering effects of liraglutide in mice

ARTICLE PUBLICATION DATE:

3-Sep-2024

4. マウスのセロトニン放出が逆境からの回復力を支える重要な媒介に

日付：2024 年 9 月 5 日
出典：ローザンヌ大学

概要：
ローザンヌ大学の神経科学者たちが『Science』誌に発表したマウス研究によると、他者がトラウマ体験に対処する様子を観察することで、自己の回復力が高まり、抑鬱などの病的状態を防ぐことができる。この「感情の伝染」は、脳内のハベヌラという構造で放出される神経伝達物質セロトニンによって媒介されていることが明らかになった。
研究チームは、回復力を促進する実験モデルを設計し、トラウマ後の病的特性の出現を測定した。特に、観察者のマウスを電気ショックを受けたマウスの近くに配置したところ、観察したマウスは自らも同様の体験をした際に病的状態に陥りにくいことが確認された。一方、他のマウスはこの経験を目撃していなかったため、回復力が低下した。
さらに、ハベヌラにおけるセロトニンの動態がこの効果の鍵であることが示された。行動実験中にセロトニンの放出が増加し、この変化がハベヌラの神経細胞の機能に持続的な影響を与えることがわかった。セロトニンのレベルを人工的に調整した結果、その増加が回復力を促進する能力を損なうことも示された。
この研究は、抑鬱のメカニズムと回復力の関連性を再考するものであり、セロトニンに着目した新たな治療法の可能性を示唆している。特に、セロトニン活性化薬やサイケデリック療法の既存の薬剤を用いることで、より良い治療アプローチを探ることが期待される。

研究関連ニュース/他のトップページに戻る

＜英文＞Serotonin to bounce back from adversity | EurekAlert!

NEWS RELEASE 5-SEP-2024

Serotonin to bounce back from adversity

Peer-Reviewed Publication

UNIVERSITY OF LAUSANNE

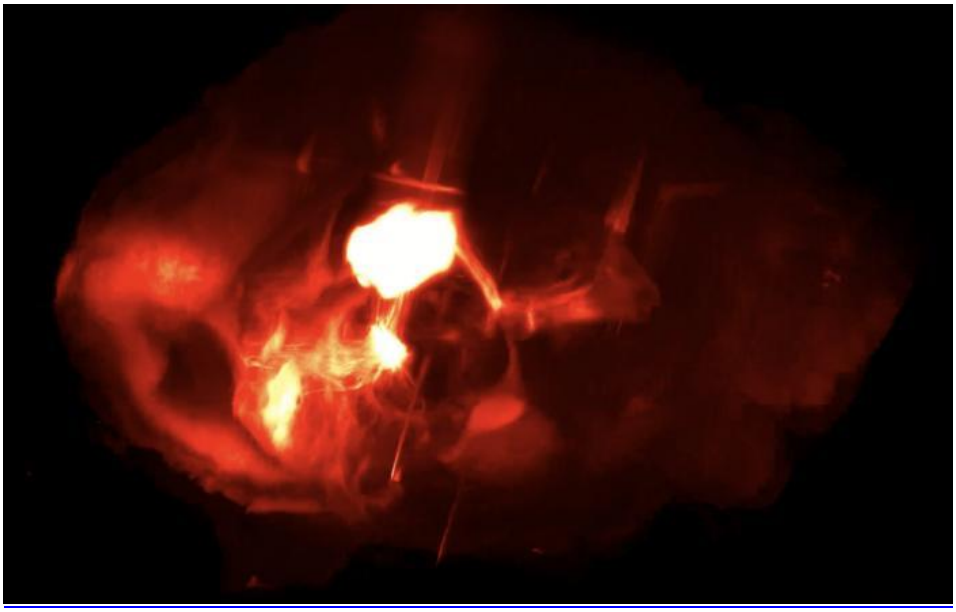


image:

The neurotransmitter serotonin, released in a brain structure called the habenula, is the key molecule mediating resilience. Image shows neurons within the mouse habenula.

view more

Credit: Laboratory of Manuel Mameli, UNIL.

The simple act of observing others cope with a traumatic experience can increase our capacity for resilience and prevent the pathological states that can result from it, notably depression. Neuroscientists at UNIL have demonstrated the presence of this "emotional contagion" in mice, and successfully deciphered its mechanism. The neurotransmitter serotonin, released in a brain structure called the habenula, has been shown to be the key to resilience. This discovery, published in Science, revisits the role of serotonin and opens up new perspectives, notably for understanding depression and its treatment.

Human beings have the ability to cope with aversive experiences while continuing to live a normal life. This ability is known as resilience. However, some individuals are more vulnerable to traumatic events. They develop a loss of motivation and drive, which are hallmarks of depression. Promoting resilience in such people at risk could counter their vulnerability and function as a preventive practice against the possible emergence of a pathological state. But there are still too many unknowns for resilience to be used as a preventive practice. "There is a lack of clinical tools or underlying mechanisms to promote this type of conditioning capable of fostering a resilient reaction as in healthy people", says Manuel Mameli, Associate Professor at the Department of Fundamental Neurosciences at the Faculty of Biology and Medicine, University of Lausanne (UNIL). To achieve this, we need to understand the brain function behind adversity – a challenge that Manuel Mameli's team has successfully undertaken.

Observing for self-preservation

To explore the underlying brain mechanisms, the UNIL neuroscientists first designed an experimental model capable of promoting resilience and measuring its consequences on the appearance of pathological traits following trauma. "We started from the recognized fact that simply observing the emotional experiences of others helps us to learn from them. It's a phenomenon known as emotional contagion, and it engages resilience", explains Manuel Mameli.

To achieve this, an "observer" mouse was placed close to a mouse subjected to small electric shocks to the paws. This simple task protected the majority of the observer mice from developing pathological states of depression when they were subsequently exposed to this unpleasant experience themselves. This was not the case for mice who had not witnessed the traumatic experiences of their fellow companions. The scientists concluded that the simple act of observing others cope with a traumatic experience increases one's own capacity for resilience and helps guard against possible pathological consequences.

Serotonin, the resilience molecule

Following the discovery of this behavioral principle, the neuroscientists successfully identified the brain mechanism mediating it. They focused on the habenula, a tiny cerebral structure located at the heart of the brain, known to participate in emotional and sensory processing, and to regulate neurotransmitters associated with depression, notably serotonin. To achieve this, they specifically developed imaging tools to track this molecule in mice. "It is very difficult to measure the variation of serotonin in the brain. Thanks to a biosensor developed by Yulong Li of Peking University, co-author of the study, we were able to identify the key mechanism", adds Manuel Mameli.

Recordings made during behavioral experiments revealed that emotional contagion coincided with a lasting change in the functioning of neurons in the habenula, together with an increase in serotonin release in this region. More specifically, according to Sarah Mondoloni, postdoctoral fellow in Manuel Mameli's laboratory at UNIL and first investigator of the study, "it is the dynamics of serotonin that change during this task, and this is the key finding of our study". By artificially altering the dynamics of serotonin levels, the research team was able to demonstrate that its non-increase not only undermines the long-lasting neuronal activity change in the habenula, but also the ability of mice to foster resilience following adversity.

Re-exploring the mechanisms of depression

A common denominator between the mechanism of resilience after adversity discovered in this study and that of depression is serotonin. Many antidepressants target serotonin to increase its concentration in the brain. Here, neuroscientists show that a transient, localized increase in the habenula can prevent the onset of apathetic behavior following a traumatic experience. "This property of the serotonergic system is an exciting information for neuroscientists. But our discovery could also pave the way for new therapeutic applications relevant to depression, for example by testing existing pharmacological serotonin activators, including psychedelic therapies that stimulate the serotonin system. Their use could be refined to achieve better therapeutic approaches", concludes Manuel Mameli.

JOURNAL:

Science

DOI:

10.1126/science.adp3897

METHOD OF RESEARCH:

Experimental study

ARTICLE TITLE:

Serotonin release in habenula during emotional contagion promotes resilience

ARTICLE PUBLICATION DATE:

6-Sep-2024

5. 棘ネズミが社会神経科学の新たな道を示す

日付：2024 年 9 月 11 日
出典：エモリー大学

概要：
エモリー大学の研究者たちは、棘ネズミの脳回路が大きな集団で生活する欲求を促進していることを発見し、哺乳類の複雑な社会行動を研究する新しいモデルを提供している。この研究は『Current Biology』誌に掲載されており、前帯状皮質から外側傍隔核への神経信号が棘ネズミの集団サイズの好みを駆動することが示されている。
棘ネズミは、野生で混合性の大きなグループで生活するよう進化しており、他の実験動物とは異なる社会行動の理解が進むと期待される。研究では、棘ネズミが知らない個体を受け入れ合うことが観察され、彼らの社会的大胆さや大きなグループへの好みが明らかになった。
実験では、棘ネズミを小グループと大グループに分け、脳の活動をスキャンした。その結果、大きなグループにいる棘ネズミでは、外側傍隔核（LS）の活動が高まることが示された。さらに、前帯状皮質（ACC）から LS への神経回路を一時的に停止させる実験を行ったところ、この回路が集団サイズの好みに強い影響を与えることが確認された。
研究者たちは今後、棘ネズミを用いて協力的な集団生活を促進する要因や、集団解散に至る環境的な転換点を探る計画だ。この研究は、社会的な行動を促進する脳の回路を理解する手がかりを提供し、人間社会の理解にもつながる可能性がある。

研究関連ニュース/他のトップページに戻る

＜英文＞Spiny mice point the way to new path in socia | EurekAlert!

NEWS RELEASE 11-SEP-2024

Spiny mice point the way to new path in social neuroscience

Neural circuitry tied to communal living in a mammal identified for first time

Peer-Reviewed Publication

EMORY UNIVERSITY

image:

Spiny mice evolved to live in the wild in large, mixed-sex groups.

view more

Credit: Aubrey Kelly

Scientists zeroed in on brain circuitry powering the desire of spiny mice to live in large groups, opening the door to a new model for the study of complex social behaviors in mammals.

Current Biology published the work led by researchers at Emory University. It shows that neural signaling from the brain's anterior cingulate cortex to the lateral septum drives the preference for spiny mice (Acomys) to affiliate with large peer groups.

"To our knowledge, this is the first study to identify neural circuitry that promotes group-size preferences in a mammal," says Aubrey Kelly, senior author of the study and associate professor of psychology at Emory. "We hope that our work paves the way for new insights into complex social behaviors in a range of mammals, including humans."

The Kelly lab made the breakthrough by developing methods to use spiny mice as a laboratory model for social neuroscience.

Unlike the rats and mice commonly used in laboratory research, spiny mice evolved to live in the wild in large, mixed-sex groups — they even allow unrelated newcomers to join their groups.

"A spiny mouse colony is not just one big family," Kelly explains. "It's more like a little society."

Brandon Fricker, first author of the study, worked on the research as a PhD student at Emory. He graduated in May and now works as a postdoctoral fellow at Harvard University.

"It was challenging, but fun, to design experiments and validate our methods for a species that is new to social neuroscience," Fricker says. "I really enjoyed working with spiny mice. They have a very different temperament than I've seen in other lab rodents. They don't show nearly as much fear or aggression towards each other, or even towards humans."

Despite the prevalence of communal living across the animal kingdom — from ants to birds to humans — methods to study the neural mechanisms that make group living possible have been lacking.

One major limitation is that the species of rats and mice commonly used in lab research do not get along well in large, mixed groups. In the wild, for instance, the classic lab rat Rattus norvegicus domesticaprimarily lives in groups of one male and many females. When males get together, they tend to fight.

The prairie vole — a small, mouse-like rodent that mates with a partner for life — has emerged in recent decades as an excellent laboratory model for the neuroscience of pair-bonding. While they are notable for their lifelong mates, however, wild prairie voles live in small family groups and are quite aggressive toward strangers.

As a graduate student Kelly, who has a PhD in evolutionary biology, explored the neural evolution of flocking behavior in birds using several finch species that ranged from being solitary to highly social.

She wanted to examine group living in mammals but was stumped by the lack of a good animal model.

"It's important to consider how an animal behaves in the real world when trying to understand how the brain works," Kelly says. "You need to have the right animal for your particular question."

Enter the spiny mouse.

Kelly first heard about these quirky rodents through a chance conversation with Ashley Seifert, a biology professor at the University of Kentucky and a co-author of the current paper.

More than a decade ago, scientists learned that the spiny mouse, which lives in arid environments in Africa, the Middle East and southern Asia, has remarkable powers of wound healing, including the ability to regenerate large suites of tissue. If a predator grabs a spiny mouse its skin slips off, allowing the mouse to escape. It then regenerates its skin, complete with stiff, spiny hairs.

Studies have also shown that the spiny mouse has unique adaptive responses related to damages to the heart, kidney and the spinal cord.

Seifert is among a growing number of scientists using the spiny mouse as a biomedical model for regeneration research. Spiny mice have also recently emerged as a model for Type 2 diabetes studies. And a handful of labs have published work on the prosocial behaviors of spiny mice and their developmental traits.

When Seifert learned that Kelly wanted a better rodent model for social neuroscience, he suggested spiny mice.

"I was feeling bold and decided to try to build a social neuroscience program around them," Kelly says.

Fricker came to Emory as a graduate student five years ago shortly after Kelly launched her lab's spiny mice program, intrigued by this new approach.

"I'm really interested in the neuroscience of social behaviors," he says. "How do neurons react to stimuli from others that we encounter and then signal how we should respond? It's critical both to our survival and to our emotional well-being. Like on the first day of school when there is a lot of pressure to make friends. Misreading a situation during that time is not ideal."

The researchers further characterized the social behaviors of spiny mice in the lab. They found that, regardless of familiarity, spiny mice rapidly approach peers, demonstrating high social boldness. They are significantly

more prosocial than aggressive with one another. Spiny mice also showed a strong preference for hanging out with large over small groups.

For the current paper, they wanted to determine the neural circuitry behind this large-group preference.

In one experiment the researchers exposed some spicy mice subjects to small groups of their peers and others to larger groups. They then scanned the brains of the subjects to look for expression of the Fos protein, a product created when neurons fire. This neuroscience technique showed that activity in the lateral septum (LS) region of the brain was higher in the spiny mice hanging out in the larger groups.

It is well-established that the lateral septum is involved in a variety of functions, including aggression and other social behaviors. In previous research, Kelly had found that this brain region is associated with flocking behavior in zebra finches.

"A brain region can be involved in so many different things, from aggression to flocking, depending on how it is interacting with other regions," Kelly says. "As technology has advanced, neuroscience is going beyond looking at single brain regions to studying the connections between different regions."

To identify circuitry involved in the large-group preference, the researchers repeated the previous experiment with the addition of neuronal tracers in the subjects. These chemical probes can map where in the brain a signal originates and the direction it travels.

The results showed a stronger signal from the anterior cingulate cortex (ACC) to the LS for the spiny mice exposed to larger, versus smaller, groups of their peers. Previous work has associated the ACC with consoling and other social behaviors in prairie voles. In humans, the ACC is involved in attention, decision-making and emotion.

The researchers then conducted experiments using chemogenetic tools that allowed them to temporarily switch off the ACC-to-LS circuit. The results showed that when this circuit was switched off, female spiny mice showed no preference when given a choice to hang out with a smaller versus a larger group. The males, however, actually flipped their preferences and chose to spend more time with a smaller group.

"I was surprised to see how strong of a change in behavior shutting down this circuit caused," Fricker says. "That shows that the ACC-LS circuit exerts a lot of influence over group-size preference."

Co-author Malvika Murugan, assistant professor in Emory's Department of Biology and an expert in viral chemogenetic techniques for neuroscience, assisted with troubleshooting the validation of the methods in the spiny mice.

The researchers used the inanimate objects of rubber ducks to test whether the ACC-LS circuit specifically promotes social preferences or just any preference for a large group of objects. While spiny mice prefer investigating a larger over a small group of rubber ducks, manipulation of this brain circuit had no effect on rubber duck preferences.

"That really highlighted that the neural circuit we identified was modulating social group-size preferences rather than something broader," Fricker says.

The researchers have now set the stage for delving deeper into the neuroscience of mammalian grouping behaviors using spiny mice as a model.

"From here, we're going to collect more behaviorally rich datasets by allowing the spiny mice to freely interact together in large groups and analyze the activity in their brains," Kelly says. "That will give us a better idea of how neural activity maps onto complex, dynamic, social behaviors."

Among the questions she wants to explore are what factors facilitate cooperative group-living and what are the environmental tipping points that lead to group dissolution and selfish behaviors.

"Studying the evolution of the social brain may generate insights into how our own brains promote getting along in groups," Kelly says. "What is the brain circuitry involved in welcoming a newcomer or cooperating and sharing food when resources are depleted?"

These are the kinds of questions the affable spiny mouse may help to answer.

JOURNAL:

Current Biology

DOI:

10.1016/j.cub.2024.08.019

METHOD OF RESEARCH:

Experimental study

SUBJECT OF RESEARCH:

Animals

ARTICLE TITLE:

Cingulate to septal circuitry facilitates the preference to affiliate with large peer groups

ARTICLE PUBLICATION DATE:

11-Sep-2024

6. 高齢マウスにおける卵巣機能を延ばす新たな治療法

日付：2024 年 9 月 16 日
出典：ノースウェスタン大学

概要：
ノースウェスタン大学の研究が、高齢マウスの卵巣機能を改善し、加齢に伴う変化を防ぐ新しい方法を発見した。この研究は、卵巣の「健康寿命」を延ばすことに焦点を当てている。健康寿命とは、深刻な病気や慢性疾患から自由な期間を指す。
研究者たちは、特発性肺線維症の治療に一般的に用いられる薬剤「ピルフェニドン」を使用した。これにより、卵巣の繊維化を抑制し、卵胞数の増加や正常なホルモンレベルの維持が見られた。著者のフランチェスカ・ダンカン教授は、卵巣の環境を改善することで、ホルモンの生成を長く維持できる可能性があると述べている。
卵巣の硬化は、卵子の質にも影響を与えることが示されており、女性の妊娠能力が低下する理由の一部を説明している。ダンカン教授は、研究の最終目的は妊娠の可能性を延ばすことだけではなく、加齢に伴うホルモン減少による健康リスクを軽減することだと強調している。
この研究は、卵巣の環境を改善することが、卵子の生産やホルモン生成に貢献する根本的な解決策であることを示している。今後、ヒトへの安全で効果的な治療薬の開発を目指すという。
この研究は『GeroScience』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

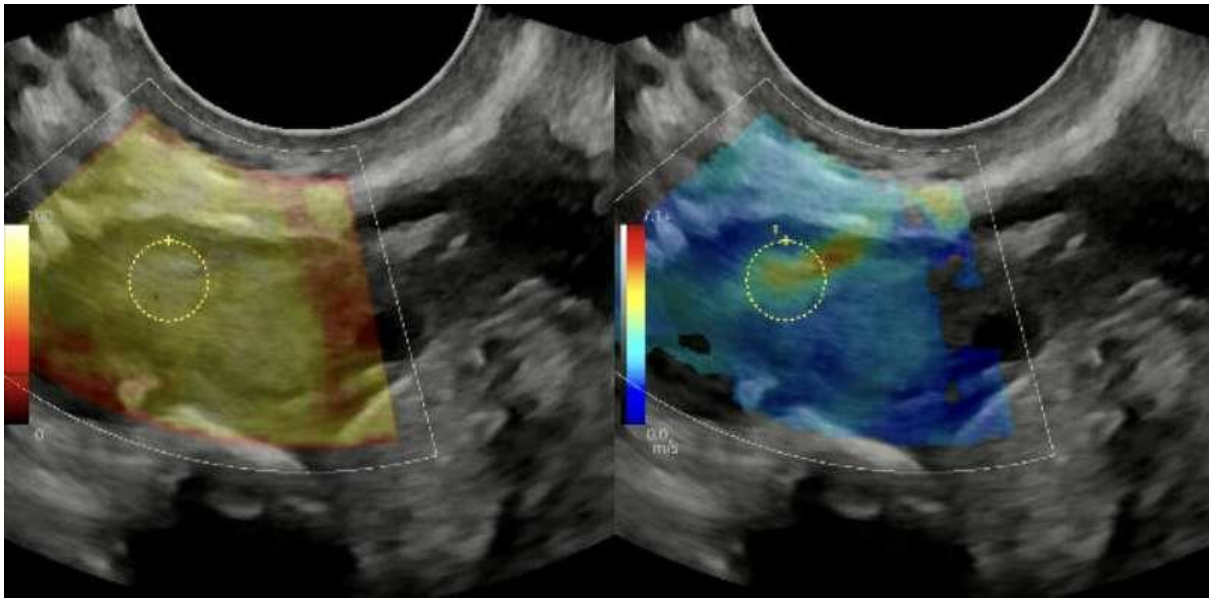
＜英文＞New treatment extends ovarian function in older mice (medicalxpress.com)

SEPTEMBER 16, 2024

EDITORS' NOTES

New treatment extends ovarian function in older mice

BY NORTHWESTERN UNIVERSITY



AN ULTRASOUND IMAGE OF A HUMAN OVARY THAT USED SHEAR WAVE ELASTOGRAPHY TO ASSESS OVARIAN STIFFNESS BY DETECTING AND MEASURING FIBROTIC TISSUE.

CREDIT: NORTHWESTERN UNIVERSITY

A woman's ovaries are like a factory where eggs grow and produce hormones that regulate everything from menstruation and pregnancy to bone density and mood. As she and her factory age, production dwindles, and by the time she hits menopause (age 51, on average), the factory is preparing to shut its doors.

A new Northwestern Medicine study in mice has discovered a novel way to lengthen the "healthspan" of this factory—improving maintenance of the ovaries and preventing key age-related changes in ovarian function. "Healthspan" refers to the length of time a person remains healthy and free from serious illness or chronic diseases.

"The average age of menopause has stayed constant over the years, but women are living decades longer than that because of health and medical advances," said corresponding author Francesca Duncan, associate professor of obstetrics and gynecology (reproductive science in medicine) at Northwestern University Feinberg School of Medicine. "We've changed the landscape of how we live, and our ovarian function needs to catch up so that we have an organ that functions proportionately to maintain women's healthspans longer."

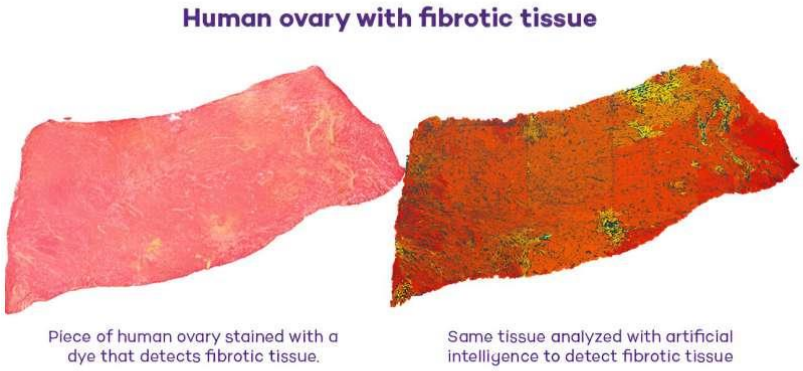
The findings are published in the journal GeroScience.

For this study, researchers used Pirfenidone, which is commonly used to treat idiopathic pulmonary fibrosis. But other ongoing studies are underway to identify optimal drug targets for ovarian fibrosis and to conduct clinical trials in women.

"This drug is not one that can be used in a clinical setting for this purpose because it has significant side effects, like liver toxicity, although we didn't see that in mice," Duncan said. "However, we demonstrated proof-of-concept: We can modulate ovarian fibrosis and improve outcomes. We are now actively working to find a safe and effective drug to do this in humans."

Consequences of stiffer ovaries in older age

In a previous study, Duncan's lab was the first to find that as ovaries age, they become excessively inflamed, fibrotic and stiff—similar to scarring in other tissues. Because cancer cells prefer collagen-rich, stiff environments, aged ovaries provide suitable conditions for cancer cells to proliferate, Duncan said.



A SIDE-BY-SIDE COMPARISON OF THE SAME HUMAN OVARY. THE LEFT WAS STAINED WITH A DYE THAT DETECTS FIBROTIC TISSUE. THE RIGHT ANALYZED THE SAMPLE WITH ARTIFICIAL INTELLIGENCE.

CREDIT: NORTHWESTERN UNIVERSITY

Stiff ovaries also affect egg quality, the earlier study found, which could help explain why women's fertility declines in their 30s and 40s.

In the new study, mice treated with medication to reduce ovarian scarring experienced higher follicle numbers, improved ovulation and maintained normal hormone levels.

"Right now, our solutions for the age-related decline in fertility, such as freezing one's eggs, are a Band-Aid," Duncan said. "You're still going to be transferring those embryos into an older woman, which has its own risks."

'Pushing the fertile window is not the ultimate goal of the study'

Lengthening a woman's fertility window is only one part of the equation, Duncan said.

"We're likely going to push the fertile window, but that is not the ultimate goal of the study," Duncan said. "Not everyone is concerned about having children."

This study focuses on ways to improve the ovarian environment, so it can continue producing critical hormones much later in a woman's life. Decreased estrogen and progesterone levels accelerate bone loss, which increases the risk of osteoporosis. Low hormones can also lead to an increased risk of cardiovascular disease; can cause thinning of the vaginal walls, leading to discomfort during sex or urinary issues; and can lead to decreased cognitive function and mood.

"If you fix the ovarian environment, you solve all the problems because you have follicles and eggs that can contribute to fertility and hormone production," Duncan said. "It's fixing the root of the issue."

More information: Systemic low-dose anti-fibrotic treatment attenuates ovarian aging in the mouse, GeroScience (2024). DOI: 10.1007/s11357-024-01322-w

7. マウスの腸内細菌叢と攻撃性との関連性に関する研究

日付：2024 年 9 月 23 日
出典：バール-イラン大学

概要：
バール-イラン大学のオムリ・コレン教授と大学院生アタラ・ウザン-ユザリによる新しい研究が、腸内細菌叢とマウスの攻撃行動との重要な関連性を明らかにした。この研究は『Brain, Behavior, and Immunity』誌に発表され、特に幼少期の抗生物質使用が腸内細菌叢に及ぼす影響と、それによる攻撃性の増加について探究している。
研究者たちは、抗生物質の影響を受けた腸内細菌を持つマウスと、抗生物質に曝露されなかった幼児から移植した腸内細菌を持つマウスを比較し、後者の方が攻撃性が顕著に高いことを観察した。コレン教授は「この発見は革命的で、重要な発達段階における腸内細菌の乱れが、後の攻撃行動に持続的な影響を与える可能性を示唆している」と述べている。
攻撃性の評価には、居住マウスのケージに外部マウスを導入する「レジデント-侵入者」パラダイムを用い、抗生物質による腸内細菌の多様性の低下が攻撃性の増加に関連していることを確認した。また、脳内の代謝物や遺伝子発現にも顕著な変化が見られた。
この研究は「ヒューマナイズドマウス」を使用しており、人間の腸内細菌が植え付けられているため、結果は人間への関連性が高い。研究は、腸脳軸が攻撃性の発達に重要な役割を果たすことを示唆し、早期の介入が長期的な行動結果にどのように影響を与えるかを理解する新たな道を開いている。

研究関連ニュース/他のトップページに戻る

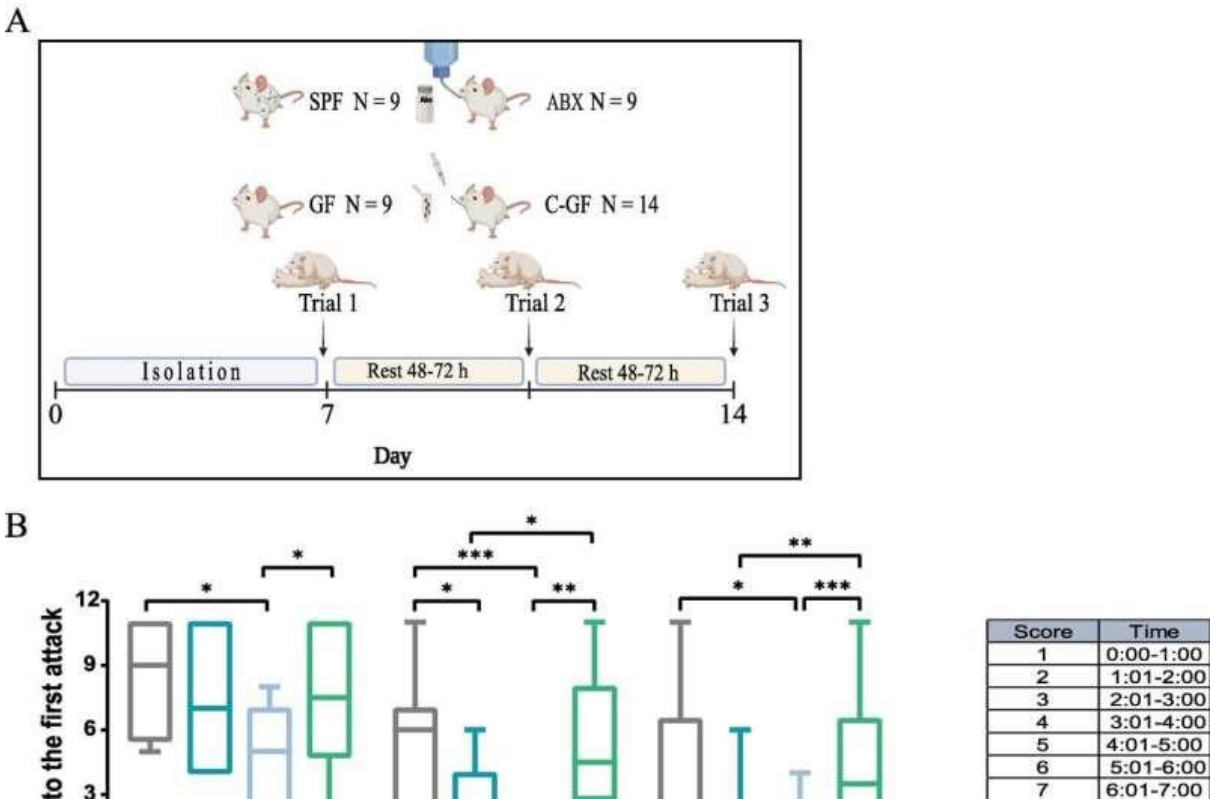
＜英文＞Study reveals link between microbiome and aggression in mice (medicalxpress.com)

September 23, 2024

Editors' notes

Study reveals link between microbiome and aggression in mice

by Bar-Ilan University



Gut microbiome modulates aggression in mice. Credit: *Brain, Behavior, and Immunity* (2024). DOI: 10.1016/j.bbi.2024.08.011

A new study led by Prof. Omry Koren and graduate student Atara Uzan-Yuzari from the Azrieli Faculty of Medicine at Bar-Ilan University has unveiled significant evidence connecting the gut microbiome to aggressive behavior in mice.

Published in the journal *Brain, Behavior, and Immunity*, the research explores how disruptions in the microbiome, particularly due to antibiotic use in early life, can lead to increased aggression.

The study builds on previous findings that demonstrated a correlation between antibiotic exposure and heightened aggression in fruit flies. By utilizing a mouse model, the researchers have taken this investigation a step further, examining behavioral, biochemical, and neurological changes in response to microbiome alterations.

The team also transplanted a microbiome derived from infants who had received antibiotics shortly after birth into mice, observing notable increases in aggression compared to those receiving a microbiome from infants not exposed to antibiotics.

"Our findings are revolutionary," said Prof. Koren. "They suggest that a disrupted microbiome during critical developmental periods can lead to persistent aggressive behaviors later in life."

To assess aggression, the research team employed the resident-intruder paradigm, where a foreign mouse is introduced into the home cage of a resident mouse. The results indicated a clear link between reduced diversity in gut bacteria—caused by antibiotic treatment—and

increased aggression. Additionally, significant changes in metabolites and gene expression related to aggression were observed in the brains of the mice.

The study is particularly noteworthy for its use of "humanized" mice, which have been implanted with human intestinal bacteria. This approach enhances the relevance of the findings to human health and behavior, providing insights into how early-life antibiotic exposure can shape future social behaviors.

The research also explores the biochemical mechanisms underlying these behavioral changes, measuring neurotransmitter levels such as serotonin and tryptophan in the brains of the mice. The team identified key patterns of gene expression in several brain regions, highlighting the septum as a crucial area in regulating aggression.

The findings of this study suggest that the gut-brain axis plays a critical role in the development of aggression, particularly when the microbiome is disrupted during crucial developmental periods, such as infancy. This opens up new avenues for understanding how early-life interventions could influence long-term behavioral outcomes and for developing strategies to mitigate these effects and improve social behavior outcomes.

More information: Atara Uzan-Yulzari et al, A gut reaction? The role of the microbiome in aggression, *Brain, Behavior, and Immunity* (2024). DOI: 10.1016/j.bbi.2024.08.011

Journal information: Brain, Behavior, and Immunity

Provided by Bar-Ilan University

8. 豚がラット肝炎ウイルスの人間への感染経路となる可能性

日付：2024 年 9 月 25 日
出典：オハイオ州立大学

概要：
オハイオ州立大学の研究によると、ラット肝炎ウイルス（HEV）の一種が豚を通じて人間に感染する可能性があることがわかった。
「ロカヘペウイルス・ラッティ（Rocahepevirus ratti）」というこのウイルスは、ラットが主な宿主であり、2018 年に香港で免疫抑制状態の人に初めて人間の感染例が報告されて以来、少なくとも 20 件の感染例が報告されている。これらの感染者はラットへの接触を報告しておらず、感染原因は不明だが、生の豚肉の摂取が疑われている。
研究者たちは、ヒトから分離されたラット HEV が豚に感染し、同じ環境で感染が広がることを確認した。ラットは豚舎に一般的に生息しており、これが感染経路になる可能性がある。感染した豚の血液や便からウイルスが検出されたが、豚に症状は見られなかった。
今後の研究では、豚肝製品にラット HEV が含まれているか調査し、食品安全対策を検討する必要がある、と指摘している。
この研究は、『PNAS Nexus』で発表されている。

研究関連ニュース/他のトップページに戻る

＜英文＞Pigs may be transmission route of rat hepatitis E to humans | ScienceDaily

Pigs may be transmission route of rat hepatitis E to humans

Study shows viral strain infects, circulates among swine

Date: September 25, 2024

Source: Ohio State University

Summary:

New research suggests that pigs may function as a transmission vehicle for a strain of the hepatitis E virus (HEV) common in rats that has recently been found to infect humans.

FULL STORY

New research suggests that pigs may function as a transmission vehicle for a strain of the hepatitis E virus (HEV) common in rats that has recently been found to infect humans.

The Rocahepevirus ratti strain is called "rat HEV" because rats are the primary reservoir of the virus. Since the first human case was reported in a person with a suppressed immune system in Hong Kong in 2018, at least 20 total human cases have been reported -- including in people with normal immune function.

People infected with rat HEV did not report exposure to rats, leaving the cause of infection undefined. The suspected cause during other human HEV infections, in many cases, is consumption of raw pork -- making it a potential route for rat HEV as well.

Researchers at The Ohio State University found that a strain of rat HEV isolated from humans could infect pigs and was transmitted among co-housed animals in farm-like conditions. Rats are common pests in swine barns -- suggesting that the pork production industry may be a setting in which rat HEV could make its way to humans.

"We always want to know which viruses might be up and coming, so we need to know the genetics behind this virus in the unlikely event something happens in the United States that would enable rat HEV to expand," said senior author Scott Kenney, an associate professor of veterinary preventive medicine at Ohio State based in the Center for Food Animal Health at the College of Food, Agricultural, and Environmental Sciences' Wooster campus.

The study was published recently in PNAS Nexus.

Hepatitis E is the leading cause of the acute viral liver infection in humans worldwide, mostly in developing regions where sanitation is poor. The virus is also endemic in pigs in the United States -- though it is present mostly in liver rather than muscle, and is killed when the meat is cooked.

Past studies testing the cross-species infectiousness of rat HEV showed the strain used in experiments did not infect non-human primates.

"It dropped off the radar for six or seven years because it was thought not to be a human pathogen. And now it's infecting humans, so we need to figure out why," Kenney said.

One strain linked to human disease is known as LCK-3110. First author Kush Yadav, who completed this work as a PhD student in the Center for Food Animal Health, used the viral genomic sequence to construct an infectious clone of LCK-3110.

The team first showed the cloned virus could replicate in multiple types of human and mammal cell cultures and in pigs. Researchers then injected pigs with an infectious solution containing the LCK-3110 strain or another HEV strain present in pigs in the U.S., as well as saline as a control condition.

Viral particles in the blood and feces were detected one week later in both groups receiving HEV strains, but levels were higher in pigs infected with rat HEV. Two weeks later, co-housed pigs that received no inoculations also began to shed rat HEV virus in their feces -- an indication the virus had spread through the fecal-oral route.

Though infected pigs' organs and bodily fluids were also positive for viral RNA, the animals did not show signs of feeling sick. Previous research suggests rats don't have clinical symptoms, either.

Even so, the rat HEV virus was detected in cerebrospinal fluid of infected pigs -- a finding that aligns with growing concern that various strains of HEV that infect humans can harm the brain. One human death linked to rat HEV was caused by meningoencephalitis.

"HEV is gaining importance for neurological disorders, and a lot of the research now points toward how neuropathology is caused by the hepatitis E virus," Yadav said. "And even though we have a small number of

known human cases, a high percentage of them are immunosuppressed. That means transplant recipients in the United States could be at risk of infection by general HEV as well as rat HEV.

"Research could now focus on whether pork liver products contain rat HEV and explore food safety procedures to block the disease."

Yadav is now a postdoctoral researcher in the Virginia-Maryland College of Veterinary Medicine at Virginia Tech. Co-authors of the study, all from Ohio State, were Patricia Boley, Carolyn Lee, Saroj Khatiwada, Kwonil Jung, Thamonpan Laocharoensuk, Jake Hofstetter, Ronna Wood and Juliette Hanson.

STORY SOURE:

MATERIALS PROVIDED BY OHIO STATE UNIVERSITY. ORIGINAL WRITTEN BY EMILY CALDWELL. *NOTE: CONTENT MAY BE EDITED FOR STYLE AND LENGTH.*

JOURNAL REFERENCE:

1. KUSH KUMAR YADAV, PATRICIA A BOLEY, CAROLYN M LEE, SAROJ KHATIWADA, KWONIL JUNG, THAMONPAN LAOCHAROENSUK, JAKE HOFSTETTER, RONNA WOOD, JULIETTE HANSON, SCOTT P KENNEY. RAT HEPATITIS E VIRUS CROSS-SPECIES INFECTION AND TRANSMISSION IN PIGS. *PNAS NEXUS*, 2024; 3 (7) DOI: 10.1093/PNASNEXUS/PGAE259

9. パーキンソン病治療が意思決定に与える悪影響 –マウス研究

日付：2024 年 9 月 24 日
出典：藤田医科大学

概要：
パーキンソン病（PD）は神経系の障害で、運動の遅れや震え、バランスの問題を引き起こす。治療薬は症状を緩和するが、一部には意思決定能力の低下や衝動制御の問題といった副作用がある。新たな研究では、外側淡蒼球（GPe）という脳の構造が、この副作用に関与していることが示された。
藤田医科大学の研究者たちは、ドーパミンを模倣する薬「プラミペキソール（PPX）」がマウスの意思決定に与える影響を調査した。マウスに毒素「6-ヒドロキシドーパミン（6-OHDA）」を投与することでパーキンソン病のような症状を持つマウスモデルを作成し、これらのマウスに PPX を投与した結果、リスクの高い選択をする傾向が強まった。脳の GPe が過剰に活性化されていることが確認され、これが意思決定の障害に関連していることがわかった。
この発見は、パーキンソン病患者の新しい治療法の開発につながる可能性があり、患者やその家族の理解を深める手助けとなる。研究者たちは、早期のケアや予防策の重要性を訴えている。
この研究は、『International Journal of Molecular Sciences』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＞A risky business: Why do some Parkinson's disease treatments affect decision making? | ScienceDaily

A risky business: Why do some Parkinson's disease treatments affect decision making?

Researchers identify a region of the brain linked to impaired decision-making skills seen in patients receiving Parkinson's disease treatment

Date: **September 24, 2024**

Source: **Fujita Health University**

Summary:

Parkinson's disease, a debilitating nervous system disorder, is treated with medications that sometimes cause impaired decision-making and poor impulse control. Now, researchers have

identified a structure in the brain called the external globus pallidus which may be responsible for this side effect, paving the way for new treatments.

FULL STORY

Parkinson's disease (PD), also known simply as Parkinson's, is a disorder of the nervous system that affects millions of people worldwide. The nerve cell damage associated with Parkinson's can cause tremors, slowed movements, problems with balance, and many other symptoms which worsen gradually over time. Although there is no cure, there are medications available that can treat PD symptoms. Some of these medications, however, have previously unexplained side effects -- including impaired decision-making that leads to potentially harmful behaviors such as pathological gambling, binge eating and compulsive shopping.

Now, in a study published online on 14 August 2024 in the *International Journal of Molecular Sciences*, researchers at Fujita Health University in Japan, led by Assistant Professor Hisayoshi Kubota from the Division of Behavioral Neuropharmacology, International Center for Brain Science (ICBS), Fujita Health University, have investigated the mechanism by which a drug called pramipexole or PPX impairs the decision-making process in mice with Parkinson's disease. The research was co-authored by Professor Taku Nagai from the Division of Behavioral Neuropharmacology, International Center for Brain Science (ICBS), and Professor Hirohisa Watanabe from the Department of Neurology, School of Medicine, both at Fujita Health University.

To take a closer look at the findings of this study, we first need to understand how PPX works to alleviate PD symptoms. PD mainly results from a loss of nerve cells or neurons that produce a compound called dopamine. Some neurons are dependent on dopamine for their regular functioning -- they have structures called 'dopamine receptors' which can be thought of as locks which can then be activated using dopamine as the 'key'. Drugs like PPX can imitate the function of dopamine and bind to these receptors instead, especially in patients with PD who lack dopamine-producing neurons.

To study the effects of PPX on PD, the researchers injected the brains of mice with a toxin called 6-hydroxydopamine (or 6-OHDA). 6-OHDA damages neurons in a very similar manner to that observed in the brains of patients with PD. The mice were treated with PPX and then subjected to a touchscreen-based 'gambling task' to test their decision-making skills. Interestingly, these mice picked the high-risk/high-reward option much more often -- they opted for a disadvantageous outcome where they received a large reward (of strawberry milkshake), which also comes with an increased risk of a large punishment by exposure to flashing lights.

But which part of the brain is responsible for this behavior? Investigating the brains of mice treated with PPX revealed that a region deep inside the brain called the external globus pallidus (GPe) was hyperactivated, or showed a much higher level of neuron activity. The researchers then chemically inhibited the neurons in the GPe, which actually reduced

disadvantageous risk-taking activity in the mice. This proved that hyperactivation of the GPe was indeed responsible for poor decision-making in the mice treated with PPX.

This study has huge implications for treating patients with Parkinson's disease. "Our findings could lead to the development of new medications or interventions that specifically target the external globus pallidus," explains Dr. Kubota. 'This would help to prevent or reduce decision-making impairments in Parkinson's disease patients.'

Besides helping medical professionals develop better treatments for Parkinson's disease, these findings can also help improve awareness among affected patients, their families, as well as the general public. Dr. Kubota, explains that "Investigating how Parkinson's disease medications affect decision-making will help the public to better understand the complexity of the disease and its treatment." He also says "This will benefit patients, their families and carers, and motivate them to consider early care and preventive strategies."

These findings shed new light on the complex processes in the brain that aid our everyday decision-making skills, and promise to improve quality of life for patients affected by Parkinson's disease. Maybe we can take away some important lessons from this study as well, and think twice before we indulge in poor decision-making in our daily lives!

Story Source:

Materials provided by Fujita Health University. *Note: Content may be edited for style and length.*

Journal Reference:

1. Hisayoshi Kubota, Xinzhu Zhou, Xinjian Zhang, Hirohisa Watanabe, Taku Nagai. Pramipexole Hyperactivates the External Globus Pallidus and Impairs Decision-Making in a Mouse Model of Parkinson's Disease. *International Journal of Molecular Sciences*, 2024; 25 (16): 8849 DOI: 10.3390/ijms25168849