Bio News – June, 2024

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

4/30　合成麻薬・大麻に似た 16 物質を指定薬物へ –厚労省

厚生労働省の専門家部会は 30 日、合成麻薬 LSD や大麻の有害成分に似た計 16 物質を新たに医薬品医療機器法（薬機法）の指定薬物とすることを了承した。5 月 11 日からこれらの物質を含む製品の販売や所持、使用が禁止される。

4/30　《JST 主催》わが国の論文力なぜ失速 第一線の研究者らシンポで激論白熱

https://scienceportal.jst.go.jp/explore/reports/20240430_e01/

5/1　Walmart が採算が合わない米国の診療所 51 ヵ所と遠隔医療を廃止

Walmart to close its 51 health centers and virtual care service - The Washington Post

5/1　Merck の Keytruda 込み胃癌初治療が Ph3 試験で生存改善達成

Pharma Industry News and Analysis | FirstWord Pharma
Merck & Co. says Keytruda combo hits survival goal in Phase III gastric cancer trial

5/2　Novartis がペプチドリーム（本社：川崎市）に 1.8 億ドルを払って両社の提携を拡大

Novartis pays PeptiDream $180M as radiopharma big bang continues (fiercebiotech.com)

5/2　アステラス製薬が Poseida（本社：カリフォルニア州サンディエゴ）との固形癌治療同種 CAR-T の提携を拡大

Astellas and Poseida Therapeutics Enter Into Research Collaboration and License Agreement to Develop Novel Allogeneic Cell Therapies in Oncology | BioSpace

5/2　Moderna が Metagenomi（本社：カリフォルニア州オークランド）との遺伝子編集治療提携を打ち切り

Moderna Walks Away from Potential $3B Gene Editing Deal with Metagenomi | BioSpace

5/3　インドの謎化石、ティラノサウルスよりでかい新種の巨大ヘビと判明

5/3　世界初の「歯生え薬」 9 月に治験開始　2030 年の発売目指す

北野病院（大阪市北区）などの研究チームは 2 日、世界初の「歯生え薬」の治験を京都大医学部付属病院で始めると発表した。すでにマウスやイヌでは歯を生やすことに成功。安全性を確認した上で、生まれつき歯の数が足りない「先天性無歯症」の患者に薬剤を投与して効果を確認する。薬は 2030 年の発売を目指すという。

5/4　Pfizer の鎌状赤血球症薬 Oxbryta が英国の医療（NHS）で使用可能に

Pharma Industry News and Analysis | FirstWord Pharma
Price cut allows Pfizer's sickle cell therapy Oxbryta to rollout on NHS

5/7　韓国、過去 50 年で「最も暑い 4 月」
フィリピンでも首都で史上最高を記録、世界的な異常高温

5/7　細胞の内部を鮮明に観察できる蛍光顕微鏡技術を開発 阪大など

https://scienceportal.jst.go.jp/newsflash/20240507_no1/index.html

5/8　需要低下により AstraZeneca のコロナワクチン Vaxzevria が全世界で取り下げ

AstraZeneca withdraws COVID-19 vaccine citing a decline in demand - ABC News

5/8　Lilly のアルツハイマー病薬 donanemab 承認申請の米国諮問委員会が 6 月 10 日開催

Eli Lilly Announces Date for Donanemab FDA AdComm Hearing (neurologylive.com)

5/8　Pfizer の筋ジストロフィー遺伝子治療 Ph2 試験被験者 1 人が死亡 ～Ph3 試験投与中断

Pfizer Pauses Gene Therapy Trial for Muscle Disease After Death (msn.com)

5/8　溶連菌感染を抑制する分子の塊を発見 神戸大など、治療薬開発へ期待

溶血性連鎖球菌（溶連菌）が原因となって臓器や組織が壊死（えし）する恐ろしい「劇症型溶血性連鎖球菌感染症」（STSS）の感染を抑制する特定の分子の塊を見つけた、と神戸大学などの研究グループが発表した。治療薬の開発などに役立つ可能性があるという。

5/9　武田薬品が利益の急減を受けて再編に取り組む

Japan's Takeda Pharma to restructure after annual profit slump | Reuters

5/10　マスト細胞を抑える抗アレルギー化合物を発見 山梨大など

花粉症やぜんそく、食物アレルギー、じんましんといったアレルギー性疾患の治療薬になり得る低分子化合物「MOD000001」を山梨大学大学院総合研究部医学域免疫学講座の中尾篤人教授（アレルギー学）らが発見した。免疫細胞でアレルギー症状を引き起こす根本要因となるマスト細胞を標的として特異的に抑え込むとみられることから、薬剤候補として少ない副作用で持続的な効果が期待できるという。
じんましんのような症状がおきるマウスを用いた実験では、MOD000001 を油のような液体に溶かして飲ませることでアレルギー症状を著しく軽くできると実証した。
マウスやヒトの細胞を培養してつくったマスト細胞を用いた実験では、MOD000001 がマスト細胞の活性化や生存の延長、生体内の移動を著しく妨げると示され、マウスを用いた実験で 7 週間の投与を経ても副作用はなかった。

5/11　Sanofi が Novavax のコロナワクチンを共同販売、12 億ドルで合意

AstraZeneca の新型コロナウイルスワクチン撤収とは対照的に、Sanofi は 12 億ドルで Novavax の SARS-CoV-2 ワクチンのライセンス契約を締結。これに伴いノババックスの株価が 130% 上昇し、10 日時点でナスダック市場断然最高の銘柄となっている。

Sanofi signs $1.2bn licensing agreement for Novavax's Covid-19 vaccine (msn.com)

Vaccine Stock Explodes After Sanofi Deal (schaeffersresearch.com)

5/11　世界初ブタ腎臓移植の患者が死亡　順調回復も術後 2 か月で「移植が原因で亡くなったとは見られない」

First person to receive genetically modified pig kidney transplant dies : NPR

5/13　世界最高速度の陽子ビーム達成　がん治療に一歩　量研機構など

体内のがん細胞をピンポイントで攻撃する「粒子線がん治療装置」の小型化に向けた研究を進めている量子科学技術研究開発機構は、ドイツなどとの国際共同研究により、小型レーザーを使って水素イオン（陽子）ビームを光速の約 50%まで加速させることに世界で初めて成功した。

5/13　メキシコで 5 月の過去最高 51.1 度記録

5/14　Sanofi に続いて、Pfizer、AstraZeneca も総額で約 10 億ドルをフランスに投資

'Choose France' investment push bags record $16 billion in pledges | Reuters

Pfizer and AstraZeneca announce new investments of nearly $1 billion in France | Reuters

5/14　腎臓がん、日本人に特有変異　7 割で確認、未知の要因か　11 カ国で全ゲノム解析・がんセンターなど

国立がん研究センターなどの国際共同研究チームは 14 日、日本を含む世界 11 カ国の腎臓がん患者 962 人のがん細胞について全ゲノム解析した結果、日本人患者の 7 割に特有の遺伝子変異があったと発表した。他国の症例ではほとんど検出されなかった。原因は不明だが、未知の発がん要因が関与した可能性が高いという。論文は 1 日付の英科学誌ネイチャーに掲載された。

5/14　塩野義製薬のコロナ薬ゾコーバの国際 Ph3 試験で目当ての効果なし

5/15　23 年夏、過去 2000 年で最も高温 研究で判明

2023 年の北半球の夏は過去 2000 年で最も暑かった。研究論文が 14 日、発表された。
科学誌「ネイチャー（Nature）」に掲載された論文は、人為的な気候変動が影響していることを示す研究結果だとしている。昨夏の気温をめぐっては、1850 年の観測開始以来で最高であることはすでに判明していた。
独ヨハネス・グーテンベルク大学（Johannes Gutenberg University）の研究者らは、北半球各地から集められた木の年輪データを分析し、1 世紀から 1850 年までの世界気温を推計した。その結果、この期間に北半球で最も暑かったのは 246 年の夏だったと判明。しかし、23 年夏の平均気温はこれよりも高く、少なくとも 0.5 度以上暑かったことが分かった。

5/15　生命科学分野に投資する Sands Capital（バージニア州アーリントン）が 5 億 5,500 万ドルを集めた

Sands Capital Launches $555M Life Sciences Fund Focusing on Private Companies | BioSpace

5/16　エーザイがアルツハイマー病薬 Leqembi 皮下注射の米国での段階的承認申請開始

https://www.eisai.co.jp/news/2024/news202430.html

5/17　武田薬品のデングワクチン TAK-003 を WHO が承認

WHO clears Takeda's dengue vaccine | Reuters

5/17　Lilly の週 1 回投与インスリンが 1 日 1 回インスリンに遜色ない血糖抑制

Eli Lilly says its experimental weekly insulin works just as well as daily doses (msn.com)

5/18　Bayer の閉経薬 elinzanetant はアステラスの Veozah に勝るとも劣らず有効

Bayer's elinzanetant data heats up rivalry with Astellas drug in menopause market / FirstWord

5/21　iPS 細胞から精子と卵子のもとを大量作製　不妊の解明も　京大研究

ヒトの iPS 細胞（人工多能性幹細胞）から、精子や卵子のもととなる細胞を大量に作る方法を開発したと、京都大の研究チームが発表した。チームの斎藤通紀（みちのり）・京大高等研究院教授（細胞生物学）は「簡単に増やせる培養法を確立できた。生殖細胞の形成過程や、不妊が起きるメカニズムなどの解明に応用できる」と期待を寄せる。成果は 20 日付の国際科学誌ネイチャー（電子版）に発表した。

5/21　AstraZeneca が 15 億ドルを投じてシンガポールに抗癌剤工場を作る

AstraZeneca to build $1.5-bln cancer drug plant in Singapore | Reuters

5/21　ALS 治療薬を承認申請　特定の遺伝子変異が対象

米製薬企業バイオジェン日本法人は 21 日、筋萎縮性側索硬化症（ALS）の治療薬「トフェルセン」の製造販売の承認を厚生労働省に申請したと発表した。SOD1 と呼ばれる遺伝子に変異のある患者を対象とした薬で患者の約 2%を占める。　バイオジェンによると、臨床試験では 28 週間後時点で神経の損傷を示す血中物質が減少。症状の進行を抑えると期待されている。米食品医薬品局（FDA）は 2023 年 4 月に迅速承認した。

5/22　Biogen が Human Immunology Biosciences（HI-Bio）（本社：カリフォルニア州サンフランシスコ）を 18 億ドルで買収

Biogen in up to $1.8 billion deal as rare diseases take center stage (msn.com)

Biogen Beefs Up Immuno Pipeline with Potential $1.8B HI-Bio Acquisition | BioSpace

5/22　Pfizer が今年中の 40 億ドルに加えて、2027 年までの 15 億ドルの経費節減計画を発表

Pfizer rolls out another cost-cutting program, sets $1.5 bln target by 2027 | Reuters

5/22　第一三共が今年ケンブリッジとミュンヘンに 2 つの新たな研究拠点を開設

Daiichi Sankyo to open two new research sites in Cambridge and Munich this year – Endpoints News (endpts.com)

5/22　自然治癒難しい半月板、人工たんぱく質を注射して再生　来春から治験

三洋化成工業（京都市）と広島大学病院は 21 日、加齢やスポーツなどで損傷したひざの半月板に人工たんぱく質を注射して再生を促す治験を来春から始めると発表した。実用化されれば、半月板を温存する新たな治療法になる。医療機器としての薬事承認などを経て早ければ 2027 年の実用化をめざすという。

5/23　血液検査で認知症判別　無症状、早期の診断期待

アルツハイマー病の原因とされるタンパク質を無症状の人らの血液中から測定し、脳内での蓄積状況を判別することに成功したと、東京大の岩坪威教授（神経病理学）らのチームが 23 日、国際専門誌に発表した。従来より効率的に早期段階の認知症診断につながると期待される。

5/23　受動喫煙による肺がん発症のメカニズム解明 –国立がん研など

周囲に流れるたばこの煙を吸う受動喫煙による肺がんの発症は、本人が喫煙する能動喫煙とは異なるメカニズムの遺伝子変異を誘発して起こることを国立がん研究センターなどの研究グループが明らかにした。炎症により特定のタンパク質が活性化することで変異が生じる。今後は大規模な調査に基づき、子どもと成人してからの受動喫煙によるゲノム情報の違いについて研究を続け、肺がん予防や薬の投与戦略などに生かしたいという。

5/24　空気中から二酸化炭素を除去するための世界最大のプラントがアイスランドで稼働開始

スタートアップのクライムワークス（Climeworks）がこのほど、世界最大の CO2 回収プラントのスイッチを入れた。空気中から二酸化炭素を取り出して、地下に閉じ込めるものだ。クライムワークスによると、このプラントはマンモス（Mammoth）と呼ばれ、キャパシティは 1 つ目の設備の約 10 倍で、完成後は年間最大 3 万 6,000 トンの炭素を、空気中から回収することができるという。これは、400 億炭素トン以上と推定される 2023 年の世界排出量のほんの一部だが、アイスランドでマンモスがオープンしたことは、新興テクノロジーにとっては画期的な出来事だ。科学者らによると、CO2 除去は気候危機鈍化の鍵となるという。

5/24　アリにもカフェイン効果　餌の場所に速く直行　駆除に応用期待・独大学

アリにカフェインを適量加えた砂糖水を与えると、餌がある場所に再び向かう際に迷わず直行し、到達時間が短くなったと、ドイツのレーゲンスブルク大の研究チームが 23 日付の米科学誌アイサイエンスに発表した。実験対象は南米原産のアルゼンチンアリで、日本を含む世界各地に広がり、外来種の害虫として駆除対象とされる。
駆除にはベイト剤と呼ばれる毒入りの餌が使われることが多く、巣に持ち帰らせることで一網打尽にできるが、効率が悪い場合がある。研究チームはベイト剤に適量のカフェインを混ぜれば、より速く、多くのベイト剤が巣に運ばれる可能性があると考え、自然環境に近い条件で試しているという。

5/24　Esperion（本社：ミシガン州アンアーバー）/第一三共のコレステロール薬ベンペド酸の心血管一大事予防効能を欧州が承認

Esperion's (ESPR) Drugs Get EU Nod for Lowering Heart Risk (msn.com)

5/24　水虫が足裏のがんに関与　治療で発生予防に効果か　慈恵医大

東京慈恵会医科大の研究グループは 24 日までに、水虫と、皮膚がんの一種である足の裏の「メラノーマ」の発生に相関が認められたと発表した。これまで足裏のがん発生には物理的な刺激が関わっていると想定されていたが、感染症である水虫との関連が初めて示された。水虫の治療や予防により、これまで困難とされてきたメラノーマ予防に一定の効果が期待できるという。
研究成果は 6 日付の国際学術雑誌「ジャーナル・オブ・ダーマトロジー」に掲載された。

5/24　10 代の大麻使用、精神病の発症リスクが「11 倍増加」 –カナダの研究

5/25　Eli Lilly、53 億ドルを投じてインディアナ州レバノン製造拠点を拡大

Eli Lilly To Invest Record $5.3B To Expand Plant That Manufactures Weight-Loss Drugs (bisnow.com)

5/25　「心筋シート」承認申請へ　阪大開発、ベンチャー企業

大阪大の澤芳樹特任教授らのチームが開発した人工多能性幹細胞（iPS 細胞）から作った「心筋シート」について、澤氏が最高技術責任者を務めるベンチャー企業クオリプス（東京）が秋ごろをめどに、厚

生労働省に製造販売承認を申請する方向で検討していることが 24 日、関係者への取材で分かった。iPS 細胞由来の医療製品の承認申請は初めてとみられる。

5/25　武田薬品が中国を拠点とする Degron と組んで癌、神経科学、炎症分野の標的分解剤に取り組む

武田薬品工業は、さまざまな腫瘍学、神経科学、炎症性疾患の標的向け新規分子接着剤分解剤開発のために、中国に本拠を置くデグロン・セラピューティクスと独占的ライセンス契約を結んだと発表。

Takeda Joins Hot Molecular Glue Market With $1.2B Deal | BioSpace

5/25　大塚製薬が Ph3 試験失敗のアルツハイマー病アジテーション薬 AVP-786 開発中止

Japan's Otsuka to stop development of Alzheimer's disease drug | Reuters

Otsuka gives up on Alzheimer's drug after second failed trial (fiercepharma.com)

5/25　世界の平均寿命、新型コロナで約 2 歳短縮 WHO

新型コロナウイルスが猛威を振るった 2019～21 年に世界の平均寿命（出生時平均余命）は 2 年近く短くなったとする調査結果を世界保健機関（WHO）が 24 日、世界保健統計の 2023 年版で発表した。

5/26　アラスカ州の氷河から高濃度メタン　最大 40 倍、高い温室効果も

アラスカ州の氷河を起源とする河川から、通常の最大 40 倍となる高濃度メタンが検出されたと、国立極地研究所や海洋研究開発機構などのチームが発表した。周辺の大気中のメタン濃度も 3 倍高かった。メタンは二酸化炭素より二十数倍も強い温室効果を持つ。地球温暖化対策を考える上で、どのような仕組みで氷河中に蓄積されたか解明が急がれる。

5/27　難治性の水虫、高濃度の胃酸抑制剤が効くことを発見 武蔵野大学など

5/28　てんかん発作のきっかけ発見　神経支援細胞が関与か　東北大

脳の神経細胞が過剰に活動して起きるてんかん発作は、脳内で神経細胞を支援する「グリア細胞」の一種の活動がきっかけとなっている可能性が高いことを、東北大の研究グループがマウスを用いた実験で突き止めた。グリア細胞の活動を制御できれば、てんかんの新たな治療法開発につながる可能性があるという。

5/28　米国で取り急ぎ承認済みの日本新薬の筋ジストロフィー薬 Viltepso の Ph3 試験失敗

NS Pharma's DMD Candidate Viltespo Fails Confirmatory Phase III Trial | BioSpace

5/28　iPS 細胞製造施設も入居 「中之島クロス」6 月 29 日オープン　再生医療の産業化目指す

一般財団法人「未来医療推進機構」（大阪市、澤芳樹理事長）は 28 日、大阪市北区中之島で開業を予定する未来医療国際拠点「Nakanoshima Qross」（中之島クロス）が 6 月 29 日にグランドオープンすると発表した。再生医療の産業化を目指す産学医連携の拠点となる。

5/29　武田薬品が米国本拠ボストン 2 か所の従業員 641 人を削減

Takeda, amid restructuring campaign, plots 641 layoffs at two Massachusetts sites | Fierce Pharma

5/29　移植用肝臓の保存時間延長、長崎大などが保存液循環させる臨床研究計画…治療態勢の強化期待

5/29　旭化成がスウェーデンの Calliditas を 11 億ドルで買収、その後 Calliditas の株価が急騰

Asahi Kasei to buy Swedish drugmaker Calliditas for $1.1 billion | Reuters

Calliditas Therapeutics' stock surges after $1.1 billion takeover bid (msn.com)

5/29　マウスの母乳中の抗体 子の脳にも届くことを実証 群馬大など

マウスの母乳中に含まれる抗体は子の脳にも届き、脳の発達や社会性に影響を与えている可能性があることを群馬大学などの研究グループが発表した。
抗体が脳に入らないようにした遺伝子改変マウスでは、脳内の特定の神経細胞などが通常のマウスより少ないほか、ペアのマウスと長い接触行動を示すことが分かった。母乳中の抗体が脳に果たす役割を詳細に解明するために今後、ヒトを対象にした研究を続けたいとしている。

5/29　Roche の提携部門責任者の James Sabry 氏が 14 年の勤務を経て退職

グループ事業開発責任者の Boris Zaïtra 氏が、7 月 1 日付けでコーポレート事業開発部門責任者に任命される。これは、製薬提携部門とグループ事業開発部門を統合する新しい役職である。

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. 父親の腸内細菌が次世代に影響を与える -マウス研究
2. 高度な遺伝子技術で、トゥレット障害の特徴を持つマウスを作成
3. 「指揮者」はマウスの初期胚のカオスをどのように理解するのか
4. ジェルが体内のアルコールを分解 -マウス実験
5. 肥満治療薬「トロイの木馬」、現行治療薬よりも効果的 -マウス実験
6. 遺伝子治療がマウスの背中の痛みを和らげ、損傷した椎間板を修復
7. ある種のマウスが一夫一妻制に至る理由が新たに進化した細胞にある可能性
8. 男性用避妊薬開発への有望なアプローチ -マウス実験

1. 父親の腸内細菌が次世代に影響を与える –マウス研究

日付：2024 年 5 月 1 日
ソース：欧州分子生物学研究所
概要：

欧州分子生物学研究所（EMBL）による研究によって、雄マウスの腸内細菌叢を破壊すると、将来の子孫の疾患リスクが増加することが示された。
EMBL の研究者らは、雄マウスの腸内細菌叢の構成を血液に入らない抗生物質で変化させることで、腸内細菌叢の不均衡な状態である「ディスバイオシス」を誘発した。その結果、ディスバイオシスが、精巣の生理学、代謝物の組成、ホルモンシグナル伝達に影響を与えることが分かった。この影響の一部は、キーとなるホルモンであるレプチンの血液中および精巣中のレベルの変化によって仲介された。
さらに、未処理またはディスバイオシスを誘発した雄と未処理の雌を交配させた結果、ディスバイオシスを誘発した父親から生まれたマウスの子供は、生まれた時の体重が有意に低く、乳幼児死亡率が増加した。また、この影響は可逆的であり、抗生物質が撤去されると父親の腸内細菌叢が回復し、回復した腸内細菌叢を持つマウスが未処理の雌と交配すると、その子供は通常の出生体重で生まれ、通常に成長した。
この研究は、父親の腸内細菌叢が子孫の健康に影響を与える可能性があることを示している、として『Nature』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

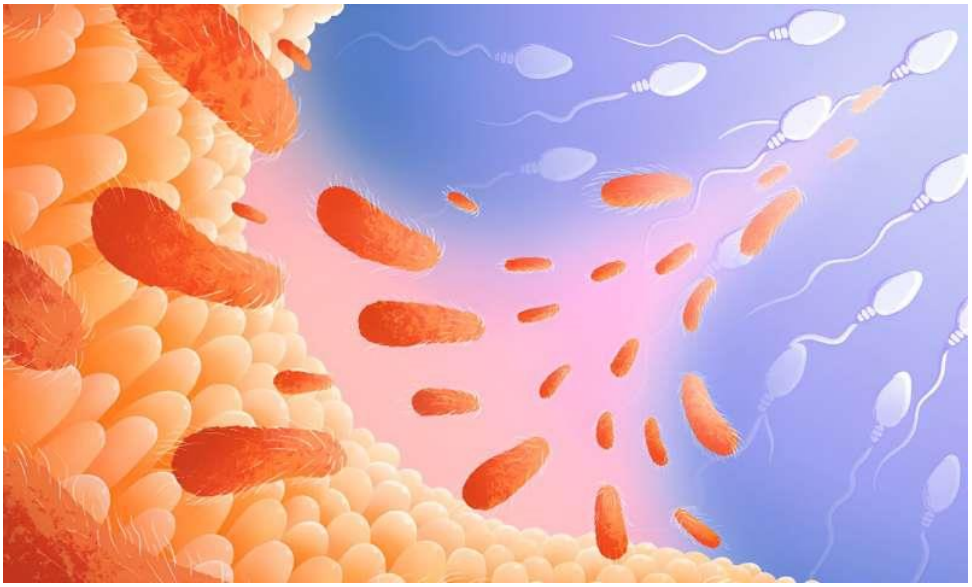
＜英文＞Father's gut microbes affect the next generation in mouse study (medicalxpress.com)

MAY 1, 2024

Editors' notes

Father's gut microbes affect the next generation in mouse study

by European Molecular Biology Laboratory



The 'gut-germline axis' is a connection between the gut, its microbiota and the germline. Credit: Joana Carvalho/Isabel Romero Calvo/EMBL

A study from the Hackett group at the European Molecular Biology Laboratory (EMBL) in Rome shows that disrupting the gut microbiome of male mice increases the risk of disease in their future offspring.

The gut microbiota is the microbial community that occupies the gastrointestinal tract. It is responsible for producing enzymes, metabolites, and other molecules crucial for host metabolism and in response to the environment.

Consequently, a balanced gut microbiota is important for mammalian health in many ways, such as helping to regulate the immune and endocrine systems. This in turn, impacts the physiology of tissues throughout the body. However, little was known about the impact of the gut microbiota on host reproduction, and whether an altered microbiota in a father could influence the fitness of his offspring.

The Hackett group at EMBL Rome, in collaboration with the Bork and the Zimmermann groups at EMBL Heidelberg, set out to answer this question, with their results published in *Nature*. The scientists showed that disrupting the gut microbiota in male mice increases the probability that their offspring are born with low weight, and are more likely to die prematurely.

What is passed on to the next generation

To study the effects of the gut microbiota on male reproduction and their offspring, the researchers altered the composition of gut microbes in male mice by treating them with common antibiotics that do not enter the bloodstream. This induces a condition called dysbiosis, whereby the microbial ecosystem in the gut becomes unbalanced.

The scientists then analyzed changes in the composition of important testicular metabolites. They found that in male mice dysbiosis affects the physiology of the

testes, as well as metabolite composition and hormonal signaling. At least part of this effect was mediated by changes in the levels of the key hormone leptin in blood and testes of males with induced dysbiosis.

These observations suggest that in mammals, a 'gut-germline axis' exists as an important connection between the gut, its microbiota, and the germline.

To understand the relevance of this 'gut-germline' axis to traits inherited by offspring, the scientists mated either untreated or dysbiotic males with untreated females. Mouse pups sired by dysbiotic fathers showed significantly lower birth weights and an increased rate of postnatal mortality. Different combinations of antibiotics as well as treatments with dysbiosis-inducing-laxatives (which also disrupt microbiota) affected offspring similarly.

Importantly, this effect is reversible. Once antibiotics are withdrawn, paternal microbiota recover. When mice with recovered microbiota were mated with untreated females, their offspring were born with normal birthweight and developed normally as well.

"We have observed that intergenerational effects disappear once a normal microbiota is restored. That means that any alteration to the gut microbiota able to cause intergenerational effects could be prevented in prospective fathers," said Peer Bork, EMBL Heidelberg Director, who participated in the study.

"The next step will be to understand in detail how different environmental factors such as medicinal drugs including antibiotics can affect the paternal germline and, therefore, embryonic development."

Ayele Denboba, first author of the publication and former postdoc in the Hackett Group, now Group Leader at the Max Planck Institute of Immunology and Epigenetics in Freiburg, Germany added, "The study originated to understand environmental impacts on fathers by considering the gut microbiota as a nexus of host-environment interactions, thus creating a sufficient-cause model to assess intergenerational health risks in complex ecological systems."

Paternal impact on pregnancy disease risk

In their work, Hackett and his colleagues also discovered that placental defects, including poor vascularization and reduced growth, occurred more frequently in pregnancies involving dysbiotic males. The defective placentas exhibited hallmarks of a common pregnancy complication in humans called pre-eclampsia, which leads to impaired offspring growth and is a risk factor for developing a wide range of common diseases later in life.

"Our study demonstrates the existence of a channel of communication between the gut microbiota and the reproductive system in mammals. What's more, environmental factors that disrupt these signals in prospective fathers increase the risk of adverse health in offspring, through altering placental development," said

Jamie Hackett, coordinator of the research project and an EMBL Rome Group Leader.

"This implies that in mice, the environment of a father just prior to conception can influence offspring traits independently of genetic inheritance."

"At the same time, we find the effect is for one generation only, and I should be clear that further studies are needed to investigate how pervasive these effects are and whether they have relevance in humans. There are intrinsic differences to be considered when translating results from mouse models to humans."

Hackett continued, "But given the widespread prevalence of dietary and antibiotic practices in Western culture that are known to disrupt the gut microbiota, it is important to consider paternal intergenerational effects more carefully—and how they may be affecting pregnancy outcomes and population disease risk."

More information: Jamie Hackett, Paternal microbiome perturbations impact offspring fitness, *Nature* (2024). DOI: 10.1038/s41586-024-07336-w. www.nature.com/articles/s41586-024-07336-w

Journal information: Nature

Provided by European Molecular Biology Laboratory

2. 高度な遺伝子技術で、トゥレット障害の特徴を持つマウスを作成

日付：2024 年 5 月 6 日
ソース：ラトガーズ大学
概要：

トゥレット障害は、神経系の障害であり、寿命には影響しないとされているが、子供、思春期、成人に影響する。この状態は、急激な無意識の動きや音、チックと呼ばれるもので特徴付けられる。チックは軽度から中等度、重度まであり、場合によっては障害となる。疾病管理予防センターによると、162 人に 1 人がこの障害を持っていると推定されているが、実際の数はそれ以上の可能性がある。
ラトガーズ大学の研究者らは、進化した遺伝子技術を用いて、トゥレット障害の特性を持つマウスを作成した。遺伝子操作されたマウスは、脳障害を持つ人間と同様の行動と脳の異常を示し、トゥレット障害に対する個別化された治療法の発見に向けた一歩となる可能性がある、としている。
この研究は、国立科学アカデミー紀要に報告されており、CRISPR/Cas9 DNA 編集技術を使用して、トゥレット障害の遺伝子変異をマウスの胚に挿入した。その後、マウスが生まれると、遺伝子変異を持つマウスと持たない兄弟マウスの行動を比較した。挿入された変異は、同じ研究チームの一部のメンバーによって発見されたもので、彼らは、トゥレット障害の遺伝的要因を調査するのに 10 年以上を費やしている。
研究者らは、これらのマウスが、トゥレット障害の神経生物学を研究し、新しい薬物を試験するための非常に有用な「モデル」である、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞Using advanced genetic techniques, scientists create mice with traits of Tourette disorder | ScienceDaily

Using advanced genetic techniques, scientists create mice with traits of Tourette disorder

Gene-altered rodents could aid the development of new treatments for a brain disorder

Date:

May 6, 2024

Source:

Rutgers University

Summary:

In research that may be a step forward toward finding personalized treatments for Tourette disorder, scientists have bred mice that exhibit some of the same behaviors and brain abnormalities seen in humans with the disorder.

FULL STORY

In research that may be a step forward toward finding personalized treatments for Tourette disorder, scientists at Rutgers University-New Brunswick have bred mice that exhibit some of the same behaviors and brain abnormalities seen in humans with the disorder.

As reported in the *Proceedings of the National Academy of Sciences*, the researchers, using a technique known as CRISPR/Cas9 DNA editing that selectively modifies the DNA of living organisms, inserted the same genetic mutations found in humans with Tourette disorder into the corresponding genes in mouse embryos. After the mice were born, the scientists observed their behavior compared with littermates without the gene mutation insertion. The mutations that were inserted were discovered by some members of the same research team who have spent more than a decade focused on investigating genetic factors in Tourette disorder.

The researchers said the findings indicate that these mice are a highly useful "model" to study the neurobiology of Tourette disorder and to test new medications.

"There are no medicines specifically developed for Tourette disorder and repurposing other drugs has worked poorly, with too many side effects," said co-senior author Jay Tischfield, the Duncan and Nancy MacMillan Distinguished Professor of Genetics in the Department of Genetics in the Rutgers School of Arts and Sciences and a pioneer in the study of Tourette disorder. "Until now, the problem has been a lack of an animal model by which to test new or existing medications."

Tourette disorder is a disorder of the nervous system that affects children, adolescents and adults. The condition is characterized by sudden, involuntary movements or sounds called tics. Tics can be mild, moderate or severe, and are disabling in some cases.

Tourette disorder doesn't affect lifespan, but it often adversely impacts the experience of people with the disorder and the people with whom they interact. The Centers for Disease Control and Prevention has estimated that one of every 162 children have the disorder, though the number may be higher.

Using cameras that recorded the mice's actions and employing a form of artificial intelligence known as machine learning, the researchers found the genetically engineered mice exhibited two key characteristics seen in humans with Tourette disorder: They engaged in repetitive motor behaviors or tics, and they exhibited what

neuroscientists call "sensorimotor gating deficits," a neural process whereby the brain filters out redundant or irrelevant stimuli.

Cara Nasello, a research associate in the Departments of Genetics and Cell Biology and Neuroscience and the first author of the study, said gating deficits in people with Tourette syndrome can be viewed as a difficulty in processing sensory information. A person without the disorder who listens to a series of sounds such as a beeping car horn wouldn't be startled after the first honk because that person's brain can link the second and subsequent sounds to the first one. A person with Tourette disorder might be startled by each separate sound, especially if it increases in volume.

The genetically engineered mice reacted the same way humans with the disorder would react to individual sounds that were part of a pattern -- they showed a startle response to each tone, Nasello said.

In collaboration with Miriam Bocarsly from the Department of Pharmacology, Physiology and Neuroscience at Rutgers New Jersey Medical School, the team found evidence that the gene mutations altered the levels of a brain chemical known as dopamine. As with humans with Tourette disorder who are treated with a drug that alters the levels of dopamine, the processing deficits and repetitive behaviors seen in the mice decreased in intensity when they were administered the same drug.

"An easy way to think about this is that we have inserted a gene mutation and it's changed the neural circuitry of the mice's brains," said Max Tischfield, an assistant professor in the Department of Cell Biology and Neuroscience in the Rutgers School of Arts and Sciences, and the senior corresponding author of the study. "And those changes are altering how a brain chemical like dopamine, which in humans is important for cognition and motor behavior, allows the mice brain cells to communicate."

The researchers credited much of the success of their work to the contributions of families with Tourette disorder who over the past 15 years donated genetic samples to the research group.

"These families did this out of the goodness of their hearts with the idea of moving the field forward," said Gary Heiman, a co-senior author of the study and a professor in the Department of Genetics who recruited families of members with Tourette disorder throughout the world and organized blood collection and genetic repositories. "They want to have a better understanding of this mysterious disorder and for us to come up with better treatments, not only for the people who are currently suffering with the disorder but also for future generations."

The scientists said the techniques they employed in their research are applicable to researchers studying other complex disorders caused by multiple genes, including autism and schizophrenia.

They also hope this advance will attract more researchers to study Tourette disorder.

"So why would a researcher jump into something if there's little known and they're left wondering, 'How do I even start? What do I have at my disposal that would allow me to even scratch the surface of this very complex disorder?'" Max Tischfield said. "And with these mice, not only can we scratch the surface, but we can dig underneath."

Story Source:

Materials provided by **Rutgers University**. Original written by Kitta MacPherson. *Note: Content may be edited for style and length.*

Journal Reference:

1. Cara Nasello, Lauren A. Poppi, Junbing Wu, Tess F. Kowalski, Joshua K. Thackray, Riley Wang, Angelina Persaud, Mariam Mahboob, Sherry Lin, Rodna Spaseska, C. K. Johnson, Derek Gordon, Fadel Tissir, Gary A. Heiman, Jay A. Tischfield, Miriam Bocarsly, Max A. Tischfield. **Human mutations in high-confidence Tourette disorder genes affect sensorimotor behavior, reward learning, and striatal dopamine in mice**. *Proceedings of the National Academy of Sciences*, 2024; 121 (19) DOI: 10.1073/pnas.2307156121

3. 「指揮者」はマウスの初期胚のカオスをどのように理解するのか

日付：2024 年 5 月 7 日
ソース：ジェノミック レギュレーション センター
概要：

早期のマウス胚の発生において、どのようにしてカオスを把握するのかという問いに対する答えが新たに明らかにされた。バルセロナのジェノミック レギュレーション センター（CRG）と、ニューヨークのチャン・ザッカーバーグ・バイオハブの研究チームによる新しい研究によれば、NKX1-2 というタンパク質が、オーケストラの指揮者のように振る舞い、胚の発育のための遺伝子の指示が正しく適切なタイミングで実行されるように巧みに指導している、として『Stem Cell Reports』誌で発表されている。
研究者らは、マウスで NKX1-2 の機能を実験的に阻害すると、核小体（リボソームを組み立てる核の一部）が大幅に変化し、胚が正しくリボソームを生成する能力が妨げられることを発見した。また、2 から 4 細胞期の胚は、細胞分裂中に染色体を適切に分配できず、この非常に早い発生段階で成長が停止した。
この発見は、マウスとヒトの間での早期発生プロセスの類似性を考慮すると、胎児異常の未解明の原因、特に流産の原因に新しい手がかりを提供する。流産は、染色体異常によって起こることが多く、この研究で観察されたような問題（不適切な染色体分離や細胞分裂のエラー）から生じる可能性がある。
研究者らは、早期胚の発生における NKX1-2 の重要性の指摘と同時に、まだ他の「指揮者」が発見される可能性がある、ともしている。

研究関連ニュース/他のトップページに戻る

＜英文＞How a 'conductor' makes sense of chaos in ear | EurekAlert!

NEWS RELEASE 7-MAY-2024

How a 'conductor' makes sense of chaos in early mouse embryos

Peer-Reviewed Publication

CENTER FOR GENOMIC REGULATION

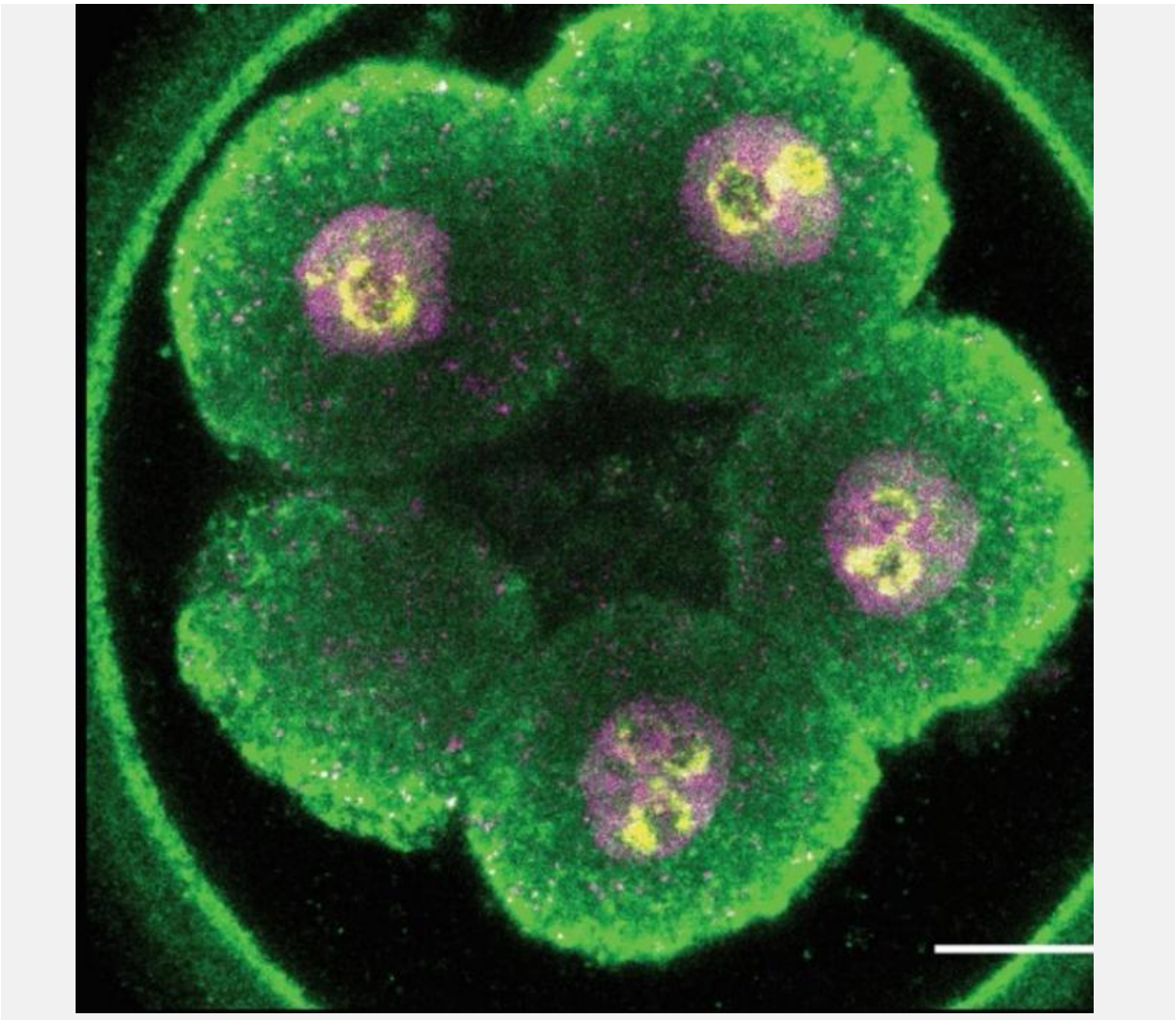


IMAGE:

MOUSE EMBRYOS AT A VERY EARLY STAGE OF DEVELOPMENT

view more

CREDIT: SHOMA NAKAGAWA/CENTRO DE REGULACIÓN GENÓMICA

Early embryonic development is tumultuous. It involves a rapid sequence of events, including cell division, differentiation, and lots of compartments moving around within each cell. Like an orchestra performance where each member of the band must start playing at the exact right moment and in perfect harmony, these processes need to be precisely timed and coordinated to ensure the embryo develops normally.

How cells make sense of this chaos at the very beginning of an embryo's development is an open question. The protein NKX1-2 a crucial role, according to a new study published today in the journal *Stem Cell Reports* by ICREA Research Professor Pia Cosma at the Centre for Genomic Regulation (CRG) in Barcelona and Professor Andrea Califano President of the Chan Zuckerberg Biohub New York and Professor at Columbia University.

NKX1–2 behaves like an orchestra's conductor, skilfully ensuring that the genetic instructions for developing the embryo are executed correctly and at the right times. The protein helps manage the production and organisation of the cell's machinery for making proteins (like ribosomes) and is also crucial for keeping chromosomes organized and properly distributed when cells divide.

When the researchers experimentally inhibited the function of NKX1–2 in mice, they found the nucleolus (a part of the nucleus that assembles ribosomes) was severely altered, disrupting the embryo's ability to produce ribosomes correctly. They also found the 2- to 4-cell embryos could not distribute chromosomes correctly during cell division, and would stop growing at these very early stages of development.

"NKX1–2 belongs to a protein family which is known to play crucial roles in early development and organ formation. While we knew that members of this family were important in general development, NKX1–2's specific role, especially in early embryonic stages, wasn't well understood," explains ICREA Research Professor Pia Cosma, corresponding author of the study.

"It is intriguing that such mechanistic determinants of embryogenesis could be identified by assembling and interrogating a mouse embryonic stem cell regulatory network, using methodologies originally developed for cancer research," adds Dr. Califano, co-corresponding author on the study.

Given the similarities in early developmental processes between mice and humans, the findings offer new clues into unexplained causes of developmental problems, including miscarriages. Miscarriages often result from chromosomal abnormalities, which can arise from issues like those observed in the study — improper chromosome segregation and cell division errors. Further research could explore if there is a human counterpart that influences these fundamental processes as it does in mice, and what happens when it fails.

Despite the importance of NKX1–2 in early embryo development, the researchers suspect more 'conductors' remain to be discovered. "NKX1–2 is expressed at very low levels, which makes it extremely difficult to detect. It's like trying to find a needle in a haystack using traditional methods in biology. Repeating our methods could help find other rare and critical elements that have been historically overlooked," adds Dr. Cosma.

JOURNAL

Stem Cell Reports

DOI

10.1016/j.stemcr.2024.04.004

METHOD OF RESEARCH

Experimental study

SUBJECT OF RESEARCH

Cells

ARTICLE TITLE

The Wnt-dependent master regulator NKX1-2 controls mouse pre-implantation development

ARTICLE PUBLICATION DATE

2-May-2024

4. ジェルが体内のアルコールを分解 –マウス実験

日付：2024 年 5 月 13 日
ソース：ETH チューリッヒ校
概要：

スイスの ETH チューリッヒ校の研究者らは、体に害を与えることなく消化管内でアルコールを分解するたんぱく質ベースのゲルを開発した。このゲルを服用することで、アルコールの有害な効果や中毒効果を軽減することができる可能性があるとして、この研究成果を『Nature Nanotechnology』誌で発表している。
アルコールのほとんどは、胃と腸の粘膜層を介して血流に入る。アルコールの消化が肝臓ではなく消化管で行われるようにすることで、アルコールから有害なアセトアルデヒドが生成されなくなる。これにより、アルコールの有害な消費量を減らすことができる。
研究者らは、通常のホエイタンパク質を使用してゲルを製造した。ホエイタンパク質を長時間煮沸し、長くて細い線維を形成し、次に塩と水を溶媒として添加し、線維を交差させてゲル化させる。
研究者らは、この新しいゲルの効果をマウスで試験した。単回のアルコール摂取後、ゲルの投与により、マウスの血中アルコール濃度が 40%減少した。アルコール摂取後 5 時間後、血中アルコール濃度は、対照群と比較して 56%も低下した。これらのマウスでは、アルコール摂取に伴う有害なアセトアルデヒドが蓄積されず、肝臓のストレス反応も大幅に減少した。
また、10 日間アルコールを摂取したマウスでは、ゲルの投与により、体重減少や肝障害の減少、肝臓内の脂質代謝の改善など、持続的な治療効果が示された。このゲルは、アルコールによる他の臓器や組織の損傷も軽減した。
このゲルの特許はすでに出願されており、ヒトの使用に許可される前にいくつかの臨床試験が必要であるが、研究者らは成功すると確信している、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞New gel breaks down alcohol in the body | ScienceDaily

New gel breaks down alcohol in the body

Date:

May 13, 2024

Source:

ETH Zurich

Summary:

Researchers have developed a protein-based gel that breaks down alcohol in the gastrointestinal tract without harming the body. In the future, people who take the gel could reduce the harmful and intoxicating effects of alcohol.

FULL STORY

Most alcohol enters the bloodstream via the mucous membrane layer of the stomach and the intestines. These days, the consequences of this are undisputed: even small amounts of alcohol impair people's ability to concentrate and to react, increasing the risk of accidents. Drinking large quantities on a regular basis is detrimental to one's health: common consequences include liver disease, inflammation of the gastrointestinal tract and cancer. According to the World Health Organization, around 3 million people die every year from excessive alcohol consumption.

Researchers at ETH Zurich have now developed a protein gel that breaks down alcohol in the gastrointestinal tract. In a study recently published in the journal *Nature Nanotechnology*, they show that in mice, the gel converts alcohol quickly, efficiently and directly into harmless acetic acid before it enters the bloodstream, where it would normally develop its intoxicating and harmful effects.

Reducing health damage caused by alcohol

"The gel shifts the breakdown of alcohol from the liver to the digestive tract. In contrast to when alcohol is metabolised in the liver, no harmful acetaldehyde is produced as an intermediate product," explains Professor Raffaele Mezzenga from the Laboratory of Food & Soft Materials at ETH Zurich. Acetaldehyde is toxic and is responsible for many health problems caused by excessive alcohol consumption.

In the future, the gel could be taken orally before or during alcohol consumption to prevent blood alcohol levels from rising and acetaldehyde from damaging the body. In contrast to many products available on the market, the gel combats not only the symptoms of harmful alcohol consumption but also its causes. Yet, the gel is only effective as long as there is still alcohol in the gastrointestinal tract. This means it can do very little to help with alcohol poisoning, once the alcohol has crossed into the bloodstream. Nor does it help to reduce alcohol consumption in general. "It's healthier not to drink alcohol at all. However, the gel could be of particular interest to people who don't want to give up alcohol completely, but don't want to put a strain on their bodies and aren't actively seeking the effects of alcohol," Mezzenga says.

Main ingredients: Whey, iron and gold

The researchers used ordinary whey proteins to produce the gel. They boiled them for several hours to form long, thin fibrils. Adding salt and water as a solvent then causes the fibrils to cross-link and form a gel. The advantage of a gel over other delivery systems is that it is digested very slowly. But to break down the alcohol, the gel needs several catalysts.

The researchers used individual iron atoms as the main catalyst, which they distributed evenly over the surface of the long protein fibrils. "We immersed the fibrils in an iron bath, so to speak, so that they can react effectively with the alcohol and convert it into acetic acid," says ETH researcher Jiaqi Su, the first author of the study. Tiny amounts of hydrogen peroxide are needed to trigger this reaction in the intestine. These are generated by an upstream reaction between glucose and gold nanoparticles. Gold was chosen as a catalyst for hydrogen peroxide because the precious metal is not digested and therefore stays effective for longer in the digestive tract. The researchers packed all these substances -- iron, glucose and gold -- into the gel. This resulted in a multi-stage cascade of enzymatic reactions that ultimately converts alcohol into acetic acid.

Gel works in mice

The researchers tested the effectiveness of the new gel on mice that were given alcohol just once as well as on mice that were given alcohol regularly for ten days. Thirty minutes after the single dose of alcohol, the prophylactic application of the gel reduced the alcohol level in the mice by 40 percent. Five hours after alcohol intake, their blood alcohol level had dropped by as much as 56 percent compared to the control group. Harmful acetaldehyde accumulated less in these mice, and they exhibited greatly reduced stress reactions in their livers, which was reflected in better blood values.

In the mice that were given alcohol for ten days, the researchers were able to demonstrate not only a lower alcohol level but also a lasting therapeutic effect of the gel: the mice that were given the gel daily in addition to alcohol showed significantly less weight loss, less liver damage and hence better fat metabolism in the liver as well as better blood values. Other organs in the mice, such as the spleen or the intestine, as well as their tissues also showed much less damage caused by alcohol.

Patent pending

In an earlier study of administering iron through whey protein fibrils, the researchers had discovered that iron reacts with alcohol to form acetic acid. As this process was too slow and too ineffective at the time, they changed the form in which they attached the iron to the protein fibrils. "Instead of using larger nanoparticles, we opted for individual iron atoms, which can be distributed more evenly on the surface of the fibrils and therefore react more effectively and quickly with the alcohol," Mezzenga says.

The researchers have already applied for a patent for the gel. While several clinical tests are still required before it can be authorised for human use, the researchers are confident that this step will also be successful, as they already showed that the whey protein fibrils that make up the gel are edible.

Story Source:

Materials provided by **ETH Zurich**. Original written by Christoph Elhardt. *Note: Content may be edited for style and length.*

Journal Reference:

1. Jiaqi Su, Pengjie Wang, Wei Zhou, Mohammad Peydayesh, Jiangtao Zhou, Tonghui Jin, Felix Donat, Cuiyuan Jin, Lu Xia, Kaiwen Wang, Fazheng Ren, Paul Van der Meeren, F. Pelayo García de Arquer, Raffaele Mezzenga. **Single-site iron-anchored amyloid hydrogels as catalytic platforms for alcohol detoxification**. *Nature Nanotechnology*, 2024; DOI: 10.1038/s41565-024-01657-7

5. 肥満治療薬「トロイの木馬」、現行治療薬よりも効果的 −マウス実験

日付：2024 年 5 月 15 日
ソース：コペンハーゲン大学医学部
概要：

『Nature』誌に発表されたコペンハーゲン大学による研究では、減量ホルモン GLP-1 の新しい使用法が示されている。GLP-1 は「トロイの木馬」として特定の分子をマウスの脳に運び、脳の可塑性に影響を与えて体重を減らすことに成功した。GLP-1 とこれらの分子を組み合わせた効果は非常に強力で、場合によっては、GLP-1 のみを投与されたマウスの 2 倍の体重減少が見られた、としている。
この新薬は、既存の減量薬に反応しない患者への代替手段となる可能性もある。マウスの研究では、現在市場に出ている減量薬と同様の副作用（吐き気など）が見られたが、薬が非常に効果的であるため、将来的には用量を減らすことで副作用を軽減できる可能性がある。
この新しい減量薬のテストは現在プレ臨床段階にあり、次のステップはヒトでの臨床試験である。この薬は GLP-1 をベースにしており、GLP-1 は腸のホルモンであり、効果的に脳の食欲制御センターを標的にする。これに分子を結合させることで、食欲を制御するニューロンに特異的に作用する。
この研究は肥満と体重減少に焦点を当てているが、将来的には神経変性疾患や精神障害の治療薬の開発にもつながる可能性がある、としている。
Ousia Pharma というバイオテクノロジー企業も設立され、この研究成果を基に重度の肥満治療薬の開発を進めている。

研究関連ニュース/他のトップページに戻る

＜英文＞'Trojan horse' weight loss drug more effective than available therapies | ScienceDaily

'Trojan horse' weight loss drug more effective than available therapies

Date:

May 15, 2024

Source:

University of Copenhagen - The Faculty of Health and Medical Sciences

Summary:

A groundbreaking article describes a promising new therapy for obesity that leads to greater weight loss in mice than existing medications. The approach smuggles molecules into the brain's appetite center and affects the brain's neuroplasticity.

FULL STORY

"I consider the drugs available on the marked today as the first generation of weight-loss drugs. Now we have developed a new type of weight-loss drug that affects the plasticity of the brain and appears to be highly effective."

So says Associate Professor and Group Leader Christoffer Clemmensen, from the Novo Nordisk Foundation Center for Basic Metabolic Research at the University of Copenhagen, who is senior author of the new study, which has been published in the scientific journal *Nature*.

In the study, Christoffer Clemmensen and colleagues demonstrate a new use of the weight loss hormone GLP-1. GLP-1 can be used as a 'Trojan Horse' to smuggle a specific molecule into the brain of mice, where it successfully affects the plasticity of the brain and results in weight loss.

"The effect of GLP-1 combined with these molecules is very strong. In some cases, the mice lose twice as much weight as mice treated with GLP-1 only," Christoffer Clemmensen explains.

This means that future patients can potentially achieve the same effect with a lower dosage. Moreover, the new drug may be an alternative to those who do not respond well to existing weight-loss drugs.

"Our studies in mice show side effects similar to those experienced by patients treated with the weight loss drugs available on the market today, including nausea. But because the drug is so effective, we may be able to lower the dosage and thus mitigate some of the side effects in the future -- though we still don't know how humans respond to the drug," he says.

Testing of the new weight loss drug is still in the so-called preclinical phase, which is based on studies with cells and on experimental animals. The next step is clinical trials with human participants.

"We already know that GLP-1-based drugs can lead to weight loss. The molecule that we have attached to GLP-1 affects the so-called glutamatergic neurotransmitter system, and in fact, other studies with human participants suggest that this family of compounds has significant weight loss potential. What is interesting here is the effect we get when we combine these two compounds into a single drug," Christoffer Clemmensen stresses.

The drug must undergo three phases of clinical trials on human participants. According to Christoffer Clemmensen, it can therefore take eight years before the drug could be available on the market.

The brain defends excessive body weight

Christoffer Clemmensen and colleagues developed an interest in molecules that are used to treat chronic depression and Alzheimer's disease.

The molecules block a receptor protein called the NMDA receptor, which play a key role in long-term changes in brain connections and have received scientific attention within fields of learning and memory. Drugs targeting these receptors will strengthen and/or weaken specific nerve connections.

"This family of molecules can have a permanent effect on the brain. Studies have demonstrated that even a relative infrequent treatment can lead to persistent changes to the brain pathologies. We also see molecular signatures of neuroplasticity in our work, but in this case in the context of weight loss," he explains.

The human body has evolved to protect a certain body weight and fat mass. From an evolutionary perspective, this has probably been to our advantage, as it means that we have been able to survive periods of food scarcity. Today, food scarcity is not a problem in large parts of the world, where an increasing part of the population suffers from obesity.

"Today, more than one billion people worldwide have a BMI of 30 or more. This makes it increasingly relevant to develop drugs to aid this disease, and which can help the organism to sustain a lower weight. This topic is something we invest a lot of energy in researching," says Christoffer Clemmensen.

A Trojan Horse smuggles small molecule modulators of neuroplasticity into appetite-regulating neurons

We know that drugs based on the intestinal hormone GLP-1 effectively target the part of the brain that is key to weight loss, namely the appetite control centre.

"What is spectacular -- on a cellular level -- about this new drug is the fact that it combines GLP-1 and molecules that block the NMDA receptor. It exploits GLP-1 as a Trojan Horse to smuggle these small molecules exclusively into the neurons that affect appetite control. Without GLP-1, the molecules that target the NMDA receptor would affect the entire brain and thus be non-specific," says Postdoc Jonas Petersen from the Clemmensen Group, who is the first author on the study and the chemist who synthesized the molecules.

Non-specific drugs are often associated with severe side effects, which has previously been seen in drugs for treating different neurobiological conditions.

"A lot of brain disorders are difficult to treat, because the drugs need to cross the so-called blood-brain barrier. Whereas large molecules like peptides and proteins generally have difficulties accessing the brain, many small molecules have unlimited access to the entire brain. We have used the GLP-1 peptide's specific access to the appetite control centre in the brain to deliver one of these otherwise non-specific substances to this region only," Christoffer Clemmensen says and adds:

"In this study, we have focused on obesity and weight loss, but in fact this is a completely new approach for delivering drugs to specific parts of the brain. So, I hope our research can pave the way for a whole new class of drugs for treating conditions like neurodegenerative diseases or psychiatric disorders."

What is neuroplasticity?

The plasticity of the brain, also known as neuroplasticity, is the brain's ability to restructure itself by forming new neural connections. This ability allows the brain to adjust to new experiences, learn new skills, absorb new information and recover from injuries.

Neuroplasticity is found in several levels of the nervous system and can be anything from microscopic changes in the structure and function of individual neurons to major changes such as the formation of new neural connections or reorganisation of areas of the brain.

Christoffer Clemmensen, along with postdoc Jonas Petersen and a former scientist from the University of Copenhagen (Anders Klein), have co-founded of the biotech company Ousia Pharma, which is a spinout company from the University of Copenhagen. The company is continuing to develop the medical concept presented in this study for the treatment of severe obesity.

Story Source:

Materials provided by **University of Copenhagen - The Faculty of Health and Medical Sciences**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Jonas Petersen, Mette Q. Ludwig, Vaida Juozaityte, Pablo Ranea-Robles, Charlotte Svendsen, Eunsang Hwang, Amalie W. Kristensen, Nicole Fadahunsi, Jens Lund, Alberte W. Breum, Cecilie V. Mathiesen, Luisa Sachs, Roger Moreno-Justicia, Rebecca Rohlfs, James C. Ford, Jonathan D. Douros, Brian Finan, Bryan Portillo, Kyle Grose, Jacob E. Petersen, Mette Trauelsen, Annette Feuchtinger, Richard D. DiMarchi, Thue W. Schwartz, Atul S. Deshmukh, Morten B. Thomsen, Kristi A. Kohlmeier, Kevin W. Williams, Tune H. Pers, Bente Frølund, Kristian Strømgaard, Anders B. Klein, Christoffer Clemmensen. **GLP-1-directed NMDA receptor antagonism for obesity treatment**. *Nature*, 2024; DOI: 10.1038/s41586-024-07419-8

6. 遺伝子治療がマウスの背中の痛みを和らげ、損傷した椎間板を修復

日付:2024 年 5 月 16 日
ソース:オハイオ州立大学
概要:

椎間板関連の背中の痛みに、遺伝子治療が有望な治療法となる可能性がある。
『Biomaterials』誌オンライン版で発表されたオハイオ州立大学の研究によると、自然由来のナノキャリアを使った遺伝子治療が、マウスの脊椎の損傷した椎間板を修復し、痛みの症状を軽減することが示された。この発見は、痛みの管理においてオピオイドに代わる効果的で長続きする治療法を提供する可能性がある。
科学者らは、マウスの結合組織細胞(線維芽細胞)をモデルとしてナノキャリアを設計し、組織発達に重要なタンパク質の遺伝子材料を搭載した。これをマウスの損傷した椎間板に注入し、12 週間にわたる評価で、遺伝子治療が椎間板の構造的な完全性と機能を回復させ、痛みの兆候を減少させることが確認された。
この研究によると、ナノキャリアは、ヒトの血流や生体液に自然に存在する細胞間のメッセージを運ぶ小胞の複製であり、研究チームは、電荷を使用してドナー細胞の膜に一時的に穴を開け、外部から得た DNA を内部に導入し、特定のタンパク質を生成する分子を運んだ。この研究では、発達と成長に重要な「パイオニア」転写因子タンパク質である FOXF1 を生成する材料を使用した。
遺伝子治療を受けたマウスの椎間板は、対照群と比較して、組織が再生し、痛みの症状が減少した。
今後の研究では、他の転写因子の影響や、年齢関連の変性をモデルとした高齢マウスでの効果をテストし、最終的には臨床試験を行いたい、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞Gene therapy relieves back pain, repairs damaged disc in mice | ScienceDaily

Gene therapy relieves back pain, repairs damaged disc in mice

Study suggests nanocarriers loaded with DNA could replace opioids

Date:

May 16, 2024

Source:

Ohio State University

Summary:

Disc-related back pain may one day meet its therapeutic match: gene therapy delivered by naturally derived nanocarriers that, a new study shows, repairs damaged discs in the spine and lowers pain symptoms in mice.

FULL STORY

Disc-related back pain may one day meet its therapeutic match: gene therapy delivered by naturally derived nanocarriers that, a new study shows, repairs damaged discs in the spine and lowers pain symptoms in mice.

Scientists engineered nanocarriers using mouse connective-tissue cells called fibroblasts as a model of skin cells and loaded them with genetic material for a protein key to tissue development. The team injected a solution containing the carriers into damaged discs in mice at the same time the back injury occurred.

Assessing outcomes over 12 weeks, researchers found through imaging, tissue analysis, and mechanical and behavioral tests that the gene therapy restored structural integrity and function to degenerated discs and reduced signs of back pain in the animals.

"We have this unique strategy that's able to both regenerate tissue and inhibit some symptoms of pain," said co-senior author Devina Purmessur Walter, associate professor of biomedical engineering at The Ohio State University.

Though there is more to learn, the findings suggest gene therapy could offer an effective and long-lasting alternative to opioids for the management of debilitating back pain.

"This can be used at the same time as surgery to actually boost healing of the disc itself," said co-senior author Natalia Higuita-Castro, associate professor of biomedical engineering and neurological surgery at Ohio State. "Your own cells are actually doing the work and going back to a healthy state."

The study was published online recently in the journal *Biomaterials*.

An estimated 40% of low-back pain cases are attributed to degeneration of the cushiony intervertebral discs that absorb shocks and provide flexibility to the spine, previous research suggests. And while trimming away bulging tissue from a herniated disc during surgery typically reduces pain, it does not repair the disc itself -- which continues to degenerate with the passage of time.

"Once you take a piece away, the tissue decompresses like a flat tire," Purmessur Walter said. "The disease process continues, and impacts the other discs on either side because you're losing that pressure that is critical for spinal function. Clinicians don't have a good way of addressing that."

This new study builds upon previous work in Higuita-Castro's lab, which reported a year ago that nanocarriers called extracellular vesicles loaded with anti-inflammatory

cargo curbed tissue injury in damaged mouse lungs. The engineered carriers are replicas of the natural extracellular vesicles that circulate in humans' bloodstream and biological fluids, carrying messages between cells.

To create the vesicles, scientists apply an electrical charge to a donor cell to transiently open holes in its membrane, and deliver externally obtained DNA inside that converts to a specific protein, as well as molecules that prompt the manufacture of even more of a functional protein.

In this study, the cargo consisted of material to produce a "pioneer" transcription factor protein called FOXF1, which is important in the development and growth of tissues.

"Our concept is recapitulating development: FOXF1 is expressed during development and in healthy tissue, but it decreases with age," Purmessur Walter said. "We're basically trying to trick the cells and give them a boost back to their developmental state when they're growing and at their healthiest."

In experiments, mice with injured discs treated with FOXF1 nanocarriers were compared to injured mice given saline or mock nanocarriers and uninjured mice.

Compared to controls, the discs in mice receiving gene therapy showed a host of improvements: The tissue plumped back up and became more stable through production of a protein that holds water and other matrix proteins, all helping promote range of motion, load bearing and flexibility in the spine. Behavioral tests showed the therapy decreased symptoms of pain in mice, though these responses differed by sex -- males and females showed varying levels of susceptibility to pain based on the types of movement being assessed.

The findings speak to the value of using universal adult donor cells to create these extracellular vesicle therapies, the researchers said, because they don't carry the risk of generating an immune response. The gene therapy also, ideally, would function as a one-time treatment -- a therapeutic gift that keeps on giving.

"The idea of cell reprogramming is that you express this transcription factor and the cell is then going to convert to this healthier state and stays committed to that healthier phenotype -- and that conversion is not normally transient," Higuita-Castro said. "So in theory, you would not expect to have to re-dose significantly."

There are more experiments to come, testing the effects of other transcription factors that contribute to intervertebral disc development. And because this first study used young adult mice, the team also plans to test the therapy's effects in older animals that model age-related degeneration and, eventually, in clinical trials for larger animals known to develop back problems.

Higuita-Castro, director of advanced therapeutics and engineering in the College of Medicine Davis Heart and Lung Research Institute and a core faculty member of Ohio State's Gene Therapy Institute, and Purmessur Walter, an investigator in Ohio State's Spine Research Institute and director of the Spinal Therapeutics Laboratory in the College of Engineering, are co-principal investigators on National Institutes of Health grants funding this research.

Additional co-authors include co-first authors Shirley Tang and Ana Salazar-Puerta, Mary Heimann, Kyle Kuchynsky, María Rincon-Benavides, Mia Kordowski, Gilian Gunsch, Lucy Bodine, Khady Diop, Connor Gantt, Safdar Khan, Anna Bratasz, Olga

Kokiko-Cochran, Julie Fitzgerald and Benjamin Walter, all of Ohio State; Damien Laudier of Icahn School of Medicine at Mount Sinai; and Judith Hoyland of the University of Manchester.

Ohio State has filed a patent application on nonviral gene therapy for minimally invasively treating painful musculoskeletal disorders.

Story Source:

Materials provided by **Ohio State University**. Original written by Emily Caldwell. *Note: Content may be edited for style and length.*

Journal Reference:

1. Shirley N. Tang, Ana I. Salazar-Puerta, Mary K. Heimann, Kyle Kuchynsky, María A. Rincon-Benavides, Mia Kordowski, Gilian Gunsch, Lucy Bodine, Khady Diop, Connor Gantt, Safdar Khan, Anna Bratasz, Olga Kokiko-Cochran, Julie Fitzgerald, Damien M. Laudier, Judith A. Hoyland, Benjamin A. Walter, Natalia Higuita-Castro, Devina Purmessur. **Engineered extracellular vesicle-based gene therapy for the treatment of discogenic back pain**. *Biomaterials*, 2024; 308: 122562 DOI: 10.1016/j.biomaterials.2024.122562

7. ある種のマウスが一夫一妻制に至る理由が新たに進化した細胞にある可能性

日付：2024 年 5 月 15 日
ソース：コロンビア大学
概要：

フロリダとジョージア州に生息するハイイロシロアシマウス（oldfield mouse）の両親はどちらも子の世話をするが、北米で最も豊富な哺乳類であるシカシロアシマウス（deer mouse）はたいてい母親のみが子育てをする。コロンビア大学の Zuckerman Institute の科学者らは、その違いに寄与していると思われる新たな副腎細胞を発見し、シカシロアシマウスが多夫多妻制であるのに対し、ハイイロシロアシマウスが一生を通じて一夫一妻制を守る理由を解明するための新たな研究として『Nature』誌のオンライン版で発表している。
この副腎細胞からのホルモンは数十年前に人間で初めて発見されたが、その役割は不明であった。そして彼らはこのホルモンがマウスにおいて育児行動を促進することを発見した。
科学者らは、これら 2 種のマウスの副腎を調査し、一夫一妻制のマウスの副腎が多夫多妻制のマウスの副腎よりも 6 倍重いことを発見した。遺伝子解析により、一夫一妻制のマウスは Akr1c18 という遺伝子の活動が非常に高いことが判明した。この遺伝子は 20α-OHP というホルモンの生成を助け、このホルモンが育児行動を促進することが分かった。
研究者らは、ホルモン 20α-OHP を注入されたマウスが子育て行動を示すことも発見した。具体的には、ホルモンを注入された多夫多妻制のマウスの 17%が子供を巣に戻すなどの行動を見せた。
さらに、ハイイロシロアシマウスの副腎は普通の 3 層構造ではなくもう一層多い 4 層構造をしており、Akr1c18 発現細胞は新たに発見されたその一層を構成しており、研究者らはその層を zona inaudita と名付けた。このゾーンでは Akr1c18 を含む 194 の遺伝子が高い活動を示した。この新しい細胞タイプは急速に進化したものだと推測される。
この発見は、人間の育児行動やホルモンの役割についての新たな洞察を提供する可能性があり、研究者らは、20α-OHP と人間の育児の関連研究が今回の成果をきっかけに更に進むことを望んでいる。

研究関連ニュース/他のトップページに戻る

＜英文＞Some mice may owe their monogamy to a newly e | EurekAlert!

NEWS RELEASE 15-MAY-2024

Some mice may owe their monogamy to a newly evolved type of cell

Scientists discover the cells and hormones that inspire mice to nurture their young; the same hormones are also present in humans

Peer-Reviewed Publication

COLUMBIA UNIVERSITY

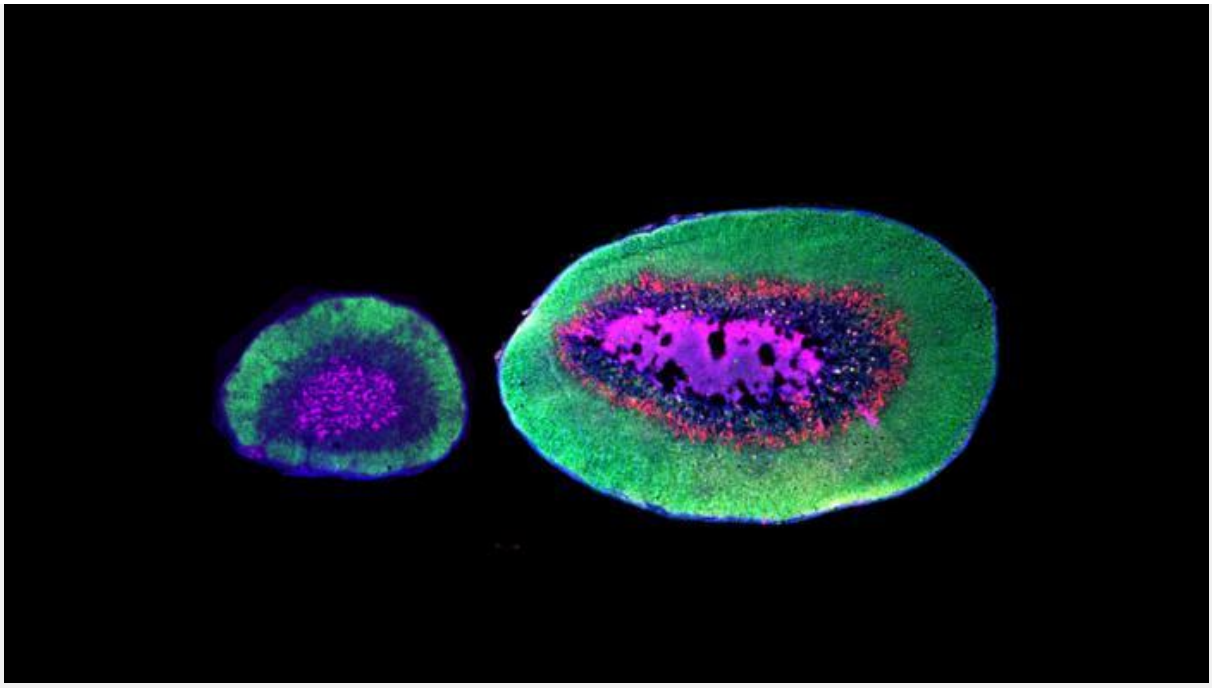


IMAGE:

THE ADRENAL GLANDS OF A DEER MOUSE (LEFT) AND OLDFIELD MOUSE (RIGHT), SHOWING THE RELATIVE SIZE OF THE ZONA FASCICULATA (GREEN) AND THE NOVEL ZONA INAUDITA (RED).

view more

CREDIT: BENDESKY LAB/COLUMBIA'S ZUCKERMAN INSTITUTE

NEW YORK, NY — What makes the oldfield mouse steadfastly monogamous throughout its life while its closest rodent relatives are promiscuous? The answer may be a previously unknown hormone-generating cell, according to a new study published online today in *Nature* from scientists at Columbia's Zuckerman Institute.

"The hormone from these cells was actually first discovered in humans many decades ago, but nobody really knew what it did," said Andrés Bendesky, MD, PhD, a principal investigator at Columbia's Zuckerman Institute. "We've discovered that it can promote nurturing in mice, which gives us an idea of what it might be doing in humans."

The new study investigated two species of mice. One is the most abundant mammal in North America — the deer mouse (*Peromyscus maniculatus*), which ranges from Alaska to Central America. The other,

the oldfield mouse (*Peromyscus polionotus*), lives in Florida and Georgia, and is a bit smaller, weighing in at roughly 13 grams compared with the deer mouse's 18 grams.

More than 100 years of previous research has shown that the mice species behave in strikingly different ways. Whereas the deer mouse is promiscuous — even a single litter of pups can have four different fathers — the oldfield mouse mates for life.

However, prior work also suggested these species are evolutionary siblings, based on similarities in their skulls, teeth and other anatomical features, as well as their genetics. To find out why these close mouse relatives behave so differently, the scientists examined their adrenal glands.

"This pair of organs, located in the abdomen, produces many hormones important for behavior," said Dr. Bendesky, who is also an assistant professor of ecology, evolution and environmental biology at Columbia University. "These include stress hormones such as adrenaline, but also a number of sex hormones."

The adrenal glands of these mice proved startlingly different in size. In adults, the adrenals of the monogamous mice are roughly six times heavier than those of promiscuous mice (after adjusting for differences in the body weight between the species).

"This extraordinary difference in the size of an internal organ between such closely related species is unprecedented," Dr. Bendesky said.

Genetic analysis of the adrenal cells revealed that one gene, *Akr1c18*, saw far more activity in the monogamous mice than in the promiscuous rodents. The enzyme this gene encodes helps create a little-studied hormone known as 20α-OHP, which is also found in humans and other mammals.

The researchers observed that increasing 20α-OHP hormone boosted nurturing behavior in both mouse species. For instance, 17 percent of the promiscuous mice who were given the hormone groomed their pups and brought them back to their nests, whereas none behaved this way if not given the hormone.

"This marks the first time we found anything that could increase parental care in the promiscuous group," Dr. Bendesky said.

Normally these glands are divided into three zones. But the scientists discovered that the adrenals of the monogamous mice possessed a fourth zone.

"We called this the *zona inaudita*, which is Latin for 'previously unheard-of zone,' because no one has ever observed this type of cell in another animal," said Natalie Niepoth, PhD, a co-first author on the study who is now a senior scientist at Regeneron.

In *zona inaudita* cells, the researchers found that 194 genes, including *Akr1c18*, were far more active compared with the same genes in other adrenal cells. Their analyses also identified key genes underlying the development and function of the *zona inaudita* in the oldfield mice.

This completely unheard-of structure apparently evolved rapidly. Genetic mutations accumulate in genomes at roughly predictable rates over time. By measuring the number of mutations distinguishing these species, the scientists estimated this novel cell type evolved within the past 20,000 years, "which is just an eyeblink when it comes to evolution," Dr. Bendesky said.

Much remains uncertain about what drives the evolution of monogamous behavior. One argument suggests that monogamy can increase the chances that parents will cooperate to care for their offspring, since fathers are more confident the young are theirs. This kind of teamwork can improve the chances that the progeny will survive, especially when resources are limited, Dr. Bendesky said. The newly found adrenal cells promote parenting behavior typical of monogamy, the researchers noted.

The new findings could provide insights when it comes to parenting behavior and challenges in humans, Dr. Niepoth suggested. For example, in mice, 20α-OHP is often converted into a compound very similar to the molecule allopregnanolone, which naturally occurs in humans and has been approved by the FDA as a drug to help treat the postpartum depression that people often experience after childbirth, Dr. Bendesky said.

"I hope that our study motivates further investigation into the link between 20α-OHP and parenting in humans," said Jennifer R. Merritt, PhD, a co-first author on the study and postdoctoral researcher in the Bendesky lab.. "We have so much to learn about the role this hormone plays in human parental behavior."

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The paper, "Evolution of a novel adrenal cell type that promotes parental care," was published online in *Nature* on May 15, 2024.

The full list of authors includes Natalie Niepoth, Jennifer R. Merritt, Michelle Uminski, Emily Lei, Victoria S. Esquibies, Ina B. Bando, Kimberly Hernandez, Christoph Gebhardt, Sarah A. Wacker, Stefano Lutzu, Asmita Poudel, Kiran K. Soma, Stephanie Rudolph and Andres Bendesky.

The authors report no conflicts of interest.

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COI STATEMENT

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8. 男性用避妊薬開発への有望なアプローチ –マウス実験

日付:2024 年 5 月 23 日
ソース:ベイラー医科大学
概要:

『サイエンス』誌に発表されたベイラー医科大学によるこの研究の焦点は、精子形成に必須なタンパク質であるセリン/スレオニンキナーゼ 33（STK33）を阻害する小分子を特定することであった。
マウスでの研究では、STK33 遺伝子を欠損させると異常な精子が形成され、不妊になることが分かっており、ヒト男性でも同様の変異が不妊を引き起こすが、他の障害は見られない。このため、STK33 は安全性の懸念が少ない避妊ターゲットと見なされている。
今回、研究者らは DNA エンコード化学技術（DEC-Tec）を用いて、STK33 を強力に阻害する化合物を発見した。その中で、改良された CDD-2807 という化合物が最も効果的であることが判明した。
この化合物をマウスに投与した結果、精子の運動性と数が減少し、不妊状態になったと同時に、毒性は示されず、治療中止後には再び精子の運動性と数が回復した。
研究は、STK33 の結晶構造の解明と、その構造に基づいた化合物の設計にも成功した。
今後数年間で、サルを用いた試験を通じて、STK33 阻害剤の効果をさらに評価する予定だとしている。
重要ポイント:

- 非ホルモン性で精子特異的なアプローチ
- STK33 の阻害による可逆的な不妊効果
- マウスでの安全性と有効性の確認
- 今後のサルでの試験計画

この研究は、男性用避妊薬の実現に向けた重要な一歩を示している。

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

A promising approach to develop a birth control pill for men

Date:

May 23, 2024

Source:

Baylor College of Medicine

Summary:

Researchers show in animal models that a novel, non-hormonal sperm-specific approach offers a promising option for reversible human male contraception.

FULL STORY

The world's population has increased by more than 2.6-fold in the last 60 years. The growing trend continues -- projections indicate that the number of people living on our planet will grow to 9 billion by 2037 from 8 billion in 2022. These numbers underscore the need for considering family planning; however, there have been limited breakthroughs in contraception in recent decades. Specifically for men, there are no oral contraceptive pills available.

In a study published in the journal *Science*, researchers at Baylor College of Medicine and collaborating institutions show in animal models that a novel, non-hormonal sperm-specific approach offers a promising option for reversible human male contraception.

"Although researchers have been investigating several strategies to develop male contraceptives, we still do not have a birth control pill for men," said corresponding author Dr. Martin Matzuk, director of the Center for Drug Discovery and chair of the Department of Pathology and Immunology at Baylor. "In this study we focused on a novel approach -- identifying a small molecule that would inhibit serine/threonine kinase 33 (STK33), a protein that is specifically required for fertility in both men and mice."

Previous research has shown that STK33 is enriched in the testis and is specifically required for the formation of functional sperm. In mice, knocking out the *Stk33* gene renders the mice sterile due to abnormal sperm and poor sperm motility. In men, having a mutation in the *STK33* gene leads to infertility caused by the same sperm defects found in the *Stk33* knockout mice. Most importantly, mice and men with these mutations have no other defects and even have normal testis size.

"STK33 is therefore considered a viable target with minimal safety concerns for contraception in men," said Matzuk, who has been on faculty at Baylor for 30 years and is Baylor's Stuart A. Wallace Chair and Robert L. Moody, Sr. Chair of Pathology and Immunology. "STK33 inhibitors have been described but none are STK33-specific or potent for chemically disrupting STK33 function in living organisms."

Finding an effective STK33 inhibitor

"We used DNA-Encoded Chemistry Technology (DEC-Tec) to screen our multi-billion compound collection to discover potent STK33 inhibitors," said first author Dr. Angela Ku, staff scientist in the Matzuk lab. "Our group and others have used this approach before to uncover potent and selective kinase inhibitors."

The researchers uncovered potent STK33-specific inhibitors, from which they successfully generated modified versions to make them more stable, potent and selective. "Among these modified versions, compound CDD-2807 turned out to be the most effective," Ku said.

"Next, we tested the efficacy of CDD-2807 in our mouse model," said co-author Dr. Courtney M. Sutton, postdoctoral fellow in the Matzuk lab. "We evaluated several doses and treatment schedules and then determined sperm motility and number in the mice as well as their ability to fertilize females."

Compound CDD-2807 effectively crossed the blood-testis barrier and reduced sperm motility and numbers and mice fertility at low doses. "We were pleased to see that the mice did not show signs of toxicity from CDD-2807 treatment, that the compound did not accumulate in the brain, and that the treatment did not alter testis size, similar to the *Stk33* knockout mice and the men with the *STK33* mutation," Sutton said. "Importantly, the contraceptive effect was reversible. After a period without compound CDD-2807, the mice recovered sperm motility and numbers and were fertile again."

"In our paper, we also present the first crystal structure for STK33," said co-author Dr. Choel Kim, associate professor of biochemistry and molecular pharmacology and member of the Dan L Duncan Comprehensive Cancer Center at Baylor. "Our crystal structure showed how one of our potent inhibitors interacts with STK33 kinase in three dimensions. This enabled us to model and design our final compound, CDD-2807, for better drug-like properties."

"This study was a tour de force by our team in the Center for Drug Discovery at Baylor and our collaborators," said co-author Dr. Mingxing Teng, assistant professor of pathology and immunology and of biochemistry and molecular pharmacology at Baylor. Teng also is a Cancer Prevention Research Institute of Texas Scholar and a member of the Dan L Duncan Comprehensive Cancer Center at Baylor. "Starting with a genetically validated contraceptive target, we were able to show that STK33 is also a chemically validated contraceptive target."

"In the next few years, our goal is to further evaluate this STK33 inhibitor and compounds similar to CDD-2807 in primates to determine their effectiveness as reversible male contraceptives," Matzuk said.

Additional co-authors of the paper affiliated with Baylor College of Medicine are Kiran L. Sharma, Hai Minh Ta, Kurt M. Bohren, Yong Wang, Srinivas Chamakuri, Ruihong Chen, John M. Hakenjos, Ravikumar Jimmidi, Katarzyna Kent, Feng Li, Jian-Yuan Li, Lang Ma, Chandrashekhar Madasu, Murugesan Palaniappan, Stephen S. Palmer, Xuan Qin, Zhi Tan, Yasmin M. Vasquez, Jian Wang, Zhifeng Yu, Qiuji Ye and Damian W. Young. Co-authors Matthew B. Robers and Jennifer Wilkinson are affiliated with Promega Corp., and Banumathi Sankaran is affiliated with Lawrence Berkeley National Laboratory.

Story Source:

Materials provided by **Baylor College of Medicine**. Original written by Graciela Gutierrez. *Note: Content may be edited for style and length.*

Journal Reference:

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