BIO NEWS

October, 2018

In-Vivo Science International Inc.

1230 Bordeaux Drive

Sunnyvale, CA 94089, USA

目次

2018 年 9 月のニュース

＝研究編（詳細については各番号をクリックして下さい)＝

1. アマゾンの果実カムカムがマウスの肥満を予防
2. 淋菌感染の重症度を正確に反映するマウスモデルの必要性
3. 体温調節：発熱の仕組み
4. 食事間隔を長くすることで健康が改善され長寿に　-マウス実験
5. 暴飲が脳に与える影響の男女差について　-マウス実験
6. 肝臓の RNA サイレンシング蛋白質をブロックしてマウスの肥満や糖尿病を予防
7. BPA 代替のプラスティックであっても、実験用マウスの生殖問題の原因に
8. マウスのコカイン嗜癖を治す遺伝子治療
9. 新薬がマウスの膵臓癌増殖を阻止
10. 再生医療 iPS 関連２本　-京大

2018 年 9 月のニュース

＝企業関連ニュース他＝

・米投資銀行がバイオテック有力アナリストを年収 300 万ドル以上で引き抜いている（8/30)

Wall Street Journal によると、バイオテックの隆盛を背景にして、投資銀行 Leerink Partners、Cantor Fitzgerald & Co.、Jefferies Group LLC が大銀行のバイオテック分野有力アナリストを 300 万ドル以上の年収を約束して引き抜いている。

・ニホンザルの iPS 細胞作製 神経幹細胞誘導に成功 -京大 (8/30)

・大気汚染 知能レベルも低下 -中国（9/1)

・中国の豚コレラ 5 省に拡大（9/3)

・骨折しやすさと関連する 15 の遺伝子座を同定（9/3)

・インド洪水「ネズミ熱」拡大（9/4)

・前 CDC（米疾病管理センター）長 Tom Frieden 氏が女性に痴漢行為をしたとして逮捕された（9/4)

・１個３億円「金の卵」産む鶏 ゲノム編集で量産可能に -産業技術総合研究所など（9/4)

・CRISPR 遺伝子編集治療の初の企業主催臨床試験を CRISPR と Vertex が独で開始（9/5)

ヒトへの CRISPR 遺伝子編集治療の初の企業主催臨床試験を CRISPR Therapeutics が Vertex Pharmaceuticals と組んでドイツで開始。Vertex は CRISPR に 1 億 500 万ドルを払い、CTX001 を共同で開発して販売する権利を得ている。今回の企業主催試験開始に先立ち、中国の研究チームは既にヒトへの CRISPR 治療の試験を開始している。

・GSK の元癌研究者 Yu Xue 氏が同社の秘密を盗もうと目論んだ罪を認めた（9/5)

・R&D 全般の見直しの一環として Bayer が従業員削減を検討している/Reuters (9/5)

・米国成人の 1 型糖尿病と 2 型糖尿病の有病率はそれぞれ 0.5%と 8.5%（9/6)

・どの妊婦も早めの梅毒検診が必要～米国予防医療特別委員会見解（9/6)

・GSK、米国の営業と事務部門のあわせて 650 職を削減（9/7)

・科学誌 PNAS が来年 2109 年から印刷を止める（9/8)

・CRISPR 研究の先駆者 Jennifer Doudna 氏が Gladstone Institutes に研究室を新設（9/10)

・Teva の元会長 Phillip Frost 氏等 10 人が株価操作で不正に稼いだとしてアメリカ証券取引委員会（SEC）が起訴（9/11)

・肥満は脳の免疫細胞・ミクログリアにシナプスを食べさせて頭を悪くするらしい（9/11)

・CRISPR/Cas9 特許の控訴裁判でも Editas Medicine が頼る Broad Institute が勝利（9/11）

CRISPR Therapeutics, Intellia Therapeutics, Caribou Biosciences が頼りとするカリフォルニア州立大学（UC）側の CRISPR- Cas9 遺伝子編集技術特許を、Broad Institute の Feng Zhang 氏の研究室由来の特許は侵害していない、とのこれまでの判断を控訴裁判所が支持。Broad Institute に有利な今回の判断は揺るぎないが、UC 側はどうにかすることを検討している。

・Novartis、スピンオフして上場する眼科事業 Alcon が本拠地をスイス ジュネーブに移転（9/12）
・武田薬品、従業員約 1000 人が働く米国シカゴ近郊ディアフィールド拠点を閉鎖（9/12）
・ニホンザル iPS 細胞の作製に成功 -京都大学（9/13）
・針がさらに 14 分進み、危機感は過去最高 環境危機時計、地球温暖化を懸念（9/14）
・座る大腸検査、内視鏡自らに挿入、邦人医師にイグ・ノーベル賞（9/14）
・Regeneron、ニューヨーク州拠点を 8 億ドルを投じて拡張～1500 人を追加雇用（9/14）
・合計で数百万ドルともされる企業との金銭的繋がりの公表を怠った Jose Baselga 氏がニューヨーク・メモリアル・スローン・ケタリング（MSK）がんセンターの医務部長を退職（9/15）
・患者毎作製不要 CAR-T 開発の Allogene が早くも 1 億ドルの IPO 調達に向かう（9/15）
・Allergan、BOTOX を脅かしうるボツリヌス毒素を擁する Bonti を買収（9/15）
・心房細動を検出しうる心電図機能付きの Apple Watch 最新版 Series 4 がお目見え（9/15）
・武田薬品が湘南ヘルスイノベーションパーク（湘南アイパーク、神奈川県藤沢市）への創薬 VB 誘致を 10 倍の 200 社目標へ（9/16）
・実験用マウスに生じる 40 年来謎の腎不全の原因が判明 -パルボウイルス感染（9/16）
・カリフォルニア州が独自の大気監視衛星打ち上げを計画 -トランプ政権の環境対策縮小方針に対抗（9/17）
・米コカ・コーラ、健康飲料への大麻成分配合を研究（9/18）
・中国 Huahai 起源バルサルタン製品から NDMA とは別の発癌性物質が見つかった（9/18）
・Akili Interactive、認知機能を改善するように運動させる治療用ビデオゲームをカリフォルニア大学サンフランシスコ校（UCSF）から取得（9/18）
・SpaceX による月旅行 最初の乗客はゾゾタウン前沢氏（9/18）
・小野薬品、米 iPS ベンチャーFate Therapeutics と提携 がん治療薬開発（9/18）

・グラム陰性細菌を手当たり次第に滅ぼしうる外膜透過化合物ができた（9/18）

グラム陰性細菌は薬の透過が著しく困難な外膜を有するが、その外膜を越えて内膜-外膜間に到達して 1 型ペプチダーゼを阻害して数あるグラム陰性細菌を選り好みせず手当たり次第に滅ぼしうる化合物を Genentech の科学者等が発見。その化合物 G0775 は外膜を透過しうる天然成分アリロマイシン（arylomycin）の最適化によって作られた。

・GSK 元科学者もう 1 人が中国政府支援企業への秘密情報横流しの罪を認めた（9/19）

・そーせい/Allergan、サルでの毒性を受けてアルツハイマー病薬の臨床試験を中断（9/19）

・Novo、研究開発の再編の一環としてデンマークと中国の 400 人を削減（9/19）

・武田、Molecular Templates の技術を利用した CD38 標的骨髄腫治療を開発（9/20）

・副作用をもみ消す看護師等を使って Humira を販促したとして AbbVie がカリフォルニア州から訴えられた（9/20）

・Novartis、欧州医薬品庁の引っ越し先アムステルダムにオランダ拠点を移す（9/20）

・Merck を追う Pfizer の次世代肺炎球菌ワクチン開発が FDA の画期性優遇指定獲得（9/21）

・Mylan、Humira のバイオシラミーの欧州承認獲得～来月から販売を始める（9/21）

・Amicus、Celenex を 1 億ドルで買って遺伝子治療開発（9/21）

・Immune-Onc、3,300 万ドル超を調達～Genentech 出身の 2 人を経営陣に迎える（9/21）

・ロサンゼルスをバイオ技術一大集積地にする取り組みに Amgen が出資（9/23）

カリフォルニア州サウザンドオークスを拠点とする Amgen が、すでにバイオ集積地となっているサンフランシスコとサンディエゴの間にある同州ロサンゼルス地域に生命科学発明を集積させて起業を促す取り組み BioLA 設立に出資。

・植物は痛みを感じるのか -ダメージを全身に伝える仕組みを埼玉大が発見（9/24）

・受精卵「ゲノム編集」来年４月にも解禁へ...基礎研究に限定（9/25）

・インフル感染を最短 3 分で陽性判定、キャノンメディカルシステムズが販売（9/25）

・Novartis、スイス/英国の 2,550 職を削減～世界の従業員を 2022 年までに 19%減らす（9/26）

・乳がん手術後の生存率 23 の遺伝子関係か -九州大グループ（9/27）

・先天性梅毒が米国で増えている（9/28）

・Merck、CEO は 65 歳で辞任という就業規則を撤廃し、現 CEO・Ken Frazier 氏が 65 歳の誕生日を迎えた後も続投を決定（9/28）

・驚異的奏効率の中国 Legend Biotech の CAR-T 治療データ粉飾が報告された（9/28）

2017 年の ASCO 年次総会で奏効率 94%が発表され、J&J との前金 3 億 5,000 万ドルの提携を同年にものにした Nanjing Legend Biotech の CAR-T 抗癌治療 LCAR-B38M の試験デ

ータが良い結果に限って公表されていたとの報告が中国で広く報じられ、Legend Biotech を所有する中国 CRO・Genscript の株価が大暴落。

目次に戻る

1．アマゾンの果実カムカムがマウスの肥満を予防

2018 年 8 月 30 日

カナダ ケベック州の Laval 大学の研究者らは、アマゾン産の果物カムカムの抽出物がマウス実験で、砂糖と脂肪が豊富な食餌を与えられたマウスの肥満を予防することを発見し、最近その研究成果が科学誌 *Gut* で発表された。
カムカムの化学組成は、キウイより 20～30 倍多くのビタミン C を含み、ブラックベリーよりも 5 倍多くのポリフェノールを含むという点で独特だ。
研究者らは、2 つのグループのマウスに、砂糖と脂肪を豊富に含む食餌を 8 週間与え、マウスの半分には毎日カムカムの抽出物を与えた。すると、カムカム処置のマウスにおける体重増加は対照マウスで観察されたものより 50%低かったし、低糖低脂肪食を摂取したマウスの体重増加と同様であった。 研究者らは、カムカムの抗肥満効果は、抽出物を受けたマウスの安静代謝の増加によって説明できると考えている。
研究者らは、又、カムカムが耐糖能とインスリン感受性を改善し、血液エンドトキシンと代謝性炎症の濃度を低下させることも発見した。今後はカムカムが人間に同じ代謝作用をもたらすかどうかを調べたい、としている

英文記事：
https://www.sciencedaily.com/releases/2018/08/180830102540.htm

---

Amazonian fruit prevents obesity in overfed mice

Date:

August 30, 2018

Source:

Université Laval

Summary:

An extract of camu camu -- a fruit native to the Amazon -- prevents obesity in mice fed a diet rich in sugar and fat, say researchers. The discovery suggests that camu camu phytochemicals could play a leading role in the fight against obesity and metabolic disease.

FULL STORY

An extract of camu camu -- a fruit native to the Amazon -- prevents obesity in mice fed a diet rich in sugar and fat, say researchers at Université Laval and the Quebec Heart and Lung Institute Research Centre. The discovery, which was recently published in the scientific journal *Gut*, suggests that camu camu phytochemicals could play a leading role in the fight against obesity and metabolic disease.

The chemical composition of camu camu is unique in that it contains 20 to 30 times more vitamin C than kiwis and 5 times more polyphenols than blackberries. "We demonstrated the beneficial health effects of polyphenol-rich berries in previous studies," explains André Marette, a professor at Université Laval's Faculty of Medicine and principal investigator for the study. "That's what gave us the idea to test the effects of camu camu on obesity and metabolic disease."

The researchers fed two groups of mice a diet rich in sugar and fat for eight weeks. Half the mice were given camu camu extract each day. At the end of the experiment, weight gain in camu camu-treated mice was 50% lower than that observed in control mice and was similar to the weight gain of mice consuming a low-sugar, low-fat diet. The researchers believe the anti-obesity effect of camu camu could be explained by an increase in resting metabolism in the mice that received the extract.

The researchers also found that camu camu improved glucose tolerance and insulin sensitivity and reduced the concentration of blood endotoxins and metabolic inflammation. "All these changes were accompanied by a reshaping of the intestinal microbiota, including a blooming of A. muciniphila and a significant reduction in Lactobacillus bacteria," explains Dr. Marette.

Transplantation of intestinal microbiota from the camu camu group to germ-free mice lacking an intestinal microbiota temporarily reproduced similar metabolic effects. "Camu camu thus exerts its positive metabolic effects at least in part through the modulation of the gut microbiota," concludes the researcher.

André Marette now wants to examine whether camu camu produces the same metabolic effects in humans. The toxicity of the fruit extract should not pose a problem since it is already commercialized to combat fatigue and stress and stimulate the immune system.

In addition to André Marette, the study's co-authors are Fernando Anhê, Renato Nachbar, Thibault Varin, Jocelyn Trottier, Stéphanie Dudonné, Mélanie Le Barz, Perrine Feutry, Geneviève Pilon, Olivier Barbier, Yves Desjardins, and Denis Roy.

Story Source:

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

Journal Reference:

1. Fernando F Anhê, Renato T Nachbar, Thibault V Varin, Jocelyn Trottier, Stéphanie Dudonné, Mélanie Le Barz, Perrine Feutry, Geneviève Pilon, Olivier Barbier, Yves Desjardins, Denis Roy, André Marette. **Treatment with camu camu (Myrciaria dubia) prevents obesity by altering the gut microbiota and increasing energy expenditure in diet-induced obese mice**. *Gut*, 2018; gutjnl-2017-315565 DOI: 10.1136/gutjnl-2017-315565

Cite This Page:

- MLA
- APA

- Chicago

Université Laval. "Amazonian fruit prevents obesity in overfed mice." ScienceDaily. ScienceDaily, 30 August 2018. <www.sciencedaily.com/releases/2018/08/180830102540.htm>.

目次に戻る

2. 淋菌感染の重症度を正確に反映するマウスモデルの必要性

2018 年 8 月 31 日

発症率が急速に増加し、抗生剤耐性が増す中、淋菌感染を予防するワクチン開発が急務となっている。ボストン大学医学部（BUSM）の研究者らは、トロント大学の研究者らと共同で、感染がどのように進化し、次世代ワクチンの有効性を決定する研究をするためのマウスモデルの使用について調査している。
淋病は今現在急速に悪化している公衆衛生上の脅威となっており、2017 年には WHO が年間 1 億 610 万件の症例発生を記録する一方で、55 万件以上の新たな淋菌が報告された。更に、淋病が益々薬剤耐性になっているという重要な証拠を踏まえて、今後効果的な淋菌ワクチンを開発し、その有効性をテストするための適切な動物モデルを有することが必要不可欠だとしている。

英文記事：
https://eurekalert.org/pub_releases/2018-08/buso-mmm083118.php

---

PUBLIC RELEASE: 31-AUG-2018

Mouse models may not accurately mimic severity of gonorrhea infection

Boston University School of Medicine

(BOSTON) - There is an urgent need to develop a vaccine to prevent gonorrhea infection due to rapidly increasing incidence and growing antibiotic resistance. BUSM researchers (in collaboration with University of Toronto researchers) have been investigating the use of animal models of gonorrhea, to study how the infection evolves and for potential use to determine the efficacy of next generation vaccines. They found that the mouse model may not fully reflect the severity of the infection and the types of immune responses seen in humans.

Gonorrhea is a rapidly worsening public health threat. In 2017 more than 550,000 new cases of gonorrhea were reported to the Centers for Disease Control and Prevention (a 67 percent increase from 2013), while the World Health Organization places global yearly incidence at 106.1 million cases. Researchers believe these figures may underestimate the actual disease burden by up to two-thirds. In addition, there is significant evidence that gonorrhea is becoming increasingly drug-resistant. According to most experts in the field, these factors make it even more essential that we develop effective gonorrhea vaccines and have adequate animal models in which to test their efficacy.

""The use of models in infectious diseases to examine pathogenesis and potential vaccine development is fraught with difficulties as many of these human specific pathogens have evolved mechanisms of infection and immune evasion specific for humans. It is essential that when models are used, the details of their infections are fully examined to ensure they at least somewhat mimic what occurs in humans," said Lee M. Wetzler, MD, Professor of Medicine and Microbiology.

###

These findings appeared online in *BMC Genomics*.

目次に戻る

3. 体温調節：発熱の仕組み

2018 年 9 月 4 日

発熱は、体温調節に重要な役割を果たすプロスタグランジン E2 (PGE2) と呼ばれる脂質化合物の視床下部における放出と密接に関係しているとされるが、どのようにして PGE2 が脳に供給/維持されるのか、そして膜の輸送体（特に SLCO2A1 遺伝子によってコード化されるプロスタグランジン輸送体の OATP2A1）の役割が解明される必要がある。
そこで今回金沢大学の薬物動態学研究室准教授の中西猛夫氏らは、マウスの微小透析研究を行って、脳の炎症反応の根底にあるメカニズムを洞察し、*Journal of Neuroscience* 誌に発表した。
研究者らは、正常な SLCO2A1、全 SLCO2A1 欠損又は単球/マクロファージ特異的 SLCO2A1 欠損を有するマウスを使用した。SLCO2A1 の有無が基礎体温に影響しないことを示した後で、発熱物質のリポ多糖類をマウスに投与、SLCO2A1 を有するマウスは 2 時間後に発熱したが、リポ多糖の熱分解効果は全 SLCO2A1 欠損マウスでは観察されなかった、としている。

英文記事：
https://www.sciencedaily.com/releases/2018/09/180904103238.htm

---

Body temperature regulation: How fever comes

Date:

September 4, 2018

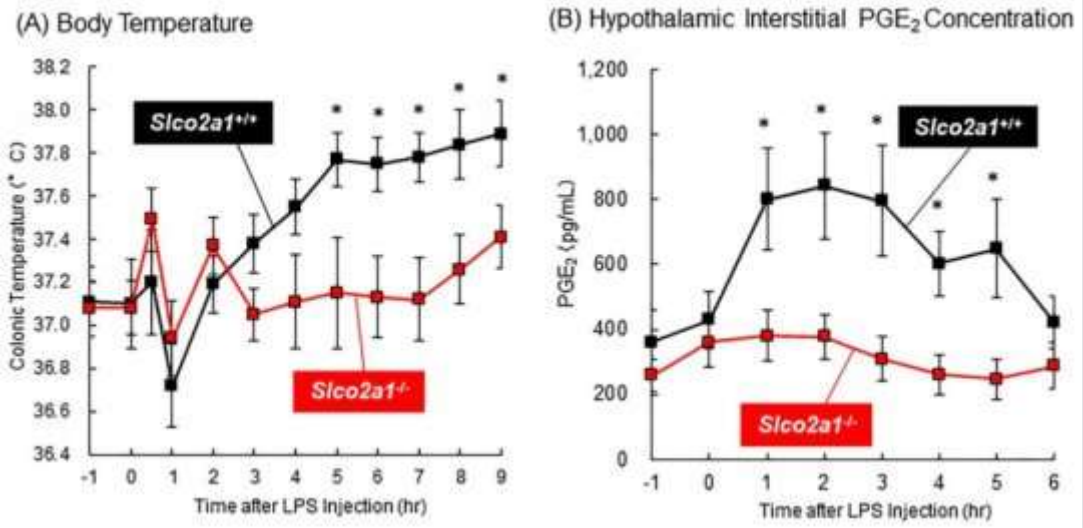
Source:

Kanazawa University

Summary:

Researchers performed a microdialysis study on mice to determine mechanisms underlying the inflammatory response in the brain associated with fever that might be used to develop new strategies for treatment.

FULL STORY



Changes in body core temperature (A) and hypothalamic interstitial PGE2 concentration (B) in mice injected with lipopolysaccharide (LPS). LPS was intraperitoneally injected to Slco2a1+/+ or Slco2a1-/- mice at time 0 hr. Body temperature was measured by monitoring colonic temperature. For PGE2 measurements, samples were collected by means of microdialysis, and subjected to LC-MS/MS analysis. (A) and (B) show mean values ± S.E.M of 10 and 6 mice in each group, respectively.

Credit: Kanazawa University

The appearance of fever is associated with the release in the hypothalamus of a lipid compound called prostaglandin E2 (PGE2), which has an important role in the regulation of body temperature. However, how PGE2 is supplied to or maintain in the brain, and the role of membrane transporters (in

particular of the prostaglandin transporter OATP2A1, encoded by the gene SLCO2A1) in this process still needs to be elucidated.

To shed light on this question, Takeo Nakanishi at Kanazawa University, Japan, and colleagues performed a microdialysis study on mice, published in the *Journal of Neuroscience*. The researchers used mice with normal Slco2a1, with total Slco2a1 deficiency or with monocyte-/macrophage-specific Slco2a1 deficiency. They first injected the mice with physiological saline, observing the same body temperature for mice with and without SLCO2A1, indicating that the presence of OATP2A1 does not affect the basal body temperature. They then administered to the mice a pyrogen, lipopolysaccharide, that normally causes a fever. Indeed, mice with Slco2a1 developed a fever after 2h, whereas the pyrogenic effect of lipopolysaccharide was not observed in mice with total SLCO2A1 deficiency. They further demonstrate the body temperature of mice with monocyte-/macrophage-specific Slco2a1 deficiency was partially attenuated. Intriguingly, an inhibitor of OATP2A1 injected to the brain of rats with normal Slco2a1 inhibited the febrile response -- in this case only an initial rise in body temperature was observed.

The study reveals that the onset of fever is associated with increased PGE2 concentration in the hypothalamus interstitial fluid, but not in the cerebrospinal fluid, thus OATP2A1 seems to work by maintaining high levels of PGE2 in the hypothalamus, either by stimulating its secretion from glial cells in the hypothalamus and from brain capillary endothelial cells or by facilitating its transport through the blood-brain barrier. OATP2A1 seems to be involved in the secretion of PGE2 from macrophages, but OATP2A1 in cells other than macrophages may also contribute to the febrile response.

This newly gained insight of the mechanisms underlying the inflammatory response in the brain associated with fever might be used to develop new strategies for treatment, pointing to OATP2A1 as a useful therapeutic target.

Story Source:

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

Journal Reference:

1. Yoshinobu Nakamura, Takeo Nakanishi, Hiroaki Shimada, Junya Shimizu, Rika Aotani, Shio Maruyama, Kei Higuchi, Takashi Okura, Yoshiharu Deguchi, Ikumi Tamai. **Prostaglandin transporter OATP2A1/SLCO2A1is essential for body temperature regulation during fever**. *The Journal of Neuroscience*, 2018; 3276-17 DOI: 10.1523/JNEUROSCI.3276-17.2018

Cite This Page:

- MLA
- APA
- Chicago

Kanazawa University. "Body temperature regulation: How fever comes." ScienceDaily. ScienceDaily, 4 September 2018. <www.sciencedaily.com/releases/2018/09/180904103238.htm>.

目次に戻る

４．食事間隔を長くすることで健康が改善され長寿に -マウス実験

2018 年 9 月 6 日

9 月 6 日に *Cell Metabolism* 誌 9 月号に発表された新しい研究によると、食事間隔を長くすることで、雄のマウスが全体的に健康になり、頻繁に食事するマウスに比べて長生きするようになった。
米国国立衛生研究所（NHI）の国立長寿研究所（NIA)、ルイジアナ州バトンルージュのペニントン・バイオメディカル・リサーチ・センターからなる研究者チームによると、マウスが何を食べたかとか何カロリーを消費したかにかかわらず、食時間隔を長くするにつれてマウスの健康状態と寿命が改善された、としている。

英文記事：
https://www.nih.gov/news-events/news-releases/longer-daily-fasting-times-improve-health-longevity-mice

---

Thursday, September 6, 2018

Longer daily fasting times improve health and longevity in mice

Increasing time between meals made male mice healthier overall and live longer compared to mice who ate more frequently, according to a new study published in the Sept. 6, 2018 issue of *Cell Metabolism*. Scientists from the National Institute on Aging (NIA) at the National Institutes of Health, the University of Wisconsin-Madison, and the Pennington Biomedical Research

Center, Baton Rouge, Louisiana, reported that health and longevity improved with increased fasting time, regardless of what the mice ate or how many calories they consumed.

"This study showed that mice who ate one meal per day, and thus had the longest fasting period, seemed to have a longer lifespan and better outcomes for common age-related liver disease and metabolic disorders," said NIA Director Richard J. Hodes, M.D. "These intriguing results in an animal model show that the interplay of total caloric intake and the length of feeding and fasting periods deserves a closer look."

The scientists randomly divided 292 male mice into two diet groups. One group received a naturally sourced diet that was lower in purified sugars and fat, and higher in protein and fiber than the other diet. The mice in each diet group were then divided into three sub-groups based on how often they had access to food. The first group of mice had access to food around the clock. A second group of mice was fed 30 percent less calories per day than the first group. The third group was meal fed, getting a single meal that added up to the exact number of calories as the round-the-clock group. Both the meal-fed and calorie-restricted mice learned to eat quickly when food was available, resulting in longer daily fasting periods for both groups.

The scientists tracked the mice's metabolic health through their lifespans until their natural deaths and examined them post-mortem. Meal-fed and calorie-restricted mice showed improvements in overall health, as evidenced by delays in common age-related damage to the liver and other organs, and extended longevity. The calorie-restricted mice also showed significant improvement in fasting glucose and insulin levels compared to the other groups. Interestingly, the researchers found that diet composition had no significant impact on lifespan in the meal fed and calorie restricted groups.

According to the study's lead author, Rafael de Cabo, Ph.D., chief of the Translational Gerontology Branch of the NIA Intramural Research Program, scientists have studied the beneficial effects of caloric restriction for more than a century, but the impact of increased fasting times has recently come under closer scrutiny.

"Increasing daily fasting times, without a reduction of calories and regardless of the type of diet consumed, resulted in overall improvements in health and survival in male mice," said de

Cabo. “Perhaps this extended daily fasting period enables repair and maintenance mechanisms that would be absent in a continuous exposure to food.”

The researchers say their findings are encouraging for future studies on how these types of time-restricted eating patterns might help humans to maintain healthy weight and reduce some common age-related metabolic disorders. According to de Cabo, next steps for this research include expanding these findings to other strains of mice and other lab animal species using both sexes, and to find the potential translation of the findings in humans.

For more information on what the research shows about calorie restriction and fasting diets in humans, visit https://www.nia.nih.gov/health/calorie-restriction-and-fasting-diets-what-do-we-know.

This press release describes a basic research finding. Basic research increases our understanding of human behavior and biology, which is foundational to advancing new and better ways to prevent, diagnose, and treat disease. Science is an unpredictable and incremental process — each research advance builds on past discoveries, often in unexpected ways. Most clinical advances would not be possible without the knowledge of fundamental basic research.

About the National Institute on Aging (NIA): The NIA leads the federal government effort conducting and supporting research on aging and the health and well-being of older people. The Institute’s broad scientific program seeks to understand the nature of aging and to extend the healthy, active years of life. For more information on research, aging, and health, go to www.nia.nih.gov.

About the National Institutes of Health (NIH): NIH, the nation's medical research agency, includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. NIH is the primary federal agency conducting and supporting basic, clinical, and translational medical research, and is investigating the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.

NIH…Turning Discovery Into Health®

###

目次に戻る

5. 暴飲が脳に与える影響の男女差について -マウス実験

2018 年 9 月 10 日

繰り返される暴飲によって、脳のある領域内の中毒に関連する遺伝子が活性化されるが、これは男性と女性では異なっている。反復暴飲の影響は、雌マウスではホルモンのシグナリングおよび免疫機能に関連する遺伝子が受け、雄マウスでは神経シグナル伝達に関連する遺伝子が受ける、との研究成果が、9 月 10 日 *Frontiers in Genetics* 誌で発表された。
アルコール依存症発症の危険因子は、反復暴飲による飲酒である可能性が高く、研究者らは、反復暴飲の飲酒が、アルコール依存性の雄および雌マウスの脳において異なる応答を生じたかどうかを調べるために、中毒に関連する脳の領域、すなわち側坐核の遺伝子発現を分析した。
これらの知見は、男性および女性患者に対する効果的な治療法を調整することの重要性を強調しており、アルコール障害治療に重要な意味を有する、としている。

英文と記事：
https://www.sciencedaily.com/releases/2018/09/180910111246.htm

---

Binge drinking affects male and female brains differently

Date:

September 10, 2018

Source:

Frontiers

Summary:

Repeated binge drinking activates genes in an area of the brain linked to addiction differently in males and females. Genes associated with hormone signaling and immune function are affected by repeated binge drinking in female mice, whereas genes associated with nerve signaling are affected in the males. These findings have implications for alcohol abuse treatment, emphasizing the importance of considering the sex of patients when developing effective pharmaceutical therapies.

FULL STORY

Gene expression in an area of the brain linked to addiction is affected differently by repeated binge drinking in males and females, finds a new study published today in *Frontiers in Genetics*. It reveals for the first time that genes associated with hormone signaling and immune function are affected by repeated binge drinking in female mice, whereas genes associated with nerve signaling are affected in males. These findings have significant implications for the treatment of alcohol use disorder as they emphasize the importance of tailoring effective therapies towards male and female patients.

"We show that repeated binge drinking significantly alters molecular pathways in the nucleus accumbens, a region of the brain linked to addiction. A comparison of activated pathways reveals different responses in each sex, similar to that reported in recent research on male and female mice tested during the withdrawal phase following chronic alcohol intoxication," says Deborah Finn, a Professor of Behavioral Neuroscience at Oregon Health & Science University and a Research Pharmacologist at the VA Portland Health Care System, USA.

She continues, "These findings are important as they increase our understanding of male and female differences in molecular pathways and networks that can be influenced by repeated binge drinking. This knowledge can help us identify and develop new targeted treatments for alcohol use disorder in males and female patients."

Repeated binge drinking can be a risk factor for the development of alcohol dependence. Finn and her colleagues wanted to determine whether repeated binge drinking produced different

responses in the brains of male and female mice, as has been found in alcohol-dependent mice tested during the withdrawal phase.

To do this, they analyzed gene expression in an area of the brain linked to addiction, the nucleus accumbens. Gene expression is the process where specific genes are activated to produce proteins for use by the cell, e.g. as building blocks for new tissues or hormones. Gene regulation governs the amount and timing of gene expression.

"We examined the effect of repeated binge drinking on the expression of 384 genes previously identified as important in addiction and mood disorders," says Finn. "Of a total of 106 genes regulated by binge drinking, only 14 were regulated in both males and females, representing common targets to binge drinking. Interestingly, only 4 of these 14 genes were regulated in the same direction and the top 30 genes regulated by binge drinking in each sex differed markedly."

The researchers analyzed the data further, to examine the likely overall effect the regulation and expression of these genes would have on males and females.

"Our results suggested repeated binge drinking had a very different effect on the neuroadaptive responses of the nucleus accumbens in males and females, with different pathways being activated in each sex. Pathway analysis suggests hormone signaling and immune function were altered by binge drinking in females, whereas nerve signaling was a central target of binge drinking in males," reports Finn.

This has important implications for the treatment of alcohol addiction and emphasizes the need to tailor individual pharmaceutical treatments for male and female patients.

Finn explains, "We have shown that pharmacologically manipulating a pathway in both sexes that only was affected by binge drinking in males did not decrease binge drinking in females; binge drinking was only decreased in males. A consideration of sex is critical in the development of potential pharmacological therapies for the treatment of alcohol use disorder."

She concludes, "Future studies will determine whether the current gene expression changes correspond to behavioral and/or physiological differences."

Story Source:

Materials provided by **Frontiers**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Deborah A. Finn, Joel G. Hashimoto, Debra K. Cozzoli, Melinda L. Helms, Michelle A. Nipper, Moriah N. Kaufman, Kristine M. Wiren, Marina Guizzetti. **Binge Ethanol Drinking Produces Sexually Divergent and Distinct Changes in Nucleus Accumbens Signaling Cascades and Pathways in Adult C57BL/6J Mice**. *Frontiers in Genetics*, 2018; 9 DOI: 10.3389/fgene.2018.00325

Cite This Page:

- MLA
- APA
- Chicago

Frontiers. "Binge drinking affects male and female brains differently." ScienceDaily. ScienceDaily, 10 September 2018. <www.sciencedaily.com/releases/2018/09/180910111246.htm>.

目次に戻る

6. 肝臓の RNA サイレンシング蛋白質をブロックしてマウスの肥満や糖尿病を予防

2018 年 9 月 10 日

肥満および 2 型糖尿病や脂肪肝疾患のような肥満関連疾患は、世界的にも主要な健康負担となっている。今回シンシナティー小児病院医療センターの中村能久博士と彼の同僚らの研究チームは、マウスの肝臓の RNA サイレンシング蛋白質 Argonaute 2 (Ago2) を遺伝的に欠損させることによって、マウスが脂肪および糖尿病状態になるのを防ぐことに成功し、この知見が *Nature Communications* 誌で発表された。
研究者らは、この研究がまだ早い段階であるとしながらも、これからの作業に対して確かな基礎を提供するものだ、としている。

英文記事：
https://www.sciencedaily.com/releases/2018/09/180910111249.htm

---

Scientists block RNA silencing protein in liver to prevent obesity and diabetes in mice

New treatment for a major health problem?

Date:

September 10, 2018

Source:

Cincinnati Children's Hospital Medical Center

Summary:

Obesity and its related ailments like type 2 diabetes and fatty liver disease pose a major global health burden, but researchers report that blocking an RNA-silencing protein in the livers of mice keeps the animals from getting fat-related and diabetic conditions.

FULL STORY

Obesity and its related ailments like type 2 diabetes and fatty liver disease pose a major global health burden, but researchers report in *Nature Communications* that blocking an RNA-silencing protein in the livers of mice keeps the animals from getting fat and diabetic conditions.

Takahisa Nakamura, PhD, and colleagues at Cincinnati Children's Hospital Medical Center genetically deleted a protein called Argonaute 2 (Ago2) from the livers of mice. Ago2 controls the silencing of RNA in cells, affecting energy metabolism in the body, according to the study. When Ago2 silences RNA in the liver, it slows metabolism and liver's ability to process a high-fat diet, the scientists report.

When they deleted Ago2 from the livers of mice, it was not toxic to the animals but it did stabilize energy metabolism. This helped stave off obesity and prevented the mice from developing diabetes and fatty liver disease, which can severely damage the vital organ -- which helps rid the body of toxic substances.

"Although this is still basic science, we propose that there may be important translational implications for our findings for chronic metabolic disorders like diabetes, fatty liver diseases, and other obesity associated illnesses," said Nakamura, senior investigator and a member of the Division of Endocrinology. "This allows us to explore the potential of finding a novel therapeutic approach that alters energy balance in obesity and modulates the associated diseases."

Novel Science

The scientists caution the research is early stage. Their findings still need additional study and verification in laboratory models and the development of a practical therapeutic to inhibit Ago2 in a clinical setting for patients. But the current paper provides a solid basis for subsequent work.

Ago2 was identified after the researchers conducted a thorough screen and analysis of the activity of genes and their molecular targets in the liver, such as critical proteins. They analyzed wild type and genetically modified mice with high-fat diets by deleting certain proteins that are critical to liver metabolism -- such as one called AMPK (AMP-activated protein kinase).

Nakamura said that identifying Ago2's role in the process "connects the dots" between how proteins are translated in the liver, how energy is produced and consumed and the activity of AMPK in these processes. He pointed out that disruption of these events is already a common feature in obesity and its related illnesses.

Story Source:

Materials provided by **Cincinnati Children's Hospital Medical Center**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Cai Zhang, Joonbae Seo, Kazutoshi Murakami, Esam S. B. Salem, Elise Bernhard, Vishnupriya J. Borra, Kwangmin Choi, Celvie L. Yuan, Calvin C. Chan, Xiaoting Chen, Taosheng Huang, Matthew T. Weirauch, Senad Divanovic, Nathan R. Qi, Hala Einakat Thomas, Carol A. Mercer, Haruhiko Siomi, Takahisa Nakamura. **Hepatic Ago2-mediated RNA silencing controls energy metabolism linked to AMPK activation and obesity-associated pathophysiology**. *Nature Communications*, 2018; 9 (1) DOI: 10.1038/s41467-018-05870-6

Cite This Page:

- MLA
- APA

- Chicago

Cincinnati Children's Hospital Medical Center. "Scientists block RNA silencing protein in liver to prevent obesity and diabetes in mice: New treatment for a major health problem?." ScienceDaily. ScienceDaily, 10 September 2018. <www.sciencedaily.com/releases/2018/09/180910111249.htm>.

目次に戻る

7. BPA 代替のプラスティックであっても、実験用マウスの生殖問題の原因に

2018 年 9 月 13 日

20 年前、研究者らは、ビスフェノール A（BPA）と呼ばれるプラスティック成分が、実験室で雌のマウスを収容するプラスティックケージから不用意に滲出し、マウスの染色体異常卵の増加を引き起こす、という偶然の発見を行った。
今回ワシントン州立大学の研究者らは、BPA を含まないペットボトルやカップやケージなどの BPA の代替品であっても、マウスに同様の問題を引き起こしているように見えることを 9 月 13 日の *Current Biology* 誌で発表した。
研究者らの消費者へのアドバイスは簡単で、「BPA フリーであってもなくても、物理的な損傷や老化の徴候を示すプラスティック製品は安全ではない」ということのようだ。

英文記事：
https://www.sciencedaily.com/releases/2018/09/180913113940.htm

---

BPA replacements in plastics cause reproductive problems in lab mice

Date:

September 13, 2018

Source:

Cell Press

Summary:

Twenty years ago, researchers made the accidental discovery that BPA had leached out of plastic cages used to house female mice in the lab, causing an increase in chromosomally abnormal eggs. Now, the same team is back to report that the array of alternative bisphenols now used to replace BPA in BPA-free bottles, cups, cages, and other items appear to come with similar problems for their mice.

Collection of water bottles

Credit: © Gresei / Fotolia

Twenty years ago, researchers made the accidental discovery that the now infamous plastics ingredient known as bisphenol A or BPA had inadvertently leached out of plastic cages used to house female mice in the lab, causing a sudden increase in chromosomally abnormal eggs in the animals. Now, the same team is back to report in the journal *Current Biology* on September 13 that the array of alternative bisphenols now used to replace BPA in BPA-free bottles, cups, cages, and other items appear to come with similar problems for their mice.

"This paper reports a strange déjà vu experience in our laboratory," says Patricia Hunt of Washington State University.

The new findings were uncovered much as before as the researchers again noticed a change in the data coming out of studies on control animals. Again, the researchers traced the problem to contamination from damaged cages, but the effects this time, Hunt says, were more subtle than before. That's because not all of the cages were damaged and the source of contamination remained less certain.

However, she and her colleagues were able to determine that the mice were being exposed to replacement bisphenols. They also saw that the disturbance in the lab was causing problems in the production of both eggs and sperm.

Once they got the contamination under control, the researchers conducted additional controlled studies to test the effects of several replacement bisphenols, including a common replacement known as BPS. Those studies confirm that replacement bisphenols produce remarkably similar chromosomal abnormalities to those seen so many years earlier in studies of BPA.

Hunt notes that the initial inadvertent exposure of their animals was remarkably similar to what might happen in people using plastics in that the exposure was accidental and highly variable. Not all of the animals' cages were damaged, and so the findings differed among animals in different cages.

She adds that -- although determining the levels of human exposure is difficult -- their controlled experiments were conducted using low doses of BPS and other replacement bisphenols thought to be relevant to exposure in people using BPA-free plastics.

These problems, if they hold true in people as has been shown in the case of BPA, will carry over to future generations through their effects on the germline. The researchers showed that, if it were possible to eliminate bisphenol contaminants completely, the effects would still persist for about three generations.

Hunt says more work is needed to determine whether some replacement bisphenols might be safer than others, noting that there are dozens of such chemicals now in use. She also suspects that other widely used and endocrine-disrupting chemicals, including parabens, phthalates, and flame retardants, may be having similarly adverse affects on fertility that warrant much more study.

"The ability to rapidly enhance the properties of a chemical has tremendous potential for treating cancer, enhancing medical and structural materials, and controlling dangerous infectious agents," the researchers write. "Importantly, this technology has paved the way for 'green chemistry,' a healthier future achieved by engineering chemicals to ensure against hazardous effects. Currently, however, regulatory agencies charged with assessing chemical safety cannot keep pace with the introduction of new chemicals. Further, as replacement bisphenols illustrate, it is easier and more cost effective under current chemical regulations to replace a chemical of concern with structural analogs rather than determine the attributes that make it hazardous."

Hunt's advice to consumers now is simple: BPA-free or not, "plastic products that show physical signs of damage or aging cannot be considered safe."

Support for these studies was provided from the NIH.

Story Source:

Materials provided by **Cell Press**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Tegan S. Horan, Hannah Pulcastro, Crystal Lawson, Roy Gerona, Spencer Martin, Mary C. Gieske, Caroline V. Sartain, Patricia A. Hunt. **Replacement Bisphenols Adversely Affect Mouse Gametogenesis with Consequences for Subsequent Generations**. *Current Biology*, 2018; DOI: 10.1016/j.cub.2018.06.070

Cite This Page:

- MLA
- APA

- Chicago

Cell Press. "BPA replacements in plastics cause reproductive problems in lab mice." ScienceDaily. ScienceDaily, 13 September 2018. <www.sciencedaily.com/releases/2018/09/180913113940.htm>.

目次に戻る

8. マウスのコカイン嗜癖を治す遺伝子治療

2018 年 9 月 18 日

遺伝的に改変した皮膚幹細胞が、マウスのコカイン探索行動の発現やコカインの過剰摂取を防ぐことを示唆するシカゴ大学医学部の論文が、今週 *Nature Biomedical Engineering* 誌に掲載される。今回の知見が臨床応用可能かを明らかにするにはさらに研究を行う必要があるが、この手法は、薬物乱用を長期的に管理するための新たな治療法に道を開くと考えられる。

薬物、とりわけコカインの乱用は、強迫的な薬物探索を伴い、長期にわたる摂取中止を経ても再発する場合が多い。コカインの過剰摂取による救急患者を治療するための効果的な戦略が求められているが、これまでに開発された行動的・薬理学的治療戦略の奏効率は低い。コカイン分解用に最適化された酵素ブチリルコリンエステラーゼ（BChE）の筋肉内注射による治療は、BChE の半減期が短いこともあり、動物モデルでの効果は限定的である。

薬物、とりわけコカインの乱用は、強迫的な薬物探索を伴い、長期にわたる摂取中止を経ても再発する場合が多い。コカインの過剰摂取による救急患者を治療するための効果的な戦略が求められているが、これまでに開発された行動的・薬理学的治療戦略の奏効率は低い。コカイン分解用に最適化された酵素ブチリルコリンエステラーゼ（BChE）の筋肉内注射による治療は、BChE の半減期が短いこともあり、動物モデルでの効果は限定的である。

http://www.natureasia.com/ja-jp/research/highlight/12692

英文記事：

https://www.sciencedaily.com/releases/2018/09/180917111609.htm

---

Gene therapy via skin protects mice from lethal cocaine doses

Modified skin grafts quickly degrade the drug and reduce drug-seeking behavior

Date:

September 17, 2018

Source:

University of Chicago Medical Center

Summary:

A new study shows that skin stem cells, modified via CRISPR and transplanted back to donor mice, can protect addicted mice from cocaine-seeking and overdose.

FULL STORY

There are no approved medications to treat either cocaine addiction or overdose. Frequent users tend to become less and less sensitive to the drug, leading to stronger or more frequent doses. The typical result is addiction. Exposure to the drug, or to drug-associated cues, even after long periods of abstention, often leads to relapse.

In the September 17, 2018 issue of *Nature Biomedical Engineering*, a University of Chicago research team led by Ming Xu, PhD, professor of Anesthesia & Critical Care, and Xiaoyang Wu, PhD, assistant professor in the Ben May Department for Cancer Research, describe a novel approach that was able to stifle the desire for cocaine and to protect against an overdose -- when tested in in mice.

The researchers had the three crucial mechanisms necessary to treat overdose and prevent addiction, according to Xu.

"We had an effective enzyme that can degrade cocaine with high efficiency," he said. "We had CRISPR, a genetic tool that enabled us to introduce a gene of interest inside the cell without

affecting other genes. And, most importantly we had technology, developed by my colleague Xiaoyang Wu, to put genetically modified skin cells back into an immunocompetent recipient. That saved us a lot of trouble."

The enzyme, butyrylcholinesterase (BChE), can degrade cocaine. But because of its short half-life, injecting BChE directly into muscle tissue has a profoundly limited effect.

To make long-lasting BChE, the authors collected primary epidermal basal progenitor/stem cells from newborn mice. They used CRISPR to deliver engineered human BChE to the cells.

Then they used a technique, developed by Wu, to prepare skin organoids and transplant them back to the donor animals, where they act as a depot for robust expression and secretion of hBChE into the blood stream. This efficiently protected the mice from cocaine-seeking and cocaine-induced relapse. It even prevented the death of mice exposed to uniformly lethal doses of cocaine.

Cutaneous gene therapy can be used as a "safe and effective way for treatment of non-skin diseases, including drug abuse, a scenario that has not been explored before," the authors note. "We demonstrated key evidence that engineered skin transplants can efficiently deliver hBChE in vivo and protect against cocaine-seeking and overdose."

These stem cells were well tolerated by the injected mice. The grafted skin cells exhibited normal epidermal stratification, proliferation and cell death.

Mice who received these skin grafts were able to remove cocaine from the bloodstream much faster than normal mice. They were able to withstand cocaine overdoses that would be lethal to 100 percent of unprotected mice.

Treated mice were less likely than untreated mice to enter environments previously associated with cocaine use. Mice exposed to alcohol, however, retained a learned fondness for that drug.

"Our study demonstrates that transplantation of genome-edited skin stem cells can be used to deliver an active cocaine hydrolase long term in vivo," the authors concluded. They showed that epidermal stem cells "can be successfully employed for ex vivo gene therapy, as efficient genetic manipulation is possible with minimal risk."

Skin transplantation protocols have been in clinical use for decades in the treatment of burn wounds, as well as vitiligo and skin genetic disorders, the authors note. These regenerated skin grafts "are stable and have been shown to survive long-term."

The skin-derived expression of hBChE in host mice with intact immune systems was stable for more than 10 weeks without significant decrease in hBChE. This suggests that the skin environment may limit any potential immune reaction toward hBChE.

The oldest mice in this study are now 12 months old and healthy, the authors note, which supports the feasibility of cutaneous gene therapy. "Taken together, our results show promise of cutaneous gene therapy as a safe and cost-effective therapeutic option for cocaine abuse in the future."

For cocaine addicts or those prone to cocaine abuse, this approach could reduce drug-seeking and protect against cocaine overdose, potentially making them "immune" to further cocaine abuse. This skin cell-based approach can potentially be used to treat alcohol, nicotine and opioid abuse and co-abuse.

Creative thinking about cocaine addiction and overdose is needed. About five percent of young adults in the United States (1.7 million people aged 18 to 25) have used cocaine at least once, according to the 2015 National Survey on Drug Use and Health. More than 900,000 Americans are dependent on, or abuse, this popular but illegal drug.

This study was funded by grants from the National Institutes of Health, the American Cancer Society and the V Foundation. Additional authors were Yuanyuan Li, Qingyao Kong, Jiping Yue and Xuewen Gou, all from the University of Chicago.

Story Source:

Materials provided by **University of Chicago Medical Center**. Original written by John Easton.
Note: Content may be edited for style and length.

Journal Reference:

1. Yuanyuan Li, Qingyao Kong, Jiping Yue, Xuewen Gou, Ming Xu, Xiaoyang Wu. **Genome-edited skin epidermal stem cells protect mice from cocaine-seeking behaviour and cocaine overdose**. *Nature Biomedical Engineering*, 2018; DOI: 10.1038/s41551-018-0293-z

---

Cite This Page:

- MLA
- APA
- Chicago

University of Chicago Medical Center. "Gene therapy via skin protects mice from lethal cocaine doses: Modified skin grafts quickly degrade the drug and reduce drug-seeking behavior." ScienceDaily. ScienceDaily, 17 September 2018. <www.sciencedaily.com/releases/2018/09/180917111609.htm>.

目次に戻る

9．新薬がマウスの膵臓癌増殖を阻止

2018 年 9 月 25 日

カリフォルニア州ロサンゼルス近郊の Cedars-Sinai 医療センター主導の研究によって、新たに開発された薬が最も一般的なタイプの膵臓癌が増殖して広がるのを防ぐことができるというマウス実験が示された。
最近 *Gastroenterology* 誌に掲載されたこの研究は、メタバート (Metavert) と呼ばれる新薬が、患者が現在使用している膵臓癌化学療法に対する抵抗性を発症するのを防ぐ可能性があることを示している。
研究者らは 4 年間にわたり癌細胞の活動を阻害する新化合物を設計合成する中で、メタバートが薬剤耐性を阻止し、またヒトにおいて一般に使用される放射線および化学療法のプラスの効果を有意に高めることを発見した。マウス実験の 1 つでは、メタバートは生存率を約 50%増加させた、としている。

英文記事：
https://www.sciencedaily.com/releases/2018/09/180925075105.htm

---

New drug blocks pancreatic cancer growth in mice, study finds

Date:

September 25, 2018

Source:

Cedars-Sinai Medical Center

Summary:

A newly developed drug can prevent the most common type of pancreatic cancer from growing and spreading in laboratory mice, according to a new study. The study also demonstrated in mice that the drug, Metavert, may prevent patients from developing a resistance to currently used pancreatic cancer chemotherapies.

FULL STORY

A newly developed drug can prevent the most common type of pancreatic cancer from growing and spreading in laboratory mice, according to a study led by Cedars-Sinai.

The study, published recently in the journal *Gastroenterology*, also demonstrated in mice that the drug, called Metavert, may prevent patients from developing a resistance to currently used pancreatic cancer chemotherapies.

"This is an exciting step toward improving survival rates in pancreatic cancer patients," said study lead author Mouad Edderkaoui, PhD, assistant professor of Medicine and Biomedical Sciences at the Samuel Oschin Comprehensive Cancer Institute at Cedars-Sinai. "If the results are confirmed in humans, we could have a drug with the potential to significantly extend the lives of patients with pancreatic ductal adenocarcinoma (PDAC), which is very difficult to treat."

Pancreatic cancer is the third-leading cause of cancer-related death in the United States, according to the American Cancer Society. This year, about 55,000 people in the U.S. will be diagnosed with the disease and more than 44,000 will die, making it one of the deadliest cancers. The pancreatic cancer five-year survival rate is 7 percent.

Ninety-five percent of pancreatic cancer patients are diagnosed with PDAC, which develops from cells lining small tubes in the pancreas. PDAC can be difficult to treat because the cancer cells prompt normal cells that reside in the pancreas -- called stellate cells -- to produce pancreatic scar tissue. Scar tissue makes it difficult for chemotherapy agents and blood to enter the pancreas, said study senior author Stephen J. Pandol M.D., director of Basic and Translational Pancreas Research at Cedars-Sinai.

The cancer and stellate cell interaction also creates an environment that stimulates local tumor growth and cancer spread to distant sites in the body, said Pandol, a professor of Medicine at Cedars-Sinai. Additionally, the activity levels of certain enzymes rev up, fueling resistance to cancer treatments.

"I've seen patients who respond to therapy for a while, and then the disease takes off because the cancer becomes smart -- it blocks chemotherapy from working," Pandol said. "Metavert targets that action."

Over a four-year period, the investigators designed and synthesized new chemicals that inhibit cancer cell activity. They discovered that Metavert blocked drug resistance and also significantly boosted the positive effects of radiation and two chemotherapy agents commonly used in humans. In one of the mouse studies, Metavert increased the survival rate by about 50 percent.

The investigators currently are developing a version of the drug to test in humans, Pandol said.

Story Source:

Materials provided by **Cedars-Sinai Medical Center**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Mouad Edderkaoui, Chintan Chheda, Badr Soufi, Fouzia Zayou, Robert Hu, V. Krishnan Ramanujan, Xinlei Pan, Laszlo G. Boros, Jian Tajbakhsh, Anisha Madhav, Neil Bhowmick, Qiang Wang, Michael Lewis, Richard Tuli, Aida Habtezion, Ramachandran Murali, Stephen J. Pandol. **An Inhibitor of GSK3B and HDACs Kills Pancreatic Cancer Cells and Slows Pancreatic Tumor Growth and Metastasis in Mice**. *Gastroenterology*, 2018; DOI: 10.1053/j.gastro.2018.08.028

Cite This Page:

- MLA
- APA
- Chicago

Cedars-Sinai Medical Center. "New drug blocks pancreatic cancer growth in mice, study finds." ScienceDaily. ScienceDaily, 25 September 2018. <www.sciencedaily.com/releases/2018/09/180925075105.htm>.

目次に戻る

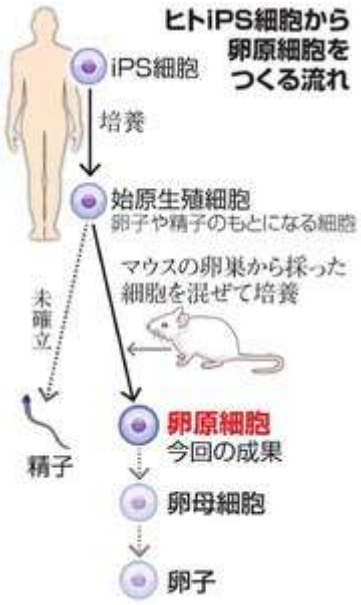
10. 再生医療 iPS 関連２本 -京大

2018 年 9 月 21、22 日

ヒトiPSから卵子「手前」の細胞　不妊症の解明へ道

野中良祐

2018 年 9 月 21 日 05 時 03 分



ヒトiPS細胞から卵原細胞をつくる流れ

ヒトの iPS 細胞から、卵子になる手前の段階にある「卵原細胞」の作製に成功したと、京都大の斎藤通紀教授（細胞生物学）らのチームが発表した。この細胞から、卵子をつくれるようになれば、不妊症の原因解明など、生殖医療に役立つ可能性がある。米科学誌サイエンス電子版に２１日、掲載される。

マウスでは、京大のチームが iPS 細胞から２０１１年に精子を、１２年に卵子をつくり、それぞれ子どもを誕生させることに成功している。一方、ヒトの iPS 細胞では、京大のチームが１５年、卵子と精子のもとになる「始原生殖細胞」の作製に成功した。しかし、マウスでは始原生殖

細胞から数日で卵原細胞になるのに対し、ヒトでは７０日以上かかり、その間に死滅してしまうなど、培養が難しく、作製の手法は確立していなかった。

今回、チームは、ヒトの iPS 細胞から変化させた始原生殖細胞を、マウスの赤ちゃんの卵巣から採った細胞と混ぜて培養した。この手法を使うと、一部は７０日を超えても生き残り、卵原細胞になることが分かった。卵原細胞に特徴的な複数の遺伝子が働いていることなどが確認できたという。

斎藤教授は「生殖細胞の発生のしくみはほとんどわかっておらず、卵子に誘導する技術を確立して解明していきたい」と話す。

卵原細胞ができたことで、そこから卵母細胞、卵子へと作製が進む道筋が見えてきた。ただ、人工的に卵子や精子をつくることには、倫理的な問題も指摘されている。このため、国の指針では、ヒトの iPS 細胞から卵子や精子をつくることは認める一方、受精させることは禁じている。

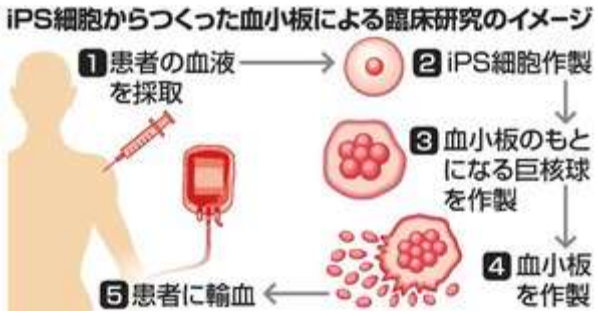
（野中良祐）

https://www.asahi.com/articles/ASL9M3HGRL9MPLBJ006.html

iPS血小板輸血、臨床へ　血液の難病治療　厚労省部会了承

野中良祐

2018 年 9 月 22 日 05 時 00 分



出血を止める働きをする血小板を iPS 細胞からつくり、血液の難病「再生不良性貧血」の患者に輸血する京都大の臨床研究について、厚生労働省の部会は２１日、計画を了承した。

血液の病気では iPS 細胞からつくった細胞を実際の患者に使うのは、世界で初めて。1 年以内には輸血を始めたいという。

■献血頼み解消に道

血小板製剤を含む血液製剤は献血によってつくられているが、少子高齢化などの影響で献血する人が減っている。iPS 細胞から血液製剤ができるようになれば、将来の血液製剤の供給にも役立ち、献血に依存している医療現場に与える影響は大きい。

再生不良性貧血は、免疫の異常などで、体内で白血球や血小板などの血液成分が十分につくれなくなる難病。国内の患者数は約 1 万人とされる。京大の江藤浩之教授らのチームが進める計画では、献血による血小板製剤では拒絶反応が起きて効果が出ない、特殊なタイプの患者 1 人に実施する。すでに患者は決まっており、募集はしない。

患者自身の血液をもとにした iPS 細胞から血小板を作製。半年ほどの間に 3 回輸血し、1 年かけて安全性や有効性を確かめる。

血液の病気に詳しい金沢大の中尾真二教授（血液内科）は「血小板がつくれない病気はほかにもあり、応用範囲は広い。現状は、（拒絶反応が起きないように）免疫の型が合う献血者に個別に依頼し、血小板を採るケースもある。献血者の負担軽減の面でも、意義は大きい」と話す。

iPS 細胞を使った再生医療は、２０１４年に目の難病患者に対する網膜組織の移植から始まった。今年に入り、心不全やパーキンソン病でも計画が進展。ほかに、角膜の病気や脊髄（せきずい）損傷などでも計画が進み、臨床応用への動きが加速している。

（野中良祐）

https://www.asahi.com/articles/ASL9P7SBSL9PUBQU01G.html?iref=pc_ss_date