BIO NEWS

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In-Vivo Science International Inc.

1230 Bordeaux Drive

Sunnyvale, CA 94089, USA

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・英国の EU 離脱に伴う本拠移転で欧州医薬品庁（EMA）職員の約 25%が失われる（1/15)
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・Bayer が米国事業のかつての重要拠点、ペンシルバニア州ピッツバーグ近郊 Robinson 拠点、を閉鎖～12,000 職削減を伴う大規模再編（1/17）
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・世界のコーヒー生産維持に不可欠な野生種の半数超が絶滅の恐れあり（1/20）
・Novartis、オックスフォード大学の AI 技術で治療効果の予測因子同定の試み（1/21）
・「ゲノム編集の双子」中国当局が事実と認める　世界初（1/21）

中国広東省の南方科技大の賀建奎副教授が「ゲノム編集により遺伝子を改変した受精卵で双子を誕生させた」と発表した問題で、同省の調査チームは賀氏の主張は事実だと認定した。動機については自分の名声や利益を追い求めるため、としている。国営新華社通信が２ １日に伝えた。ゲノム編集された子どもが生まれたのは世界で初めて。

賀氏は昨年１ １月、香港大で開かれた国際会議で、ゲノム編集を経た双子の誕生を発表した。しかし、根拠となる具体的な情報を明らかにしなかったため、「真偽不明」として国内外で疑問視されていた。当局が事実だと認めたことで、今後、倫理面や安全性に問題があるとする批判が、さらに高まりそうだ。（広州＝益満雄一郎）

https://headlines.yahoo.co.jp/hl?a=20190121-00000057-asahi-int

・慶応大名誉教授/物理学者　米沢富美子さん死去　日本女性科学者の草分け的存在（1/21）
・遺伝子編集赤ちゃんを作った中国研究者が倫理報告を捏造したと報じられている（1/22）

https://www.sciencemag.org/news/2019/01/scientist-behind-crispr-twins-sharply-criticized-government-probe-loses-job?utm_campaign=news_daily_2019-01-21&et_rid=375979900&et_cid=2612200

・武田薬品が 30 億ドルの新興市場資産売却を検討（1/22）

620 億ドルでの Shire 買い取りに伴う膨大な負債を減らす取り組みの一環として武田薬品が新興市場薬の売却を検討しているとの垂れ込み情報を Bloomberg が報じている。

・米国の 1 型糖尿病患者 1 人あたりのインスリン費用が 2012-2016 年におよそ 2 倍に　（1/23）
・Vertex の長年の CFO・Ian Smith が不埒な振る舞いにより解雇された（1/24）
・ゲノム編集サルから５匹のクローン誕生、世界初か　-中国（1/24）
・Merck & Co、エボラワクチンを流行が続くコンゴ共和国に出荷（1/25）
・Roche、戦略事業長 Alexander Hardy 氏を Genentech の CEO に任命（1/25）
・フィンランドの 50 万人のゲノム解析試験 FinnGen に GSK と Sanofi が参加（1/27）

フィンランドの 50 万人の医療データとゲノム情報を解析して医学や治療に活かす取り組み FinnGen に GlaxoSmithKline（GSK）と Sanofi が加わる。Abbvie, AstraZeneca, Biogen, Celgene, Roche 子会社 Genentech, Merck & Co, Pfizer も既に FinnGen のメンバー。

・AbbVie の総売上げの 6 割を担う Humira が 200 億ドル達成ならず（1/28)

AbbVie の売り上げのおよそ 6 割を生み出している超大成功関節リウマチ（RA）薬 Humira（adalimumab）の 2018 年の売り上げはアナリストや同社経営陣が予想していた 200 億ドルには至らず、残念ながら来年もその達成は難しいようだ。

達成すれば史上初の 200 億ドル薬となったが、2018 年の米国での売り上げは 136 億 8,500 万ドル、米国外では 62 億 5,100 万ドル、それらを合わせた総額は 199 億 3,600 万ドル。

欧州で去年 10 月に発売されたばかりの Humira バイオシミラーは既に非常に好調で、発売から最初の 1 年間で Humira の 50%がバイオシミラーと入れ替わると Bernstein のアナリスト Ronny Gal 氏は予想している。

・英国、次世代の人工知能（AI）技術に取り組む 1000 の博士課程を新設（1/28)

・米国の薬局大手 CVS が Teva と Lilly の CGRP 片頭痛薬を採用～Amgen のは落選（1/29)

・遺伝子改変した受精卵での妊娠認めず　日本政府有識者会議（1/31)

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1. 第 37 回 JP モルガン・ヘルスケアカンファレンス

2019 年 1 月 4 日

1 月 7 日から 10 日まで、サンフランシスコ ユニオンスクエアで、「第 37 回 JP モルガン・ヘルスケアカンファレンス」が開催される。同カンファレンスは、ライフサイエンス業界最大の年間会議の 1 つで、世界中の何千人もの投資家や役員がサンフランシスコに集まり、最新の技術革新を発表して次のパートナーや投資家を探す場となっている。

英文記事：
https://www.jpmorgan.com/global/healthcareconference

37th Annual J.P. Morgan

HEALTHCARE

CONFERENCE

January 7 - 10, 2019

Westin St. Francis Hotel | San Francisco, California

About

The annual J.P. Morgan Healthcare Conference is the largest and most informative healthcare investment symposium in the industry, bringing together industry leaders, emerging fast-growth companies, innovative technology creators, and members of the investment community.

9,000450 +TOTAL ATTENDEESPRIVATE + PUBLICCOMPANIES

History

What is today known as the annual J.P. Morgan Healthcare Conference began in 1983 and was hosted by Hambrecht & Quist (H&Q). H&Q was acquired by Chase in 2000 and a year later Chase was acquired by J.P. Morgan. At its infancy, the conference featured just 20 companies, had about 200 attendees and focused on the biotech industry.

Today, while it is still at the Westin St. Francis in San Francisco, the annual J.P. Morgan Healthcare Conference brings thousands of investors from around the world together. The hundreds of companies presenting run the gamut, from start-ups to those with more than $300 billion in market cap, and encompass the entire global healthcare landscape, including pharmaceutical

firms, healthcare service providers, profit and not-for-profits, and medical device companies.

Keynotes

Monday

Jamie Dimon

Chairman and Chief Executive Officer, JPMorgan Chase & Co.

Tuesday

Dr. Scott Gottlieb

Commissioner of the Food & Drug Administration (FDA)

Wednesday

James Carville

Political Icon

Interviewed by:

Maria Bartiromo

Anchor and Global Markets Editor, FOX Business Network

Interviewed by:

Cory Kasimov

Managing Director and Senior Biotechnology Analyst, J.P.

Morgan

&

Mary Matalin

Celebrated Conservative Voice and Former Presidential Advisor

&

Chris Schott

Managing Director and Senior Analyst, U.S. Major and Specialty Pharmaceuticals, J.P. Morgan

Interviewed by:

Peter Engel

Vice Chairman, Investment Banking, J.P. Morgan

FAQs

What are the dates for the 2019 conference (displays following content on page)

January 7-10, 2019

How do I register for the conference? (displays following content on page)

The J.P. Morgan Healthcare conference is for clients of the firm, by invitation only. Please reach out to your J.P. Morgan representative to inquire about passes.

Can I register onsite? (displays following content on page)

Registration closes prior to the conference date. There is no onsite registration.

Can I listen to company presentations if I'm unable to attend in-person? **(displays following content on page)**

Yes. Some company presentations will also be available via webcasts.

Where do I get a copy of the agenda? **(displays following content on page)**

The agenda is made available only to confirmed attendees.

Are media permitted to attend the conference? **(displays following content on page)**

Yes; there are a limited number of press passes for the event.

What is your media policy? **(displays following content on page)**

All company presentations are considered on-the-record unless otherwise specified. Luncheon keynotes are off-the-record.

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2. ヒルシュスプルング病の新しいマウスモデルの開発

2019 年 1 月 7 日

約 5,000 人に 1 人の割合で乳児が遠位結腸の腸管神経細胞なしで生まれ、その結果ヒルシュスプルング病を発症する。ニューロンを欠くため、腸の内容物は正常に通過することができず、便秘および結腸の拡大をもたらす。
この状態は、冒された腸の部分を外科的に除去することによって治療されるが、患者は依然として小腸結腸炎、または消化管の炎症を起こす危険性が高く、これがヒルシュスプルング病の生命を脅かす主な合併症となっている。
ヒルシュスプルング病の症例の約半分は、RET と呼ばれる遺伝子の突然変異によって引き起こされるため、ヘルシンキ大学の研究者らは、この疾患の最初のマウスモデルを開発し、それに関連した *RET* シグナル伝達の欠損を伴う腸炎の発生および特徴を説明している。この知見は、*Cellular and Molecular Gastroenterology and Hepatology* 誌に発表されている。

英文記事：
https://www.sciencedaily.com/releases/2019/01/190107131216.htm

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Scientists developed new mouse model of Hirschsprung's disease

Date:

January 7, 2019

Source:

University of Helsinki

Summary:

Researchers have developed a new mouse model of Hirschsprung's disease and associated enterocolitis and shed light on the disease progression.

FULL STORY

About one in every 5,000 babies is born without enteric neurons in distal colon resulting in Hirschsprung's disease. Because of the lacking neurons, contents of the gut cannot pass normally resulting in constipation and enlargement of colon.

The condition is treated with a surgical removal of the affected gut part, but the patients remain at high risk of enterocolitis, or inflammation of the gut. This is the major life threatening complication of Hirschsprung's disease.

About half of the Hirschsprung's disease cases are caused by mutations in a gene called RET. RET is a receptor, a large protein molecule, which is located at the surface of the cell to receive signals from other cells. During development, a complex formed by two proteins called GDNF and GFRa1 binds to RET and activates signaling required for normal development of the enteric neurons.

For developing new treatments, animal models of the disease are most often a prerequisite. This work lead by Associate Professor Jaan-Olle Andressoo describes generation and characterization of the first viable mouse model of Hirschsprung's disease and associated enterocolitis with a defect in GDNF/GFRa1/RET signaling thus representing most patients.

This is important because so far animal studies of Hirschsprung's disease have used model systems that represent a minority of the genetic mutations in Hirschsprung's disease.

Using the new mouse model scientists at the University of Helsinki were now able to shed further light on the chronology of events in enterocolitis. They found that mucin producing goblet cells, a specific type of cells responsible for lubricating the inner surface of the gut, may be a potential target for preventative treatment.

Scientists also conclude that reduced expression of GFRa1 can contribute to susceptibility to Hirschsprung's disease. The new mouse model will serve as a useful tool for enhancing understanding of the disease and for defining treatment in the future.

Story Source:

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

Journal Reference:

1. L Lauriina Porokuokka, Heikki T. Virtanen, Jere Lindén, Yulia Sidorova, Tatiana Danilova, Maria Lindahl, Mart Saarma, Jaan-Olle Andressoo. **Gfra1 under-expression causes Hirschsprung's disease and associated enterocolitis in mice**. *Cellular and Molecular Gastroenterology and Hepatology*, 2018; DOI: 10.1016/j.jcmgh.2018.12.007

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University of Helsinki. "Scientists developed new mouse model of Hirschsprung's disease." ScienceDaily. ScienceDaily, 7 January 2019. <www.sciencedaily.com/releases/2019/01/190107131216.htm>.

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3. マウスで不眠症研究

2019 年 1 月 9 日

セントルイスのワシントン大学医学部の研究者らは、遺伝性疾患　1 型神経線維腫症 (NF1) を患う人が経験するのと類似した睡眠障害のあるマウスを研究している。このマウスは、NF1 を模倣するように遺伝子操作されており、NF1 または他の要因に関連する不眠症について解明するのに役立つとして、その調査結果を 1 月 4 日の *Journal of Sleep Research* 誌に発表した。
これによると、通常、マウスは日中に眠り、ヒトと同様に、深い眠り（夢なし）から REM 睡眠（夢あり）まで、数回の周期を繰り返す。しかし、NF1 変異を持つマウスは、深い眠りに入った直後に目覚める傾向にあり、その結果、断片化した、おそらく安らかではない睡眠を繰り返すことになる、としている。

英文記事：
https://www.sciencedaily.com/releases/2019/01/190109102425.htm

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Mice sleeping fitfully provide clues to insomnia

Genetically engineered mice mimic common sleep problems

Date:

January 9, 2019

Source:

Washington University School of Medicine

Summary:

Researchers working with mice with sleep problems similar to those experienced by people with the genetic disease neurofibromatosis type 1 (NF1) -- believe the animals will help shed light on insomnia linked to NF1 or other factors.

FULL STORY

Mice that sleep fitfully could help researchers unravel the mystery of insomnia.

Researchers at Washington University School of Medicine in St. Louis studied mice genetically modified to mimic the genetic disease neurofibromatosis type 1 (NF1), which is associated with sleep problems. They found that the animals, like some people with NF1, slept in short, irregular spurts. Studying these mice could help identify the molecular and cellular mechanisms that go awry and cause fragmented sleep patterns in people with and without the disease, the researchers said.

"The mice are a tool for us to understand how sleep disturbances arise and how sleep disruption contributes to problems with learning and attention," said David H. Gutmann, MD, PhD, the Donald O. Schnuck Family Professor of Neurology and the study's senior author. "This could apply both to people with NF1 and others without NF1 who also have sleep problems."

The findings were published Jan. 4 in the *Journal of Sleep Research*.

As many as half of people with NF1 -- a condition that causes benign tumors in the brain and on nerves throughout the body -- have difficulty falling or staying asleep. Learning disabilities and attention problems also are common in children with NF1, and both may be exacerbated by poor sleep. But doctors don't know why some children with NF1 develop sleep problems and others don't, nor can they do much to help them sleep better.

"Right now we just treat children and adults with NF1 and sleep problems like we treat patients without NF1 because we don't understand what causes them," said Gutmann, who also directs the Neurofibromatosis Center at Washington University.

Co-first author Corina Anastasaki, PhD, an instructor in neurology, bred mice with a mutation in their Nf1 gene similar to what is seen in people with NF1. Then, co-first author Nicholas Rensing and Michael J. Wong, MD, PhD, the Allen P. and Josephine B. Green Professor of Pediatric

Neurology, fitted onto the mice miniature versions of the caps people wear for sleep studies, enabling them to measure brain waves and identify sleep patterns.

Mice normally sleep during the day and, like people, cycle several times from deep, dreamless sleep to REM sleep -- or dreaming -- and back again. Mice with an Nf1 mutation, however, tended to wake up soon after they entered deep sleep. The result was a fragmented, and probably not restful, day of sleep.

"Throughout the whole night and day, they fell asleep and woke up when they shouldn't have," Anastasaki said. "They fell into deep sleep, but they didn't stay there."

Although the mice were engineered to mimic human NF1 disease, they could yield insights about the biological underpinnings of sleep in general, which could help people with sleep problems unrelated to NF1. About a third of American adults report some degree of insomnia, and 15 percent have chronic insomnia that lasts three months or more.

"It is hard to study sleep problems in people because there are so many factors that influence how well you sleep -- maybe you're stressed out, maybe you're sick, maybe you're taking care of a new baby," Gutmann said. "But now we have a controlled system that we can use to start looking at which cells and proteins are involved, and which biological factors influence sleep quality. Only when we understand the problem better will we be able to find better ways to treat it."

Story Source:

Materials provided by **Washington University School of Medicine**. Original written by Tamara Bhandari. *Note: Content may be edited for style and length.*

Journal Reference:

1. Corina Anastasaki, Nicholas Rensing, Kevin J. Johnson, Michael Wong, David H. Gutmann. **Neurofibromatosis type 1 (Nf1)-mutant mice exhibit increased sleep fragmentation**. *Journal of Sleep Research*, 2019; e12816 DOI: 10.1111/jsr.12816

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- Chicago

Washington University School of Medicine. "Mice sleeping fitfully provide clues to insomnia: Genetically engineered mice mimic common sleep problems." ScienceDaily. ScienceDaily, 9 January 2019. <www.sciencedaily.com/releases/2019/01/190109102425.htm>.

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４．健康な乳児からの腸内微生物がマウスのミルクアレルギー発症を阻止

2019 年 1 月 14 日

NHI/国立アレルギー感染症研究所によると、シカゴ大学の研究者らの新しい研究で、腸内微生物が牛乳アレルギーの発症の予防に役立つ可能性があることが発見された。
研究者らは、マウスに移植された健康なヒトの乳児ドナーからの腸内微生物が、牛乳にさらされたマウスに対してアレルギー反応を起こさないように保護することを発見した。また、牛乳にアレルギーのある乳児から移植された場合には、このような保護効果は観られなかった、としている。
研究者らは、以前、牛乳アレルギーの乳児は、非アレルギー性の乳児とは異なる組成の腸内微生物を持っていること、又、いくつかの微生物は食物アレルギー発症の危険性が低いことと関連があることを明らかにしている。
今日 *Nature Medicine* 誌のオンライン版で説明されているこの知見は、食物アレルギーの予防・治療に対して微生物叢ベースの治療法開発に役立つ可能性がある。

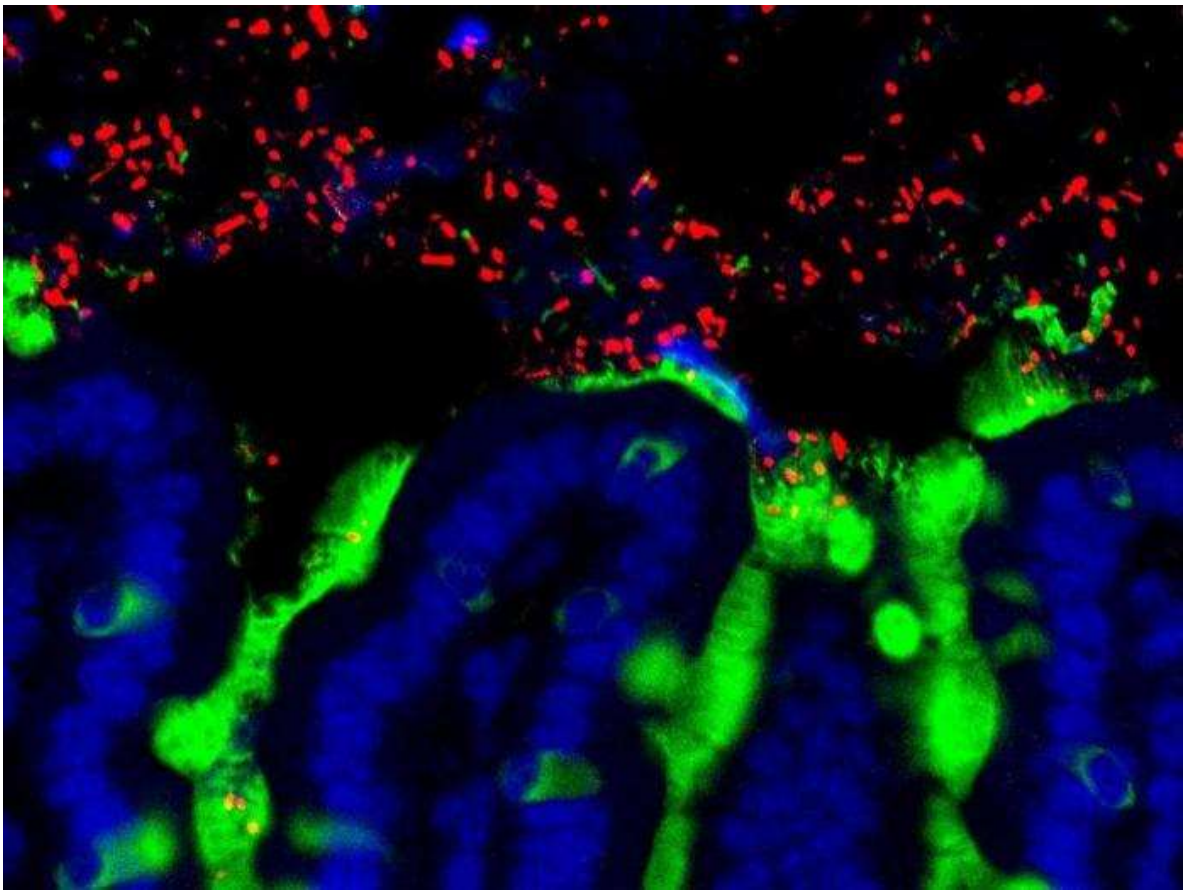
英文記事：
https://www.scienceandtechnologyresearchnews.com/gut-microbes-from-healthy-infants-block-milk-allergy-development-in-mice/

Health Gut Microbes from Healthy Infants Block Milk Allergy Development in Mice

Gut Microbes from Healthy Infants Block Milk Allergy Development in Mice

NIH-funded study links gut microbiome to food allergy.

January 16, 2019



Commensal bacteria (red) reside amongst the mucus (green) and epithelial cells (blue) of a mouse small intestine.
The University of Chicago

New research suggests that the gut microbiome may help prevent the development of cow's milk allergy. Scientists at the University of Chicago found that gut microbes from healthy human infant donors transplanted into mice protected animals exposed to milk from experiencing allergic reactions, while gut microbes transplanted from infants allergic to milk did

not. The work, described online today in *Nature Medicine*, was supported in part by NIH's National Institute of Allergy and Infectious Diseases. The findings may inform research to develop microbiome-based therapies to prevent or treat food allergy.

Scientists previously found that infants allergic to cow's milk had different compositions of gut microbes than non-allergic infants. Previous studies also revealed that some microbes are associated with a lower risk of developing food allergy, leading researchers to examine whether gut microbes of infants without milk allergy might be protective.

Researchers transplanted gut microbes from each of eight infant donors into groups of mice raised in a sterile environment and sensitized to milk protein—meaning the animals' immune systems created allergic antibodies to milk. When later exposed to milk, mice receiving no microbes or microbes from milk-allergic children produced allergic antibodies and experienced anaphylaxis, a potentially life-threatening allergic reaction. Mice receiving gut microbes from non-allergic infants had no reactions.

Investigators then analyzed microbes in infant stool samples, finding many differences between the stool of infants who were allergic to milk and those who were not. Mice transplanted with microbes from non-allergic infants also harbored a family of microbes previously found to protect against developing food allergies. Further experiments identified one microbe, *Anaerostipes caccae*, that prevented the development of milk allergy when transplanted alone into groups of mice. Researchers then sampled cells along the mice's gut linings—where food allergies in mice and humans begin to develop. They found that mice that received microbes from non-allergic infants expressed different genes compared to those that did not, suggesting that microbes residing in the gut impact the host's immune system. The researchers conclude that intestinal microbes play a

critical role in regulating allergic responses to food and suggest that further research could lead to microbiome-modifying therapies to prevent or treat food allergy.

SOURCE National Institutes of Health (NIH)

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5. 代謝の「魔法の弾丸」タンパク質の健康への効果

2019 年 1 月 15 日

代謝タンパク質 AMPK は、健康のための一種の魔法の弾丸と言われてきた。動物モデルの研究では、このタンパク質を活性化する化合物が、糖尿病の回復、心血管の健康改善、ミトコンドリア病の治療、更には寿命を延ばすための健康増進効果を持つことを示している。しかし、これらの化合物の影響のうちどれだけが AMPK に完全に起因し得るかは分かっていない。
そこで、今回ソーク研究所の研究者らは、この代謝タンパク質 AMPK が、その分子的機能および治療的機能をどのように、どこで、いつ発揮するのか、これまで以上に詳細に研究できる新システムを開発し、その論文が 1 月 2 日に *Cell Reports* 誌に掲載された。
この論文によると、研究チームは、脂肪肝疾患の成体マウスの肝臓で AMPK を活性化するために新しいモデルを使用している。
この新しいマウスモデルでは、マウスが特別なバージョンの AMPK を持つことを可能にしており、これによって研究者が成体マウスに抗生物質を与えることによって遺伝子を活性化することができる。さらに、マウスの誘導性 AMPK 遺伝子をダブルエンジニアリングすることによって、体内のどこでこの AMPK 活性化が起こるのかを制御することもできる、としている。

英文と記事：
https://www.sciencedaily.com/releases/2019/01/190115111944.htm

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Health effects of metabolic 'magic bullet' protein

New model lets scientists activate health-promoting enzyme AMPK at any time and in any tissue

Date:

January 15, 2019

Source:

Salk Institute

Summary:

Researchers have developed a new system that lets them study in more detail than ever exactly how, where and when the metabolic protein AMPK carries out its molecular and therapeutic functions.

FULL STORY

The metabolic protein AMPK has been described as a kind of magic bullet for health. Studies in animal models have shown that compounds that activate the protein have health-promoting effects to reverse diabetes, improve cardiovascular health, treat mitochondrial disease -- even extend life span. However, how much of the effects of these compounds can be fully attributed to AMPK versus other potential targets is unknown.

Now, Salk researchers have developed a new system that lets them study in more detail than ever exactly how, where and when AMPK carries out its molecular and therapeutic functions. In the paper, published January 2, 2019 in the journal *Cell Reports*, the Salk team uses the new model to activate AMPK in the livers of adult mice with fatty liver disease.

"This model will allow us to answer questions that scientists could not answer before," says Salk Professor and Salk Cancer Center Director Reuben Shaw, who led the new work. "It really gives us a new way to define the health benefits of this specific enzyme in a wide variety of diseases."

AMP-activated protein kinase, or AMPK, is known as a master regulator of metabolism. Cells activate AMPK when they are running low on energy, and AMPK is activated in tissues throughout the body following exercise or during calorie restriction. In response, AMPK alters the activity of many other genes and proteins, helping keep cells alive and functioning even when they're running low on fuel. In different tissues throughout the body and at different time points in development, AMPK likely has varying effects. Until now, the only way to study the specific impact

of genetically increasing AMPK activity was to change its activity in an organism for its entire life, starting at embryogenesis.

"When AMPK is overactivated from the very beginning of embryogenesis, we don't know what effects it's having on normal development," says Daniel Garcia, a senior research associate at Salk and first author of the new paper.

So Garcia, Shaw and their colleagues enabled a mouse to have a special version of AMPK that lets the researchers activate the gene by feeding the adult mouse an antibiotic.

"The model we've developed is much more similar to what you would see in a clinic if you target AMPK with drugs," says Garcia.

Moreover, by double-engineering the inducible AMPK gene in the mice, the researchers can also control where in the body this AMPK activation happens -- everywhere, or just in a select tissue or tissues.

To test the utility of the new model, the researchers developed mice that could have AMPK activated in the liver. Then, they fed a subset of these mice high-fat diets leading to diet-induced obesity and an excess accumulation of fats in the liver. This condition is equivalent to nonalcoholic fatty liver disease (NAFLD) in humans, the leading form of chronic liver disease in American adults.

In both mice with and without NAFLD, levels of fats in the liver dropped when AMPK was activated -- new fat production was slowed and existing fats were metabolized. Moreover, when AMPK was activated in mice that were fed a high-fat diet, the mice were protected against weight gain and obesity and had fewer signs of liver inflammation.

"This paper confirms that AMPK is a good target for treating NAFLD," says Garcia. "It's further confirmation that AMPK activators should be tested clinically."

In addition to the effects on liver fat, AMPK activation -- even though it was limited to the liver -- also lowered levels of fats elsewhere in the body, suggesting that hormones released by the liver into the rest of the body were affected.

"These results indicate that AMPK could potentially be a powerful treatment to a host of diseases in humans," says Shaw, who holds the William R. Brody Chair.

The researchers next plan to study AMPK activation in a plethora of other tissues, including muscles, where scientists have hypothesized AMPK could have a dramatic effect.

"There are broader questions beyond NAFLD to ask about whether genetic activation of AMPK in muscle mimics exercise and whether activation of AMPK later in an organism's life can promote life span," says Shaw.

Story Source:

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

Journal Reference:

1. Daniel Garcia, Kristina Hellberg, Amandine Chaix, Martina Wallace, Sébastien Herzig, Mehmet G. Badur, Terry Lin, Maxim N. Shokhirev, Antonio F.M. Pinto, Debbie S. Ross, Alan Saghatelian, Satchidananda Panda, Lukas E. Dow, Christian M. Metallo, Reuben J. Shaw. **Genetic Liver-Specific AMPK Activation Protects against Diet-Induced Obesity and NAFLD**. *Cell Reports*, 2019; 26 (1): 192 DOI: 10.1016/j.celrep.2018.12.036

Cite This Page:

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- APA
- Chicago

Salk Institute. "Health effects of metabolic 'magic bullet' protein: New model lets scientists activate health-promoting enzyme AMPK at any time and in any tissue." ScienceDaily. ScienceDaily, 15 January 2019. <www.sciencedaily.com/releases/2019/01/190115111944.htm>

目次に戻る

6. 糖尿病治療に幹細胞アプローチで新たな希望

2019 年 1 月 17 日

糖尿病のより効果的な治療法を開発しようとしている科学者らは幹細胞に注目している、幹細胞は血糖を制御するホルモンであるインスリンを生産する細胞に変換させることが可能だからだ。しかし、ここでの大きな課題は、これらの細胞によって生産されるインスリンの量を制御することである。

セントルイスのワシントン大学医学部の研究チームは、ヒト幹細胞をインスリン分泌β細胞に同軸化するためのレシピを調整することによって、得られた細胞が血中グルコースレベルの変動に対してより敏感であることを示した。

インスリンを作ることができないマウスにこのβ細胞を移植した時、新たな細胞が数日以内にインスリンを分泌し始め、数ヶ月間マウスの血糖をコントロールすることができた、としている。

この研究は、1 月 17 日に *Stem Cell Reports* 誌で発表された。

英文記事：

https://medicalxpress.com/news/2019-01-stem-cell-approach-diabetes.html

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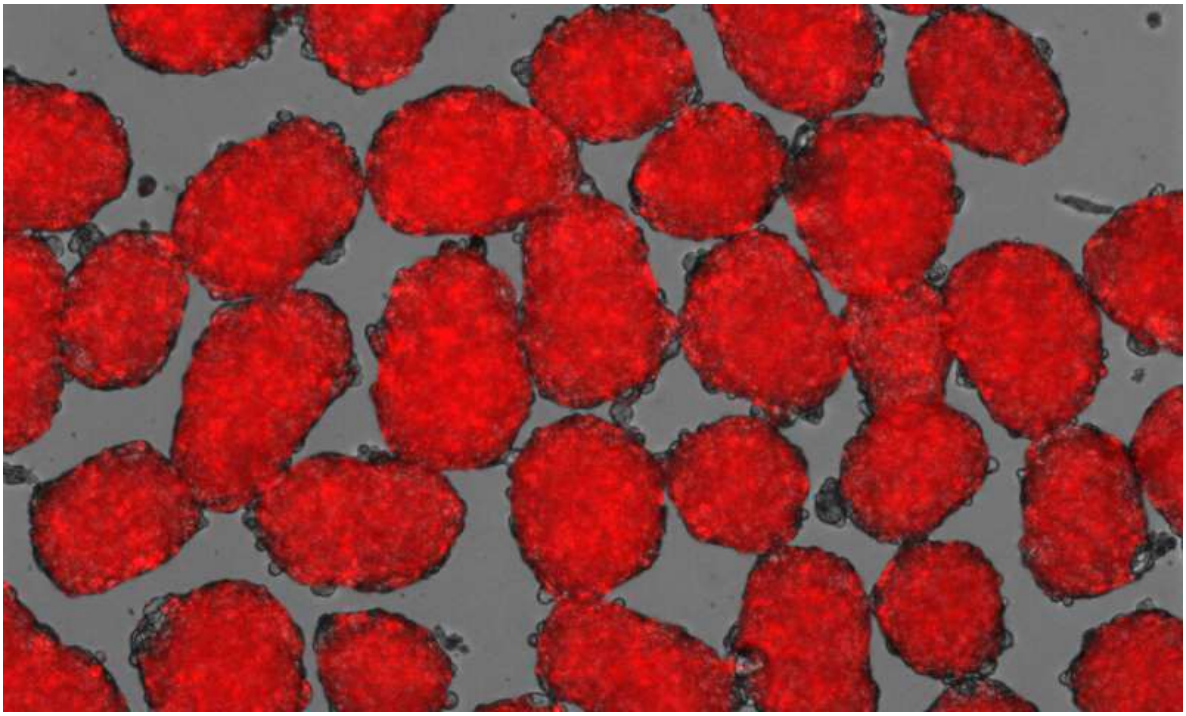
JANUARY 17, 2019

New hope for stem cell approach to treating diabetes

by Jim Dryden, Washington University School of Medicine



Researchers at Washington University School of Medicine in St. Louis have tweaked the recipe for coaxing human stem cells into insulin-secreting beta cells and shown that the resulting cells are more responsive to fluctuating glucose levels in the blood. Here, the new beta cells appear red as they secrete insulin in response to glucose. Credit: Millman lab, Washington University

Scientists working to develop more effective treatments for diabetes are turning to stem cells. Such cells can be transformed into cells that produce insulin, the hormone that controls blood sugar.

But there's a major challenge: the amount of insulin produced by theses cells is difficult to control.

Now, by tweaking the recipe for coaxing human stem cells into insulin-secreting beta cells, a team of researchers at Washington University School of Medicine in St. Louis has shown that the resulting cells are more responsive to fluctuating glucose levels in the blood.

When they transplanted the beta cells into mice that could not make insulin, the new cells began secreting insulin within a few days, and they continued to control blood sugar in the animals for months.

The new study is published Jan. 17 in the journal *Stem Cell Reports*.

"We've been able to overcome a major weakness in the way these cells previously had been developed. The new insulin-producing cells react more quickly and appropriately when they encounter glucose," said principal investigator Jeffrey R. Millman, Ph.D., an assistant professor of medicine and of biomedical engineering. "The cells behave much more like beta cells in people who don't have diabetes."

The researchers now believe it may be time to evaluate whether the same stem-cell approach could produce insulin and effectively control blood sugar in people.

Millman was a part of a research team at Harvard that, in 2014, converted skin cells into stem cells and, in 2016, did the same thing with skin cells from a patient with diabetes. Each time, the stem cells

were then treated with various growth factors to coax them into insulin-secreting beta cells. The beta cells, however, didn't work as well as the researchers had hoped.

"Previously, the beta cells we manufactured could secrete insulin in response to glucose, but they were more like fire hydrants, either making a lot of insulin or none at all," he said. "The new cells are more sensitive and secrete insulin that better corresponds to the glucose levels."

For this study, Millman's laboratory still grew beta cells from human stem cells, but they made numerous changes to the "recipe" for producing insulin-producing beta cells, treating the cells with different factors at different times as they grew and developed to help the cells mature and function more effectively.

After that process was complete, the researchers transplanted the beta cells into diabetic mice with suppressed immune systems so that they wouldn't reject the human cells. Those transplanted cells produced insulin at levels that effectively controlled blood sugar in the mice, functionally curing their diabetes for several months, which, for most of the mice in the study, was about the length of their lives.

As laboratory researcher rather than a clinician, Millman said he can't predict exactly when such cells may be ready for human trials

but believes there are at least two ways that stem cell-derived beta cells could be tested in human patients.

"The first would be to encapsulate the cells in something like a gel—with pores small enough to prevent immune cells from getting in but large enough to allow insulin to get out," he said. "Another idea would be to use gene-editing tools to alter the genes of beta cells in ways that would allow them to 'hide' from the immune system after implantation."

Millman said that if stem cell-derived beta cells are proven safe and effective for people with diabetes, his method of manufacturing the cells quickly could be ramped up to an industrial scale. In his laboratory alone, his team is able to grow and develop more than a billion beta cells in just a few weeks.

Explore further

Scientists discover mechanisms behind neonatal diabetes

More information: Velazco-Cruz L, Song J, Maxwell KG, Goedegebuure MM, Augsornworawat P, Hogrebe NJ, Millman JR. Acquisition of dynamic function in human stem cell-derived beta cells. *Stem Cell Reports*, Jan 17, 2019. DOI: 10.1016/j.stemcr.2018.12.012

Provided by Washington University School of Medicine

目次に戻る

7. 免疫系を活性化して癌を食す

– 抗腫瘍反応を高めるためにマクロファージをプライミングする方法

2019 年 1 月 21 日

ペンシルベニア大学 Abramson Cancer Center の研究者らは、癌細胞を攻撃して食べるのに必要なエネルギーをいかにしてマクロファージと呼ばれる免疫細胞に補給するか、その方法を特定した、として今日の *Nature Immunology* 誌上で発表している。
マクロファージが癌細胞の増殖を支えて広げるか、または妨げるかは充分に確立されているが、ほとんどの腫瘍は CD47 と呼ばれるシグナルを発現しており、これがマクロファージを深い眠りへと誘い込み、それらが機能しないようにすることがある。研究者らは、マクロファージの代謝を再配線することでこのシグナルを克服し、目覚まし時計のように機能してマクロファージを作動させて仕事に行かせる方法を発見した、としている。

英文記事：
https://www.sciencedaily.com/releases/2019/01/190121115403.htm

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Energizing the immune system to eat cancer

Method of priming macrophages to boost anti-tumor response

Date:

January 21, 2019

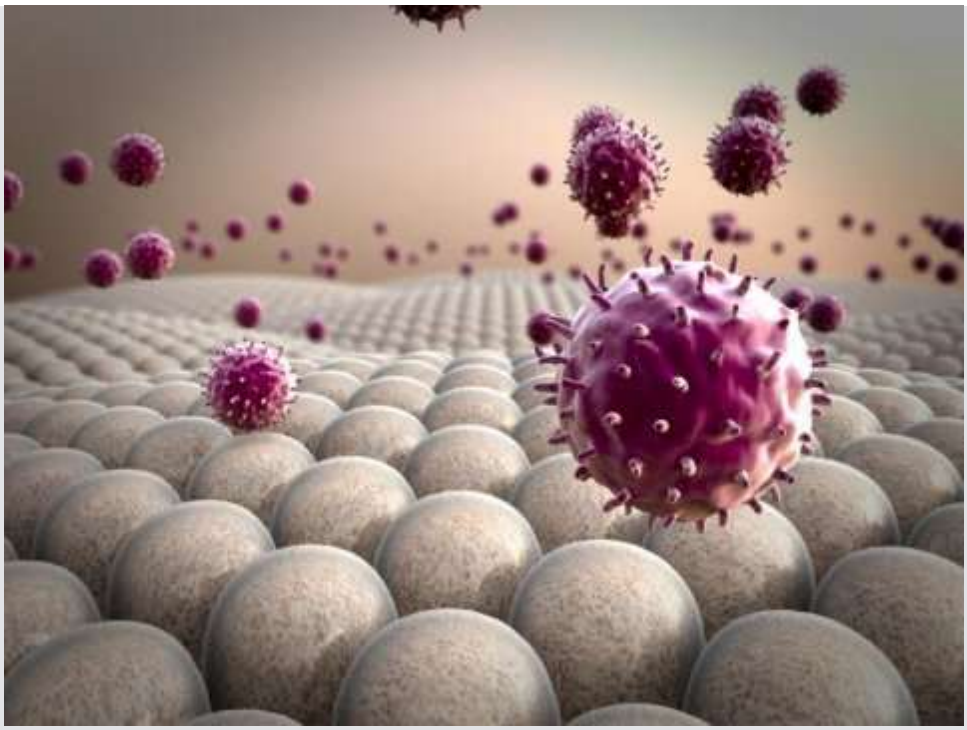
Source:

University of Pennsylvania School of Medicine

Summary:

Researchers say they've identified how to fuel macrophages with the energy needed to attack and eat cancer cells.

FULL STORY



Macrophages are immune cells just like T and B cells, but differ in that they can eat cells that are not supposed to be in the body.

Credit: Penn Medicine

Immune cells called macrophages are supposed to serve and protect, but cancer has found ways to put them to sleep. Now researchers at the Abramson Cancer Center of the University of Pennsylvania say they've identified how to fuel macrophages with the energy needed to attack and eat cancer cells. It is well established that macrophages can either support cancer cell growth and spread or hinder it. But most tumors also express a signal called CD47, which can lull macrophages into a deep sleep and

prevent them from eating. Researchers have found that rewiring macrophage metabolism can overcome this signal and act like an alarm clock to rouse and prepare macrophages to go to work. Their findings were published in *Nature Immunology* today.

Macrophages are immune cells just like T and B cells, but differ in that they can eat cells that are not supposed to be in the body. In fact, they are the most prominent immune cell found in cancer, but unfortunately, most are often convinced to help cancer grow and spread. Cancer cells frequently stop macrophages from attacking them by expressing CD47, a "don't eat me" signal. Researchers now say that merely blocking inhibitory signals like CD47 is not always sufficient to convince macrophages to attack cancer. Instead, two signals are required. First, they need a signal to activate them -- such as a toll-like receptor agonist. After that, a second signal -- such as a CD47 inhibitor -- can lower the threshold needed to wage battle on the cancer.

"It turns out macrophages need to be primed before they can go to work, which explains why solid tumors may resist treatment with CD47 inhibitors alone," said the study's senior author Gregory L. Beatty, MD, PhD, an assistant professor of Hematology-Oncology at Penn's Perelman School of Medicine. Jason Mingen Liu, an MD and PhD graduate student in Beatty's lab, is the study's lead author.

The team used this approach by activating macrophages with CpG, a toll-like receptor agonist that sends the first signal, and found that it rapidly induced shrinkage of tumors and prolonged survival of mice even without the requirement of T cells. Unexpectedly, they also found that the activated macrophages were able to eat cancer cells even in the presence of high levels of CD47.

To understand the molecular basis of this phenomenon, the team traced the metabolic activity of macrophages and determined that activated macrophages began to utilize both glutamine and glucose as fuel to support the energy requirements needed for them to eat cancer cells. This rewiring of the macrophages metabolism was necessary for CpG to be effective, and the researchers say these findings point to the importance of macrophage metabolism in determining the outcome of an immune response.

"Cancer does not shrink without the help of macrophages and macrophages need the right fuel to eat cancer cells and shrink tumors," Liu said. "To do this, a shift in metabolism is needed to steer the energy in the right direction. It is the metabolism that ultimately allows macrophages to override signals telling them not to do their job."

Beatty points out that patients with diabetes, cardiovascular disease, and other conditions are routinely treated with drugs that could affect macrophage metabolism, but virtually nothing is known about how these drugs might impact immunotherapy responses in cancer, meaning the team's discovery has implications even for existing treatments.

Story Source:

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

Cite This Page:

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- Chicago

University of Pennsylvania School of Medicine. "Energizing the immune system to eat cancer: Method of priming macrophages to boost anti-tumor response." ScienceDaily. ScienceDaily, 21 January 2019. <www.sciencedaily.com/releases/2019/01/190121115403.htm>.

目次に戻る

8. 揺動運動で睡眠と記憶を改善 -マウスおよびヒト実験

2019 年 1 月 24 日

スイスの研究チームによる 2 つの新しい研究、1 つはヒト若年成人、もう 1 つはマウスで行われたが、それらの研究によって、睡眠において揺動運動が幅広く利点になることが示され、1 月 24 日に *Current Biology* 誌で報告されている。
研究者らは以前ヒトの実験で、連続的な揺れがより速く眠りに落ちたり、より健全に眠るのを助けることを示していたが、今回彼らは、睡眠中の揺れの影響とそれに関連した脳波を探求した。データは、参加者が揺れている間に速く眠りに落ちたこと、眠りについたらより深く眠り目が覚め難くなったことを示した。また、その睡眠が記憶に与える影響について、朝行った記憶テストでより良い結果が得られた、としている。
マウス実験においては、ケージを揺り動かすために市販の往復式シェーカーを使用、揺動によって眠りに落ちる時間が短縮され、睡眠時間も長くなったが、より深く眠るという証拠は示されなかった、としている。
この 2 つの研究は、「睡眠に対する揺動刺激の影響の根底にある神経生理学的メカニズムへの新しい洞察を提供する」としており、睡眠障害や記憶障害を患うことが多い高齢者だけでなく、不眠症や気分障害のある患者を治療するための新たなアプローチ開発に役立つかもしれない、としている。

英文記事：
https://www.sciencedaily.com/releases/2019/01/190124110844.htm

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Rocking motion improves sleep and memory, studies in mice and people show

Date:

January 24, 2019

Source:

Cell Press

Summary:

Two new studies, one conducted in young adults and the other in mice, add to evidence for the broad benefits of a rocking motion during sleep. In fact, the studies in people show that rocking not only leads to better sleep, but it also boosts memory consolidation during sleep.

FULL STORY

Asleep in a hammock.

Credit: © Monkey Business / Fotolia

Anyone who has ever put a small child to bed or drifted off in a gently swaying hammock will know that a rocking motion makes getting to sleep seem easier. Now, two new studies reported in *Current Biology* on January 24, one conducted in young adults and the other in mice, add to evidence for the broad benefits of a rocking motion during sleep. In fact, the studies in people show that rocking not only leads to better sleep, but it also boosts memory consolidation during sleep.

"Having a good night's sleep means falling asleep rapidly and then staying asleep during the whole night," says Laurence Bayer of the University of Geneva, Switzerland. "Our volunteers -- even if they were all good sleepers -- fell asleep more rapidly when rocked and had longer periods of deeper sleep associated with fewer arousals during the night. We thus show that rocking is good for sleep."

Bayer and their colleagues had earlier shown that continuous rocking during a 45-minute nap helped people to fall asleep faster and sleep more soundly. In the new study, led by Laurence Bayer and Sophie Schwartz, University of Geneva, Switzerland, they wanted to explore the effects of rocking on sleep and its associated brain waves throughout the night.

The researchers enlisted 18 healthy young adults to undergo sleep monitoring in the lab. The first night was intended to get them used to sleeping there. They then stayed two more nights -- one sleeping on a gently rocking bed and the other sleeping on an identical bed that wasn't moving.

The data showed that participants fell asleep faster while rocking. Once asleep, they also spent more time in non-rapid eye movement sleep, slept more deeply, and woke up less.

Next, the researchers wanted to know how that better sleep influenced memory. To assess memory consolidation, participants studied word pairs. The researchers then measured their accuracy in recalling those paired words in an evening session compared to the next morning when they woke up. They found that people did better on the morning test when they were rocked during sleep.

Further studies showed that rocking affects brain oscillations during sleep. They saw that the rocking motion caused an entrainment of specific brain oscillations of non-rapid eye movement sleep (slow oscillations and spindles). As a result, the continuous rocking motion helped to

synchronize neural activity in the thalamo-cortical networks of the brain, which play an important role in both sleep and memory consolidation.

The second study in mice by Konstantinos Kompotis and colleagues is the first to explore whether rocking promotes sleep in other species. And, indeed, it did. The researchers, led by Paul Franken, University of Lausanne, Switzerland, used commercial reciprocating shakers to rock the cages of mice as they slept.

While the best rocking frequency for mice was found to be four times faster than in people, the researchers' studies show that rocking reduced the time it took to fall asleep and increased sleep time in mice as it does in humans. However, the mice did not show evidence of sleeping more deeply.

Researchers had suspected that the effects of rocking on sleep were tied to rhythmic stimulation of the vestibular system, the sensory system that contributes to the sense of balance and spatial orientation. To explore this notion in the mouse, the researchers studied animals whose vestibular systems were disrupted by non-functioning otolithic organs, found in their ears. Their studies showed that mice lacking working otolithic organs experienced none of the beneficial effects of rocking during sleep.

Taken together, the two studies "provide new insights into the neurophysiological mechanisms underlying the effects of rocking stimulation on sleep," Bayer and Perrault write. The findings may be relevant for the development of new approaches for treating patients with insomnia and mood disorders, as well as older people, who frequently suffer from poor sleep and memory impairments.

The researchers say it will be essential in future work to explore the precise deeper brain structures involved in the effects of rocking on sleep.

"Current tools, such as optogenetics, can help us decipher which structures, or even neuronal populations, receive the stimulus from the otolithic organs and transfer it further to the structures of the sleep circuitry," Franken says. "Mapping the network of communication between the two systems will provide with basic understanding, as well as novel clinical targets to cope with sleep disorders, like insomnia."

Story Source:

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

Journal References:

1. Perrault et al. **Whole-Night Continuous Rocking Entrains Spontaneous Neural Oscillations with Benefits for Sleep and Memory**. *Current Biology*, DOI: 10.1016/j.cub.2018.12.028
2. Kompotis et al. **Rocking Promotes Sleep in Mice through Rhythmic Stimulation of the Vestibular System**. *Current Biology*, 2019 DOI: 10.1016/j.cub.2018.12.007

Cite This Page:

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Cell Press. "Rocking motion improves sleep and memory, studies in mice and people show." ScienceDaily. ScienceDaily, 24 January 2019. <www.sciencedaily.com/releases/2019/01/190124110844.htm>.

目次に戻る

9. 抗癌ウィルス設計

2019 年 1 月 29 日

北海道大学の研究者らは、癌細胞を選択的に標的として殺すウィルスを開発、その遺伝子操作されたウィルスは現在治療に使用されている他のウィルスよりも効果的に癌細胞を殺す、として *Oncology Reports* 誌に発表している。
それによると、研究者らはアデノウィルスの一種からウィルス複製に関与する遺伝子 E4orf6 を削除した。そこからできた dl355 と呼ばれる遺伝子操作されたアデノウィルスは、癌細胞内で、複製しその数を著しく増加させることを発見した。いくつかのウィルスは、それらが破裂して死滅するまで細胞内で増殖する為、癌治療に使用することができる。
マウスで増殖したヒト腫瘍細胞に dl355 を投与した場合、腫瘍増殖は優位に抑制された。
研究チームは最後に、dl355 の抗癌効果を現在臨床診療で使用されている dl1520 と呼ばれる別の抗癌アデノウィルスと比較したところ、dl355 の方は子宮頸癌細胞および肺癌細胞を含む、試験した全ての癌細胞株において、癌細胞を殺すことにおいて優れた結果を示した、としている。

英文記事：
https://www.sciencedaily.com/releases/2019/01/190129093709.htm

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Engineering a cancer-fighting virus

Date:

January 29, 2019

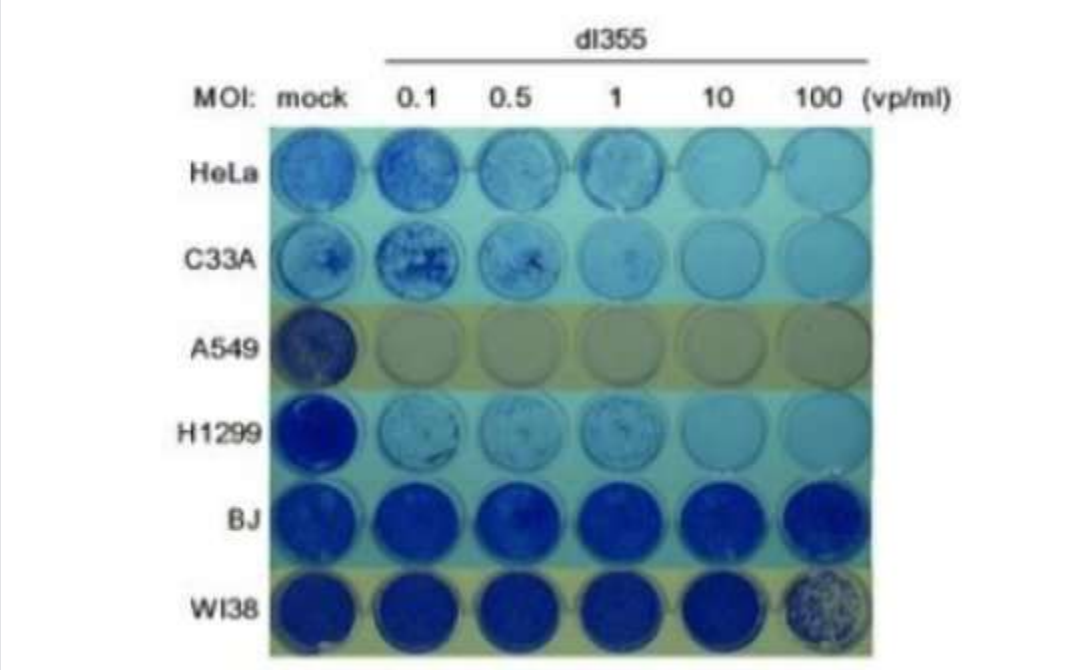
Source:

Hokkaido University

Summary:

An engineered virus kills cancer cells more effectively than another virus currently used in treatments, according to researchers.

FULL STORY



This is a comparison of cancer cells and normal cells after being infected with the dl355 adenovirus. The top four cell types listed on the left (HeLa, C33A, A549, and H1299) are cancer cells, and the bottom two (BJ and WI38) are normal cells. As the amount of dl355 virus administered to the cancer cells increased (represented by MOI), more cancer cells died in 7 days, while the normal cells continued to live.

Credit: Yanagawa-Matsuda, et. al, Oncology Reports, November 12, 2018

An engineered virus kills cancer cells more effectively than another virus currently used in treatments, according to Hokkaido University researchers.

Hokkaido University researchers have engineered a virus that selectively targets and kills cancer cells. The virus, called dl355, has an even stronger anticancer effect than another engineered virus currently used in clinical practice, according to a study published in the journal *Oncology Reports*.

Molecular oncologist Fumihiro Higashino and colleagues deleted a gene involved in viral replication, called E4orf6, from a type of adenovirus. The team previously discovered that E4orf6 stabilizes a type of mRNA called ARE-mRNAs in the infected cells enabling viral replication. ARE-mRNAs are known to be stable in stressed cells and cancer cells, but rapidly degrade in normal cells.

In laboratory tests, they found that their modified adenovirus, called dl355, replicated and increased its number significantly more in cancer cells than it did in normal cells. Higashino explains "The E4orf6-lacking virus relies on the stable ARE-mRNAs in cancer cells for its replication."

Some viruses can be used to treat cancers, as they replicate within the cells until they burst and die. The researchers infected several types of cultured cancer cells with 100 dl355 virus particles per cell and found that nearly all the cancer cells died within seven days. In contrast, most normal cells infected with the virus did not die, even after seven days. Several cancer cell lines managed to survive low doses of dl355, but all cancer cells were killed by the virus as the dose was increased. Tumour growth was also significantly suppressed when dl355 was administered to human tumour cells grown in mice.

Finally, the team compared the anticancer effects of dl355 with another anticancer adenovirus currently used in clinical practice, called dl1520. dl355 replication was higher in all cancer cell lines tested, including cervical and lung cancer cells, and was better at killing all but one type of cancer cell, compared to dl1520. Both viruses only killed very few normal cells.

The findings suggest that dl355 has potential to be an effective anticancer treatment, the team concludes. They suggest enhancing the stabilization of ARE-mRNAs in cancer cells could even further strengthen its effect, but Professor Higashino notes that further research is required. "While we think dl355 has the potential to be an effective treatment method in dealing with many types of cancers, much more research needs to be done. When we think of a timeline, at least five more years of further research may be required, possible more, on top of clinical trials," Professor Higashino noted.

Story Source:

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

Journal Reference:

1. Aya Yanagawa-Matsuda, Yohei Mikawa, Umma Habiba, Tetsuya Kitamura, Motoaki Yasuda, Mohammad Towfik-Alam, Yoshimasa Kitagawa, Kazuyuki Minowa, Masanobu Shindoh, Fumihiro Higashino. **Oncolytic potential of an E4-deficient adenovirus that can recognize the stabilization of AU-rich element containing mRNA in cancer cells**. *Oncology Reports*, 2018; DOI: 10.3892/or.2018.6865

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- MLA
- APA
- Chicago

Hokkaido University. "Engineering a cancer-fighting virus." ScienceDaily. ScienceDaily, 29 January 2019. <www.sciencedaily.com/releases/2019/01/190129093709.htm>.

目次に戻る

10. エピジェネティック遺伝子に基づく新・自閉症マウスモデル開発

2019 年 1 月 30 日

自閉症スペクトラム障害（ASD）の原因は多様で、不明な部分が多い。カリフォルニア大学サンディエゴ校医学部の研究者らは、1 月 17 日に *Translational Psychiatry* 誌に掲載された論文で、新規マウスモデルにおいて、エピジェネティックな調節が神経発達とそれに関連する行動に特異的に関与する下流遺伝子にどのように悪影響を及ぼすか、説明している。
研究者らによると、この遺伝子が自閉症に関連しているという臨床的および遺伝的証拠のみがあったが、このマウスモデルによって、この遺伝子と ASD 様の行動をもたらす神経分子と細胞の変化を結び付ける直接的な因果的証拠を得ることができた、としている。また、エピジェネティクスとは、遺伝暗号自体の変更ではなく、遺伝子発現の変更によって引き起こされる生物の変化を意味するが、エピジェネティックな調節メカニズムの重要性は、ヒトの神経発達および ASD など神経発達において益々注目されていく、としている。

英文記事：
https://www.sciencedaily.com/releases/2019/01/190130133043.htm

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Novel autism mouse model based on an epigenetic gene developed

Mouse model offers new way to test potential therapeutic interventions

Date:

January 30, 2019

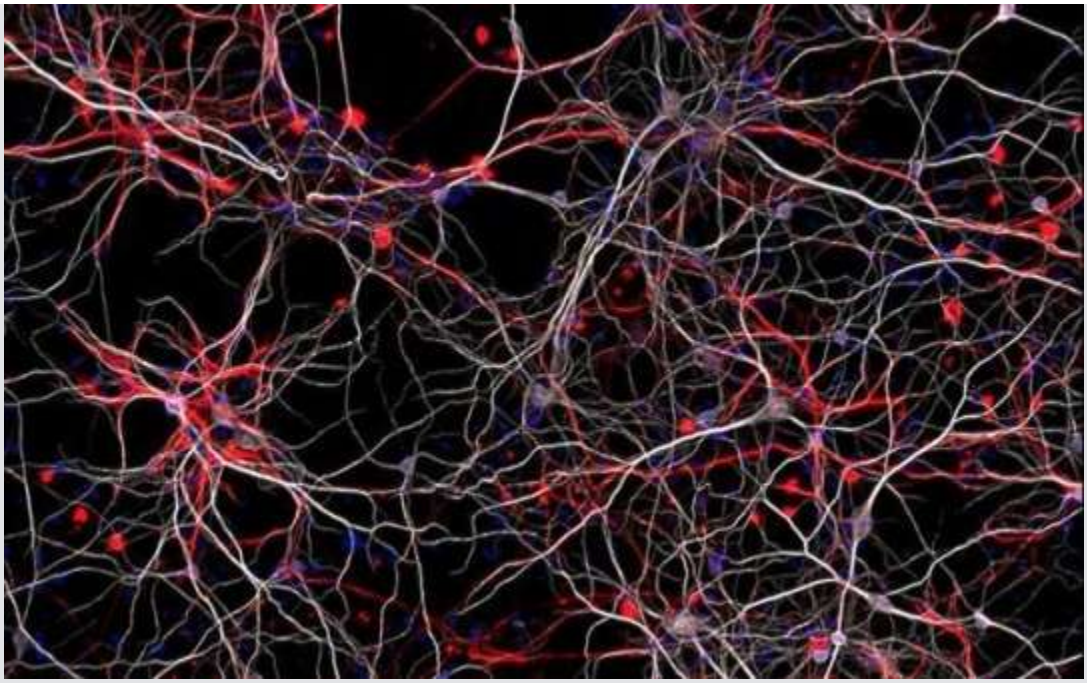
Source:

University of California - San Diego

Summary:

In a new study, researchers describe how, in a novel mouse model, epigenetic regulation negatively impacts a downstream gene specifically involved in neurodevelopment and associated behaviors.

FULL STORY



A network of Setd5-mutant neuronal cultures extracted from the cortex of a mouse cortex. Cell nuclei are blue. Neurons are white. Astrocytes, a type of brain cell, are red.

Credit: Alysson Muotri, UC San Diego

The causes of autism spectrum disorder (ASD) are diverse and to some extent, unknown. But without doubt, they are complex, layered and deeply

nuanced. In a study published January 17, 2019 in *Translational Psychiatry*, researchers at University of California San Diego School of Medicine describe how, in a novel mouse model, epigenetic regulation negatively impacts a downstream gene specifically involved in neurodevelopment and associated behaviors.

"We only had clinical and genetic evidence that the gene was related to autism. Now, with this mouse model, we have direct causal evidence linking this gene with neuronal molecular and cellular alterations leading to ASD-like behavior," said senior author Alysson R. Muotri, PhD, professor in the UC San Diego School of Medicine departments of Pediatrics and Cellular and Molecular Medicine, director of the UC San Diego Stem Cell Program and a member of the Sanford Consortium for Regenerative Medicine.

"This animal model might be useful when testing potential therapeutic alternatives for this subgroup of ASD in people. Our plans also include the development of human brain organoids derived from reprogrammed cells from ASD individuals."

Epigenetics refers to changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself. Epigenetic control of chromatin structure -- how DNA is efficiently packaged within a cell's nucleus -- mediates many critical cellular processes, from gene expression to cell division and neural development.

"The importance of epigenetic regulatory mechanisms is increasingly appreciated in human neurodevelopment and neurodevelopmental conditions, such as ASD," said Muotri. "Indeed, mutations in chromatin-related epigenetic genes can cause several neurological disorders."

Muotri and colleagues looked specifically at a group of proteins called the SET domain which write instruction code for histone methylation, a process of adding or subtracting proteins to increase or decrease gene transcription. It is critical to the regulation of gene expression and the ability of different cells to express different genes.

SET domain proteins mediate a gene called SETD5, which is essential to neurodevelopment and has been categorized, in clinical genetic studies, as a top ASD-risk gene, "but until now there was no causal relation between SETD5 loss of function and alterations in neurodevelopment," said Muotri.

In a mouse model with haploinsufficiency of SETD5 (only one functional copy of the gene), the researchers found that cortical neurons displayed morphological alterations and reduced connectivity. "As a consequence, the neuronal networks showed a delayed in development in these mice compared to controls," said Muotri.

The researchers then traced which genes were affected, identifying neurodevelopmental pathways that are targeted by the SETD5 gene. They hypothesized that the affected gene expression would likely result in altered behavior and, in fact, observed abnormal patterns of social interaction and "autism-compatible" behavior in the mice.

Magnetic resonance imaging analyses revealed subtle anatomical differences in the mutant adult brain of affected mice. A more detailed anatomical investigation revealed aberrant cortical lamination -- a phenotype observed in other ASD mouse models as well.

The Muotri lab has developed a large collection of cells carrying unexplored ASD-risk genes generated from the Tooth Fairy Project.

Co-authors include: Spencer M. Moore, Jason S. Seidman, Richard Gao, Alex Savchenko, Ty D. Troutman, Yohei Abe, Josh Stender, Sicong Wang and Christopher K. Glass, UC San Diego; Jacob Ellegood, Hospital for Sick Children, Toronto, CA; Daehoon Lee and Hoonkyo Suh, Cleveland Clinic; Bradley Voytek, UC San Diego and Kavli Institute for Brain and Mind; and Jason P. Lerch, Hospital for Sick Children and University of Toronto.

Disclosure: Alysson Muotri is a co-founder and has an equity interest in TISMOO, a company dedicated to genetic analysis focusing on therapeutic applications customized for autism spectrum disorder and other neurological disorders with genetic origins. The terms of this arrangement have been reviewed and approved by the University of California San Diego according to its conflict of interest policies.

Story Source:

Materials provided by **University of California - San Diego**. Original written by Scott LaFee. *Note: Content may be edited for style and length.*

Journal Reference:

1. Spencer M. Moore, Jason S. Seidman, Jacob Ellegood, Richard Gao, Alex Savchenko, Ty D. Troutman, Yohei Abe, Josh Stender, Daehoon Lee, Sicong Wang, Bradley Voytek, Jason P. Lerch, Hoonkyo Suh, Christopher K Glass, Alysson R. Muotri. **Setd5 haploinsufficiency alters neuronal network connectivity and leads to autistic-like behaviors in mice**. *Translational Psychiatry*, 2019; 9 (1) DOI: 10.1038/s41398-018-0344-y

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