BIO NEWS

June, 2018

In-Vivo Science International Inc.

1230 Bordeaux Drive

Sunnyvale, CA 94089, USA

目次

2018 年 5 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)＝

2018 年 5 月のニュース

＝企業関連ニュース他＝

・昨年最も稼いだ製薬会社 CEO は United Therapeutics の Martine Rothblatt 氏（5/1）
・Datavant、医療データの匿名化サービスを手がける Universal Patient Key を取得（5/1）
・GSK の帯状疱疹ワクチンの 1Q 売り上げは期待を遥かに上回る 1 億 1,000 万ポンド（5/2）
・Microsoft と Google の設立者が組んで万能インフルエンザワクチン開発を支援（5/2）
・J&J、殺癌ウイルスを開発している BeneVir を買う（5/3）
・遺伝子編集技術を生み出す Feng Zhang 氏が新会社 Beam Therapeutics を設立（5/3）
・人工知能研究者 Daphne Koller 氏が創薬 R&D 改善を目指す新会社 insitro を設立（5/3）
・韓国が Samsung BioLogics に会計ルール違反を通知（5/4）
・Aslan、目標の半分にも満たない 4,200 万ドルの IPO 調達を達成（5/5）
・犬の腸内細菌群 マウスよりヒトに類似 -欧州分子生物学研究所（5/6）
・超低炭水化物（30g 以下/日）食で 1 型糖尿病患者の血糖制御が改善（5/7）
・Novartis の降圧薬 Diovan の日本での試験論文さらに 3 つの撤回が必要とされた（5/7）
・武田薬品が Shire を 460 億ポンド（620 億ドル）相当で買う合意に至った（5/8）
・スポーツ飲料を毎日飲む米国高校生の割合は低下（5/8）
・Valeant が Bausch Health Companies へと社名変更（5/9）
・安全な抗癌 T 細胞を開発している Autolus が 1 億ドルの IPO 調達を計画（5/9）
・京大 アマゾン流域に研究拠点（5/9）
・土壌微生物 DNA からの創薬企業 Lodo が Genentech と提携（5/10）
・コンゴ民主共和国でエボラウイルス疾患が再び流行（5/10）
・Novartis がトランプ大統領の弁護士に 120 万ドルを見返り無しで払ったことを認めた（5/10）
・Provention Bio が 5,000 万ドルの IPO 調達を計画（5/10）
・微生物薬の Evelo Biosciences が 8,500 万ドルの IPO 調達達成（5/10）
・ADHD 治療ビデオゲームを間もなく FDA に承認申請する Akili が 5,500 万ドル調達（5/10）
・米国医師のおよそ 5 人に 2 人が 100 万ドルを超える資産を保有（5/11）
・ロボットとデジタルツイン導入で Sanofi 米国工場の生産力が高まる、従業員は減少（5/11）
・抗生剤への細菌の耐性の研究で名を馳せた Stanley Falkow 氏死去（5/11）
・Novartis の細胞/遺伝子治療事業の元リーダーBastiano Sanna が Semma を率いる（5/11）
・Eli Lilly が抗癌免疫治療を揃えた Armo Biosciences を 16 億ドルで買収（5/11）

・低湿度で皮膚が傷むのを防ぎうる蛋白質 CLCA2 が見つかった（5/12）
・標識なしで細胞の中身をはっきりと立体で示す人工知能技術が開発された（5/12）
・リボゾーム合成を促す tRNA 由来短鎖 RNA（tsRNA）の阻害でマウス肝癌が退縮（5/12）
・サルからサルに子宮移植し妊娠 慶大が成功（5/13）
・世界初クローン牛「のと」死ぬ…19 歳 10 か月（5/14）
・「記憶を移植」 米研究者らがアメフラシの遺伝子で成功（5/15）
・コンゴでのエボラ流行への対策に WHO が Merck の承認前ワクチン接種を準備（5/15）
・第一三共、更に 2 つの二重特異性抗癌抗体を開発する権利を Zymeworks から取得（5/15）
・Lilly が Aurka Pharma を買収（5/15）
・塩基編集により変異を直す Beam Therapeutics（マサチューセッツ州ケンブリッジ）が 8,700 万ドル調達と共にお披露目（5/15）
・米国では小児への ADHD や喘息薬の処方が増えている（5/15）
・武田薬品、今年度営業利益 17%減少を予想～Velcade の米国独占販売終了が背景（5/15）
・トランス脂肪を含む食品の販売を無くすための 6 段階の手順を WHO が発表（5/16）
・ノースウェスタン大学のインキュベーター発足（5/16）
・喫煙経験がない米国成人の電子タバコ使用が増えている（5/16）
・トランプ大統領弁護士への支払い問題で Novartis の最高弁護士が辞任（5/16）
・細胞内に届くミニ蛋白質技術を擁する FogPharma が 6,600 万ドル調達（5/17）
・昨年の売り上げ首位の製薬会社は Johnson & Johnson の 760 億ドル（5/17）
・2017 年の米国の出生数は 2016 年に比べて 2%少ないおよそ 385 万人（5/18）
・目薬 Restasis の特許を嘘をついて取得したとして米国の小売 4 社（Walgreen, Kroger, Albertsons, HEB Grocery Company）が Allergan を告訴（5/19）
・HIV の遺伝子壊す技術開発 神戸大、細胞実験に成功（5/19）
・米国の糖尿病成人の死亡率は 10 年あたり 20%低下（5/21）
・より太りやすくする遺伝子情報は喫煙しやすくもする（5/21）
・潰瘍性大腸炎患者はパーキンソン病を発症しやすい（5/22）
・逆風続きの Celgene の事業開発長が先月半ばに辞任（5/22）
・Celgene、Evotec に前金 6,500 万ドルを払って抗癌治療を協力して開発（5/22）
・ヒト ES 細胞 国内で初の提供へ –京都大（5/22）
・やせた高齢女性 糖尿リスク高 -順天堂大 研究（5/22）

・生物の 24 時間周期 決める酵素発見 –京都大（5/22)
・武田薬品、中国の合弁会社の持ち分を 2 億 8,000 万ドルで売却 （5/23)
・厚労省 遺伝性乳がん薬承認へ（5/24)
・アステラス製薬、4 事業の全てまたは大半を解消/譲渡して 600 人を削減 （5/24)
・抗うつ薬使用と体重増加が関連（5/24)
・抗癌剤開発の Kronos Bio が Gilead の元 R&D 長を CEO に任命（5/24)
・Novartis の遺伝子治療事業 AveXis が 5,500 万ドルを投じて米国ノースキャロライナ州に新工場を建設予定（5/24)
・iPS 細胞から免疫細胞を作製 -京大 iPS 細胞研究所（5/25)
・すい臓がん 発生構造を解明 -京大 iPS 細胞研究所（5/25)
・中国に最先端の薬を広める新会社を GSK の感染症事業リーダーZhi Hong 氏が設立(5/25)
・米国の若い女性の肺癌発現率は喫煙率は同程度でも若い男性より高い（5/25)
・カキのノロ 極小の泡で除去 -電子部品メーカーのトスレック（京都市南区）(5/26)
・Allergan が 2015 年に買った Naurex から独立した Aptinyx が 8,000 万ドルの IPO 調達を計画（5/26)
・認知症薬 米で相次ぐ開発撤退 -Pfizer、Merck、Eli Lilly、J&J など(5/27)
・再生医療の特許 日本は出遅れ -日本:294 件、米国:1436 件、中国:607 件、韓国:507 件、欧州:438 件（5/28)
・米国の抗癌剤出費は 2022 年までに 1,000 億ドルに達する予測 （5/28)
・753 の癌治療細胞製品が世界で開発中～米国 1 位:378 品、中国 2 位;203 品 （5/29)

目次に戻る

1．高脂肪食でも体型維持 -マウス実験

2018 年 5 月 3 日

私達の身体は食べ物からの脂肪を脂肪組織に貯蔵することを非常に効率的にやってのける。これは食べ物の入手が簡単ではなかった長い歴史の中で進化した結果と言える。
しかし、今日私達の多くが高カロリー食品に絶えずアクセスできるようになり、私達の持つこの食べ物を脂肪に変換する‘素晴らしい’能力が、逆に世界中に肥満者の数を急増させるという大きな問題を作っている。
今回コペンハーゲン大学の研究者らは、新しい研究の一環として、マウス実験により、身体の脂肪蓄積能力を阻害することに成功した。彼らはマウスの脂肪組織中の酵素 NAMPT を遺伝的に欠損させ、これによって、非常に高脂肪の食事であっても過体重または肥満にならなかった、としている。ただし、NAMPT は今までの研究において、体内の組織で代謝機能を高めることも示されている。従って、NAMPT を減少させること、イコール、ヒトにおける実行可能な肥満治療戦略となるとは必ずしもいかないかもしれないが、少なくとも肥満に対するより良い治療の新たな道を開くと期待される。

英文記事：
https://www.sciencedaily.com/releases/2018/05/180503142706.htm

---

Researchers defy biology: Mice remain slim on burger diet

Date:

May 3, 2018

Source:

University of Copenhagen The Faculty of Health and Medical Sciences

Summary:

Our bodies are extremely efficient at storing fat from food into our fat tissue. In a new study, researchers have managed to completely block the development of obesity. The researchers deleted an enzyme and made it impossible for mice to increase their amount of fat tissue, despite the mice eating an extremely fatty diet. They are hoping the findings will open new avenues for better treatment of obesity.

FULL STORY

Mouse eating cheese. (stock image)

Credit: © BillionPhotos.com / Fotolia

We are our own worst enemy when it comes to developing obesity. The body is naturally geared to assimilate energy from the food we eat and store

it as fat until it is needed. This is the result of millions of years of evolution under the pressure of low food availability.

But today, where many of us have constant access to high calorie foods, our body's impressive ability to convert food into fat has, ironically, become problematic. Consequently, the number of overweight people worldwide is skyrocketing, leading to large health consequences for both the individual and society.

However, as part of a new study, researchers at the University of Copenhagen have now managed to inhibit the body's ability to store fat. They genetically delete the enzyme NAMPT in fat tissue of mice, and this renders the animals completely resistant to becoming overweight or obese, even on a very fatty diet.

'We gave the mice a diet that more or less corresponds to continuously eating burgers and pizza. Still, it was impossible for them to expand their fat tissue. Our ultimate goal is that by understanding these fundamental underpinnings of how we become obese, we can apply our finding to the development of novel treatment strategies for metabolic disease,' says Karen Nørgaard Nielsen, first author on the publication and a Ph.D. student at the Novo Nordisk Foundation Center for Basic Metabolic Research.

High-Fat Food, Same Weight

The findings are in line with results obtained from humans. Several studies have shown that the presence of large amounts of the enzyme NAMPT in blood and in stomach fat tissue is significantly connected with being overweight or obese. However, this study provides the first evidence that NAMPT is absolutely required to become overweight or obese and that lack of NAMPT in fat tissue fully protects against obesity.

In the University of Copenhagen study, the researchers compared how normal mice and mice lacking NAMPT in fat tissue gained weight when given either high-fat food or a healthier, lower-fat diet. When on the healthy diet, there was no difference in body weight or the amount of fat between the normal mice and the mice lacking NAMPT.

However, when the mice were given high-fat food, the control mice became very obese, yet the mice lacking NAMPT gained no more weight from high-fat food than when they were on the healthier diet. In addition, the mice lacking NAMPT maintained better control of blood glucose than normal mice when eating high-fat food.

Contradicts the General View

The result challenges the general view of NAMPT, which is largely seen as an enzyme that should be boosted for therapeutic purposes.

'NAMPT appears to increase the metabolic functionality of almost every tissue in the body in which it has been studied. For example, there are indications that the liver and skeletal muscle may benefit from increased NAMPT activity. We similarly find that NAMPT is critical for fat tissue function. Unfortunately, that function is efficiently storing fat. NAMPT in fat tissue was likely once an extraordinary benefit to our ancestors but in today's society full of high-fat, calorically-dense foods, it may now pose a liability', says Associate Professor Zachary Gerhart-Hines from the Novo Nordisk Foundation Center for Basic Metabolic Research and corresponding author on the study.

He does not necessarily believe that generally decreasing NAMPT is a viable treatment strategy in humans. There would be too great a risk for potentially harmful consequences in other tissues of the body.

However, he suggests that this study may pave the way for more research into how NAMPT is linked to the storage of fat from the food we eat. By learning biologically how we become obese in the first place, he hopes that it will eventually be possible to target one of the underlying mechanisms in humans to treat obesity and metabolic disease.

Story Source:

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

Journal Reference:

1. Karen Nørgaard Nielsen, Julia Peics, Tao Ma, Iuliia Karavaeva, Morten Dall, Sabina Chubanava, Astrid L. Basse, Oksana Dmytriyeva, Jonas T. Treebak, Zachary Gerhart-Hines. **NAMPT-mediated NAD biosynthesis is indispensable for adipose tissue plasticity and development of obesity**. *Molecular Metabolism*, 2018; DOI: 10.1016/j.molmet.2018.02.014

Cite This Page:

- MLA
- APA
- Chicago

University of Copenhagen The Faculty of Health and Medical Sciences. "Researchers defy biology: Mice remain slim on burger diet." ScienceDaily. ScienceDaily, 3 May 2018. <www.sciencedaily.com/releases/2018/05/180503142706.htm>.

目次に戻る

2. 絶食が幹細胞の再生能力を高める -マウス実験

2018 年 5 月 3 日

ヒトの腸の幹細胞は、年齢と共に再生能力を失い始める。これらの幹細胞は全ての新しい腸細胞の供給源であるため、この減少は胃腸感染などの疾患からの回復をより困難にする可能性がある。今回マサチューセッツ工科大学（MIT）の研究者らは、絶食が幹細胞の再生能力を劇的に改善することを発見し、この研究成果が 5 月 3 日の *Cell Stem Cell* 誌に掲載されている。この 24 時間の絶食効果は老化したマウスおよび若いマウスの両方において見出された。
また、この絶食したマウスからの幹細胞を含む更なる研究として、絶食が糖などの炭水化物を燃やす通常の代謝から脂肪酸の代謝へと切り替えるよう細胞に働くことも明らかになった。このスイッチは、脂肪酸の代謝に関与する多くの遺伝子を活性化する PPAR と呼ばれる転写因子の活性化によって起こる。研究者らは、この経路をオフにすれば、断食がもはや幹細胞再生を促進できないことも発見した。
更に興味深いことに、研究者らは、PPAR の効果を模倣する幹細胞をマウスに処理することによって、絶食の有益な効果を再現できることも見出した。

英文記事：
https://www.sciencedaily.com/releases/2018/05/180503142852.htm

---

Fasting boosts stem cells' regenerative capacity

A drug treatment that mimics fasting can also provide the same benefit, study finds

Date:

May 3, 2018

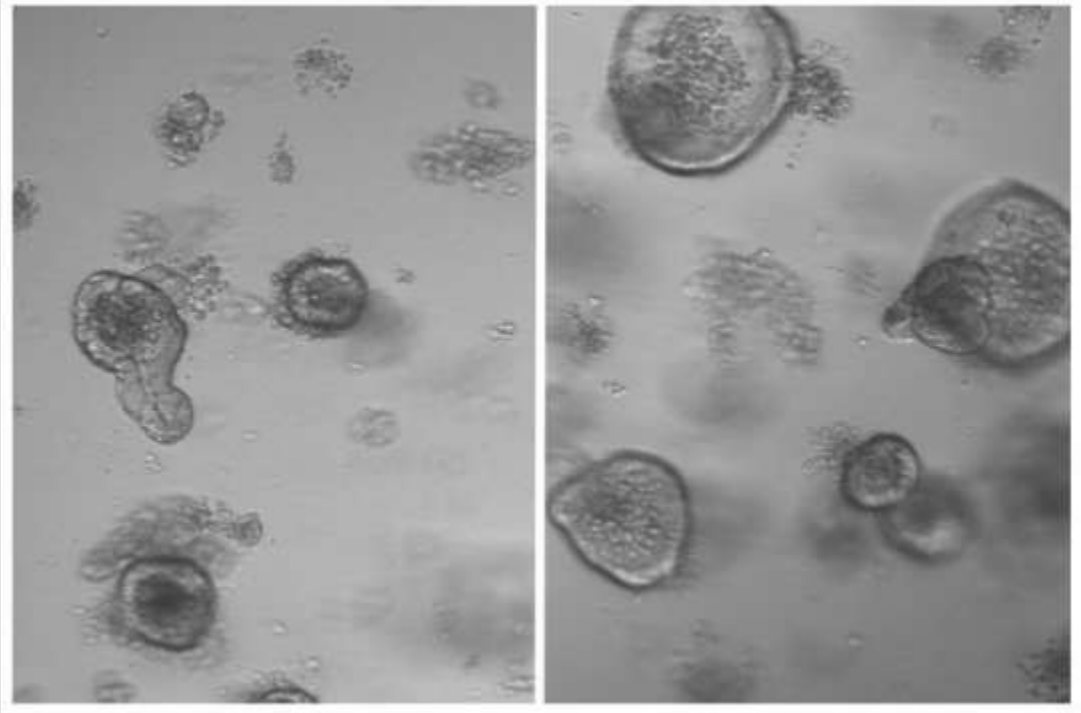
Source:

Massachusetts Institute of Technology

Summary:

Age-related declines in stem cell function can be reversed by a 24-hour fast, according to a new study. Biologists found fasting dramatically improves stem cells' ability to regenerate, in both aged and young mice.

FULL STORY



Intestinal stem cells from mice that fasted for 24 hours, at right, produced much more substantial intestinal organoids than stem cells from mice that did not fast, at left.

Credit: Maria Mihaylova and Chia-Wei Cheng

As people age, their intestinal stem cells begin to lose their ability to regenerate. These stem cells are the source for all new intestinal cells, so this

decline can make it more difficult to recover from gastrointestinal infections or other conditions that affect the intestine.

This age-related loss of stem cell function can be reversed by a 24-hour fast, according to a new study from MIT biologists. The researchers found that fasting dramatically improves stem cells' ability to regenerate, in both aged and young mice.

In fasting mice, cells begin breaking down fatty acids instead of glucose, a change that stimulates the stem cells to become more regenerative. The researchers found that they could also boost regeneration with a molecule that activates the same metabolic switch. Such an intervention could potentially help older people recovering from GI infections or cancer patients undergoing chemotherapy, the researchers say.

"Fasting has many effects in the intestine, which include boosting regeneration as well as potential uses in any type of ailment that impinges on the intestine, such as infections or cancers," says Omer Yilmaz, an MIT assistant professor of biology, a member of the Koch Institute for Integrative Cancer Research, and one of the senior authors of the study. "Understanding how fasting improves overall health, including the role of adult stem cells in intestinal regeneration, in repair, and in aging, is a fundamental interest of my laboratory."

David Sabatini, an MIT professor of biology and member of the Whitehead Institute for Biomedical Research, is also a senior author of the paper, which appears in the May 3 issue of *Cell Stem Cell*.

"This study provided evidence that fasting induces a metabolic switch in the intestinal stem cells, from utilizing carbohydrates to burning fat," Sabatini says. "Interestingly, switching these cells to fatty acid oxidation enhanced their function significantly. Pharmacological targeting of this pathway may provide a therapeutic opportunity to improve tissue homeostasis in age-associated pathologies."

The paper's lead authors are Whitehead Institute postdoc Maria Mihaylova and Koch Institute postdoc Chia-Wei Cheng.

Boosting regeneration

For many decades, scientists have known that low caloric intake is linked with enhanced longevity in humans and other organisms. Yilmaz and his colleagues were interested in exploring how fasting exerts its effects at the molecular level, specifically in the intestine.

Intestinal stem cells are responsible for maintaining the lining of the intestine, which typically renews itself every five days. When an injury or infection occurs, stem cells are key to repairing any damage. As people age, the regenerative abilities of these intestinal stem cells decline, so it takes longer for the intestine to recover.

"Intestinal stem cells are the workhorses of the intestine that give rise to more stem cells and to all of the various differentiated cell types of the intestine. Notably, during aging, intestinal stem function declines, which impairs the ability of the intestine to repair itself after damage," Yilmaz says. "In this line of investigation, we focused on understanding how a 24-hour fast enhances the function of young and old intestinal stem cells."

After mice fasted for 24 hours, the researchers removed intestinal stem cells and grew them in a culture dish, allowing them to determine whether the cells can give rise to "mini-intestines" known as organoids.

The researchers found that stem cells from the fasting mice doubled their regenerative capacity.

"It was very obvious that fasting had this really immense effect on the ability of intestinal crypts to form more organoids, which is stem-cell-driven," Mihaylova says. "This was something that we saw in both the young mice and the aged mice, and we really wanted to understand the molecular mechanisms driving this."

Metabolic switch

Further studies, including sequencing the messenger RNA of stem cells from the mice that fasted, revealed that fasting induces cells to switch from their usual metabolism, which burns carbohydrates such as sugars, to metabolizing fatty acids. This switch occurs through the activation of transcription factors called PPARs, which turn on many genes that are involved in metabolizing fatty acids.

The researchers found that if they turned off this pathway, fasting could no longer boost regeneration. They now plan to study how this metabolic switch provokes stem cells to enhance their regenerative abilities.

They also found that they could reproduce the beneficial effects of fasting by treating mice with a molecule that mimics the effects of PPARs. "That was also very surprising," Cheng says. "Just activating one metabolic pathway is sufficient to reverse certain age phenotypes."

The findings suggest that drug treatment could stimulate regeneration without requiring patients to fast, which is difficult for most people. One group that could benefit from such treatment is cancer patients who are receiving chemotherapy, which often harms intestinal cells. It could also benefit older people who experience intestinal infections or other gastrointestinal disorders that can damage the lining of the intestine.

The researchers plan to explore the potential effectiveness of such treatments, and they also hope to study whether fasting affects regenerative abilities in stem cells in other types of tissue.

Story Source:

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

Journal Reference:

1. Maria M. Mihaylova, Chia-Wei Cheng, Amanda Q. Cao, Surya Tripathi, Miyeko D. Mana, Khristian E. Bauer-Rowe, Monther Abu-Remaileh, Laura Clavain, Aysegul Erdemir, Caroline A. Lewis, Elizaveta Freinkman, Audrey S. Dickey, Albert R. La Spada, Yanmei Huang, George W. Bell, Vikram Deshpande, Peter Carmeliet, Pekka Katajisto, David M. Sabatini, Ömer H. Yilmaz. **Fasting Activates Fatty Acid Oxidation to Enhance Intestinal Stem Cell Function during Homeostasis and Aging**. *Cell Stem Cell*, 2018; 22 (5): 769 DOI: 10.1016/j.stem.2018.04.001

Cite This Page:

- MLA
- APA

- Chicago

Massachusetts Institute of Technology. "Fasting boosts stem cells' regenerative capacity: A drug treatment that mimics fasting can also provide the same benefit, study finds." ScienceDaily. ScienceDaily, 3 May 2018. <www.sciencedaily.com/releases/2018/05/180503142852.htm>.

目次に戻る

3．体のサイズをコントロールできる遺伝的な「ダイアル」-ブタ実験

2018 年 5 月 7 日

ノースカロライナ州立大学の研究者らは、HMGA2 遺伝子の発現とブタの体のサイズとの間に関連性があることを実証し、米国科学アカデミー紀要に発表した。
身体の大きさおよび体格指数の決定に関与する 2 つの異なる遺伝子として、HMGA2 および HMGA1 があり、研究者らは、以前からマウスにおいて HMGA2 類似体を研究していた。今回は、ブタにおいて、両方の遺伝子のコピー、一つのコピー、両方発現していないものについて、そのサイズが調査された。一つのコピーのみ発現したものは正常よりも 25%小さくなり、両方発現しなかった場合には 75%小さくなった、としている。
この研究は、哺乳類動物全体の体のサイズ調節における遺伝子の重要性を示し、遺伝子改変の標的を提供するものである。

英文記事：
https://www.sciencedaily.com/releases/2018/05/180507174015.htm

---

Researchers find genetic 'dial' can control body size in pigs

Date:

May 7, 2018

Source:

North Carolina State University

Summary:

Researchers have demonstrated a connection between the expression of the HMGA2 gene and body size in pigs. The work further demonstrates the gene's importance in body size regulation across mammalian species, and provides a target for gene modification.

FULL STORY

Researchers from North Carolina State University have demonstrated a connection between the expression of the HMGA2 gene and body size in pigs. The work further demonstrates the gene's importance in body size regulation across mammalian species, and provides a target for gene modification.

"Essentially, HMGA2 is a gene that controls the total number of cells that an animal has," says Jorge Piedrahita, the Randall B. Terry Distinguished Professor of Translational Medicine and Director of the Comparative Medicine Institute at NC State. "The gene is only active during fetal development, and 'programs' in the number of cells that the animal will be able to generate. When the animal is born, it will only be able to grow to the size dictated by the number of cells that it can produce."

Researchers had previously studied the HMGA2 analogue in mice, which have two different genes (HMGA2 and HMGA1) involved in body size and body mass index determination. Pigs and humans share the HMGA2 gene responsible for growth regulation in their species. The NC State study looked at body size in pigs that expressed both copies of the gene, one copy, or neither copy.

"We found that the amount of the gene expressed is proportional to the size of the animal," Piedrahita says. "If both copies were expressed the pig was 'normal' sized. If one copy was expressed the pig was roughly 25 percent smaller than normal, and if neither copy was expressed the pig was 75 percent smaller.

"The animals grow and develop normally, although the boars with both copies of the gene deleted were sterile. Overall, it seems that controlling the expression of HMGA2 is like using a dial to control body size."

The researchers also found that the deletion of HMGA2 affected the resources that the pig fetuses received in utero. In litters containing fetuses with both copies of the gene deleted and fetuses with one or more copy of the gene expressed, the fetuses with both copies deleted did not survive

the pregnancy. However, if the litter only contained fetuses with both copies deleted, the fetuses survived and developed normally.

Story Source:

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

Journal Reference:

1. Jaewook Chung et al. **High Mobility Group A2 (HMGA2) deficiency in swine leads to dwarfism, abnormal fetal resource allocation and cryptorchidism**. *PNAS*, 2018 DOI: 10.1073/pnas.1721630115

Cite This Page:

- MLA
- APA
- Chicago

North Carolina State University. "Researchers find genetic 'dial' can control body size in pigs." ScienceDaily. ScienceDaily, 7 May 2018. <www.sciencedaily.com/releases/2018/05/180507174015.htm>.

目次に戻る

４．組織操作したヒト膵臓細胞で、糖尿病マウスの治療に成功

2018 年 5 月 8 日

シンシナティー子供病院医療センターおよび横浜市立大学（YCU）の研究者らは、ヒトの膵島を実験室で組織工学処理して、それを移植したマウスにおいて循環系を発達させインスリン様のホルモンを分泌し急性発症 1 型糖尿病の治療に成功した。
Cell Reports 誌で発表されたこの研究では、自己凝縮細胞培養と呼ばれる新しいバイオエンジニアリングプロセスを使用している。彼らはこの技術が、再生医療として、人間の臓器組織を本人自身の細胞から成長させることにこれから少しでも近付いていく助けになる、としている。

英文記事：
https://www.sciencedaily.com/releases/2018/05/180508111745.htm

---

Tissue-engineered human pancreatic cells successfully treat diabetic mice

Self-condensation process for cells generates vascularized organ tissues for transplant

Date:

May 8, 2018

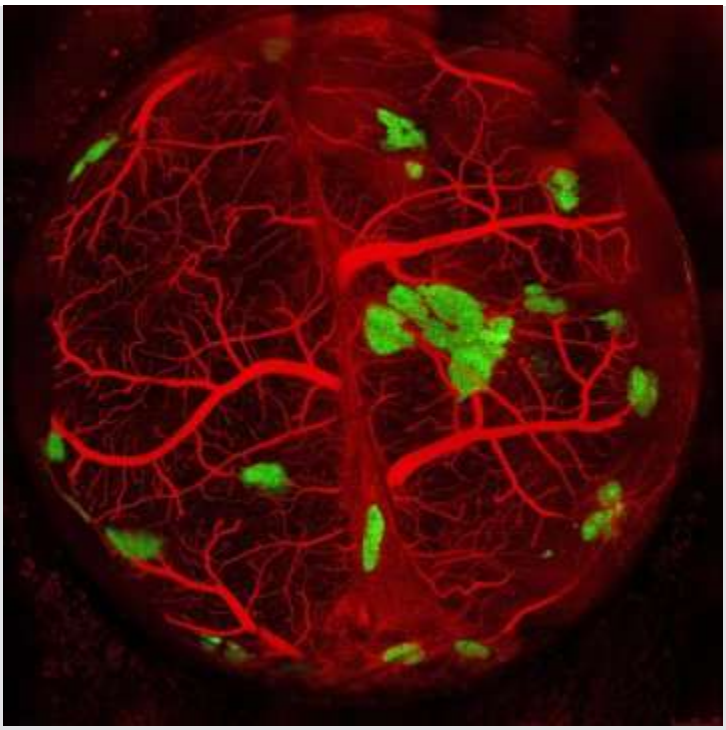
Source:

Cincinnati Children's Hospital Medical Center

Summary:

Researchers tissue-engineered human pancreatic islets in a laboratory that develop a circulatory system, secrete hormones like insulin and successfully treat sudden-onset type 1 diabetes in transplanted mice. The scientists use a new bioengineering process they developed called a self-condensation cell culture. The technology helps nudge medical science closer to one day growing human organ tissues from a person's own cells for regenerative therapy, say study investigators.

FULL STORY



This image shows vascularized pancreatic islets (areas in green) bioengineered by researchers and transplanted into a mouse. The bioengineered islets -- which have a network of blood vessels (shown in red) and secrete hormones like insulin -- are shown seven days after transplant. Scientists reporting research data in Cell Reports say their goal is to one day translate the bioengineering process used to generate and transplant mouse pancreatic islets to human patients with diabetes.

Credit: Cincinnati Children's

Researchers tissue-engineered human pancreatic islets in a laboratory that develop a circulatory system, secrete hormones like insulin and successfully treat sudden-onset type 1 diabetes in transplanted mice.

In a study published by *Cell Reports*, the scientists use a new bioengineering process they developed called a self-condensation cell culture. The technology helps nudge medical science closer to one day growing human organ tissues from a person's own cells for regenerative therapy, say study investigators at Cincinnati Children's Hospital Medical Center in the U.S. and Yokohama City University (YCU) in Japan.

"This method may serve as a principal curative strategy for treating type 1 diabetes, of which there are 79,000 new diagnoses per year," said Takanori Takebe, MD, a physician-scientist at the Cincinnati Children's Center for Stem Cell and Organoid Medicine. "This is a life-threatening disease that never goes away, so developing effective and possibly permanent therapeutic approaches would help millions of children and adults around the world."

Takebe, who has a dual appointment in the Department of Regenerative Medicine at YCU, stressed the technology needs additional research before it can be used therapeutically in a clinic. He is the study's co-lead investigator along with YCU colleague, Hideki Taniguchi, MD, PhD.

Getting out of Nature's Way

Scientists tested their processing system with donated human organ cells (pancreas, heart, brain, etc.), with mouse organ cells and with induced pluripotent stem cells (iPS). Reprogrammed from a person's adult cells (like skin cells), iPS cells act like embryonic cells and can form any tissue type in the body.

The tissue-engineering process also uses two types of embryonic-stage progenitor cells, which support formation of the body and its specific organs. The progenitor cells are mesenchymal stem cells (MSNs) and human umbilical vascular endothelial cells (HUVECs).

Using either donated organ cells, mouse cells or iPS cells, the researchers combined these with MSNs, HUVECs along with other genetic and biochemical material that cue the formation of pancreatic islets. In conditions that nourish and nurture the cells, the ingredients condensed and self-organized into pancreatic islets.

After the tissue-engineered islets were transplanted into humanized mouse models of severe type 1 diabetes, they resolved the animals' disease, report researchers.

Blood Source Challenge

Human pancreatic islets already can be transplanted into diabetic patients for treatment. Unfortunately, the engraftment success rate is relatively low because the tissues lose their vascularization and blood supply as islets are being processed before transplant. This makes it difficult to get the maximum health benefit for patients getting these procedures, the authors write.

And although stem cell-based tissue engineering has tremendous therapeutic potential, its future clinical use still faces the critical challenge of ensuring a blood supply to nourish the transplanted tissues, according to researchers.

"We need a strategy that ensures successful engraftment through the timely development of vascular networks," said Taniguchi. "We demonstrate in this study that the self-condensation cell culturing system promotes tissue vascularization."

Pancreatic islets tissue-engineered in the current generated by the process not only quickly developed a vascular network after transplant into animal models of type 1 diabetes, the tissues also functioned efficiently as part of the endocrine system -- secreting hormones like insulin and stabilizing glycemic control in the animals.

Takebe's and Taniguchi's research team already demonstrated the ability to use a "self-condensation" cell culture process using iPS cells to tissue engineer three-dimensional human liver organoids that can vascularize after transplant into laboratory mice. But the ability to generate organ tissue fragments that vascularize in the body -- like pancreatic islets -- had been an elusive goal until the current study, investigators said.

Story Source:

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

Journal Reference:

1. Yoshinobu Takahashi, Keisuke Sekine, Tatsuya Kin, Takanori Takebe, Hideki Taniguchi'. **Self-Condensation Culture Enables Vascularization of Tissue Fragments for Efficient Therapeutic Transplantation**. *Cell Reports*, 2018; 23 (6): 1620-1629 DOI: 10.1016/j.celrep.2018.03.123

Cite This Page:

- MLA
- APA
- Chicago

Cincinnati Children's Hospital Medical Center. "Tissue-engineered human pancreatic cells successfully treat diabetic mice: Self-condensation process for cells generates vascularized organ tissues for transplant." ScienceDaily. ScienceDaily, 8 May 2018. <www.sciencedaily.com/releases/2018/05/180508111745.htm>.

目次に戻る

5. 高繊維食がマウスをインフルエンザ感染から保護

2018 年 5 月 15 日

5 月 15 日に *Immunity* 誌で発表された前臨床試験によると、免疫システムを健康なレベルの応答性に設定することにより、インフルエンザ感染マウスの生存率を高めることが示された。喘息やアレルギーを含む様々な慢性炎症性疾患に対して、食物繊維と短鎖脂肪酸（SCFA）の有益な効果は近年大きな注目を集めている、が、これらの治療法が一般的には免疫応答を弱め、感染の感受性を高める可能性があることが懸念されていた。今回 Monash University（オーストラリア）の研究者らは、発酵性の高い繊維イヌリンあるいは SCFA のいずれかを補充した食事によって、マウスがインフルエンザ感染から保護されていることを発見した。高繊維食は、肺の有害な過剰免疫反応を鈍らせ、T 細胞を活性化することによって抗ウィルス免疫を高める。これらの二重の利点は、食物繊維の微生物発酵による SCFA の生産増加をもたらす腸内細菌組成の変化によって媒介された、としている。

英文記事：
https://www.sciencedaily.com/releases/2018/05/180515113805.htm

---

A high-fiber diet protects mice against the flu virus

Date:

May 15, 2018

Source:

Cell Press

Summary:

Dietary fiber increases survival in influenza-infected mice by setting the immune system at a healthy level of responsiveness, according to a preclinical study published May 15 in the

journal Immunity. A high-fiber diet blunts harmful, excessive immune responses in the lungs while boosting antiviral immunity by activating T cells. These dual benefits were mediated by changes in the composition of gut bacteria.

FULL STORY

Dietary fiber increases survival in influenza-infected mice by setting the immune system at a healthy level of responsiveness, according to a preclinical study published May 15th in the journal *Immunity*. A high-fiber diet blunts harmful, excessive immune responses in the lungs while boosting antiviral immunity by activating T cells. These dual benefits were mediated by changes in the composition of gut bacteria, leading to an increase in the production of short-chain fatty acids (SCFAs) through the microbial fermentation of dietary fiber.

"The beneficial effects of dietary fiber and SCFAs on a variety of chronic inflammatory diseases, including asthma and allergies, have received substantial attention in recent years and have supported momentum toward their use in clinical studies," says senior study author Benjamin Marsland of Monash University. "But we were concerned that these treatments might lead to a general dampening of immune responses and could increase susceptibility to infections."

From a public health perspective, influenza A infection is especially relevant because it is one of the most common viral diseases worldwide. Up to 20% of people are infected each year, resulting in substantial morbidity and mortality. In the new study, Marsland and his team found that mice were protected from influenza infection by a diet supplemented with either the highly fermentable fiber inulin or SCFAs.

Specifically, these treatments led to both the dampening of the innate immune response that is typically associated with tissue damage, and also the enhancement of the adaptive immune response that is charged with eliminating pathogens.

"We typically find that a certain treatment turns our immune system either on or off," Marsland says. "What surprised us was that dietary fiber was selectively turning off part of our immune system, while turning on another, completely unrelated part of our immune system."

Taken together with past studies, the new findings suggest that the modern Western diet consisting of food high in sugar and fat and low in fiber could increase susceptibility to inflammatory diseases while decreasing protection against infections. From a therapeutic standpoint, additional research is needed to determine how much fiber, and what type of fiber, would be most effective in humans.

For their own part, Marsland and his team will further examine how dietary changes influence the immune system, and particularly how changes in the gut can influence lung diseases. Currently, they are planning dietary intervention studies in humans to determine how their results could best be translated to day-to-day living.

"There is a need for carefully designed and controlled dietary or SCFA intervention studies in humans to address how these findings could be exploited to benefit people with asthma, or for preventing viral infections," Marsland says. "We should also look further into these pathways as a means of supplementing other therapies or enhancing vaccine efficacy."

Story Source:

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

Journal Reference:

1. Aurélien Trompette, Eva S. Gollwitzer, Céline Pattaroni, Isabel C. Lopez-Mejia, Erika Riva, Julie Pernot, Niki Ubags, Lluis Fajas, Laurent P. Nicod, Benjamin J. Marsland. **Dietary Fiber Confers Protection against Flu by Shaping Ly6c – Patrolling Monocyte Hematopoiesis and CD8 T Cell Metabolism**. *Immunity*, 2018; 48 (5): 992 DOI: 10.1016/j.immuni.2018.04.022

Cite This Page:

- MLA
- APA
- Chicago

Cell Press. "A high-fiber diet protects mice against the flu virus." ScienceDaily. ScienceDaily, 15 May 2018. <www.sciencedaily.com/releases/2018/05/180515113805.htm>.

目次に戻る

6. ゲノム編集でアルツハイマー病を予防 -マウス実験

2018 年 5 月 16 日

理化学研究所 脳神経科学研究センター（理研 CBS）の研究者らは、マウスのアルツハイマー病を防御できる突然変異を発見した。
アルツハイマー病の特徴の一つは、ニューロン間でのプラークの蓄積であり、これらのプラークは、切断される前のアミロイド前駆体タンパク質（APP）の残りの部分であるアミロイドベータから作られる。これまでの研究で 300 を超える遺伝子変異が疾患発症の原因となることが分かっているが、この疾患の発症リスクを低下させる遺伝子変異については同定されていなかった。
今回 *Nature Communications* 誌に掲載されたこの研究は、正常遺伝子を変異型と置き換えるために CRISPR 技術を使用し、この疾患のマウスモデルにおいてこの変異起こすことによって、アミロイドベータの蓄積が制御されることを観察した。

参考記事：
www.riken.jp/pr/press/2018/20180504_2/

英文記事：
https://www.sciencedaily.com/releases/2018/05/180516101445.htm

---

Mutation protects against Alzheimer's-like disease in mice

Date:

May 16, 2018

Source:

RIKEN

Summary:

Researchers have discovered a mutation that can protect against Alzheimer's disease in mice. The study found that a specific mutation can reduce the characteristic accumulation of the amyloid-beta peptide that occurs.

FULL STORY

Researchers at the RIKEN Center for Brain Science have discovered a mutation that can protect against Alzheimer's disease in mice. Published in the scientific journal *Nature Communications*, the study found that a specific mutation can reduce the characteristic accumulation of the amyloid-beta peptide that occurs.

Most of us are aware of the mental and behavioral changes that occur in people with Alzheimer's disease. Perhaps less well-known outside the scientific world are the physical changes that happen in the brain. One of the hallmarks of the disease is the accumulation of plaques between neurons. These plaques are made from amyloid-beta, which is the leftover part of the amyloid precursor protein (APP) before it has been cut up. Building off of previous research, the team led by Takaomi Saido created mice with a mutated *App* gene, hoping that it could reduce the formation of amyloid-beta plaques.

Previous research had led the team to believe that an *App* gene with a specific deletion might reduce amyloid-beta build up. They used CRISPR technology to replace the normal gene with the mutated version, and indeed observed less amyloid-beta accumulation in the mouse model of the disease.

This knock-in process is a little messier than it sounds, and as expected, sample mice varied in how much of the desired deletion was actually deleted. This was useful because the team was able to see that most drastic reductions in amyloid-beta plaques were the mice with the most compete

deletions. Further analysis showed that expression levels of the APP protein correlated with those of amyloid-beta, which was also expected.

This process for finding beneficial mutations is powerful. Random screening of human populations is not easy if the frequency of the mutation is low, and of course it only works with naturally occurring mutations. Additionally, the study shows the usefulness of gene-editing targeted screening in a disease that affects millions of people worldwide, but despite decades of research, still has no effective treatment.

Story Source:

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

Journal Reference:

1. Kenichi Nagata, Mika Takahashi, Yukio Matsuba, Fumi Okuyama-Uchimura, Kaori Sato, Shoko Hashimoto, Takashi Saito, Takaomi C. Saido. **Generation of App knock-in mice reveals deletion mutations protective against Alzheimer's disease-like pathology**. *Nature Communications*, 2018; 9 (1) DOI: 10.1038/s41467-018-04238-0

Cite This Page:

- MLA
- APA
- Chicago

RIKEN. "Mutation protects against Alzheimer's-like disease in mice." ScienceDaily. ScienceDaily, 16 May 2018. <www.sciencedaily.com/releases/2018/05/180516101445.htm>.

目次に戻る

7．バイオエンジニアリングゲルによって脳卒中後脳組織を再増殖させる-マウス実験

2018 年 5 月 21 日

脳卒中で損傷した脳を持つマウスでは、新しいストローク　ヒーリングゲルがニューロンや血管の再成長を助けた、と UCLA の研究者らが *Nature Materials* 誌の 5 月 21 日号で報告している。

脳は、脳卒中および他の疾患後回復する能力が限られている。肝臓や皮膚のような体内の他の臓器とは異なり、脳は新たな繋がりや血管や新しい組織構造を再生しない。脳卒中のために脳内で死亡した組織は吸収され、血管やニューロンや軸索のない空洞を残す。そこで研究者らは、脳組織の特性を模倣するように卒中腔に注射するようにゲルを設計し、新たな成長の足場を作った。16 週間後、マウスの卒中腔には新しいニューラルネットワークを含む再生脳組織が見られた。

この結果は、このようなアプローチがヒトの脳卒中の新しい治療法となる可能性があることを示唆するものだ、としている。

英文記事：

https://www.sciencedaily.com/releases/2018/05/180521131811.htm

---

Mice regrow brain tissue after stroke with bioengineered gel

Replacement neurons, blood vessels fill in stroke cavity; gel provides scaffolding

Date:

May 21, 2018

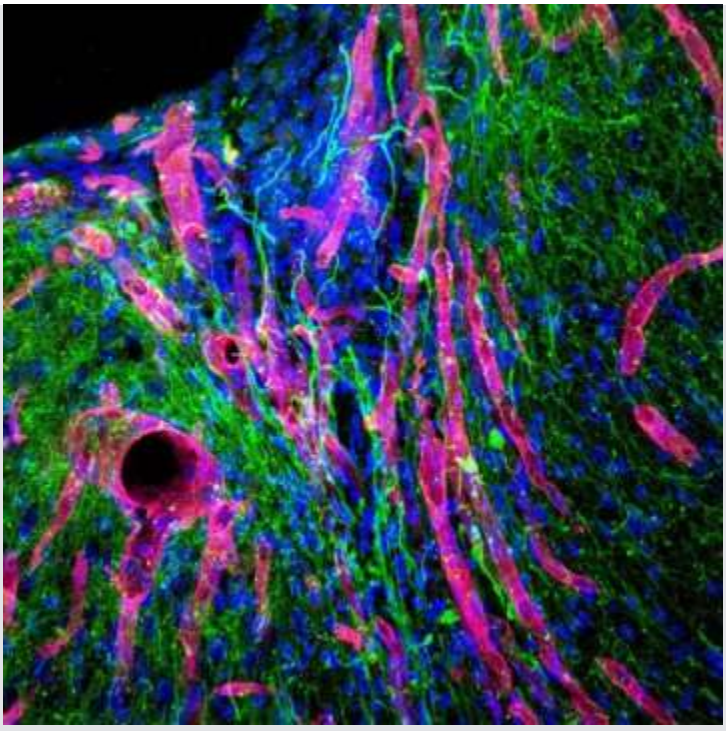
Source:

University of California - Los Angeles

Summary:

In a first-of-its-kind finding, a new stroke-healing gel helped regrow neurons and blood vessels in mice with stroke-damaged brains, researchers report.

FULL STORY



This is a photomicrograph of tissue that has grown into the stroke cavity in the stroke-healing gel. The red tubes are blood vessels. They are growing into the site of the stroke in the center of the image. The green filaments are axons. These grow along the blood vessels as they enter the gel and infarct area. The blue ovoids are cell nuclei in the tissue.

Credit: UCLA Health

In a first-of-its-kind finding, a new stroke-healing gel helped regrow neurons and blood vessels in mice with stroke-damaged brains, UCLA researchers report in the May 21 issue of *Nature Materials*.

"We tested this in laboratory mice to determine if it would repair the brain in a model of stroke, and lead to recovery," said Dr. S. Thomas Carmichael, Professor and Chair of neurology at UCLA. "This study indicated that new brain tissue can be regenerated in what was previously just an inactive brain scar after stroke."

The results suggest that such an approach may someday be a new therapy for stroke in people, said Dr. Tatiana Segura, a former Professor of Chemical and Biomolecular Engineering at UCLA who is now a professor at Duke University. Carmichael and Segura collaborated on the study.

The brain has a limited capacity for recovery after stroke and other diseases. Unlike some other organs in the body, such as the liver or skin, the brain does not regenerate new connections, blood vessels or new tissue structures. Tissue that dies in the brain from stroke is absorbed, leaving a cavity, devoid of blood vessels, neurons or axons, the thin nerve fibers that project from neurons.

To see if healthy tissue surrounding the cavity could be coaxed into healing the stroke injury, Segura engineered a gel to inject into the stroke cavity that thickens to mimic the properties of brain tissue, creating a scaffolding for new growth.

The gel is infused with molecules that stimulate blood vessel growth and suppress inflammation, since inflammation results in scars and impedes regrowth of functional tissue.

After 16 weeks, stroke cavities in mice contained regenerated brain tissue, including new neural networks -- a result that had not been seen before. The mice with new neurons showed improved motor behavior, though the exact mechanism wasn't clear.

"The new axons could actually be working," said Segura. "Or the new tissue could be improving the performance of the surrounding, unharmed brain tissue."

The gel was eventually absorbed by the body, leaving behind only new tissue.

This research was designed to explore recovery in acute stroke, or the period immediately following stroke -- in mice, that is five days; in humans, that is two months. Next, Carmichael and

Segura are determining if brain tissue can be regenerated in mice long after the stroke injury. More than 6 million Americans are living with the long-term outcomes of stroke, known as chronic stroke.

Story Source:

Materials provided by **University of California - Los Angeles**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Lina R. Nih, Shiva Gojgini, S. Thomas Carmichael, Tatiana Segura. **Dual-function injectable angiogenic biomaterial for the repair of brain tissue following stroke**. *Nature Materials*, 2018; DOI: 10.1038/s41563-018-0083-8

Cite This Page:

- MLA
- APA
- Chicago

University of California - Los Angeles. "Mice regrow brain tissue after stroke with bioengineered gel: Replacement neurons, blood vessels fill in stroke cavity; gel provides scaffolding." ScienceDaily. ScienceDaily, 21 May 2018. <www.sciencedaily.com/releases/2018/05/180521131811.htm>.

目次に戻る

8. 結核とパーキンソン病との関連性 発見

2018 年 5 月 22 日

英国フランシス・クリック研究所およびニューカッスル大学と GSK が主導する新たな共同研究によると、免疫細胞が結核（TB）のような細菌感染を除去するために使用するメカニズムは、パーキンソン病にも関与している可能性がある、としている。
細胞におけるこれらの知見は、マウス実験によって支持された。 パーキンソン病患者の最も一般的な遺伝子変異は、LRRK2 と呼ばれる遺伝子であり、LRRK2 タンパク質を過活動状態にする。研究者らはマウスで LRRK2 の遺伝子を欠失したところ、結核感染に対する早期免疫応答の増強を示し、感染後 2 週間まで対照マウスよりも肺の結核菌レベルが有意に低いことを発見した。このメカニズムは、パーキンソン病においても起こりうると考えられている。
この発見は、パーキンソン病の原因について説明し、パーキンソン病を治療するために設計された薬物が結核にも働く可能性があることを示唆している。
この研究は、*EMBO Journal* 誌に掲載されている。

英文記事：
https://www.sciencedaily.com/releases/2018/05/180522082131.htm

---

Link between tuberculosis and Parkinson's disease discovered

The mechanism our immune cells use to clear bacterial infections like tuberculosis (TB) might also be implicated in Parkinson's disease

Date:

May 22, 2018

Source:

The Francis Crick Institute

Summary:

The mechanism our immune cells use to clear bacterial infections like tuberculosis (TB) might also be implicated in Parkinson's disease, according to a new study. The findings provide a possible explanation of the cause of Parkinson's disease and suggest that drugs designed to treat Parkinson's might work for TB too.

FULL STORY

The mechanism our immune cells use to clear bacterial infections like tuberculosis (TB) might also be implicated in Parkinson's disease, according to a new collaborative study led by the Francis Crick Institute, Newcastle University and GSK.

The findings, which will be published in *The EMBO Journal*, provide a possible explanation of the cause of Parkinson's disease and suggest that drugs designed to treat Parkinson's might work for TB too.

Parkinson's protein

The most common genetic mutation in Parkinson's disease patients is in a gene called LRRK2, which makes the LRRK2 protein overactive.

Drugs that block LRRK2 are a promising new treatment for Parkinson's, with many pharmaceutical companies developing drugs to target LRRK2 and clinical trials underway. But how overactive LRRK2 causes Parkinson's and why LRRK2 blockers work was a mystery.

The biological causes of Parkinson's remain largely unknown, making it more difficult to develop and improve treatments. Discovering a mechanism that causes Parkinson's and how drugs affect it could significantly advance efforts to improve treatments.

Insights from TB

By studying what LRRK2 does in immune cells called macrophages that are infected with *Mycobacterium tuberculosis (Mtb)* -- the bacterium that causes TB -- researchers believe they have uncovered a potential cause of Parkinson's.

Macrophages recognise and engulf Mtb securing it within tight-fitting internal compartments called phagosomes. Another part of the cell called the lysosome then fuses with the phagosome to destroy the bacterium inside.

Using a combination of experimental approaches, Crick and GSK researchers, in collaboration with proteomics specialist Matthias Trost from Newcastle University, found that LRRK2 prevents phagosomes from fusing with lysosomes in both human and mouse macrophages, making them less efficient at clearing bacteria. Deleting the LRRK2 gene or treating the cells with an LRRK2 blocker significantly reduced levels of Mtb.

These findings in cells were supported by experiments in mice. When the researchers deleted the gene for LRRK2 in mice, they found that they exhibited an enhanced early immune response to TB infection, and had significantly lower levels of Mtb in their lungs than control mice up to two weeks after infection.

"We think that this mechanism might also be at play in Parkinson's disease, where abnormal masses of protein called 'Lewy bodies' build up in neurons in the brain and cause damage," said Susanne Herbst, joint first author of the paper and post-doctoral fellow at the Crick.

The team suspect that LRRK2 might be preventing immune cells in the brain from degrading cell debris properly, leading to a build-up of protein in neurons that disrupts their function.

Susanne added: "By studying TB, we have found a possible explanation for why LRRK2 mutations are a genetic risk factor for Parkinson's disease. It's exciting when different fields of research connect up in unexpected ways like this!"

Co-author Patrick Lewis, Associate Professor in Cellular and Molecular Neuroscience at the University of Reading, said: "The dogma in the Parkinson's field has been to focus almost exclusively on what is happening to neurons in the brain to make them degenerate. But over the last few years, there has been a growing appreciation of the integral role of other cells in the brain and particularly the immune system in keeping neurons healthy. This study reinforces why we should think more broadly about the events that cause neurodegeneration, and that some of the answers to Parkinson's disease might come from immunology."

New TB treatments

The findings also suggest that LRRK2 inhibitors could be a powerful new way of combating TB, which kills 1.67 million people every year.

"Drug-resistant TB is a serious emerging problem, and boosting the body's own immune defence against TB is an important step in the battle against antibiotic resistant strains," said Max Gutierrez, Group Leader at the Crick and senior author of the paper.

"LRRK2 inhibiting drugs are already being developed to treat Parkinson's disease and we're trying to see if we can repurpose them as a potential new TB therapy. This should be relatively straightforward because TB infects the lungs, so the LRRK2 inhibitors wouldn't need to cross the blood-brain barrier like they do in Parkinson's disease."

Story Source:

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

Journal Reference:

1. Anetta Härtlova, Susanne Herbst, Julien Peltier, Angela Rodgers, Orsolya Bilkei-Gorzo, Antony Fearns, Brian D Dill, Heyne Lee, Rowan Flynn, Sally A Cowley, Paul Davies, Patrick A Lewis, Ian G Ganley, Jennifer Martinez, Dario R Alessi, Alastair D Reith, Matthias Trost, Maximiliano G Gutierrez. **LRRK2 is a negative regulator of Mycobacterium tuberculosis phagosome maturation in macrophages**. *The EMBO Journal*, 2018; e98694 DOI: 10.15252/embj.201798694

Cite This Page:

- MLA

- APA
- Chicago

The Francis Crick Institute. "Link between tuberculosis and Parkinson's disease discovered: The mechanism our immune cells use to clear bacterial infections like tuberculosis (TB) might also be implicated in Parkinson's disease." ScienceDaily. ScienceDaily, 22 May 2018. <www.sciencedaily.com/releases/2018/05/180522082131.htm>.

目次に戻る

9．腸内細菌がケトン体食の抗発作作用に重要な役割 -マウス実験

2018 年 5 月 24 日

先ごろ何かと耳にする、ロバート・アトキンス博士の考案したケトン体ダイエットだが、カリフォルニア大学ロサンゼルス校（UCLA）の科学者らは、高脂肪＆低炭水化物のケトン体ダイエットの抗てんかん発作作用に本質的な役割を果たす特定の腸内細菌を同定した。今日の *Cell* 誌に掲載されたこの研究は、ヒトの腸内細菌と発作の感受性との因果関係を初めて確立するものである。

研究者らは、微生物叢が発作に対して保護効果を持つかどうか調べる為に、滅菌実験室環境において無菌で飼育されたマウスと腸内微生物を枯渇させる抗生物質で治療されたマウスの 2 種類でケトン飼料の効果を分析したところ、どちらにも効果が見られなかった。さらに、研究者らは、腸内微生物の DNA からヌクレオチドとして知られる有機分子の正確な順序を特定し、この保護を提供する上で重要な役割を果たす 2 種類の細菌が Akkermansia muciniphila および Parabacteroides 種であることを突き止めた。

この成果に基づいててんかん治療微生物薬の開発会社 Bloom Science が既に発足している。

英文記事：

https://www.sciencedaily.com/releases/2018/05/180524141700.htm

---

Gut bacteria play key role in anti-seizure effects of ketogenic diet

Date:

May 24, 2018

Source:

University of California - Los Angeles

Summary:

Scientists have identified specific gut bacteria that play an essential role in the anti-seizure effects of the ketogenic diet. The study is the first to establish a causal link between seizure susceptibility and the gut microbiota -- the 100-trillion-or-so bacteria and other microbes that reside in our intestines.

FULL STORY

UCLA scientists have identified specific gut bacteria that play an essential role in the anti-seizure effects of the high-fat, low-carbohydrate ketogenic diet. The study, published today in the journal *Cell*, is the first to establish a causal link between seizure susceptibility and the gut microbiota -- the 100 trillion or so bacteria and other microbes that reside in the human body's intestines.

The ketogenic diet has numerous health benefits, including fewer seizures for children with epilepsy who do not respond to anti-epileptic medications, said Elaine Hsiao, UCLA assistant professor of integrative biology and physiology, and senior author of the study. However, there has been no clear explanation for exactly how the diet aids children with epilepsy.

Researchers in Hsiao's laboratory hypothesized that the gut microbiota is altered through the ketogenic diet and is important for the diet's anti-seizure effects. Hsiao's research team conducted a comprehensive investigation into whether the microbiota influences the ability of the diet to protect against seizures and if so, how the microbiota achieves these effects.

In a study of mice as a model to more thoroughly understand epilepsy, the researchers found that the diet substantially altered the gut microbiota in fewer than four days, and mice on the diet had significantly fewer seizures.

To test whether the microbiota is important for protection against seizures, the researchers analyzed the effects of the ketogenic diet on two types of mice: those reared as germ-free in a sterile laboratory environment and mice treated with antibiotics to deplete gut microbes.

"In both cases, we found the ketogenic diet was no longer effective in protecting against seizures," said lead author Christine Olson, a UCLA graduate student in Hsiao's laboratory. "This suggests that the gut microbiota is required for the diet to effectively reduce seizures."

The biologists identified the precise order of organic molecules known as nucleotides from the DNA of gut microbiota to determine which bacteria were present and at what levels after the diet was administered. They identified two types of bacteria that were elevated by the diet and play a key role in providing this protection: Akkermansia muciniphila and Parabacteroides species.

With this new knowledge, they studied germ-free mice that were given these bacteria.

"We found we could restore seizure protection if we gave these particular types of bacteria together," Olson said. "If we gave either species alone, the bacteria did not protect against seizures; this suggests that these different bacteria perform a unique function when they are together."

The researchers measured levels of hundreds of biochemicals in the gut, blood and hippocampus, a region of the brain that plays an important role in spreading seizures in the brain. They found that the bacteria that were elevated by the ketogenic diet alter levels of biochemicals in the gut and the blood in ways that affect neurotransmitters in the hippocampus.

How do the bacteria do this? "The bacteria increased brain levels of GABA -- a neurotransmitter that silences neurons -- relative to brain levels of glutamate, a neurotransmitter that activates neurons to fire," said co-author Helen Vuong, a postdoctoral scholar in Hsiao's laboratory.

"This study inspires us to study whether similar roles for gut microbes are seen in people that are on the ketogenic diet," Vuong said.

"The implications for health and disease are promising, but much more research needs to be done to test whether discoveries in mice also apply to humans," said Hsiao, who has helped to develop a company that will examine the potential clinical applications of her laboratory's findings.

Story Source:

Materials provided by **University of California - Los Angeles**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Christine A. Olson, Helen E. Vuong, Jessica M. Yano, Qingxing Y. Liang, David J. Nusbaum, Elaine Y. Hsiao. **The Gut Microbiota Mediates the Anti-Seizure Effects of the Ketogenic Diet**. *Cell*, 2018; DOI: 10.1016/j.cell.2018.04.027

Cite This Page:

- MLA
- APA
- Chicago

University of California - Los Angeles. "Gut bacteria play key role in anti-seizure effects of ketogenic diet." ScienceDaily. ScienceDaily, 24 May 2018. <www.sciencedaily.com/releases/2018/05/180524141700.htm>.

目次に戻る

10. 前立腺癌における大きな課題への手がかり -マウス実験

2018 年 5 月 28 日

ミシガン大学ローゲル癌センターの研究者らは、前立腺癌において重要な役割を果たすアンドロゲン受容体からのシグナルを制御する ARLNC1 という新遺伝子を同定した。この長い非コード RNA をマウスにおいてノックダウンすると、癌細胞死が起こった。
Nature Genetics 誌に掲載されたこの研究は、この発見が生来の治療の重要な標的になる可能性がある、としている。

英文記事：
https://medicalxpress.com/news/2018-05-genome-dark-clues-major-prostate.html

---

Published: March 29, 2018.

Genome's dark matter offers clues to major challenge in prostate cancer

May 28, 2018, University of Michigan

Arul Chinnaiyan, M.D., Ph.D. Credit: Rogel Cancer Center

The dark matter of the human genome may shed light on how the hormone androgen impacts prostate cancer.

Researchers at the University of Michigan Rogel Cancer Center identified a novel gene they named ARLNC1 that controls signals from the androgen receptor, a key player in prostate cancer. Knocking down this long non-coding RNA in mice led to cancer cell death, suggesting this may be a key target for future therapies. The study is published in *Nature Genetics*.

Current prostate cancer treatments aim to block the androgen receptor to stop cancer growth. But most patients become resistance to androgen-specific therapies, developing a challenging form of the disease called metastatic castration-resistant prostate cancer.

"The androgen receptor is an important target in prostate cancer. Understanding that target is important. This study identifies a feedback loop that we could potentially disrupt as an alternative to blocking the androgen receptor directly,"

says study senior author Arul Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology.

Chinnaiyan's lab identified thousands of lncRNAs in a 2015 paper. Long non-coding RNAs are considered the dark matter of the genome because so little is known about them.

While searching for lncRNAs that might play a role in prostate cancer, the team discovered that ARLNC1 is elevated in prostate cancer relative to benign prostate tissue, which suggests a role in cancer development. And it was associated with androgen receptor signaling, which made it more intriguing.

The researchers found that the androgen receptor actually induces ARLNC1 expression. Then ARLNC1 binds to the androgen receptor messenger RNA transcript. This stabilizes the level of androgen receptor, which then feeds back to sustain ARLNC1.

"At the end of the day, you're creating or stabilizing more androgen receptor signaling in general and driving this oncogenic pathway forward. We're envisioning a potential therapy against ARLNC1 in combination with therapy to block the androgen receptor—which would hit the target and also this positive feedback loop," Chinnaiyan says.

When researchers blocked ARLNC1 in cell lines expressing androgen receptor, it led to cancer cell death and prevented tumor growth. In mouse models, elevating ARLNC1 caused large tumors to form. Knocking down ARLNC1 in mice caused tumors to shrink.

Researchers plan to continue studying the biology of ARLNC1 to understand how it's involved in prostate cancer progression and androgen receptor signaling.

"We want to further characterize the dark matter of the genome," Chinnaiyan says. "There are a number of these lncRNAs that we don't understand how they functionally work. Some of them will certainly be very useful as cancer biomarkers and we think a subset are important in biological processes."

Explore further: A new method for prostate cancer imaging

More information: Yajia Zhang et al, Analysis of the androgen receptor–regulated lncRNA landscape identifies a role for ARLNC1 in prostate cancer progression, *Nature Genetics* (2018). **DOI: 10.1038/s41588-018-0120-1**

Journal reference: Nature Genetics