BIO NEWS

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目次

2018 年 8 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 8 月のニュース

＝企業関連ニュース他＝

・BeiGene、香港での IPO で 8 億ドル超調達を計画（7/31）

・1Q 決算が不調の武田にとって Shire の開発品は頼もしい（8/1）

今年の 1Q（4-6 月）営業利益が昨年同期に比べておよそ半減（49%減少）した武田薬品と同社が買う Shire の開発品をまとめて最大の年間売り上げ予想額が大きい順に並べると上位 10 品のうち殆ど（7 品）が Shire の開発品

・GSK、バングラディシュの古い工場を閉鎖～1000 人程度解雇（8/1）

・LEO Pharma が Bayer の皮膚科処方薬事業を買収（8/1）

・Ascletis Pharma の設立者兼 CEO が香港 IPO で 11 億ドルの財を成した（8/2）

・BeiGene が香港での IPO で 9 億 300 万ドルを調達（8/3）

2016 年に米国ナスダック市場に上場して既に 1 億 5,800 万ドルを集めた中国北京拠点の BeiGene だが、規制緩和で可能になった香港証券取引所で再度 IPO して 9 億 300 万ドルを調達

・Janssen と Bayer が人件費の上昇と労働組合との対立を背景にして韓国工場を閉鎖（8/5）

・英国の EU 離脱後用の製品備蓄を製薬会社が増やしている（8/5）

・英国の EU 離脱で欧州医薬品庁職員が予想以上に失われる（8/5）

・身近なプラスチック成分は日光を浴びて温暖化ガス・メタンやエチレンを放つ（8/5）

・英国で大麻製品が医療で合法的に使用できるようになる（8/6）

・シエラレオネのコウモリからエボラウイルスの新種が見つかった～人への感染能はまだ不明（8/6）

・京都大学、パーキンソン病患者脳への iPS 細胞由来神経前駆細胞投与試験を開始（8/6）

・コンゴでの新たなエボラ流行に対して Merck のワクチン接種が始まる（8/7）

・ニュージャージー州の Antares Pharma、Pfizer の薬と一体化した応急ペン型自己注射器を開発（8/7）

・AI 利用創薬支援会社 Sensyne Health がロンドン証券取引所 AIM に来週上場予定（8/8）

・米国の薬剤給付管理会社 Express Scripts が 48 の薬剤を保険支払い対象から除外（8/8）

・肝疾患治療を開発する Ambys Medicines が武田薬品との提携と共に発足（8/9）

・Salk Institute が性差別を訴えた女性研究者 3 人のうち 2 人と和解（8/9）

・協和発酵キリン、リンパ腫薬 Poteligeo が FDA に承認された（8/9）

・アステラス製薬、英国の Quethera 買収～遺伝子治療の取り組みを更に強化（8/10）

・英国の Vernalis を米国サンディエゴ拠点の Ligand Pharmaceuticals が 4,300 万ドルで買収（8/13）
・スマホのブルーライトで失明早まる可能性 -米研究（8/14）
・J&J が Remicade バイオシミラーを不当に締め出しているとの Pfizer 訴訟が前進（8/15）
・Pfizer などが投資する神経保護薬開発会社 Magnolia が 3,100 万ドルを調達して発足（8/15）
・メリーランド州の Emergent BioSolutions がワクチン会社 PaxVax を現金 2 億 7,000 万ドルで買収（8/15）
・Insilico, Juvenescence, Buck Institute が老化疾患治療薬を開発する新会社を設立（8/15）
・Gilead、この 3 月に最高医学責任者（CMO）に就任したばかりの Andrew Cheng 氏が辞任（8/16）
・Roche 子会社 Genentech がカリフォルニア州サウスサンフランシスコ拠点の従業員 223 人を解雇（8/17）
・Foundation Medicine の元リーダーが Third Rock Ventures に加入（8/17）
・麻薬過剰摂取で米国人 72,000 人が昨年死亡（8/19）
・がんゲノム登録義務化 -厚労省（8/19）
・iPS で血小板 輸血へ臨床申請 -京大（8/20）
・英国と米国の寿命は他の高所得国と違って低下し続けている（8/20）
・炭水化物が摂取カロリーの半分ほどの人が最も死亡率が低い -米研究（8/20）
・eLife 設立者兼編集長の Randy Schekman 氏が同職を去る（8/21）
・ニューヨーク大学医学部の授業料がただになる（8/22）
・「ディオバン」の論文データ改ざん事件を受けて、名大の研究論文を科学誌が撤回（8/24）
・コンゴ共和国が米 NIH 開発抗体のエボラ患者への投与開始（8/24）
・Sangamo の元役員 Winson Tang 氏等がインサイダー取引で告訴された（8/24）
・楽天の三木谷 CEO が率いる抗癌剤の Rakuten Aspyrian が 1 億 5,000 万ドル調達（8/24）
・米国立衛生研究所（NIH）への前年より 5%多い予算配分を議会上院が承認（8/26）
NIH の予算増加を米国議会上院が 4 年連続で承認。2019 年 10 月 1 日から始まる 2019 年度の NIH 予算を前年に比べて約 5%（20 億ドル）上げて 391 億ドルとすることが承認された。

・容器に残った抗がん剤、使用可能に -厚労省が初の指針 (8/27)
・ニューヨーク拠点の Y-mAbs、最大 9,200 万ドルの IPO を計画 (8/28)
・処方薬の値段を広告に記すことを製薬会社に義務付ける法案が米議会上院を通過 (8/28)
・筋ジス仕組み解明 酸化ストレスで悪化 -京大 iPS 細胞研究所 (8/28)
・「レム睡眠」二つの必須遺伝子を特定 -マウス実験 -理化学研など (8/29)

目次に戻る

1．老化と繁殖の慣習に反するハダカデバネズミ

2018 年 8 月 1 日

ハダカデバネズミは地中に 300 匹近い大規模なコロニーを作って生活する。そのコロニーの中では 1 つのペアのみが繁殖を行い、それ以外は全て非繁殖個体の労働力となる。繁殖ペアには生殖の代謝コストが伴うわけだが、女王ネズミを例にとると、他のネズミよりも長寿で、生涯通じて繁殖する。通常、哺乳動物は繁殖することにより個体の生存期間は短縮され寿命が短くなるが、ハダカデバネズミの場合はその逆なのだ。
今回ドイツのライプニッツ老化研究所（Leibniz Institute on Aging）の研究者らは、この明らかなパラドックスの元での遺伝子メカニズムを調べ、オープンアクセスジャーナル *BMC Biology* に発表した。

英文記事：
https://www.sciencedaily.com/releases/2018/08/180801224420.htm

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Naked mole-rats defy conventions of aging and reproduction

Date:

August 1, 2018

Source:

BioMed Central

Summary:

Naked mole-rats live in colonies of two breeders and around 300 non-breeding workers. Although the breeding pair carries the metabolic cost of reproduction and, in the queen's case, lactation, they live longer than non-breeders and remain fertile throughout their lives. Researchers investigated the genetic mechanisms beneath this apparent paradox.

FULL STORY

Naked mole-rats live in colonies of two breeders and around 300 non-breeding workers. Although the breeding pair carries the metabolic cost of reproduction and, in the queen's case, lactation, they live longer than non-breeders and remain fertile throughout their lives. Researchers at the Leibniz Institute on Aging in Germany investigated the genetic mechanisms beneath this apparent paradox. Their findings are published in the open access journal *BMC Biology*.

Dr Martin Bens, the corresponding author said: "Our results indicate that when naked mole-rats mature into breeders, it changes their aging rates, meaning that breeders are able to live longer than non-breeders. This is surprising, as evidence from other species suggest that reproduction, which ensures the survival of the species as a whole, reduces the lifespan of the individual. In naked mole-rats reproduction appears to prolong the breeders' lifespan. This goes against the common expectation that mammals either invest resources in a long life or in reproduction."

The researchers analyzed the transcriptomes -- the sum of all transcribed genes -- for tissue samples taken from a range of organs, including heart, liver, and gonads. They compared the transcriptomes of naked mole-rat breeders to that of non-breeders, as well as to breeding and non-breeding guinea pigs, which are close relatives of the naked mole-rat but have a shorter lifespan.

The authors found that genes related to aging were expressed differently in samples from breeding naked mole-rats than those from guinea pigs and non-breeding naked mole-rats. For example, a gene related to muscle regeneration showed higher expression in naked mole-rat breeders which may be linked to higher resistance to muscle loss during aging. Gene expression changes like this may contribute to the exceptionally long lifespan of naked mole-rat breeders.

Dr Bens said: "Unlike non-breeding guinea pigs and other rodents, non-breeding naked mole-rats are not sexually dimorphic; they show no differences in body size, body mass or external genitalia, as well as few behavioral differences. One of the main and surprising findings of our study is that transcribed genes in non-breeding naked mole-rats also show no significant differences between females and males. However, we found that the transcriptome changes significantly when they mature into breeders."

When the authors separated non-breeding naked mole-rats from colonies and paired them with naked mole-rats of the opposite sex, the workers transitioned into breeders. The transition was accompanied by physical and behavioral changes that differed between males and females -- the animals became sexually dimorphic. Sexual maturation was also associated with a change in gene expression levels linked to extended life and health span.

Dr Bens said: "Deeper investigations of naked mole-rat transcriptome data can help us understand how sexual maturation is regulated. This could potentially help us better understand sexual maturation in humans, where the onset of puberty varies between individuals and is influenced by a variety of factors such as stress and nutrition. Variations in puberty onset have implications for the risk for diseases such as breast cancer or cardiovascular diseases. Our data may help identify targets to mitigate these variations."

In another study titled 'Species comparison of liver proteomes reveals links to naked mole-rat longevity and human aging,' published in *BMC Biology* on the same day, Dr Bens and colleagues compared the liver of naked mole-rats with those of guinea pigs to further investigate the molecular mechanisms that underlie naked mole-rat longevity.

Alessandro Ori, the corresponding author of the study said: "We found that naked mole-rat livers have a unique expression pattern of mitochondrial proteins that result in distinct metabolic features of their mitochondria, including an increased capacity to utilize fatty acids. We were also able to show that similar molecular networks are affected during aging in both naked mole-rats and humans, which suggests that there may be a direct link between these networks and the longevity of these species, both of which would be expected to have much shorter lives based on their body mass."

Story Source:

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

Journal Reference:

1. Martin Bens, Karol Szafranski, Susanne Holtze, Arne Sahm, Marco Groth, Hans A. Kestler, Thomas B. Hildebrandt, Matthias Platzer. **Naked mole-rat transcriptome signatures of socially suppressed sexual maturation and links of reproduction to aging**. *BMC Biology*, 2018; 16 (1) DOI: 10.1186/s12915-018-0546-z

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目次に戻る

2. マウスの雌の繁殖能力は細胞の通信システムによって制御される

2018 年 8 月 2 日

ウィスコンシン大学マディソン校獣医学部の比較バイオサイエンス学科の教授である Joan Jorgense 氏は学部生時代にルームメートから、高校で閉経してしまうまでに生理が来たのは一回だけ、医者には将来的にも生物学的子供を授かることはないと言われた、と打ち明けられた。このルームメートの言葉に触発されて、Jorgense 氏は早発性卵巣不全のような妊娠の問題に焦点を当てた研究を行っている。
8 月 2 日に *PLOS Genetics* 誌に発表された新しい研究では、卵巣の発達によってどのようにマウスの雌の繁殖能力が影響を受けるかを理解しようとし、健康な卵を維持するために 2 つの遺伝子、IRX3 と IRX5、が一緒に働いてマウスの卵巣に細胞の通信システムを構築することを発見した、と発表している。

英文記事：
https://www.sciencedaily.com/releases/2018/08/180802102357.htm

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Muscle 'switch' may control the benefits of exercise

Scientists identify a biological pathway that boosts our ability to build aerobic capacity or muscle

Date:

August 2, 2018

Source:

Joslin Diabetes Center

Summary:

Studying lab animals and humans, researchers discovered that a protein called JNK helps to drive response to exercise. If JNK is activated during exercise, the researchers say, that stimulates skeletal muscle growth. If it's not activated, muscles improve their adaptation for endurance and aerobic capacity.

FULL STORY

Some people respond well to both aerobic exercise and strength training, while others don't. And some of us respond well to only one of those things, but not both. Scientists at Joslin Diabetes Center now have uncovered a surprising molecular "switch" that may help to explain why this happens.

"We've identified an exercise-activated biological pathway that hasn't been studied at all," says Sarah Lessard, PhD, an Assistant Investigator in Joslin's section of Clinical, Behavioral and Outcomes Research and first author on a paper presenting the research in the journal *Nature Communications*.

Studying lab animals and humans, Lessard and her colleagues discovered that a protein called c-Jun N-terminal kinase (JNK)helps to drive response to exercise. If JNK is activated during exercise, the researchers say, that stimulates skeletal muscle growth. If it's not activated, muscles improve their adaptation for endurance and aerobic capacity.

"It's like a switch," Lessard remarks. "If the switch is on, you'll have muscle growth. If it's turned off, you have endurance adaptation in the muscle."

Exercise is a foundation for our overall health, and exercise that promotes aerobic capacity is a powerful factor in preventing diabetes, cardiovascular disease and other chronic metabolic diseases. However, that capacity is not evenly distributed among us.

"If a hundred people do the exact same aerobic training program, some will have huge improvements in aerobic capacity, and some will have little to no response," Lessard notes. Her lab studies the biological signals that tell a muscle to adapt for aerobic capacity or for muscle growth.

In previous work, the Joslin team looked at which genes were activated in two groups of lab rats that had been bred for many generations to respond either very well or very poorly to endurance exercise training (running on treadmills). The scientists found that activation of the JNK biological pathway predicted that an animal would respond poorly to endurance exercise training.

That finding was a bit unexpected, since the researchers knew that JNK was associated with inflammation in metabolic diseases such as type 2 diabetes and obesity. So why would the protein be activated by exercise?

Lessard and her colleagues began their current study with mice that had been genetically modified to knock out production of JNK in their muscles. These "JNK knockout" mice remain perfectly healthy and will run vigorously on wheels in their cages very much like normal mice. ("Mice actually enjoy running several kilometers a night," Lessard remarks.)

But when both groups of mice were trained to run, the investigators found the JNK knockout mice had a much higher increase than normal mice in aerobic exercise capacity, along with higher levels of blood vessels and of a type of muscle fiber specialized to give endurance.

Next, the Joslin researchers ran an experiment that promotes muscle growth in animals. Normal mice doubled the mass of their affected muscles, but the JNK knockout mice didn't increase their muscle mass nearly as much.

Diving deeper into the biological mechanisms underlying these results, the scientists found that JNK works through a well-studied pathway involving myostatin, a protein that restrains muscle growth. Myostatin is targeted in some clinical trials that seek to increase muscle mass in aging and in diseases such as advanced cancer where muscle loss is often a serious problem.

The Joslin investigators then collaborated with Vernon Coffey, associate professor of exercise and sports science at Bond University in Gold Coast, Queensland, Australia, on tests in healthy, human volunteers. Results from Coffey's group indicated that similar biological mechanisms were at work.

The tests showed that JNK was highly activated in the muscles of humans lifting leg weights, a resistance exercise. In contrast, JNK generally was not activated in muscle when the volunteers performed cycling, an endurance exercise.

But a significant minority of test subjects did show some JNK activation in their leg muscles during endurance exercise. That activation might prevent endurance adaptations, and it might explain why some people don't respond as well to endurance exercise.

The Joslin team is looking at various ways to inhibit JNK activation. Among them, the scientists think that the activation of JNK during exercise depends on the amount of mechanical stress on the muscle, and that some people experience a higher level of mechanical stress during aerobic exercise. If so, developing approaches to reduce this stress might improve response.

Additionally, the researchers are doing experiments with animal models to try to treat this condition with drugs that inhibit JNK or related molecular targets.

The Joslin study has direct implications for the prevention of type 2 diabetes, the reduction of diabetes complications, and the prevention of cardiovascular disease. It could also prove useful for developing therapeutic approaches for building muscle to fight muscle-wasting diseases. (It also may help explain the "interference phenomenon" experienced by athletes during concurrent training.)

"We've begun to figure out how muscle decides whether it will grow or adapt for endurance, which really hasn't been known," Lessard sums up. "And we're finding that this process is directly linked to the risk of type 2 diabetes."

Lessard and her colleagues are now testing this hypothesis in a study analyzing the JNK biological pathway during endurance exercise, comparing people at heightened risk of type 2 diabetes versus people of normal risk.

If over-activation of the JNK pathway during endurance exercise does indeed boost the risk of diabetes, and if scientists can figure out a way to stop that process, "we might be able to reverse the risk in some people," Lessard speculates.

Story Source:

Materials provided by **Joslin Diabetes Center**. *Note: Content may be edited for style and length.*

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目次に戻る

3. マウスの社会性と結び付いている特定の脳回路

2018 年 8 月 8 日

スタンフォード大学医学部の研究によると、自閉症スペクトラム障害のマウスモデルにおける社会的行動は、研究者らがそのマウスの脳の一部において特定のシグナル伝達物質であるセロトニンの放出を引き起こした時に正常化した。
この研究では、実験的操作により、側坐核と呼ばれるマウスの脳の領域におけるセロトニンの広範な放出が引き起こされた。研究者らは、この領域で見出されるセロトニン受容体の特定のサブタイプを活性化する薬物が、これらの精神神経障害の社会性欠損を改善する上で治療薬となることを証明し得る、としている。
この研究成果は 8 月 8 日の *Nature* 誌に掲載されている。

英文記事：
https://www.sciencedaily.com/releases/2018/08/180808134338.htm

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Specific brain circuit tied to sociability in mice

Date:

August 8, 2018

Source:

Stanford Medicine

Summary:

Social behavior in mouse models of autism spectrum disorder normalized when investigators triggered the release of a specific signaling substance, serotonin, in a single part of the animals' brains, according to a new study.

FULL STORY

Social behavior in mouse models of autism spectrum disorder normalized when investigators triggered the release of a specific signaling substance, serotonin, in a single part of the animals' brains, according to a study from the Stanford University School of Medicine.

"This points to a previously understudied brain mechanism that contributes to an inability to derive pleasure from social interactions," said Robert Malenka, MD, PhD, professor and associate chair of psychiatry and behavioral sciences.

The brain mechanisms underlying sociability and social deficits are poorly understood, complicating attempts to find effective treatments for autism spectrum disorders, schizophrenia and other neuropsychiatric disorders marked at least in part by social withdrawal. In the study, experimental manipulations triggered extensive release of serotonin in a region of the mice's brains called the nucleus accumbens. Malenka said drugs activating a particular subtype of serotonin receptors found in this region could prove therapeutic in ameliorating the social deficits of these neuropsychiatric disorders.

The Nancy Friend Pritzker Professor in Psychiatry and Behavioral Sciences, Malenka is the senior author of the study, whose findings will be published online Aug. 8 in *Nature*. The lead author is postdoctoral scholar Jessica Walsh, PhD.

There are drugs called selective serotonin reuptake inhibitors, or SSRIs, that increase overall serotonin levels in the brain. But these widely used antidepressants take weeks to have a therapeutic effect and sometimes don't work at all -- or eventually stop working. They haven't shown efficacy in countering autism spectrum disorder's social deficits, either.

'Turning on the faucet to maximum flow'

"SSRIs increase serotonin levels about as much as a moderately leaky faucet," Malenka said. "What we did in this series of experiments in mice was more like turning on that faucet to maximum flow." The researchers also tested the effects on mice's sociability of suddenly shutting off the faucet completely.

The nucleus accumbens, a midbrain structure found in all mammals, is a crucial hub of the brain's reward circuitry, which is a collection of brain areas whose networked activity makes us feel good about something we've done or are doing. This, in turn, instructs us to do more of it.

"Evolution has ensured that certain behaviors important for survival -- eating, finding a mate, procreating, successfully escaping from predators or captivity -- feel great," Malenka said.

In most mammals, social interaction sets off the reward circuitry, too. "Hanging out with your buddies makes sense from an evolutionary survival standpoint," Malenka said. "You're more likely to find a mate and less likely to be attacked." But people with autism spectrum disorder don't interact easily with others. They don't appear to experience the same rewarding sensation that people without these illnesses do.

In the new study, the scientists performed experiments that pinpointed the relevance of serotonin release in the nucleus accumbens to social activity in mice.

"Mice aren't little human beings," Malenka said. "We can't ask them how they're feeling about their social lives. But they provide insights into the human brain. They can be very useful for studying relatively primitive mechanisms governing social behavior. For example, if something makes a mouse want to spend more time with its buddies, that something is likely to be fun for the mouse."

Controlling cell signals with light

The scientists inserted genes encoding light-sensitive proteins into sets of nerve cells in the mice's brains. The scientists could now stimulate these nerve cells to fire impulses, or inhibit them from firing, with laser light delivered by an optical fiber implanted in the animals' brains.

First, Malenka and his colleagues sensitized nerve cells to light in another brain area called the dorsal raphe. This structure, the brain's main source of serotonin, sends nerve-cell projections to many brain areas, including the nucleus accumbens. Then the scientists put mice in situations in which they could choose to socialize or not. Activating nerve cells in the dorsal raphe made the mice more sociable.

Next, some mice were bioengineered so that only serotonin-secreting nerve cells running from the dorsal raphe to the nucleus accumbens were responsive to light. The scientists focused laser light on the nucleus accumbens, causing just the serotonin-secreting nerve cells there to release the substance -- and inducing the same increased sociability. This experimental step ruled out involvement of other types of nerve cells in the tract from the dorsal raphe.

But activating this circuitry didn't make the mice more inclined to move around or explore inanimate objects, or increase their interest in food. Serotonin release in the nucleus accumbens appears to reinforce only social behavior in the animals, Malenka said, making potential drugs that mimic or enhance this local release less likely to produce unwanted behaviors, such as drug addiction, overeating and excessive gambling.

Inhibiting rather than activating serotonin release in the nucleus accumbens dramatically reduced the sociability of normally friendly mice. This indicated that serotonin release in the nucleus accumbens plays an important role in the mice's normal social behavior.

To explore the possible connection between faulty serotonin-release circuitry in the nucleus accumbens and neuropsychiatric social deficits, the scientists zeroed in on one particular version of the more than 10 different known subtypes of receptors for serotonin. This version, called 5HT-1b, is a major subtype found in the nucleus accumbens. Drugs targeting 5HT-1b might produce fewer side effects than drugs with more general serotonin-circuitry effects.

Malenka's group next turned to mouse models of autism. The scientists deleted a specific chunk of genetic material from a chromosome in these mice to mimic an effectively identical genetic deletion in humans that accounts for about 1 percent of all clinically diagnosed cases of autism spectrum disorder. In mice, deleting this DNA either in nerve cells throughout the brain or only in serotonin-secreting nerve cells from the dorsal raphe produced social deficits in the mice that resemble some of those associated with its human counterpart.

The researchers found that this mutation significantly weakened serotonin-secreting activity in the nerve cells originating in the dorsal raphe, in a manner reminiscent of the direct inhibition of serotonin-secreting nerve cells that caused social deficits in normal mice. By using light to directly force those nerve cells' release of serotonin in the nucleus accumbens, the researchers could restore normal social behavior in the mouse models of autism. They were also able to restore normal sociability by infusing a drug that directly targets and activates 5HT-1b receptors in the nucleus accumbens, a result suggesting similar drugs might be beneficial in treating social behavior deficits.

Malenka expressed surprise at the consistency and strength of the study's results. "They couldn't have come out any better if I'd made them up," he said. "Usually you see some variability -- some mice are having a bad hair day, others are having a good hair day. This time, we got similar results in almost every single animal we tested."

Malenka is deputy director of the Stanford Neurosciences Institute and a member of Stanford Bio-X.

Story Source:

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

Journal Reference:

1. Jessica J. Walsh, Daniel J. Christoffel, Boris D. Heifets, Gabriel A. Ben-Dor, Aslihan Selimbeyoglu, Lin W. Hung, Karl Deisseroth, Robert C. Malenka. **5-HT release in nucleus accumbens rescues social deficits in mouse autism model**. *Nature*, 2018; DOI: 10.1038/s41586-018-0416-4

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Stanford Medicine. "Specific brain circuit tied to sociability in mice." ScienceDaily. ScienceDaily, 8 August 2018. <www.sciencedaily.com/releases/2018/08/180808134338.htm>.

目次に戻る

４．炭水化物摂取が変形性関節症に繋がる可能性 -マウス実験

2018 年 8 月 9 日

変形性関節症（OA）のリスクに関しては、今まで体脂肪が増えれば上昇することは知られていた。今回オクラホマ医学研究財団の新しい研究によって、実験用のマウスにおいて、食事として摂られる炭水化物組成が AO のリスクを増加させることが発見された。
OA は、米国における最も一般的な形態の関節炎の障害であり、約 2,700 万人が罹患している。関節の骨をクッションする軟骨が壊れて磨耗し、骨同士が擦れ合う。
研究者らは肥満がどのように OA に寄与するか調べるために、マウスに高脂肪食を与えたが、時間の経過と共に、低脂肪対照食であってもその炭水化物構成が OA を発症する機会を与えるに充分であることを発見。主要な犯人は繊維と砂糖であったが、この結果はマウスだけでなく、ヒトにも影響を及ぼす可能性があるとしている。
研究チームは、今後、体内微生物や腸内細菌についても、OA に果たす役割について調べる予定にしている。

英文記事：
https://www.sciencedaily.com/releases/2018/08/180809112417.htm

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Dietary carbohydrates could lead to osteoarthritis, new study finds

Do your knees ache? Your diet could be a culprit

Date:

August 9, 2018

Source:

Oklahoma Medical Research Foundation

Summary:

Researchers have found that carbohydrate composition of diets increased the risk of osteoarthritis in laboratory mice -- even when the animals didn't differ in weight.

FULL STORY

Do your knees ache? According to new findings from the Oklahoma Medical Research Foundation, your diet could be a culprit.

In a study led by OMRF scientist Tim Griffin, Ph.D., researchers found that the carbohydrate composition of diets increased the risk of osteoarthritis in laboratory mice -- even when the animals didn't differ in weight.

"We know increased body fat elevates risk, but we haven't appreciated as much how diet itself affects the disease risk," said Griffin. "These findings give us new clues that there can be significant dietary effects linked to increased OA risk even in the absence of obesity."

Osteoarthritis, or OA, is the most common form of arthritis and the most widespread form of disability in the country, affecting nearly 27 million people in the U.S. It occurs when the cartilage that cushions bones in the joints breaks down and wears away, causing the bones to rub against one another.

Several factors can increase risk, including high-impact physical jobs, previous joint injuries, age and genetics, but carrying extra body weight is among the most proven contributors.

"Obesity is the one of the most significant factors for developing disease in the knee joint," said Griffin. "However, therapeutic strategies to prevent or treat obesity-associated OA are limited because of the uncertainly about the root cause of the disease."

To study how, exactly, obesity contributes to osteoarthritis, Griffin and his lab placed groups of mice on different high-fat diets. However, over time, they observed that the carbohydrate makeup of the rodents' low-fat control diet was alone sufficient to alter their chances of developing OA.

The primary culprits: fiber and sugar.

In particular, Griffin's team found that changing the amount of sucrose -- table sugar -- and fiber in the diet altered OA pathology in the rodents. The high-sucrose diet increased signs of joint inflammation, while the high-fiber diet caused changes in cartilage genes and cellular stress-response pathways.

While the study involved mice, Griffin said the findings could ultimately have human implications.

"It's important to understand how our diet affects the health of our joints," he said. "We were surprised to see so many OA-related differences between the two high-carb diets even though body weight and body fat were the same."

Griffin next plans to investigate how different types of dietary fiber and other components of our diets can contribute to OA, and also look at the role the body's microbiome and gut bacteria play in the disease.

The new findings were published in the journal *Disease Models & Mechanisms*. OMRF researchers Erika Barboza Prado Lopes, Ph.D., Albert Batushansky, Ph.D., Mike Kinter, Ph.D., and former OMRF scientist Elise Donovan, Ph.D., contributed to the research.

The work was supported by National Institutes of Health grants P20RR018758, P20GM103441, P30GM114731, P30AG050911 and R01AG049058. Griffin also received additional funding support through the Arthritis Foundation.

Story Source:

Materials provided by **Oklahoma Medical Research Foundation**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Elise L. Donovan, Erika Barboza Prado Lopes, Albert Batushansky, Mike Kinter, Timothy M. Griffin. **Independent effects of dietary fat and sucrose content on chondrocyte metabolism and osteoarthritis pathology in mice**. *Disease Models & Mechanisms*, 2018; dmm.034827 DOI: 10.1242/dmm.034827

Cite This Page:

- MLA
- APA
- Chicago

Oklahoma Medical Research Foundation. "Dietary carbohydrates could lead to osteoarthritis, new study finds: Do your knees ache? Your diet could be a culprit." ScienceDaily. ScienceDaily, 9 August 2018. <www.sciencedaily.com/releases/2018/08/180809112417.htm>.

目次に戻る

5. 尻尾の再成長には神経幹細胞が重要（サラマンダー、トカゲ、マウス比較）

2018 年 8 月 13 日

サラマンダーの尻尾を切り落とした場合、数週間後にはほぼ完全に再生される。トカゲでは、新しい尻尾が再成長するが、それは元のものとは違っている。又、マウスの場合、尻尾は全く元に戻ることはない。
ピッツバーグ大学医学部の研究者らはサラマンダーの完璧な再生とトカゲの不完全な再生を比較することにより、脊髄の幹細胞が究極の制限因子であることを発見した。
この発見は、今週の米国立科学アカデミー紀要に掲載されている。

英文と記事：
https://www.sciencedaily.com/releases/2018/08/180813160522.htm

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When it comes to regrowing tails, neural stem cells are the key

Date:

August 13, 2018

Source:

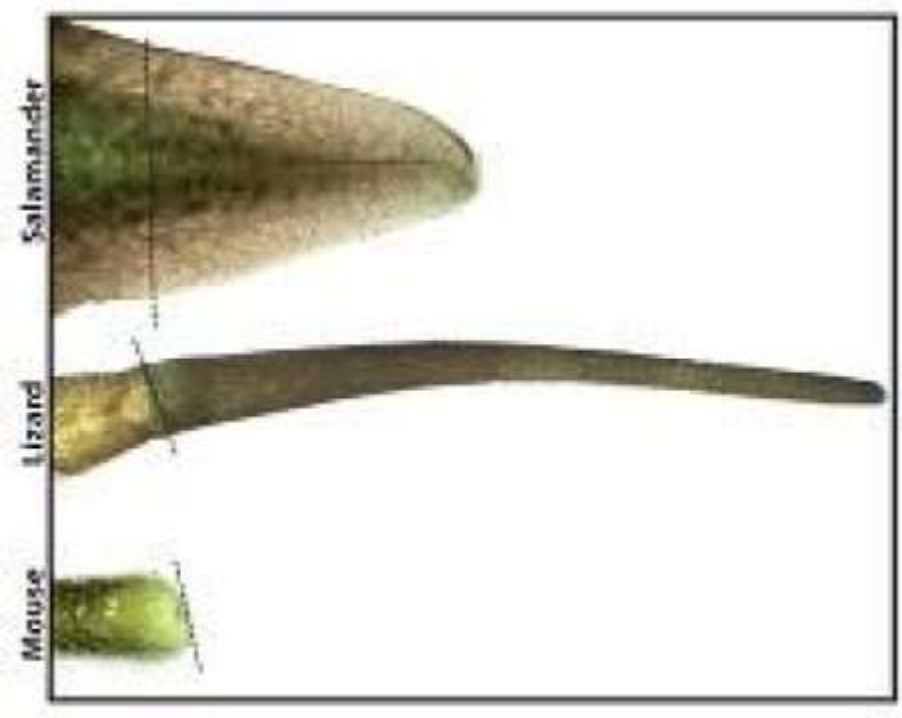
University of Pittsburgh Schools of the Health Sciences

Summary:

It's a longstanding mystery why salamanders can perfectly regenerate their tails whereas lizard tails grow back all wrong. By transplanting neural stem cells between species,

researchers have discovered that the lizard's native stem cells are the primary factor hampering tail regeneration.

FULL STORY



Salamanders tails regenerate perfectly, whereas lizard tails grow back imperfectly and mouse tails don't grow back at all.

Credit: Thomas P. Lozito

Cut off a salamander's tail and, in a few weeks, a near-perfect replacement grows. Do the same to a lizard and a new tail will regrow, but it won't be the same as the original. By comparing tail regeneration between the two animals, researchers at the University of Pittsburgh School of Medicine found that stem cells in the spinal cord are the ultimate limiting factor.

This finding, published this week in *Proceedings of the National Academy of Sciences*, answers the longstanding question of why tail regeneration is perfect in the salamander and imperfect in the lizard, and may serve as a stepping stone to understanding why mice can't regenerate their tails at all.

"The traditional animal model for regeneration is the salamander," said senior author Thomas P. Lozito, Ph.D., assistant professor in Pitt's Department of Orthopaedic Surgery, Center for Cellular and Molecular Engineering and the McGowan Institute for Regenerative Medicine. "Salamanders can regenerate a wide variety of tissues -- brain, heart, parts of their eyes, limbs, tails -- but they have whole classes of molecule types and tissues that just aren't found in mammals, so we really haven't been able to apply very much of what we found in the salamander to humans."

According to Lozito, if the goal is to translate regeneration research to non-regenerating species like humans, the lizard is a much better model than the salamander. Lizards are the closest relative to mammals that can regenerate an appendage, and they have a similar genome and biochemistry. But lizards cannot regenerate lost limbs at all, and their regenerated tails are much simpler than the originals.

"You can easily tell a lizard with a regenerated tail," Lozito said. "It doesn't get anything right. The scales are different; the color pattern is different, and then when you look inside the tail, all the tissues are different. There's no bone; the skeleton is completely cartilaginous, just tubes within tubes."

Understanding what separates perfect regeneration in the salamander from imperfect regeneration in the lizard lays the groundwork for bridging the gap to non-regenerating species, Lozito said.

Lozito's lizard of choice is the mourning gecko, which has several interesting properties, including a high tolerance for transplantation.

This feature allowed his team to take neural stem cells -- the nascent precursors of neurons and glia, the non-neuronal cells that surround them -- from the salamander and insert them into the lizard's regenerating tail stump. The goal was to see what holds back tail regeneration in the lizard: the biochemical environment or the lizard's native stem cells.

They found the transplanted salamander stem cells retained their ability to differentiate into multiple cell types, including neurons. By contrast, lizard neural stem cells could become only glial cells, which don't process the messages that direct movement and feeling.

"It was a nice surprise," said lead author Aaron Sun, Ph.D., a Pitt physician-scientist trainee who completed part of his research in Lozito's lab. "And it goes to show that maybe the regenerative processes are still somewhat conserved."

But perhaps the most surprising observation, according to Sun, is that the traditionally described "neural stem cells" driving regeneration in the lizard are not "true" neural stem cells at all. Although they check many of the classic boxes, they fall short of a defining characteristic -- the ability to spring forth a diversity of cell types.

That explains why there isn't perfect tail regeneration in the lizard, Lozito said. The neural stem cells can't produce the different cell types that would be needed to recreate the asymmetries of the original spinal cord, which in turn stymies the development of bony vertebrae.

"The spinal cord is the master regulator of tail regeneration, and these differences that we're seeing between lizard and salamander tails are due to differences in stem cell quality," Lozito said. "It's all because of the neural stem cells."

Story Source:

Materials provided by **University of Pittsburgh Schools of the Health Sciences**. *Note: Content may be edited for style and length.*

Journal Reference:

1. Aaron X. Sun, Ricardo Londono, Megan L. Hudnall, Rocky S. Tuan, Thomas P. Lozito. **Differences in neural stem cell identity and differentiation capacity drive divergent regenerative outcomes in lizards and salamanders**. *Proceedings of the National Academy of Sciences*, 2018; 201803780 DOI: 10.1073/pnas.1803780115

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University of Pittsburgh Schools of the Health Sciences. "When it comes to regrowing tails, neural stem cells are the key." ScienceDaily. ScienceDaily, 13 August 2018. <www.sciencedaily.com/releases/2018/08/180813160522.htm>.

目次に戻る

6. 大腸疾患に関するマウス実験の記事　２本

2018 年 8 月 14 日、8 月 20 日

大腸疾患に関するマウス実験の記事 2 本：

1）　**野菜に含まれる化学物質がマウスの大腸癌を予防　-フランシス・クリック研究所（イギリス）**

ケール、キャベツ、ブロッコリーなどの野菜が作る化学物質が、健康な腸を維持し大腸癌の予防に役立つ可能性があるというマウス研究で、*Immunity* 誌に掲載されている。野菜の健康上の利点は立証されているが、その背後にあるメカニズムの多くは未知のままである。この研究では、アリール炭化水素受容体（AhR）と呼ばれるタンパク質を活性化することによって、食餌中のインドール-3-カルビノール（I3C）がどのようにして大腸炎および大腸癌を予防できるかが示されている。

2）　**イチゴが大腸の有害な炎症を軽減　-マサチューセッツ大学アムハースト校**

炎症性腸疾患（IBD）は、重度の下痢や大変な痛みを伴うが、簡単な食事介入が大腸の炎症を緩和し腸の健康を改善できるとの研究が、第 256 回全米化学会（ACS）で発表された。

研究者らは、ヒトの 1 日カップ 4 分の 3 に相当する量のイチゴ消費が、IBD マウスの体重減少や血まみれの下痢症状を有意に抑制することを発見。また、炎症の減少だけでなく、大腸内の微生物組成も健全化されることを観察。イチゴが IBD マウスの異常な代謝経路にも良好な影響を与える、としている。

英文記事：

https://www.sciencedaily.com/releases/2018/08/180814173648.htm
https://www.sciencedaily.com/releases/2018/08/180820085219.htm

Chemicals found in vegetables prevent colon cancer in mice

Date:

August 14, 2018

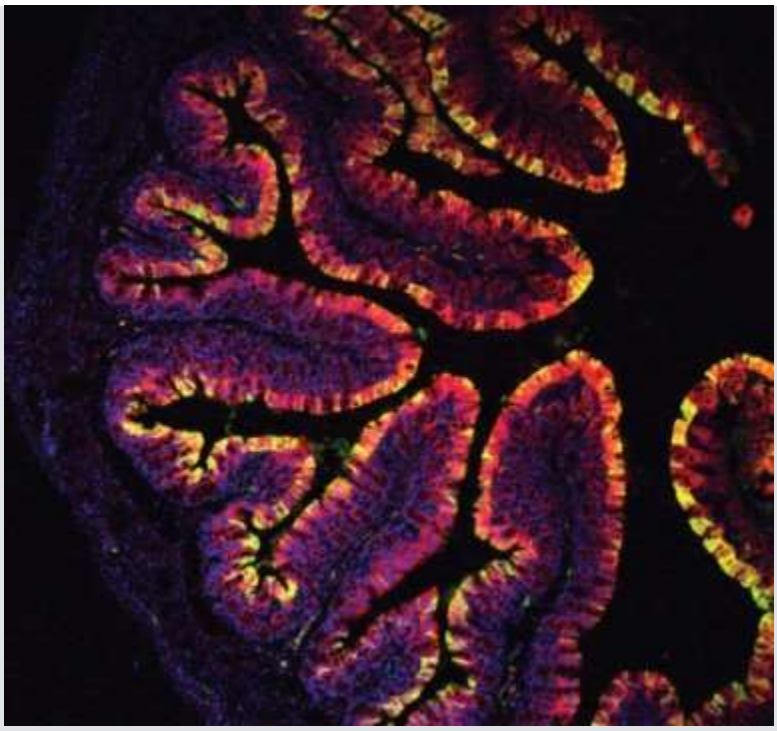
Source:

The Francis Crick Institute

Summary:

Chemicals produced by vegetables such as kale, cabbage and broccoli could help to maintain a healthy gut and prevent colon cancer, a new study shows.

FULL STORY



This is a mouse colon from Cyp1a reporter mice after feeding with I3C.

Credit: Chris Schiering, Francis Crick Institute

Chemicals produced by vegetables such as kale, cabbage and broccoli could help to maintain a healthy gut and prevent colon cancer, a new study from the Francis Crick Institute shows.

The research, published in *Immunity*, shows that mice fed on a diet rich in indole-3-carbinol -- which is produced when we digest vegetables from the Brassica genus -- were protected from gut inflammation and colon cancer.

While the health benefits of vegetables are well-established, many of the mechanisms behind them remain unknown. This study offers the first concrete evidence of how I3C in the diet can prevent colon inflammation and cancer, by activating a protein called the aryl hydrocarbon receptor (AhR).

Gut reactions

AhR acts as an environmental sensor, passing signals to immune cells and epithelial cells in the gut lining to protect us from inflammatory responses to the trillions of bacteria that live in the gut.

"We studied genetically modified mice that cannot produce or activate AhR in their guts, and found that they readily developed gut inflammation which progressed to colon cancer," explains first author Dr Amina Metidji from the Francis Crick Institute. "However, when we fed them a diet enriched with I3C, they did not develop inflammation or cancer. Interestingly, when mice whose cancer was already developing were switched to the I3C-enriched diet, they ended up with significantly fewer tumours which were also more benign."

By studying both mice and mouse gut organoids -- 'mini guts' made from stem cells -- the researchers found that AhR is vital for repairing damaged epithelial cells. Without AhR, intestinal stem cells fail to differentiate into specialised epithelial cells that absorb nutrients or generate protective mucus. Instead, they divide uncontrollably which can ultimately lead to colon cancer.

Preventing colon cancer

"Seeing the profound effect of diet on gut inflammation and colon cancer was very striking," says senior author Dr Gitta Stockinger, Group Leader at the Francis Crick Institute. "We often think of colon cancer as a disease promoted by a Western diet rich in fat and poor in vegetable content, and

our results suggest a mechanism behind this observation. Many vegetables produce chemicals that keep AhR stimulated in the gut. We found that AhR-promoting chemicals in the diet can correct defects caused by insufficient AhR stimulation. This can restore epithelial cell differentiation, offering resistance to intestinal infections and preventing colon cancer.

"These findings are a cause for optimism; while we can't change the genetic factors that increase our risk of cancer, we can probably mitigate these risks by adopting an appropriate diet with plenty of vegetables."

As well as correcting altered AhR dependent gene expression, dietary I3C also had a surprising effect on unmodified mice with normal AhR expression. While normal mice fed on standard or I3C-enriched food did not develop tumours during the study, those fed on a 'purified control diet' did.

An 'optimal' diet?

Laboratory mice are usually fed a standard grain-based 'chow' which contains a mix of ingredients and nutrients. For dietary studies, they are given a 'purified control diet' so that researchers know exactly what is in the food. These are designed to precisely fulfil the animal's nutritional needs while being free of allergens, pathogens or variable ingredients found in standard chow.

Purified control diets contain exact mixtures of carbohydrates, proteins, fats and fibres enriched with vitamins and minerals. However, the latest study suggests that these diets have fewer AhR-promoting chemicals than the standard chow or the I3C-enriched diet.

"Normal mice on the purified control diet developed colon tumours within 10 weeks, whereas mice on the standard chow didn't develop any," explains co-corresponding author Dr Chris Schiering, who worked on the study at the Crick and now works at Imperial College London. "This suggests that even without genetic risk factors, a diet devoid of vegetable matter can lead to colon cancer."

From mouse to man

To follow up on their surprising findings, the team are now hoping to do further experiments in organoids made from human gut biopsies and eventually human trials.

"A number of epidemiological studies suggested that vegetables may be protective against cancer," explains Gitta. "However, there is very little literature on which vegetables are the most beneficial or why. Now that we've demonstrated the mechanistic basis for this in mice, we're going to

investigate these effects in human cells and people. In the meantime, there's certainly no harm in eating more vegetables!"

Professor Tim Key, Cancer Research UK's expert on diet and cancer, said: "This study in mice suggests that it's not just the fibre contained in vegetables like broccoli and cabbage that help reduce the risk of bowel cancer, but also molecules found in these vegetables too. This adds to the evidence that a healthy diet, rich in vegetables, is important. Further studies will help find out whether the molecules in these vegetables have the same effect in people, but in the meantime there are already plenty of good reasons to eat more vegetables"

Story Source:

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

Journal Reference:

1. Amina Metidji, Sara Omenetti, Stefania Crotta, Ying Li, Emma Nye, Ellie Ross, Vivian Li, Muralidhara R. Maradana, Chris Schiering, Brigitta Stockinger. **The Environmental Sensor AHR Protects from Inflammatory Damage by Maintaining Intestinal Stem Cell Homeostasis and Barrier Integrity**. *Immunity*, 2018; DOI: 10.1016/j.immuni.2018.07.010

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- Chicago

The Francis Crick Institute. "Chemicals found in vegetables prevent colon cancer in mice." ScienceDaily. ScienceDaily, 14 August 2018. <www.sciencedaily.com/releases/2018/08/180814173648.htm>.

Strawberries could help reduce harmful inflammation in the colon

Date:

August 20, 2018

Source:

American Chemical Society

Summary:

Inflammatory bowel disease is a set of painful conditions that can cause severe diarrhea and fatigue. Researchers are now reporting that a simple dietary intervention could mitigate colonic inflammation and improve gut health. In this case, a strawberry -- or rather, less than a cupful of strawberries -- a day could help keep the doctor away.

FULL STORY

Inflammatory bowel disease (IBD) is a set of painful conditions that can cause severe diarrhea and fatigue. Treatments can include medications and surgery. But now researchers report that a simple dietary intervention could mitigate colonic inflammation and improve gut health. In this case, a strawberry -- or rather, less than a cupful of strawberries -- a day could help keep the doctor away.

The researchers are presenting their results today at the 256th National Meeting & Exposition of the American Chemical Society (ACS).

"The sedentary lifestyle and dietary habits of many people in this country -- high-sugar, high-animal-fat, but low-fiber diets -- may promote colonic inflammation and increase the risk of IBD," says Hang Xiao, Ph.D., who led the study.

In 2015, 3 million adults in the U.S. reported being diagnosed with IBD, according to the U.S. Centers for Disease Control and Prevention. IBD includes both Crohn's disease, which can infect any part of the gastrointestinal tract, and ulcerative colitis, which is characterized by inflammation of the colon and rectum. People with IBD also have a higher risk of colorectal cancer.

The dietary consumption of fruits and vegetables has been associated with a lowered risk of IBD. To establish an effective and practical approach to decrease colonic inflammation in both IBD patients and the general population, Xiao and his team at the University of Massachusetts Amherst focused on strawberries due to their wide consumption. According to Yanhui Han, a Ph.D. student who conducted the study, most of the previous reports focused on the effects of purified compounds and extracts from strawberries. "But when you only test the purified compounds and extracts, you miss out on a lot of other important components in the berries, such as dietary fiber, as well as phenolic compounds bound to the fibers, that can't be extracted by solvents," he says. He adds that it also makes sense to study the effects of whole berries because people mostly consume the whole fruits rather than their extracts.

In their experiment, Han and Xiao used four groups of mice -- a group of healthy mice consuming a regular diet, and three groups of mice with IBD consuming a regular diet, a diet with 2.5 percent whole strawberry powder or a diet with 5 percent whole strawberry powder. Xiao says they tried to feed the mice doses of strawberries that would be in line with what a human could reasonably consume.

The researchers found that dietary consumption of whole strawberries at a dose equivalent to as low as three-quarters of a cup of strawberries per day in humans significantly suppressed symptoms like body weight loss and bloody diarrhea in mice with IBD. Strawberry treatments also diminished inflammatory responses in the mice's colonic tissue.

But decreased inflammation wasn't the strawberry's only conferred benefit during this study. Colonic inflammation adversely impacts the composition of microbiota in the gut. With IBD, the abundance of harmful bacteria increases, while levels of beneficial bacteria decrease in the colon.

Following the dietary treatments of whole strawberries, the researchers observed a reversal of that unhealthy microbiota composition in the IBD mice. Xiao's team also obtained experimental data that indicated strawberries might impact abnormal metabolic pathways in the IBD mice, which in turn could lead to the decreased colonic inflammation they observed.

Next, the team will try to validate their findings in IBD patients. While eating three-quarters of a cup of strawberries a day could be beneficial for those looking to enhance their gut health, Xiao advises patients to consult with their doctors before changing their diets. He also suggests avoiding this type of nutritional intervention if one is allergic to the fruit.

Story Source:

Materials provided by **American Chemical Society**. *Note: Content may be edited for style and length.*

目次に戻る

7. CasPER -酵素多様化に対応する新方法

2018 年 8 月 21 日

デンマーク工科大学の科学者らは、*Metabolic Engineering Journal* 誌に掲載された新しい研究の中で、CasPER という新しいゲノム編集ツールを発表した。
これは、CRISPR/Cas9 に基づいており、エンジニアリングを追加することなく必須および非必須の酵素の柔軟なエンジニアリングを可能にする、としている。
この方法が、医薬品、食品添加物、燃料、化粧品など、バイオベースの製造開発を含む様々な局面において非常に重要になってくる可能性がある。

英文記事：
https://www.eurekalert.org/pub_releases/2018-08/tuod-c-a082118.php

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PUBLIC RELEASE :21-AUG-2018

CasPER -- a new method for diversification of enzymes

Technical University of Denmark

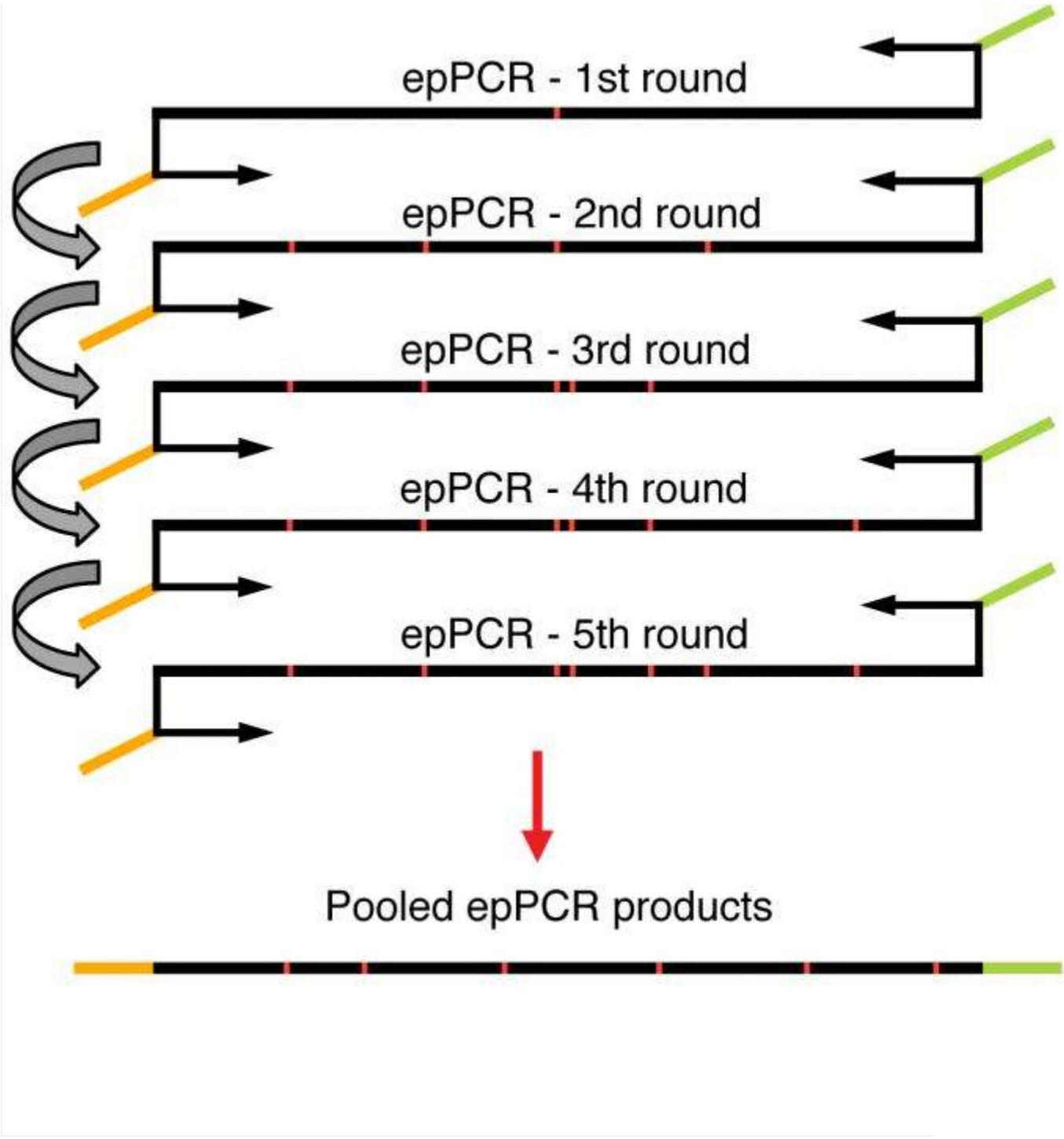

IMAGE: Scientists have invented a new method that allows for flexible engineering of essential and nonessential enzymes without additional engineering. **view more**

Credit: The Novo Nordisk Foundation Center for Biosustainability, DTU

A new study published in the *Metabolic Engineering Journal* describes a method based on CRISPR/Cas9, which enables flexible engineering of essential and nonessential enzymes without additional engineering. This could be of great importance for various aspects including the development of bio-based production of pharmaceuticals, food additives, fuels and cosmetics.

"When having a production strain this will make it easier for one to engineer certain limiting enzymes in the biosynthetic pathway and increase efficiency, specificity or diversity. People would be able to discover the best trade-off enzyme variants in the pathway and increase production of valuable compounds," says Tadas Jakociunas, Researcher at the Novo Nordisk Foundation Center for Biosustainability, DTU.

The newly developed method is named CasPER and is building on existing technologies, such as CRISPR/Cas9, that has been used for genome engineering and re-programming in yeast during the last years. However, the new tool enables scientists to engineer enzymes or their active domains by integrating much longer diversified fragments providing the opportunity to target every single nucleotide in a specific region. In yeast, CasPER was able to integrate mutagenized DNA fragments with almost 100% efficiency even in multiplex manner.

Discovery of enzymes variants

In depth characterisation of the new method concludes that the main difference between already existing CRISPR/Cas9 methods is that CasPER allows very efficient integration and in multiplex manner of large DNA fragments bearing various mutations to generate pools of cells with hundreds of thousands of enzymes variants.

While other CRISPR methods rely mostly on integration of shorter sequences to diversify DNA and require multiple rounds of engineering, CasPER significantly broadens the length of engineered DNA fragments. Furthermore, it does not require any additional steps making it faster and more effective to diversify enzymes to produce higher yields of desired chemicals.

Screening platform

Before the introduction of CRISPR/Cas9 it was a rather slow process to engineer essential enzymes in e.g. yeast. Today it is much more flexible regarding what you can target, and that

makes it more viable to engineer enzymes to be more efficient and specific allowing them to transform more substrate into a product.

"It is still very costly and time-consuming to build cell factories for production of valuable compounds so investing all that money and time on engineering it needs to pay off. You need to produce a certain amount of product to make it commercially relevant, and a tool like CasPER will definitely help to speed up and upscale this process," says Tadas Jakociunas.

As a proof-of-concept in this study, the scientists targeted several essential enzymes in the mevalonate pathway. This biosynthetic route is responsible for production of sterols and is essential in most living organisms. By studies in humans it is best known as the target of statins, a class of cholesterol lowering drugs. These drugs are based on inhibiting some of the steps in the pathway. In some bacteria and eukaryotes this pathway is responsible for producing the largest class of compounds called isoprenoids.

To prove the applicability and efficiency of CasPER scientists targeted two essential enzymes in the mevalonate pathway and were able to select cell factories with up to 11-fold increased production of carotenoids.

Great potential in industry and academia

In the future, CasPER can be widely used both in academia and industry for various purposes. Although the main application of the method was to speed up and lower the costs for engineering and optimizing cell factories, the method can also be applied for any experiment where diversification of DNA is needed.

"You can study protein functions to develop protein structure prediction tools, and study protein interactions with DNA, substrates and other molecules to diversify regulatory elements such as promoters, terminators and enhancers," says Tadas Jakociunas.

The method was validated in yeast, but it can also be applied in other organisms with efficient homologous recombination machinery.

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目次に戻る

8. 天然糖がメタボを防御 -マウス実験

2018 年 8 月 23 日

セントルイスのワシントン大学（WashU）医学部の研究者らが、新しいマウス研究によって、メタボリックシンドローム（肥満、糖尿病、脂肪肝疾患を含む関連疾患の集合体）を治療する新しい可能性を示唆している。
8 月 23 日に *JCI Insight* 誌に掲載されたこの研究は、トレハロースと呼ばれる天然糖が肝臓からグルコースを遮断し、インスリン感受性を高める遺伝子 -Aloxe3- を活性化することによって、糖尿病発症の機会を減らすことを示している。
研究者らは、絶食または通常の食事でマウスにトレハロースを与えることによって、肝臓代謝に有益な効果をもたらすことを発見、グルコースが薬物で肝臓から遮断されるのであれば、食べ物を厳密に制限することなく、断食の利益を得ることが可能になるのではないか、としている。

英文記事：
https://medicalxpress.com/news/2018-08-natural-sugar-defends-metabolic-syndrome.html

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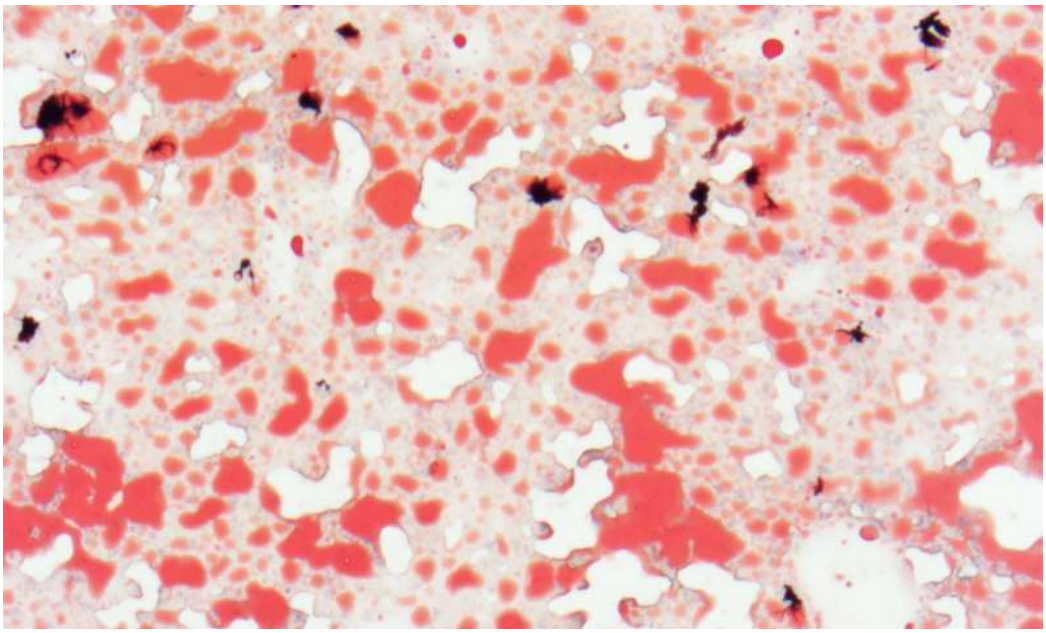
Natural sugar defends against metabolic syndrome, in mice

August 23, 2018, Washington University School of Medicine



Mice fed a diet high in trans fats and cholesterol for 12 weeks show fatty deposits in the liver (red staining). A new study from Washington University School of Medicine in St. Louis shows that the natural sugar trehalose blocks glucose …**more**

New research, in mice, indicates that a natural sugar called trehalose blocks glucose from the liver and activates a gene that boosts insulin sensitivity, reducing the chance of developing diabetes. Activating the gene also triggers an increase in calories burned, reduces fat accumulation and weight gain, and lessens measures of fats and cholesterol in the blood.

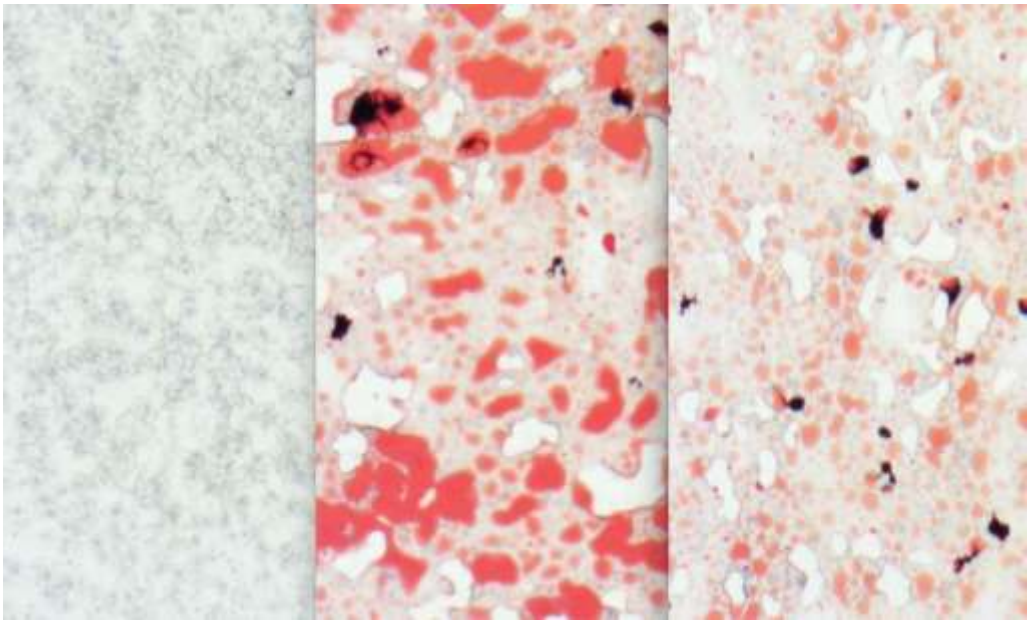
The findings, from researchers at Washington University School of Medicine in St. Louis, suggest new possibilities for treating metabolic syndrome, a cluster of related conditions that includes obesity, diabetes and fatty liver disease.

The study is published Aug. 23 in *JCI Insight*.

While potential medicinal use of trehalose still requires considerable research, the investigators found that giving mice trehalose via drinking water resulted in beneficial effects on the animals' liver metabolism—similar to benefits that resulted from fasting. In fasting mice, the liver also turns on the same gene that improves the body's ability to use insulin.

"We learned that this gene, Aloxe3, improves insulin sensitivity in the same way that common diabetes drugs—called thiazolidinediones—improve insulin

sensitivity," said Brian DeBosch, MD, Ph.D., an assistant professor of pediatrics. "And we showed that Aloxe3 activation in the liver is triggered by both trehalose and by fasting, possibly for the same reason: depriving the liver of glucose.



A new study from Washington University School of Medicine in St. Louis shows that the natural sugar trehalose blocks glucose from getting into the liver and turns on a gene, Aloxe3, that improves insulin sensitivity and other measures of …**more**

"In mice, this gene is turned on as part of what seems to be the normal fasting response. Our data suggest that fasting—or giving trehalose with a normal diet—triggers the liver to change the way it processes nutrients, in a beneficial way. And if glucose can be blocked from the liver with a drug, it may be possible to reap the benefits of fasting without strictly limiting food."

The researchers found that Aloxe3 in the liver—whether activated by fasting or trehalose—leads the mice not only to make better use of insulin, but to increase calorie burning, raise body temperature, reduce weight gain and fat accumulation—including fat deposits in the liver—and lessen measures of fats and cholesterol in the blood. Further, they found that mice fed an obesity-inducing diet and mice that eat freely and are genetically prone to obesity are protected from metabolic disease if given trehalose in their drinking water.

Studying the genes switched on in the livers of mice given trehalose, DeBosch and his colleagues became intrigued by Aloxe3, which typically is known for helping the skin maintain proper hydration in the body and had not been thought to have any role in the liver.

The researchers found that activating Aloxe3 in the mice given trehalose improves insulin sensitivity in a way that is similar to how thiazolidinediones work. Studying healthy mice given only water over a 48-hour period, they found that fasting, likewise, activates Aloxe3 in the liver. This activation could boost insulin sensitivity in the same way.

However, DeBosch said, trehalose may encounter enzymes in the digestive tract that break it apart, releasing its two glucose molecules, which would be counterproductive. The researchers investigated a similar sugar—lactotrehalose—they found has the same beneficial effects from triggering Aloxe3 but does not break apart as easily.

Explore further: Peptide improves glucose and insulin sensitivity, lowers weight in mice

More information: Higgins CB, Zhang Y, Mayer AL, Fujiwara H, Stothard AI, Graham MJ, Swarts BM, DeBosch BJ. Aloxe3 is a hepatic fasting-responsive lipoxygenase that enhances insulin sensitivity via hepatic PPAR-gamma. *JCI Insight* Aug. 23, 2018.

Provided by: Washington University School of Medicine

目次に戻る

9. 甘いもの、食べるなら「日中に」 メタボリスク抑制か

2018 年 8 月 27 日

砂糖をとるのを活発に活動する時間に限ると、自由にとり続けるより肝臓や血中にたまる脂肪量を抑えられることを、名古屋大の研究チームがラットの実験で見つけた。体が休んでいる時間の摂取を避けることで、メタボリックシンドローム（内臓脂肪症候群）などになるリスクを下げられる可能性があるとしている。１６日付の米科学誌プロスワンに発表した。

砂糖をとりすぎると肝臓や血中の脂肪量が増えるとされる。世界保健機関（ＷＨＯ）の指針では、生活習慣病の予防として１日に砂糖をとる量を、摂取する総エネルギー量の１０％未満とするよう勧めており、５％までに抑えると健康増進効果はさらに高まるとしている。

研究チームは、餌として砂糖かでんぷんをラットに与えた。その際、ラットの活動時間にあたる夜に限ったグループと、自由に食べることが出来るグループに分け、約４週間後の肝臓内や血中の脂肪量を調べた。

その結果、砂糖を活動時間に限って与えたグループは、自由な時間に食べられたグループより約２割、肝臓内や血中の脂肪量が少なかった。ただ、時間を限って与えても、でんぷんを与えたグループより脂肪量は多かった。

研究チームの名古屋大大学院生命農学研究科の小田裕昭准教授（時間栄養学）によると、休息時間は体内で砂糖を分解する働きが弱まっていたり、エネルギーとして利用されなかったりすることで脂肪がたまりやすいと考えられるという。小田准教授は「砂糖のとりすぎは体に良くないと分かっていても、実践は難しい。ただ、食べる時間を人間だと日中に限れば、悪影響を抑えられる可能性がある」と話す。（土肥修一）

https://www.asahi.com/articles/ASL8F6HDTL8FULBJ00R.html

英文記事：

https://www.sciencedaily.com/releases/2018/08/180827100431.htm

High-sugar feeding only at active times of day reduces adverse effects in rats

Date:

August 27, 2018

Source:

Nagoya University

Summary:

Researchers showed that limiting the consumption of a high-sucrose diet to the nighttime, when rats are most active, alleviated some of its most harmful effects associated with high levels of fat in the blood and liver. This work suggested that temporal controls on sugar intake in humans could also help in the fight against components of metabolic syndrome such as diabetes, obesity, and high blood pressure.

FULL STORY

A sedentary lifestyle combined with a diet dominated by processed foods has widely resulted in a range of conditions including diabetes, obesity, and high blood pressure, which are known collectively as metabolic syndrome. Although many insights into the causes of metabolic syndrome have been made, much remains to be understood about the complex interplay among the genetic, environmental, and lifestyle-related factors related to ways of preventing this condition.

Sucrose, a common form of sugar made up of glucose and fructose, is one part of the diet known to be associated with conditions such as obesity and high blood pressure when consumed in excess. However, it is still somewhat unclear how this occurs and how to minimize it. In a new paper published in *PLOS ONE*, a research team centered at Nagoya University has shown that restricting

the consumption of a high-sucrose diet in rats to the part of the day when they are active avoids many of the deleterious effects of excess sugar on the body.

The team established four groups of rats with different diets: either a high-sucrose diet or an equivalent diet with starch replacing the sucrose, with these being made available either throughout the day and night, or only when the rats were active. Given the nocturnal nature of rats, this corresponded to the nighttime.

"We chose to study rats because their body weight is ten times that of the commonly used animal model of mice, making them more similar to humans, and because they have a more stable metabolism" Hiroaki Oda of the Laboratory of Nutritional Biochemistry says. "We subjected the four groups to various analyses, including of body weight, lipids in blood and liver, and hepatic gene expression."

The results showed that, when the rats had access to high-sucrose food only at night when they were active, their levels of fat in the blood and liver were lower than those in the group in which such food was available all the time, despite the two groups consuming the same amount overall. The results also indicated that this improvement was not caused by any knock-on effect on the expression of genes for fat metabolism, indicating that it was the temporal restriction on feeding itself that produced the beneficial effects.

"Our findings could be very important for the fight against obesity and other lifestyle-related diseases in humans," lead author Shumin Sun says. "Potentially, limiting sugar intake to the part of the day when people are most active could reduce many of the damaging effects of its excessive consumption across the globe."

Story Source:

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

Journal Reference:

1. Shumin Sun, Fumiaki Hanzawa, Miki Umeki, Saiko Ikeda, Satoshi Mochizuki, Hiroaki Oda. **Time-restricted feeding suppresses excess sucrose-induced plasma and liver lipid accumulation in rats**. *PLOS ONE*, 2018; 13 (8): e0201261 DOI: 10.1371/journal.pone.0201261

目次に戻る

10. 女王の糞を食べて、母性を得る -ハダカデバネズミ

2018 年 8 月 27 日

ハダカデバネズミは、東アフリカの砂漠の地下にコロニーを作って生活している。少数の繁殖用の雄以外、コロニーのメンバーは、餌の塊茎をあさり、敵から身を守り、女王の生んだ子供達の世話をして生きている。
今日、米国立科学アカデミー紀要で発表された研究によると、この最後の行動である“子供達の世話”をするためにハダカデバネズミは女王の糞を食べる、という新しい研究が示唆されている。
哺乳動物の雌では、育児本能は通常妊娠中のホルモンによって引き起こされるが、ハダカデバネズミについて、この育児本能の源泉は何か？
研究者らは、実験室に設けたハダカデバネズミのコロニーを分析、妊娠中の女王の糞、非妊娠中の女王の糞、非妊娠の女王の糞だがエストロゲンホルモンエストラジオールをほどこしたものを食べさせたところ、妊娠した女王からの糞または非妊娠の女王のエストラジオール入りの糞を食べた雄は、録音した子供達の鳴き声に対してより反応し、他の雄に比べて糞尿中のエストロゲン濃度も高かった、と報告している。

英文記事：
http://www.sciencemag.org/news/2018/08/eating-poop-makes-naked-mole-rats-more-motherly?et_rid=375979900&et_cid=2323355

NEIL BROMHALL/SHUTTERSTOCK.COM

Eating poop makes naked mole rats more motherly

By **Michael Price** Aug. 27, 2018 , 3:00 PM

If you think you take a lot of crap from your boss, you've got nothing on the naked mole rat. Workers in this society literally eat their queen's dung in order to prepare themselves to care for her children, a new study suggests.

Naked mole rats (*Heterocephalus glaber*, pictured) live in underground colonies throughout the deserts of East Africa. Apart from a few breeding males, colony members spend their days foraging for tubers, defending against predators, and taking care of the queen's youngsters. This last behavior has puzzled biologists: In female mammals, child-rearing instincts are typically sparked by a flood of hormones during

pregnancy—yet these hormone–producing reproductive organs never develop in the subordinate females in naked mole rat society. So what kick–starts their maternal urge?

According to a study published today in the *Proceedings of the National Academy of Sciences*, the answer could be related to an unsavory aspect of mole rat behavior: coprophagy, or the eating of each other's poop. The researchers, who first reported their findings 3 years ago at a Society for Neuroscience meeting, analyzed a naked mole rat colony in a lab. One group of female subordinates dined on the pregnant queen's dung, whereas another ate poop from a nonpregnant queen. A final group ate feces from a nonpregnant queen that had been garnished with the estrogen hormone estradiol, which has been shown to jump–start maternal behaviors like grooming and nursing.

Subordinates that ate poop either from the pregnant queen or fortified with estradiol turned their heads to tune into recordings of mole rat pup cries, and had higher levels of estrogen in their poop and urine, than did the other mole rats. That suggests **naked mole rat queens pass along maternal instincts to their subordinates through fecal meals**—a strategy that appears to be unique in the animal kingdom.

Posted in:

- Plants & Animals

doi:10.1126/science.aav2331