Bio News – March, 2020

In-Vivo Science International, Inc.

今月の企業関連ニュース/他

2/2　AI 活用で創製の新薬、日本で世界初の臨床試験開始

https://www.itmedia.co.jp/news/articles/2002/02/news023.html

2/3　新型ウイルス患者、インフル・エイズ薬混合で劇的回復 タイ保健省発表

https://www.afpbb.com/articles/-/3266360

2/3　新型肺炎、中国の死者が 361 人に　SARS を超える

https://www.asahi.com/articles/ASN23323ZN23UHBI007.html

2/3　質が悪い外食が米国成人の摂取カロリーの約 2 割を占める

2/4　無料の遺伝子検査で小児のてんかんを早く見つける取り組みに Biogen 等 5 社が参加

遺伝子検査を無料で提供して小児のてんかんを早く見つける取り組み Behind the Seizure に 5 社・Biogen や PTC Therapeutics を含む 5 社が新たに加わりました。Behind the Seizure は BioMarin と Invitae が立ち上げ、今回の 5 社の参加に先立って去年には Stoke Therapeutics と Xenon Pharmaceuticals がすでに加わっている。

https://www.fiercepharma.com/marketing/more-pharma-sponsors-join-biomarin-and-invitae-genetic-testing-program-for-children

2/4　Gilead が中国の新型コロナウイルスに抗ウイルス薬提供～試験も立ち上げている

中国で猛威を振るう新型コロナウイルス（2019-nCoV）感染に、他のエボラ治療と競って負けた抗ウイルス薬 Remdesivir（レムデシビル）が効くかどうかを調べる無作為化試験を Gilead Sciences が中国と協力して立ち上げている。

2/4　日本国際賞に米欧 2 氏

国際科学技術財団は 4 日、2020 年の日本国際賞を、ネアンデルタール人の全遺伝情報（ゲノム）解読で古人類学に貢献した独マックス・プランク進化人類学研究所のスバンテ・ペーボ教授（64）と、次世代通信規格「5G」を支える「誤り訂正」技術を開発した米マサチューセッツ工科大のロバート・ギャラガー名誉教授（88）に授与すると発表した。
授賞式は 4 月 15 日に東京都内で開かれ、それぞれ賞金 5,000 万円が贈られる。

2/5　「気候の人工操作」研究に 400 万ドル投入 -アメリカ

温暖化が止まらないなら、人工的に止めてしまおうではないか、そんな研究が進んでいる。それは「気候工学(ジオエンジニアリング)」と呼ばれる分野で、新たな温暖化対策として、欧米を中心に注目されている。

2/5　iPS パーキンソン病治験、さらに2人実施　京大、経過は順調

https://www.sankei.com/life/news/200205/lif2002050040-n1.html

2/5　新型コロナウイルス・2019-nCoV 感染を Lilly/Incyte の Baricitinib で阻止しうる

2/5　新型コロナウイルス・2019-nCoV 感染治療の開発に Regeneron も参入

2/6　ゲノム編集を用いた革新的な遺伝子治療による視覚再建　マウス実験-東北大学

https://www.eurekalert.org/pub_releases_ml/2020-02/tu-4020620.php

2/6　Merck & Co が主力製品に専念するために女性健康製品やバイオシミラーを手放す

2/6　Pfizer との店頭医療品合弁事業分社化の準備を GlaxoSmithKline（GSK）が正式に開始

2/6　iPS 心筋、移植計画を承認　厚労省に申請へ―慶応大

2/6　新型コロナウイルスへの世界の取り組みにゲイツ財団が最大 1 億ドル提供

2/6　ピーナツアレルギー治療薬の Aimmune に Nestle が更に 2 億ドルを投資

2/6　Novo の GLP-1 糖尿病薬の昨年の売り上げが 10 億ドルの大台を軽く突破

2/7　妊娠左右する遺伝子発見　熊本大など、不妊治療への応用期待

https://www.nishinippon.co.jp/item/n/582155/

https://www.sciencedaily.com/releases/2020/02/200206110701.htm

2/8　Novo Nordisk がデンマーク、AstraZeneca がオーストラリアの製造拠点を拡大

2/8　AstraZeneca がオーストラリアに 2500 万本の植樹

先月末に発表された AstraZeneca の植樹計画が早速実行に移され、悲惨な森林火災を被ったオーストラリアに計画の半分の 2500 万本を植樹。
AstraZeneca は非営利緑化推進組織 One Tree Planted と協力して世界に木を 5 年間で 5000 万本植える計画を先月末に発表している。

2/10　トランプ政権、タバコ製品を規制するすべての権限を FDA から剥奪することを提案

2/10　Lilly と Roche のどちらの抗 Aβ 抗体も変異によるアルツハイマー病の進展を防げず

2/11　筋ジストロフィー薬開発が去年末に頓挫した Wave Life、従業員 22%削減

2/11　米国糖尿病市場を目指すデンマークの Zealand がインスリン投与装置メーカーValeritas を買収

2/12　新型肺炎は「COVID―19」 WHO 命名

2/12　水は「ふつう」じゃない。液体の水の構造は 2 種類あることを東大が証明

2/12　神戸で医療用ロボ研究開発　市と神戸大、産官学連携で

https://www.kobe-np.co.jp/news/iryou/202002/0013111279.shtml

2/13　Gilead の最有力の新型コロナウイルス薬候補を中国製薬会社が勝手に製造

2/13　J&J が米国政府と協力して新型コロナウイルス疾患 COVID-19 ワクチン開発を急ぐ

2/13　Sanofi から首脳部の 4 人が去る

2/13　iPS で網膜色素変性症治療　神戸の病院、厚労省に計画申請

https://www.sankei.com/life/news/200213/lif2002130037-n1.html

2/14　卵子形成が始まる仕組み解明　マウスの生殖細胞―京大

https://www.jiji.com/jc/article?k=2020021400156&g=soc

2/15　エーザイが抗肥満薬 BELVIQ/BELVIQ XR の米国での販売中止 -癌の発現率上昇が認められた事を受けて

2/15　難病「ハンチントン病」の治療につながる物質を発見 -阪大研究チーム

2/18　新型肺炎の致死率2%　SARS より「致命的ではない」 WHO 見解

https://www.sankei.com/life/news/200218/lif2002180005-n1.html

2/19　Novartis 元重役が後発品の価格操作の罪を認めた～共謀した Taro 社の重役も起訴

入札で不正を働いて価格を操作してジェネリック医薬品を売りつけた罪を Novartis 子会社 Sandoz 元経営陣 Hector Armando Kellum 氏が認めた。

2/19　新型コロナウイルスに有効かもしれない Zhejiang Hisun Pharmaceutical の抗インフルエンザ薬を中国が承認

2/19　新型コロナウイルス感染症（COVID-19）の流行を受けて米国 FDA が中国工場の査察をしばらく控える

2/19　Sanofi も米国政府と協力して新型コロナウイルスワクチンを開発

https://www.statnews.com/2020/02/18/sanofi-announces-it-will-work-with-hhs-to-develop-coronavirus-vaccine/?utm_source=STAT+Newsletters&utm_campaign=085f95a9a5-MR_COPY_12&utm_medium=email&utm_term=0_8cab1d7961-085f95a9a5-150065641

2/19　ウォーレン・バフェット氏の Berkshire Hathaway が Biogen 株式を 2 億ドル購入

米国の投資王 Warren Buffett 氏が指揮する Berkshire Hathaway がアルツハイマー病薬 aducanumab の米国 FDA 承認申請を控える Biogen の株式約 65 万株を約 2 億ドル（1 億 9,240 万ドル）で取得。
aducanumab の前途に関するアナリスト見解は分かれていて、たとえば Baird の Brian Skorney 氏は同剤の結果は FDA の承認水準に至っていないと言っているのに対して、SVB Leerink の Marc Goodman 氏は非承認より承認の可能性の方が大きいと判断している。
Biogen の他にバークシャー・ハサウェイは 2017 年後期から大規模再編を始めた Teva にもつぎ込んでいるが今の所その見返りは手にできていない。

https://www.fiercepharma.com/pharma/a-192m-moat-buffett-s-berkshire-builds-stake-biogen-ahead-key-alzheimer-s-drug-filing

2/20　アステラス製薬子会社 Audentes が米国ノースキャロライナ州に遺伝子治療製造工場を建設する

https://www.businesswire.com/news/home/20200218005989/en/Audentes-Therapeutics-Announces-Plans-Build-New-State-of-the-Art

2/21　Merck の最高デジタル責任者が辞職～Marriott ホテルに転職

Merck & Co が NIKE から引き抜いた最高電子情報技術責任者・Jim Scholefield 氏が 2 年と経たず他所に移籍。

2/24　破産した Aradigm の吸入抗生剤開発品を Grifols が引き取る

2013 年 5 月にスペインの Grifols は Aradigm のシプロフロキサシン吸入剤の世界での開発権利を得る合意を交わしていた。

2/25　Sanofi が欧州の 6 つの製造拠点を切り離して医薬品有効成分（API）製造会社を新設

2/25　GSK が中国 Clover の新型コロナウイルス COVID-19 ワクチン開発に協力

2/26　感染症の血液検査を開発する Karius（カリフォルニア州レッドウッドシティー）が 1 億 6,500 万ドル調達

感染症の血液検査を開発する Karius が、ソフトバンクの新たな投資事業 Vision Fund 2 が率いた融資で 1 億 6,500 万ドル調達。

https://jp.techcrunch.com/2020/02/25/2020-02-24-karius-raises-165-million-for-its-liquid-biopsy-technology-identifying-diseases-in-a-drop-of-blood/

2/26　米国内各地での新型コロナウイルス感染症（COVID-19）の広まりはもはや不可避 -米国疾病対策センター（CDC）

中国以外の地域での広まりを受け、米国内各地での新型コロナウイルス感染症（COVID-19）の広まりはもはや避けようがないとの見解をアメリカ疾病管理センター（CDC）が示した。また、死者が出ていることとヒトからヒトへの感染が続いていることがパンデミックと判断する 2 つの基準を満たしている、としている。
状況に応じて学校は休むか遠隔授業を実施し、企業は出勤不要の勤務体制を準備する必要があり、大勢が集まる催しは中止が必要かもしれない、としている。
米国は中国と韓国への渡航の危険度をレベル 3 に引き上げ、可能なら誰もが避ける事を要請している。また、イランとイタリアへの渡航の危険度は日本への渡航と同様にレベル 2 に引き上げ、長患いしていたり高齢の成人は可能なら避ける必要がある、としている。

2/26　2億円、「世界一高い薬」日本でも承認へ　脊髄性筋萎縮症の治療薬

https://www.tokyo-np.co.jp/s/article/2020022601001280.html

厚生労働省の専門部会は26日、世界一高い薬とされる脊髄性筋萎縮症の遺伝子治療薬「ゾルゲンスマ」の国内での製造販売を了承した。3月中に正式承認される見通し。遺伝子治療薬としては国内2例目となる。
製薬大手ノバルティスが申請。米国ではFDAが昨年5月に承認。1回の投与で治療が終わるが、米国での費用は2億円以上。日本でも承認を経て今年5月にも保険適用され、高額の薬価が公的医療保険の財源に影響する可能性がある。
脊髄性筋萎縮症は生まれて半年ごろまでに筋肉の萎縮や呼吸困難が出る難病。

2/26　自閉症と遺伝子突然変異の関係突き止める　阪大研究チーム　治療薬開発に期待

https://mainichi.jp/articles/20200226/k00/00m/040/360000c

2/27　武田薬品が PvP Biologics を買収

http://www.qlifepro.com/press/20200226-16-55009/takeda-pharmaceutical-221/

2/27　新型コロナウイルス感染症 COVID-19 を予防/治療しうる 31 の抗ウイルス薬の同定 - NORWEGIAN UNIVERSITY OF SCIENCE AND TECHNOLOGY

https://www.eurekalert.org/pub_releases/2020-02/nuos-edm022620.php

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. 21 番染色体とそのダウン症候群への影響 –マウス研究

2. パーキンソン病における認知症の潜在的な治療標的遺伝子

3. 慢性炎症や老化を逆転させる分子「スイッチ」

4. イヌの脳癌治療法発見がヒトの脳癌治療法発見に繋がる可能性

5. 口蹄疫ウイルスが最も致命的な膵臓癌の標的になる可能性

6. マウスの生殖時計 逆転法

7. パーキンソン病を阻止する分子か？

8. 成長と共に拡張する人工心臓弁の開発に成功

9. 人工知能が新しい抗生物質を作り出す

1. 21 番染色体とそのダウン症候群への影響 -マウス研究

日付:2020 年 1 月 28 日
ソース:University College London (UCL)
概要:

UCL 主導の研究チームは、ダウン症マウスの記憶および意思決定の問題を引き起こす 21 番染色体の特定の領域を初めて同定、これは人のダウン症に関する貴重な洞察を新たに提供する発見だ、としている。
ほとんどの人は、各細胞に 23 対に分けられる 46 個の染色体を持つ:ダウン症候群 (DS) の人には 200 個以上の遺伝子を運ぶ染色体 21 の余分なコピーがある。*Cell Reports* 誌に掲載されたこの研究では、Cardiff 大学と Francis Crick 研究所の支援を受けた UCL の研究者らが、マウスモデルを使用して、これらの余分な遺伝子が学習障害を引き起こす方法を調べた。
21 番染色体とその遺伝子はマウスでも見られるが、遺伝子は 3 つの異なるマウス染色体上の 3 つの小さな領域に分散している。これらは、それぞれ 148 遺伝子、62 遺伝子、19 遺伝子を含むマウス染色体 16、10、17 である。研究者らは、これら 3 つの異なるマウス領域(染色体)のそれぞれの遺伝子が学習と記憶に及ぼす影響を調べた。これを行うために、3 つの異なるマウス系統を遺伝子組み換えして、マウス染色体 16、10、または 17 に遺伝子グループの 1 つの余分なコピーを保持した。
マウスが単純な「左右」の T 迷路をネゴシエートする必要があるナビゲーションテスト中に、各グループの記憶能力と意思決定能力の両方を測定、これらのテスト中、脳波 (EEG)を使用して、記憶および意思決定に重要な脳領域の電気的活動を監視した。研究者らは、マウス系統の 1 つ(「Dp10Yey」マウス)の記憶力が低下しており、海馬と呼ばれる脳の一部に不規則な脳回路があることを発見した。また、別の系統(「Dp1Tyb」マウス)の意思決定能力が悪く、計画と意思決定に必要な海馬と前頭前野の間の脳のシグナル伝達が悪いことも発見した。また、3 番目の系統(「Dp17Yey」マウス)には、脳内で異常な電気的活動はなかった。
これによって、異なる複数の遺伝子がダウン症候群に関連するさまざまな認知問題の原因であることが初めて示された、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/01/200128114620.htm

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Novel insight into chromosome 21 and its effect on Down syndrome

Date:

January 28, 2020

Source:

University College London

Summary:

A research team has, for the first time, identified specific regions of chromosome 21, which cause memory and decision-making problems in mice with Down syndrome, a finding that provides valuable new insight into the condition in humans.

FULL STORY

A UCL-led research team has, for the first time, identified specific regions of chromosome 21, which cause memory and decision-making problems in mice with Down syndrome, a finding that provides valuable new insight into the condition in humans.

Most people have 46 chromosomes in each cell, divided into 23 pairs: people with Down syndrome (DS) have an extra copy of chromosome 21, which carries over 200 genes.

In this study, published in *Cell Reports*, researchers at UCL, supported by Cardiff University and the Francis Crick Institute, used mouse models to try and find out how having these extra genes causes learning disability.

Chromosome 21 and its genes are also found in mice, although the genes have dispersed onto three smaller regions on three different mouse chromosomes. These are mouse chromosomes 16, 10 and 17 containing 148 genes, 62 genes and 19 genes respectively.

The researchers looked at the effect of the genes in each of these three different mouse regions (chromosomes) on learning and memory. To do this three different mouse strains (groups of mice), were genetically modified to carry an extra copy of one of the gene groups on mouse chromosomes 16, 10 or 17.

During navigation tests, where mice needed to negotiate a simple 'left-right' T-maze, each group was measured for both memory and decision-making ability.

During these tests, the electrical activity of brain regions important for memory and decision making was also monitored, using an electroencephalogram (EEG).

The researchers found that one of the mouse strains ('Dp10Yey' mice) had worse memory, and had irregular brain circuity (signals) in a part of the brain called hippocampus -- which is known to be very important for memory.

They also found another strain ('Dp1Tyb' mice) had worse decision-making ability and had poor brain signalling between the hippocampus and the pre-frontal cortex -- needed for planning and decision-making. And the third strain ('Dp17Yey' mice) had no unusual electrical activity in the brain.

Co-author, Professor Matthew Walker (UCL Queen Square Institute of Neurology), said: "These findings are a complete surprise -- we did not expect the three different gene groups would act completely differently.

"Scientists have traditionally worked on the hypothesis that a single gene, or single genes, was the likely cause of intellectual disabilities associated with Down syndrome.

"We have shown -- for the first time -- that different and multiple genes are contributing to the various cognitive problems associated with Down syndrome."

Researchers will now look to discover specifically which gene or genes, within the smaller gene groups, are responsible for impaired memory and decision-making.

Corresponding author Professor Elizabeth Fisher (UCL Queen Square Institute of Neurology) said: "Our study provides critical insights into the mechanisms underlying neuro-disability in Down syndrome and indicates that intellectual disability in Down syndrome may result from different underlying genetic, functional and regional brain abnormalities.

"This implies that therapies for people with Down syndrome should perhaps target multiple processes, and we have made the initial steps in identifying what some of these processes are."

Note: Mouse strains Dp1Tyb, Dp10Yey and Dp17Yey were genetically modified to carry an extra copy of one of the gene groups on mouse chromosomes 16, 10 and 17 respectively.

Story Source:

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

Journal Reference:

1. Pishan Chang, Daniel Bush, Stephanie Schorge, Mark Good, Tara Canonica, Nathanael Shing, Suzanna Noy, Frances K. Wiseman, Neil Burgess, Victor L.J. Tybulewicz, Matthew C. Walker, Elizabeth M.C. Fisher. **Altered Hippocampal-Prefrontal Neural Dynamics in Mouse Models of Down Syndrome**. *Cell Reports*, 2020; 30 (4): 1152 DOI: 10.1016/j.celrep.2019.12.065

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University College London. (2020, January 28). Novel insight into chromosome 21 and its effect on Down syndrome. *ScienceDaily*. Retrieved February 3, 2020 from www.sciencedaily.com/releases/2020/01/200128114620.htm

University College London. "Novel insight into chromosome 21 and its effect on Down syndrome." ScienceDaily. www.sciencedaily.com/releases/2020/01/200128114620.htm (accessed February 3, 2020).

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2. パーキンソン病における認知症の潜在的な治療標的遺伝子

日付：2020 年 2 月 5 日
ソース：ワシントン大学医学部
概要：

米国では推定約 930,000 人がパーキンソン病を患っている。この病気は、運動を司る脳の一部に蓄積するアルファシヌクレインと呼ばれるタンパク質の有毒な塊によって引き起こされると考えられており、その塊は脳細胞を損傷させたり殺すことができる。又、認知障害が、その運動症状の何年も後に発生する傾向にある。運動問題に関連しているタンパク質クラスターも認知症に関連しているが、これがどのように起こるかは明らかになっていない。パーキンソン病の人の 80%は、診断から 20 年以内に認知症を発症し、遺伝子 APOE の特定のバリアントを保有する患者は特にリスクが高い、とされている。
セントルイスにあるワシントン大学医学部の科学者らは、新しい研究で、パーキンソン病、APOE、認知症の関連の手がかりを発見した。彼らは、塊になりやすいアルファシヌクレインの形態をもつマウスの研究において、マウスを APOE-APOE2、APOE3 または APOE4 のヒト変異体を運ぶように、または APOE をまったく持たないように遺伝子を組み換えた。そして、APOE4 マウスが APOE3 または APOE2 マウスよりもアルファシヌクレインクラスターを多く持っていることを発見。さらなる実験により、APOE4 マウスでも塊がより広範に広がることが示された。調査結果は APOE4 がマウスの脳の病気の徴候悪化に直接かかわったことを示した。
Science Translational Medicine 誌で 2 月 5 日に発表された調査結果は、パーキンソン病患者の認知機能低下を遅らせたり防ぐために、APOE を標的とする治療へと繋げる可能性がある、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-02/wuso-gia013120.php

NEWS RELEASE 5-FEB-2020

Gene ID'd as potential therapeutic target for dementia in Parkinson's

Targeting gene linked to Alzheimer's may reduce dementia risk in Parkinson's

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

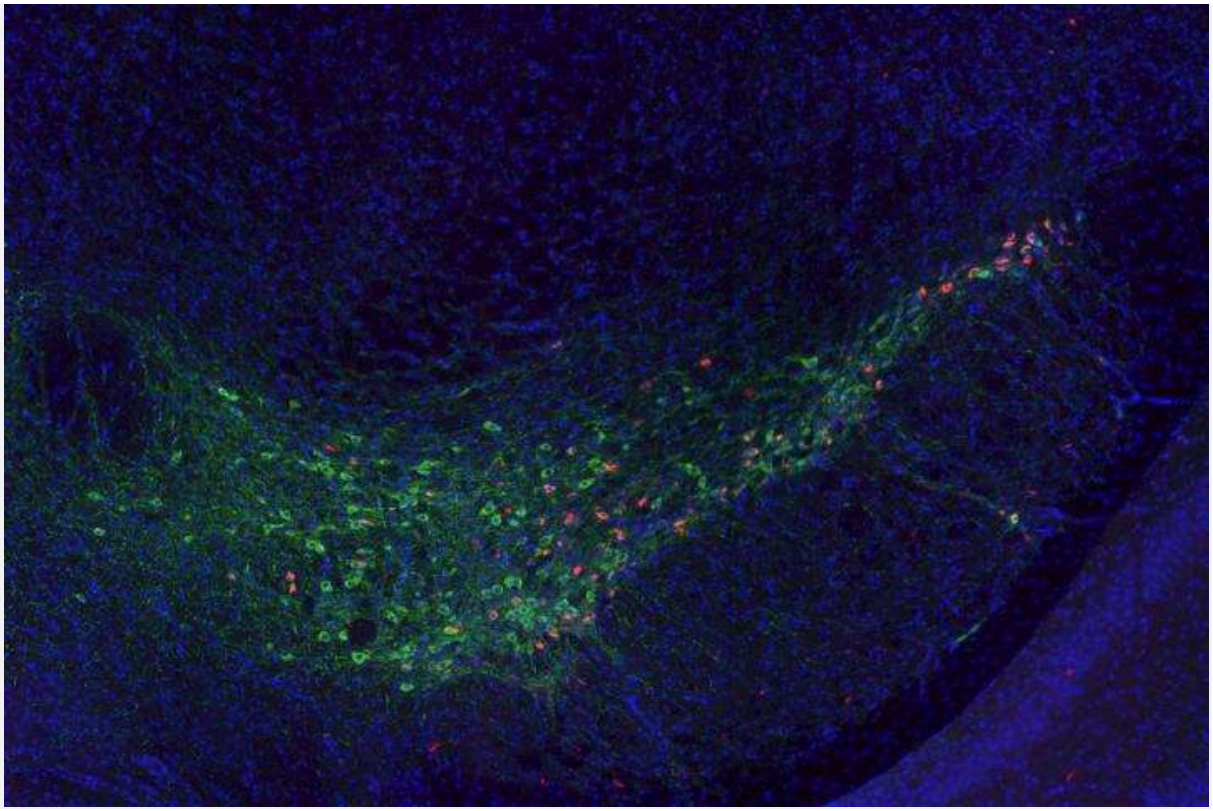

IMAGE: Clumps of the Parkinson's protein alpha-synuclein (red) are visible inside neurons (green) in the brain of a mouse. Researchers at Washington University School of Medicine in St. Louis have discovered... **view more**

Credit: Z.M. Wargel and B.M. Freeberg

Dementia is one of the most debilitating consequences of Parkinson's disease, a progressive neurological condition characterized by tremors, stiffness, slow movement and impaired balance. Eighty percent of people with Parkinson's develop dementia within 20 years of the diagnosis, and patients who carry a particular variant of the gene APOE are at especially high risk.

In new research, scientists at Washington University School of Medicine in St. Louis have found a clue to the link between Parkinson's, APOE and dementia. They discovered that harmful Parkinson's proteins spread more rapidly through the brains of mice that have the high-risk variant of APOE, and that memory and thinking skills deteriorate faster in people with Parkinson's who carry the variant. The findings, published Feb. 5 in *Science Translational Medicine*, could lead to therapies targeting APOE to slow or prevent cognitive decline in people with Parkinson's.

"Dementia takes a huge toll on people with Parkinson's and their caregivers," said Albert (Gus) Davis, MD, PhD, an assistant professor of neurology and the study's lead author. "The development of dementia is often what determines whether someone with Parkinson's is able to remain in their home or has to go into a nursing home."

An estimated 930,000 people in the U.S. live with Parkinson's. The disease is thought to be caused by toxic clumps of a protein called alpha-synuclein that build up in a part of the brain devoted to movement. The clumps damage and can kill brain cells.

Cognitive problems tend to arise many years after the motor symptoms. The protein clusters implicated in movement problems also are linked with dementia, but how this happens is not clear. Davis and his colleagues - including senior author David Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor and head of the Department of Neurology- saw a clue in the risky nature of APOE.

A variant of APOE known as APOE4 raises the risk of Alzheimer's disease threefold to fivefold. Like Parkinson's, Alzheimer's is a neurodegenerative condition caused by the spread of toxic protein clusters throughout the brain, although some of the proteins involved are different. APOE4 increases the chance of Alzheimer's dementia partly because it spurs Alzheimer's proteins to collect into clumps that injure the brain. The researchers suspected that APOE4 similarly triggers the growth of toxic clusters of Parkinson's proteins.

Studying mice with a form of alpha-synuclein prone to clumping, Davis, Holtzman and colleagues genetically modified the mice to carry human variants of APOE - APOE2, APOE3 or APOE4 - or no APOE at all.

The researchers found that APOE4 mice had more alpha-synuclein clusters than APOE3 or APOE2 mice. Further experiments showed that the clumps spread more widely in APOE4 mice as well. Together, the findings showed that APOE4 was directly involved in exacerbating signs of disease in the mice's brains.

"What really stood out is how much less affected the APOE2 mice were than the others," Davis said. "It actually may have a protective effect, and we are investigating this now. If we do find that APOE2 is protective, we might be able to use that information to design therapies to reduce the risk of dementia."

To study the effect of APOE variants on dementia in people with Parkinson's, the researchers analyzed publicly available data from three separate sets of people with Parkinson's. Two of the cohorts - one from the Parkinson's Progression Markers Initiative, with 251 patients, and the other from the Washington University Movement Disorders Center, with 170 patients - had been followed for several years. In both cohorts, cognitive skills declined faster in people with APOE4 than in those with APOE3. People with two copies of APOE2 are very rare, but none of the three patients in the group with two copies of APOE2 showed any cognitive decline over the period of the study.

The third cohort, from the NeuroGenetics Research Consortium, was made up of 1,030 people with Parkinson's whose cognitive skills had been evaluated just once. The researchers found that people with APOE4 in the cohort had developed cognitive problems at a younger age and had more severe cognitive deficits at the time they were evaluated than people with APOE3 or APOE2.

"Parkinson's is the most common, but there are other, rarer diseases that also are caused by alpha-synuclein aggregation and also have very limited treatment options," Davis said. "Targeting APOE with therapeutics might be a way to change the course of such diseases."

APOE doesn't affect the overall risk of developing Parkinson's or how quickly movement symptoms worsen, so an APOE-targeted therapy might stave off dementia without doing anything for the other symptoms. Even so, it could be beneficial, Davis said.

"Once people with Parkinson's develop dementia, the financial and emotional costs to them and their families are just enormous," Davis said. "If we can reduce their risk of dementia, we could dramatically improve their quality of life."

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3. 慢性炎症や老化を逆転させる分子「スイッチ」

日付：2020 年 2 月 6 日
ソース：カリフォルニア州立大学バークレー校
概要：

カリフォルニア州立大学バークレー校の科学者らは、体内の慢性炎症の原因となる免疫機構を制御する分子「スイッチ」を特定した。2 月 6 日の *Cell Metabolism* 誌オンライン版に掲載されているこの発見は、これら年齢関連の状態の多くを停止または逆転させる新しい治療法に繋がる可能性がある。
NLRP3 インフラマソームと呼ばれる免疫タンパク質の巨大なコレクションの過剰な活性化は、多発性硬化症、癌、糖尿病、認知症などのさまざまな慢性疾患に関連している。研究者らは、この NLRP3 インフラマソームを脱アセチル化またはスイッチオフすることを目的とする薬物が、これらの状態および一般に加齢に伴う変性の予防または治療に役立つ可能性がある、としている。すなわち、このアセチル化がスイッチとして機能し、アセチル化されると、このインフラマソームはオンになり、脱アセチル化されると、インフラマソームはオフになる。
チームは、マウスとマクロファージと呼ばれる免疫細胞の研究で、SIRT2 と呼ばれるタンパク質が NLRP3 インフラマソームの脱アセチル化に関与していることを発見した。SIRT2 の産生を妨げる遺伝的変異で飼育された 2 歳の熟年マウスは、通常のマウスよりも多くの炎症兆候を示した。これらのマウスは、2 型糖尿病とメタボリックシンドロームに関連する状態である、より高いインスリン抵抗性も示した。免疫系が放射線で破壊され、その後、NLRP3 インフラマソームの脱アセチル化またはアセチル化バージョンのいずれかを産生する血液幹細胞で再構成された熟年マウスでは、インフラマソームの脱アセチル化または「オフ」バージョンを与えられたマウスは、6 週間後にインスリン抵抗性を改善した。
研究者らは、この発見が、主要慢性疾患の治療に非常に重要な意味を持っている、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/02/200206144837.htm

Molecular 'switch' reverses chronic inflammation and aging

Date:

February 6, 2020

Source:

University of California - Berkeley

Summary:

Scientists have identified a molecular 'switch' that controls the immune machinery responsible for chronic inflammation in the body. The finding could lead to new ways to halt or even reverse many age-related conditions, from from Alzheimer's and Parkinson's to diabetes and cancer.

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FULL STORY

Hourglass, aging concept (stock image).

Credit: © photosaint / Adobe Stock

Chronic inflammation, which results when old age, stress or environmental toxins keep the body's immune system in overdrive, can contribute to a variety of devastating diseases, from Alzheimer's and Parkinson's to diabetes and cancer.

Now, scientists at the University of California, Berkeley, have identified a molecular "switch" that controls the immune machinery responsible for chronic inflammation in the body. The finding, which appears online Feb. 6 in the journal *Cell Metabolism*, could lead to new ways to halt or even reverse many of these age-related conditions.

"My lab is very interested in understanding the reversibility of aging," said senior author Danica Chen, associate professor of metabolic biology, nutritional sciences and toxicology at UC Berkeley. "In the past, we showed that aged stem cells can be rejuvenated. Now, we are asking: to what extent can aging be reversed? And we are doing that by looking at physiological conditions, like inflammation and insulin resistance, that have been associated with aging-related degeneration and diseases."

In the study, Chen and her team show that a bulky collection of immune proteins called the NLRP3 inflammasome -- responsible for sensing potential threats to the body and launching an inflammation response -- can be essentially switched off by removing a small bit of molecular matter in a process called deacetylation.

Overactivation of the NLRP3 inflammasome has been linked to a variety of chronic conditions, including multiple sclerosis, cancer, diabetes and dementia. Chen's results suggest that drugs targeted toward deacetylating, or switching off, this NLRP3 inflammasome might help prevent or treat these conditions and possibly age-related degeneration in general.

"This acetylation can serve as a switch," Chen said. "So, when it is acetylated, this inflammasome is on. When it is deacetylated, the inflammasome is off."

By studying mice and immune cells called macrophages, the team found that a protein called SIRT2 is responsible for deacetylating the NLRP3 inflammasome. Mice that were bred with a genetic mutation that prevented them from producing SIRT2 showed more signs of inflammation at the ripe old age of two than their normal counterparts. These mice also exhibited higher insulin resistance, a condition associated with type 2 diabetes and metabolic syndrome.

The team also studied older mice whose immune systems had been destroyed with radiation and then reconstituted with blood stem cells that produced either the deacetylated or the acetylated version of the NLRP3 inflammasome. Those who were given the deacetylated, or "off," version of the inflammasome had improved insulin resistance after six weeks, indicating that switching off this immune machinery might actually reverse the course of metabolic disease.

"I think this finding has very important implications in treating major human chronic diseases," Chen said. "It's also a timely question to ask, because in the past year, many promising Alzheimer's disease trials ended in failure. One possible explanation is that treatment starts too late, and it has gone to the point of no return. So, I think it's more urgent than ever to understand the reversibility of aging-related conditions and use that knowledge to aid a drug development for aging-related diseases."

Co-authors of the study include Ming He, Hou-Hsien Chiang and Hanzhi Luo, previously at UC Berkeley where the research was carried out; Zhifang Zheng, Mingdian Tan, Rika Ohkubo and Wei-Chieh Mu at UC Berkeley; Qi Qiao, Li Wang and Hao Wu at Harvard Medical School; and Shimin Zhao at Fudan University.

This research was supported in part by the National Institutes of Health under grants R01DK117481, R01DK101885, R01AG063404, R01AG 063389, DP1HD087988 and R01Al124491; the National Institute of Food and Agriculture; the France-Berkeley Fund, a Glenn/AFAR Scholarship; the Dr. and Mrs. James C.Y. Soong Fellowship; the Government Scholarship for Study Abroad (GSSA) from Taiwan; the ITO Foundation Scholarship and the Honjo International Scholarship.

Story Source:

Materials provided by **University of California - Berkeley**. Original written by Kara Manke. *Note: Content may be edited for style and length.*

Journal Reference:

1. Ming He, Hou-Hsien Chiang, Hanzhi Luo, Zhifang Zheng, Qi Qiao, Li Wang, Mingdian Tan, Rika Ohkubo, Wei-Chieh Mu, Shimin Zhao, Hao Wu, Danica Chen. **An Acetylation Switch of the NLRP3 Inflammasome Regulates Aging-Associated Chronic Inflammation and Insulin Resistance**. *Cell Metabolism*, 2020; DOI: 10.1016/j.cmet.2020.01.009

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4. イヌの脳癌治療法発見がヒトの脳癌治療法発見に繋がる可能性

日付:2020 年 2 月 10 日
ソース:ジャクソン研究所
概要:

皿の中の癌細胞からマウスに移植された患者の腫瘍に至るまで、実験モデルを使用した癌研究は、病気とその治療法についてさらに学ぶために非常に役立ってきた。ただし、一部の癌については、これらのモデルは医学の進歩に関する十分な洞察を提供できていない。最も一般的な悪性脳腫瘍であるびまん性神経膠腫はこの顕著な例であり、ほぼ普遍的な再発率と患者の予後不良が続いている。
コンパニオンドッグは、ヒトと同じくらい頻繁に神経膠腫を自然に発症する。そして、ヒト同様、非常に治療が困難である。しかし同時に、ヒトの腫瘍にどれほど似ているかは不明であった。
そこで JAX の癌研究者らは、イヌの腫瘍がヒトの腫瘍に類似しているかどうかを調べるため、83 匹のイヌから死後腫瘍サンプルを入手し、徹底的な分子検査を行い、この疾患を引き起こす共通性、類似性を特定した。
獣医の診療所は、ヒトの医療および基礎研究の設定とは多少異なるが、イヌは人間にとって潜在的に有効なモデルであり、特に神経膠腫患者の予後を改善するためのヒト治療法に対して有益な情報を与えることができる、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://medicalxpress.com/news/2020-02-fido-brain-cancer.html

FEBRUARY 10, 2020

Finding a cure for Fido's brain cancer may help us find a cure for ourselves

by Jackson Laboratory

JAX cancer researcher Roel Verhaak with his pet chihuahua Lola. Credit: The Jackson Laboratory

Cancer research using experimental models—everything from cancer cells in a dish to patient tumors transplanted in mice—has been extremely useful for learning more about the disease and how we might treat it. For some cancers, however, these models have failed to provide sufficient insight for medical progress. Diffuse glioma, the most common malignant brain tumor, is a prominent example, and it continues to have near-universal rates of recurrence and poor patient prognoses.

A significant problem with the experimental systems is that while they may model the cancer cells quite well, they don't fully capture their environment within the body, including nearby healthy tissues, immune cells and signaling, and more. So how can researchers learn how to better treat cancers within the context of a patient's body instead of isolated from it? In a paper published in *Cancer Cell*, "Comparative molecular life history of spontaneous canine and human gliomas," a team led by Jackson Laboratory (JAX) Professor Roel Verhaak, Ph.D., presents a possible answer: working to cure our beloved pet dogs.

Molecular similarity:

Companion dogs spontaneously develop gliomas about as often as humans do. They arise in adult dogs, but at the age of human children in calendar years. And, as in humans, they're sadly very difficult to treat. Caring for pet dogs with glioma can be quite challenging for their owners. Therein lies an opportunity: they may benefit from experimental approaches, which at the same time may provide clues on how to better treat glioma in humans. But it's not known how well they resemble human tumors. To investigate how similar canine tumors are to human tumors—or not—Verhaak and his team obtained posthumous tumor samples from 83 dogs for thorough molecular examination. By comparing the results in detail to those from human glioma patients, both from children and adults, they identified the commonalities driving the disease.

The molecular "life history" obtained provides a better understanding of glioma across both species.

What they found was that there are indeed important similarities between gliomas across dogs, children and adults. Shared molecular traits included mutations in particular genes and pathways such as the DNA repair system known to be altered in human glioma. These findings extended to changes in the number of chromosomes, known as aneuploidy. A remarkable outcome of the comparison was the observation that canine glioma resembled pediatric glioma much more than glioma in adult patients.

The team also assessed how well canine gliomas model human immune response and the immune microenvironment. They found that the immunological features of dogs with spontaneously arising gliomas closely resemble those in human patients. The advent of immunotherapies in human medicine has seen encouraging successes but also low patient response rates. Using them for canine gliomas may provide an effective venue to assess efficacy and to improve response in both dogs and people.

Convergent evolution:

Overall, the convergence of glioma traits across species indicates the tumors are adapting to similar selective pressures exerted by their environments in both human and dog brains. An interesting note is that the average age of the canine cohort was about nine years. Their glioma samples had a lower number of mutations than human adult gliomas but resembled pediatric gliomas, whose patients have also aged relatively few calendar years, in the rates of genetic changes found. This aspect of canine gliomas can be important for studying the functional role of such variation and how it can be targeted for therapy.

The paper's findings provide important insight into canine gliomas and indicate that the results are likely relevant to human gliomas and potential therapies, particularly in children. While the veterinarian's office is somewhat different from both human medical and basic research settings, dogs represent a potentially effective model for humans. Striving to cure them, and learning what works best—and, importantly, why it works—can inform our own therapy regimens, providing an important opportunity to improve prognoses for glioma patients.

Explore further

Study uncovers unexpected connection between gliomas, neurodegenerative diseases

More information: Samirkumar B. Amin et al, Comparative Molecular Life History of Spontaneous Canine and Human Gliomas, *Cancer Cell* (2020). DOI: 10.1016/j.ccell.2020.01.004

Journal information: Cancer Cell

Provided by Jackson Laboratory

5. 口蹄疫ウイルスが最も致命的な膵臓癌の標的になる可能性

日付:2020 年 2 月 11 日
ソース:クイーン・メアリー大学ロンドン校
概要:

ロンドンのクイーン・メアリー大学の研究者らは、Spirogen(現在 AstraZeneca の一部)および ADC Therapeutics と共同で、αvβ6(alpha-v-beta-6)と呼ばれる別のタンパク質を標的とする口蹄疫ウイルスから取られたペプチドまたはタンパク質断片を特定した。このタンパク質は、大部分の膵臓癌細胞の表面に高レベルで見られる。
チームはペプチドを使用して、テシリンと呼ばれる非常に強力な薬物を膵臓癌細胞に運び、膵臓癌腫瘍のあるマウスを薬物とペプチドの組み合わせで治療すると、腫瘍は完全に殺された、としている。
チームは、実験室とマウスの両方の細胞でペプチド/テシリンの組み合わせのテストを実施、遺伝的に同一のヒト癌細胞を使用した。マウスでのテストは、最も印象的な結果をもたらし、αvβ6 陽性腫瘍のあるマウスに、週 3 回、ペプチドと薬物の組み合わせを少量投与したところ、これにより腫瘍の増殖が完全に停止した。
チームは現在、臨床試験に移行する前に、より複雑なマウスモデルでペプチドと薬物の組み合わせテストを更に行った上で、膵臓癌の転移にも影響するかどうか判断する計画だ、としている。
Theranostics 誌で発表されたこの研究は、英国の医学研究慈善団体である膵臓癌研究基金によって資金提供されている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://medicalxpress.com/news/2020-02-foot-and-mouth-disease-virus-deadliest-cancer.html

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FEBRUARY 12, 2020

Foot-and-mouth-disease virus could help target the deadliest cancer

by Pancreatic Cancer Research Fund

Professor John Marshall, Queen Mary University of London. Credit: Cancer Research UK

The foot-and-mouth-disease virus is helping scientists to tackle a common cancer with the worst survival rate—pancreatic cancer.

Researchers at Queen Mary University of London have identified a peptide, or protein fragment, taken from the foot-and-mouth-disease virus that targets another protein, called AvB6 (alpha-v-beta-6). This protein is found at high levels on the surface of the majority of pancreatic cancer cells.

Working jointly with Spirogen (now part of AstraZeneca) and ADC Therapeutics, the team have used the peptide to carry a highly potent drug, called tesirine, to the pancreatic cancer cells. When mice with pancreatic cancer tumours were treated with the drug and peptide combination, the tumours were completely killed.

The study, published in *Theranostics*, was funded by the UK medical research charity Pancreatic Cancer Research Fund.

Lead researcher Professor John Marshall, from the Cancer Research UK Barts Centre, explains: "Foot-and-mouth-disease virus uses AvB6 as a route to infect cattle, as the virus binds to this protein on a cow's tongue. By testing pieces of the protein in the virus that attaches to AvB6, we've developed a route to deliver a drug specifically to pancreatic cancers. Our previous research had shown that 84 per cent of pancreatic cancer patients have high levels of AvB6 on their cancers."

The team performed tests of the peptide/tesirine combination in both cells in the laboratory and in mice. They used genetically identical human cancer cells, some that had AvB6 on their surface and some that had no AvB6. Both types of cells were exposed to the peptide and drug combination. The cells with AvB6 were most affected, while the AvB6 negative cells needed much higher doses of the drug for the cells to be killed.

The tests in mice gave the most impressive results. Mice that had AvB6-positive tumours were given a tiny dose of the peptide-drug combination three times a week, and this stopped the tumours growing completely. But when the dose was increased and given just twice a week, all tumours in mice that were AvB6 positive were completely killed.

"These very exciting results, that are the result of many years of laboratory testing, offer a completely new way of treating pancreatic cancer." says Professor Marshall. "One advantage of targeting AvB6 is that it is very specific to the cancer, because most normal human tissues have little or none of this protein. So we're hopeful that, if we can develop this into an effective treatment for pancreatic cancer, it would have limited side effects."

The team now plan to further test the peptide and drug combination in more complex mice models, to determine if it can also impact on pancreatic cancer metastases, before moving to clinical trials.

Dr. Emily Farthing, senior research information manager at Cancer Research UK said: "Although we have made great progress in treating many types of cancer, survival remains stubbornly low for people with pancreatic cancer and there is an urgent need for more effective treatments. This early-stage research has developed a promising new drug that reduces the growth of pancreatic tumours in the lab. And with further research to see if it's safe and effective for patients, we hope that this could one day offer new hope for people with this disease."

Explore further

Researchers modify common flu virus to attack pancreatic cancer

More information: *Theranostics*, DOI: 10.7150/thno.38702

Provided by Pancreatic Cancer Research Fund

6. マウスの生殖時計 逆転法

日付:2020 年 2 月 12 日
ソース:クイーンズランド大学(オーストラリア)
概要:

クイーンズランド大学 (UQ) の研究者らは、卵子の老化プロセスを逆転させる代謝化合物を少量投与することで、高齢の雌マウスの出生率を上げることに成功した。
UQ の Hayden Homer 教授率いるチームは、老化による卵子の質の低下は、エネルギーを生成するのに重要な細胞内の特定の分子のレベルが低いことに起因することを発見、細胞がその分子を作るために使用する「前駆体」化合物の経口投与によって、生殖老化プロセスを逆転できるかどうかを調査した。問題の分子は NAD(ニコチンアミドアデニンジヌクレオチド)として、「前駆体」は NMN(ニコチンアミドモノヌクレオチド)として知られている。
ホーマー教授は、マウスの生殖能力は、ヒトの高齢女性からの卵子で観察された変化と同様の卵質の欠陥により、約 1 歳から低下し始める、と言っている。そこで、4 週間にわたって飲料水中の NMN を低用量で処理したところ、繁殖試験中に卵子の質を劇的に回復し、出生率を高めることができた、としている。
IVF では卵子の質を改善できないため、現在のヒト高齢女性の唯一の選択肢は、若い女性から提供された卵子を使用することであるが、この発見は、卵子の質を回復し女性の生殖機能を回復する機会を与えるものだ、としている。
この研究はニューサウスウェールズ大学 (UNSW) と共同で実施され、*Cell Reports* 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＞https://www.sciencedaily.com/releases/2020/02/200212103035.htm

SCIENTISTS REVERSE REPRODUCTIVE CLOCK IN MICE

Date:

February 12, 2020

Source:

University of Queensland

Summary:

Researchers have lifted fertility rates in older female mice with small doses of a metabolic compound that reverses the aging process in eggs, offering hope for some women struggling to conceive.

FULL STORY

Lab mouse (stock image).

Credit: © filin174 / Adobe Stock

Researchers have lifted fertility rates in older female mice with small doses of a metabolic compound that reverses the aging process in eggs, offering hope for some women struggling to conceive.

The University of Queensland study found a non-invasive treatment could maintain or restore the quality and number of eggs and alleviate the biggest barrier to pregnancy for older women.

A team led by UQ's Professor Hayden Homer found the loss of egg quality through aging was due to lower levels of a particular molecule in cells critical for generating energy.

"Quality eggs are essential for pregnancy success because they provide virtually all the building blocks required by an embryo," Professor Homer said.

"We investigated whether the reproductive aging process could be reversed by an oral dose of a 'precursor' compound -- used by cells to create the molecule."

The molecule in question is known as NAD (nicotinamide adenine dinucleotide) and the 'precursor' as NMN (nicotinamide mononucleotide).

Professor Homer said fertility in mice starts to decline from around one year of age due to defects in egg quality similar to changes observed in human eggs from older women.

"We treated the mice with low doses of NMN in their drinking water over four weeks, and we were able to dramatically restore egg quality and increase live births during a breeding trial," Professor Homer said.

Professor Homer said poor egg quality had become the single biggest challenge facing human fertility in developed countries.

"This is an increasing issue as more women are embarking on pregnancy later in life, and one in four Australian women who undergo IVF treatment are aged 40 or older," he said.

"IVF cannot improve egg quality, so the only alternative for older women at present is to use eggs donated by younger women.

"Our findings suggest there is an opportunity to restore egg quality and in turn female reproductive function using oral administration of NAD-boosting agents -- which would be far less invasive than IVF. It is important to stress, however, that although promising, the potential benefits of these agents remains to be tested in clinical trials."

This study was conducted in collaboration with UNSW and published in the journal *Cell Reports.*

Story Source:

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

Journal Reference:

1. Michael J. Bertoldo, Dave R. Listijono, Wing-Hong Jonathan Ho, Angelique H. Riepsamen, Dale M. Goss, Dulama Richani, Xing L. Jin, Saabah Mahbub, Jared M. Campbell, Abbas Habibalahi, Wei-Guo Nicholas Loh, Neil A. Youngson, Jayanthi Maniam, Ashley S.A. Wong, Kaisa Selesniemi, Sonia Bustamante, Catherine Li, Yiqing Zhao, Maria B. Marinova, Lynn-Jee Kim, Laurin Lau, Rachael M. Wu, A. Stefanie Mikolaizak, Toshiyuki Araki, David G. Le Couteur, Nigel Turner, Margaret J. Morris, Kirsty A. Walters, Ewa Goldys, Christopher O'Neill, Robert B. Gilchrist, David A. Sinclair, Hayden A. Homer, Lindsay E. Wu. **NAD Repletion Rescues Female Fertility during Reproductive Aging**. *Cell Reports*, 2020; 30 (6): 1670 DOI: 10.1016/j.celrep.2020.01.058

Cite This Page:

- MLA
- APA
- Chicago

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7. パーキンソン病を阻止する分子か？

日付：2020 年 2 月 14 日
ソース：ヘルシンキ大学
概要：

ヘルシンキ大学の研究者らは、分子 BT13 が、パーキンソン病で失われる化学物質であるドーパミンのレベルを高め、ドーパミン産生脳細胞を死から保護する可能性があることを発見した。
この研究は、英国パーキンソン病協会（Parkinson’s UK）が共同出資し、*Movement Disorders* 誌のオンライン版で本日発表された。この研究結果は、分子注射後のマウスの脳のドーパミン濃度の増加を示しており、BT13 はマウスの脳の特定受容体も活性化して、細胞を保護することも示している。
研究者らは現在、BT13 の特性の改善に取り組んでおり、BT13 を潜在的な治療としてより効果的にし、成功した場合、英国のパーキンソン病とともに生きる 145,000 人に利益をもたらすことができる、としている。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-02/pu-moh021420.php

NEWS RELEASE 14-FEB-2020

Molecule offers hope for halting Parkinson's

PARKINSON’S UK

A promising molecule has offered hope for a new treatment that could stop or slow Parkinson's, something no treatment can currently do.

Researchers from the University of Helsinki found that molecule BT13 has the potential to both boost levels of dopamine, the chemical that is lost in Parkinson's, as well as protect the dopamine-producing brain cells from dying.

The results from the study, co-funded by Parkinson's UK and published online today in the journal *Movement Disorders*, showed an increase in dopamine levels in the brains of mice following the injection of the molecule. BT13 also activated a specific receptor in the mouse brains to protect the cells.

Typically, by the time people are diagnosed with Parkinson's, they have already lost 70-80 per cent of their dopamine-producing cells, which are involved in coordinating movement.

While current treatments mask the symptoms, there is nothing that can slow down its progression or prevent more brain cells from being lost, and as dopamine levels continue to fall, symptoms get worse and new symptoms can appear.

Researchers are now working on improving the properties of BT13 to make it more effective as a potential treatment which, if successful, could benefit the 145,000 people living with Parkinson's in the UK.

The study builds on previous research on another molecule that targets the same receptors in the brain, glial cell line-derived neurotrophic factor (GDNF), an experimental treatment for Parkinson's which was the subject of a BBC documentary in February 2019. While the results were not clear cut, GDNF has shown promise to restore damaged cells in Parkinson's.

However, the GDNF protein requires complex surgery to deliver the treatment to the brain because it's a large molecule that cannot cross the blood-brain barrier - a protective barrier that prevents some drugs from getting into the brain.

BT13, a smaller molecule, is able to cross the blood-brain barrier - and therefore could be more easily administered as a treatment, if shown to be beneficial in further clinical trials.

Professor David Dexter, Deputy Director of Research at Parkinson's UK, said:

"People with Parkinson's desperately need a new treatment that can stop the condition in its tracks, instead of just masking the symptoms.

"One of the biggest challenges for Parkinson's research is how to get drugs past the blood-brain barrier, so the exciting discovery of BT13 has opened up a new avenue for research to explore, and the molecule holds great promise as a way to slow or stop Parkinson's.

"More research is needed to turn BT13 into a treatment to be tested in clinical trials, to see if it really could transform the lives of people living with Parkinson's."

Dr Yulia Sidorova, lead researcher on the study, said: "We are constantly working on improving the effectiveness of BT13. We are now testing a series of similar BT13 compounds, which were predicted by a computer program to have even better characteristics.

"Our ultimate goal is to progress these compounds to clinical trials in a few coming years."

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Parkinson's UK is the largest charitable funder of Parkinson's research in Europe. The charity has invested £93 million into researching Parkinson's and treatments since 1969.

Media enquiries

For more information please contact:

Amy Dodge, Media and PR Manager, Parkinson's UK, 020 7932 1362
adodge@parkinsons.org.uk

Out of hours: 07961 460248

Notes to editors

For a preview of the paper, see: https://onlinelibrary.wiley.com/doi/full/10.1002/mds.27943

About Parkinson's

Anyone can get Parkinson's, young or old. Every hour, two more people are diagnosed.

Parkinson's is what happens when the brain cells that make dopamine start to die. There are over 40 symptoms, from tremor and pain to anxiety. Some are treatable, but the drugs can have serious side effects. It gets worse over time and there's no cure. Yet.

But we know we're close to major breakthroughs. By funding the right research into the most promising treatments, we get closer to a cure every day.

Until then, we're here for everyone affected by Parkinson's. Fighting for fair treatment and better services. Making everyone see its real impact.

We are Parkinson's UK. Powered by people. Funded by you. Together we'll find a cure.

Advice, information and support is available via our website, http://www.parkinsons.org.uk, or our free, confidential helpline on 0808 800 0303.

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8. 成長と共に拡張する人工心臓弁の開発に成功

日付：2020 年 2 月 19 日
ソース：ボストン小児病院
概要：

発育して大きくなる心臓に合わせて拡張可能な取り替え不要の人工心臓弁が開発され、意図したとおり成長にあわせて拡張可能なことが羊への移植で確認された。
先天性心疾患の子供のための現在の人工心臓弁はサイズが固定されており、小児期に弁をより大きなバージョンに交換するために開心術を繰り返す必要がある。しかし、ボストン小児病院で開発された驚くべき新しいデザインは、子供が成人まで同じ人工弁を維持することを可能にし、心臓弁欠損のある成人にも利益をもたらす可能性がある、としている。新しいデバイスは、2 月 19 日にオンラインで公開された *Science Translational Medicine* 誌に記載されている。
大型動物モデルでのベンチスタディ、コンピューターシミュレーション、および広範なテストにより、新しい人工弁の設計がさまざまなサイズで機能し、低侵襲バルーンカテーテル手順で拡張しても弁の機能が維持されることが実証された、としている。心臓の弁は 3 枚だが、今回開発された人工弁は静脈弁に倣って 2 枚で構成されており、現在出回っている人工弁でしばしば認められる問題・血栓が生じないように血流がより滑らかになるように作られている。羊への移植後 10 週間の抗凝固薬なしの観察中に血栓形成は認められていない。

研究関連ニュース/他のトップページに戻る

＜英文＞https://www.eurekalert.org/pub_releases/2020-02/bch-ntoo21820.php

NEWS RELEASE 19-FEB-2020

New type of heart valve may be the only replacement a child needs

Design breakthrough could avoid the need for valve replacement surgery as a child grows; adults could also benefit

BOSTON CHILDREN'S HOSPITAL

IMAGE: This view from above demonstrates the valve retaining its essential shape at various states of diametric expansion (from 1x to 1.8x). The prototype was created by Sophie C. Hofferberth in... view more

Credit: Sophie C. Hofferberth, Boston Children's Hospital

Current prosthetic heart valves for children with congenital heart disease are fixed in size, requiring repeated open-heart surgeries during childhood to replace the valve with a larger version. But a surprising new design created at Boston Children's Hospital could allow children to keep the same prosthetic valve until adulthood, and could also benefit adults with heart valve defects. The new device is described in *Science Translational Medicine*, published online February 19.

Benchtop studies, computer simulations and extensive testing in large animal models demonstrate that the new prosthetic valve design works across a wide range of sizes, and that the valve retains its functionality when expanded via a minimally invasive balloon catheter procedure.

"We hope to bring this new device into clinical testing fairly rapidly," says Pedro J. del Nido, MD, Chairman of Cardiovascular Surgery at Boston Children's Hospital and senior author on the paper. "If our preclinical results hold up in human testing, this could transform the field."

Less is more: Two valve leaflets versus three

More than 330,000 children worldwide are born with a heart valve defect, and millions of others develop rheumatic heart disease requiring early valve replacement. Current prosthetic heart valves are fixed in diameter, so typically need to be replaced every few years; children receiving their first replacement before age 2 will need as many as five high-risk open-heart operations before reaching adulthood.

Commercially available prosthetic heart valves have three leaflets, tiny flaps that provide a one-way inlet or outlet for blood to keep it flowing in the right direction. The new design was inspired by human venous valves, located in the deep veins of the leg. Unlike our hearts' native outflow valves, our venous valves have just two leaflets, and a geometry that is optimized to maintain closure and one-way flow even when the veins expand in diameter to accommodate larger volumes of blood passing through.

"Veins carry approximately 70 percent of our blood volume," says Sophie C. Hofferberth, MD, a surgical resident at Brigham and Women's Hospital who led the research in del Nido's lab at Boston Children's. "The vein dimensions can change dramatically depending on body position, yet the valves must remain functional. We mimicked the geometric profile of the human venous valve to design a bileaflet valve of programmed dimensions that is adaptable to growth without loss of one-way flow control."

In multiple rounds of testing, in both benchtop and large animal models, valve prototypes with the biomimetic two-leaflet design were able to expand to accommodate growth and structural asymmetries within the heart. The valves remained fully functional across a wide range of dimensions, at a range of pressure and flow rates.

Because the valve is designed to expand without requiring the frame and leaflet to stretch or enlarge, it is compatible with a range of off-the-shelf materials, the researchers say. The study showed the device could be effectively expanded at multiple timepoints in a growing animal model, using a minimally invasive balloon catheter approach.

Potential for fewer blood clots

The researchers also observed that their "geometrically adaptable" design encourages a favorable blood flow profile through the valve, potentially reducing the risk for blood clot formation often seen with existing valve replacement devices. In the growing sheep model, there was no evidence of blood clot formation over 10 weeks of observation, even without the use of blood-thinning medication typically given to prosthetic valve recipients.

"A shortcoming of many existing devices is the presence of flow disruptions that lead to blood clot formation and early valve deterioration," says Hofferberth, who is first author on the paper. "Our design achieves a favorable flow profile that seems to facilitate effective valve washout and minimize flow stagnation, which is likely to be an important determinant of long-term device durability."

The research team believes their data support initiation of a clinical study within one to two years.

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Mossab Saeed, Christopher Payne, Karl Price, and Peter Hammer of Boston Children's Department of Cardiac Surgery were coauthors on the paper, together with Lara Tomholt, Matheus Fernandes, and James Weaver of the Wyss Institute for Biologically Inspired Engineering; Gerald Marx, Jesse Esch, and David Brown of Boston Children's Department of Cardiology; Jonathan Brown and Elazer Edelman of MIT; and Richard W. Bianco of the University of Minnesota. The study was supported by a NIH-NRSA postdoctoral fellowship grant (1F32HL138993-01), an Early Career Award from the Thrasher Research Fund, and the Oakwood Foundation. A provisional patent has been filed naming several of the authors.

About Boston Children's Hospital

Boston Children's Hospital is ranked the #1 children's hospital in the nation by U.S. News & World Report and is the primary pediatric teaching affiliate of Harvard Medical School. Home to the world's largest research enterprise based at a pediatric medical center, its discoveries have benefited both children and adults since 1869. Today, 3,000 researchers and scientific staff, including 8 members of the National Academy of Sciences, 21 members of the National Academy of Medicine and 12 Howard Hughes Medical Investigators comprise Boston Children's research community. Founded as a 20-bed hospital for children, Boston Children's is now a 415-bed comprehensive center for pediatric and adolescent health care. For more, visit our Discoveries blog and follow us on social media @BostonChildrens, @BCH_Innovation, Facebook and YouTube.

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9. 人工知能が新しい抗生物質を作り出す

日付:2020 年 2 月 20 日
ソース:マサチューセッツ工科大学
概要:

MIT の研究者らは、機械学習アルゴリズムを使用して、強力な新しい抗生物質化合物を特定した。臨床検査では、この薬物は、既知のすべての抗生物質に耐性のある株を含む、世界で最も問題の多い病気の原因となる細菌の多くを殺した。また、2 つの異なるマウスモデルの感染もクリアした、としている。
数日で 1 億以上の化学物質をスクリーニングできるコンピューターモデルは、既存の薬物とは異なるメカニズムを使用して細菌を殺す潜在的な抗生物質を選択するように設計されている。
MIT の Medical Engineering and Science 研究所 (IMES) の James Collins 教授は、自分達のアプローチによって明らかにされたこの分子が、間違いなく発見された最も強力な抗生物質の 1 つである、と言っている。彼らの新しい研究では、他のいくつかの有望な抗生物質候補も特定されており、さらに試験する予定だ、としている。彼らは、薬物が細菌を殺すことを可能にする化学構造について学んだことを基に、このモデルを新しい薬物の設計にも使用できると考えている。
この研究成果は、*Cell* 誌に掲載されている。

研究関連/他のトップページに戻る

＜英文＞https://www.sciencedaily.com/releases/2020/02/200220141748.htm

Artificial intelligence yields new antibiotic

A deep-learning model identifies a powerful new drug that can kill many species of antibiotic-resistant bacteria

Date:

February 20, 2020

Source:

Massachusetts Institute of Technology

Summary:

Using a machine-learning algorithm, researchers have identified a powerful new antibiotic compound. In laboratory tests, the drug killed many of the world's most problematic

disease-causing bacteria, including some strains that are resistant to all known antibiotics. It also cleared infections in two different mouse models.

FULL STORY

Bacterial colony in dish (stock image).

Credit: © motorolka / Adobe Stock

Using a machine-learning algorithm, MIT researchers have identified a powerful new antibiotic compound. In laboratory tests, the drug killed many of the world's most problematic disease-causing bacteria, including some strains that are resistant to all known antibiotics. It also cleared infections in two different mouse models.

The computer model, which can screen more than a hundred million chemical compounds in a matter of days, is designed to pick out potential antibiotics that kill bacteria using different mechanisms than those of existing drugs.

"We wanted to develop a platform that would allow us to harness the power of artificial intelligence to usher in a new age of antibiotic drug discovery," says James Collins, the Termeer Professor of Medical Engineering and Science in MIT's Institute for Medical Engineering and Science (IMES) and Department of Biological Engineering. "Our approach revealed this amazing molecule which is arguably one of the more powerful antibiotics that has been discovered."

In their new study, the researchers also identified several other promising antibiotic candidates, which they plan to test further. They believe the model could also be used to design new drugs, based on what it has learned about chemical structures that enable drugs to kill bacteria.

"The machine learning model can explore, in silico, large chemical spaces that can be prohibitively expensive for traditional experimental approaches," says Regina Barzilay, the Delta Electronics Professor of Electrical Engineering and Computer Science in MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL).

Barzilay and Collins, who are faculty co-leads for MIT's Abdul Latif Jameel Clinic for Machine Learning in Health, are the senior authors of the study, which appears today in *Cell*. The first author of the paper is Jonathan Stokes, a postdoc at MIT and the Broad Institute of MIT and Harvard.

A new pipeline

Over the past few decades, very few new antibiotics have been developed, and most of those newly approved antibiotics are slightly different variants of existing drugs. Current methods for screening new antibiotics are often prohibitively costly, require a significant time investment, and are usually limited to a narrow spectrum of chemical diversity.

"We're facing a growing crisis around antibiotic resistance, and this situation is being generated by both an increasing number of pathogens becoming resistant to existing antibiotics, and an anemic pipeline in the biotech and pharmaceutical industries for new antibiotics," Collins says.

To try to find completely novel compounds, he teamed up with Barzilay, Professor Tommi Jaakkola, and their students Kevin Yang, Kyle Swanson, and Wengong Jin, who have previously developed machine-learning computer models that can be trained to analyze the molecular structures of compounds and correlate them with particular traits, such as the ability to kill bacteria.

The idea of using predictive computer models for "in silico" screening is not new, but until now, these models were not sufficiently accurate to transform drug discovery. Previously, molecules were represented as vectors reflecting the presence or absence of certain chemical groups. However, the new neural networks can learn these representations automatically, mapping molecules into continuous vectors which are subsequently used to predict their properties.

In this case, the researchers designed their model to look for chemical features that make molecules effective at killing E. coli. To do so, they trained the model on about 2,500 molecules, including about 1,700 FDA-approved drugs and a set of 800 natural products with diverse structures and a wide range of bioactivities.

Once the model was trained, the researchers tested it on the Broad Institute's Drug Repurposing Hub, a library of about 6,000 compounds. The model picked out one molecule that was predicted to have strong antibacterial activity and had a chemical structure different from any existing antibiotics. Using a different machine-learning model, the researchers also showed that this molecule would likely have low toxicity to human cells.

This molecule, which the researchers decided to call halicin, after the fictional artificial intelligence system from "2001: A Space Odyssey," has been previously investigated as possible diabetes drug. The researchers tested it against dozens of bacterial strains isolated from patients and grown in lab dishes, and found that it was able to kill many that are resistant to treatment, including Clostridium difficile, Acinetobacter baumannii, and Mycobacterium tuberculosis. The drug worked against every species that they tested, with the exception of Pseudomonas aeruginosa, a difficult-to-treat lung pathogen.

To test halicin's effectiveness in living animals, the researchers used it to treat mice infected with A. baumannii, a bacterium that has infected many U.S. soldiers stationed in Iraq and Afghanistan. The strain of A. baumannii that they used is resistant to all known antibiotics, but application of a halicin-containing ointment completely cleared the infections within 24 hours.

Preliminary studies suggest that halicin kills bacteria by disrupting their ability to maintain an electrochemical gradient across their cell membranes. This gradient is necessary, among other functions, to produce ATP (molecules that cells use to store energy), so if the gradient breaks down, the cells die. This type of killing mechanism could be difficult for bacteria to develop resistance to, the researchers say.

"When you're dealing with a molecule that likely associates with membrane components, a cell can't necessarily acquire a single mutation or a couple of mutations to change the chemistry of the outer membrane. Mutations like that tend to be far more complex to acquire evolutionarily," Stokes says.

In this study, the researchers found that E. coli did not develop any resistance to halicin during a 30-day treatment period. In contrast, the bacteria started to develop resistance to the antibiotic ciprofloxacin within one to three days, and after 30 days, the bacteria were about 200 times more resistant to ciprofloxacin than they were at the beginning of the experiment.

The researchers plan to pursue further studies of halicin, working with a pharmaceutical company or nonprofit organization, in hopes of developing it for use in humans.

Optimized molecules

After identifying halicin, the researchers also used their model to screen more than 100 million molecules selected from the ZINC15 database, an online collection of about 1.5 billion chemical compounds. This screen, which took only three days, identified 23 candidates that were structurally dissimilar from existing antibiotics and predicted to be nontoxic to human cells.

In laboratory tests against five species of bacteria, the researchers found that eight of the molecules showed antibacterial activity, and two were particularly powerful. The researchers now plan to test these molecules further, and also to screen more of the ZINC15 database.

The researchers also plan to use their model to design new antibiotics and to optimize existing molecules. For example, they could train the model to add features that would make a particular antibiotic target only certain bacteria, preventing it from killing beneficial bacteria in a patient's digestive tract.

Story Source:

Materials provided by **Massachusetts Institute of Technology**. Original written by Anne Trafton.
Note: Content may be edited for style and length.

Journal Reference:

1. Jonathan M. Stokes, Kevin Yang, Kyle Swanson, Wengong Jin, Andres Cubillos-Ruiz, Nina M. Donghia, Craig R. MacNair, Shawn French, Lindsey A. Carfrae, Zohar Bloom-Ackerman, Victoria M. Tran, Anush Chiappino-Pepe, Ahmed H. Badran, Ian W. Andrews, Emma J. Chory, George M. Church, Eric D. Brown, Tommi S. Jaakkola, Regina Barzilay, James J. Collins. **A Deep Learning Approach to Antibiotic Discovery**. *Cell*, 2020; 180 (4): 688 DOI: 10.1016/j.cell.2020.01.021

Massachusetts Institute of Technology. "Artificial intelligence yields new antibiotic: A deep-learning model identifies a powerful new drug that can kill many species of antibiotic-resistant bacteria." ScienceDaily. ScienceDaily, 20 February 2020. <www.sciencedaily.com/releases/2020/02/200220141748.htm>.
