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USDA/ARS
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at Baylor College of Medicine

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NUTRITION & YOUR CHILD

HOW GENES CONTRIBUTE TO OBESITY

RESEARCHERS STUDY RARE SEROTONIN 2C RECEPTOR MUTATIONS

There are many factors that contribute to obesity, including a person's genes. Scientists at the Children's Nutrition Research Center (CNRC) are conducting human and laboratory studies to better understand how an individual's genetic variation contributes to their obesity risk.

"While most people think that obesity is a simple problem of eating too many calories, in truth, there are many factors that contribute to weight gain," said Dr. Stephanie Sisley, associate professor of pediatrics at Baylor College of Medicine and medical director of the genetic disorders of obesity program at Texas Children's Hospital. "Some factors, like sleep, nutritional quality and some medications, can be changed. However, many of them cannot be modified – like the genes you inherit from your family." In fact, scientists are learning that there are many genes involved in obesity risk.

Dr. Yong Xu, professor of pediatrics and molecular and cellular biology at Baylor College of Medicine, has newly identified how a gene is connected with obesity and certain behaviors — the serotonin 2C receptor gene. His findings may be helpful for diagnosing and treating obesity, as well as understanding how genes usually work together to maintain a healthy weight.

"Serotonin is a chemical produced in the brain that acts to relay messages from one part of the brain to another. Serotonin communicates the message by binding to a specific protein, called the serotonin receptor, which is found on some brain cells. These brain cells are involved in a variety of functions, including mood, appetite and some social behaviors," Xu said.

The Xu lab and the lab of Dr. I. Sadaf Farooqi at the University of Cambridge (UK), worked together to study how the serotonin 2C receptor may be involved in weight control and behavior. By combining their expertise — animal genetic studies in the Xu lab and human genetics research in the Farooqi lab — they showed that the serotonin 2C receptor is an important regulator of body weight and certain behaviors. This study was published in *Nature Medicine.*

One gene, multiple effects

The project started with finding that some children with severe obesity carried rare mutations in their serotonin 2C receptor. They also found that the mutation often caused the receptor to no longer work.

"People who carried these rare mutations had huge appetites, some degree of uncommon behaviors and rapid, often exaggerated, changes in mood, including strong emotions like uncontrollable laughing or crying or heightened irritability or temper," Farooqi said.

The researchers found that mice with the same mutation also became obese. This finding confirmed the team's hypothesis that mutations of the serotonin 2C receptor gene prevented the receptor from working properly and contributed to the development of obesity.

"This is an important discovery from the diagnostic point of view," Xu said. "We suggest that the serotonin 2C receptor gene should be included in diagnostic gene panels used to identify if there is a genetic cause for cases of severe childhood-onset obesity."

In addition, the team identified a mechanism that would explain why these mutations can lead to obesity. "We found that activation of the serotonin 2C receptor is necessary for turning on specific neurons in the hypothalamus, a part of the brain that is important for regulating eating behavior," Xu said. "When the receptor does not function, these neurons cannot communicate information about hunger correctly, and as a result, the mice overeat and become obese. Normal activity of these neurons is required to suppress overeating."

The researchers also worked with the mouse model to explore whether the mutations could change behavior.

"We confirmed that mice with the mutation were less sociable and more aggressive," Xu said. "Before these findings, there was little evidence that this specific type of serotonin receptor (serotonin 2C receptor) was important for normal behavior and to prevent aggression. We are interested in investigating the mechanism."

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NEW NON-INVASIVE SKIN SCAN MAY QUICKLY ASSESS BABIES' FRUIT AND VEGETABLE INTAKE

Nutrition scientists are interested in developing rapid and accurate ways to determine what children and families eat. Some of the food groups scientists are most interested in monitoring are fruits and vegetables, which children of all ages notoriously do not eat enough. Children start eating fruits and vegetables in the first year of life, but getting a clear picture of an infant's food intake is a big challenge. Infants cannot tell pediatricians and scientists what they eat, and infants often have multiple caregivers making it hard to get the full story.

A new technology that uses a type of color measurement called reflection spectroscopy is used in adults and children to assess their fruit and vegetable intake. How does it work? When people eat fruits and vegetables, some of the red, orange and yellow pigments in those foods (carotenoids) accumulate in the skin. You may have heard of carotenoids before, as they are critical to healthy vision and are precursors to the essential nutrient vitamin A. The device works by taking a specific color-based measurement of the amount of carotenoids in skin. A recent study conducted at USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine and Texas Children's Hospital looked at the use of skin carotenoid scores measured by non-invasive reflection spectroscopy in 4-, 6- and 8-month-old infants, and how strongly those scores were related to carotenoid intake and plasma carotenoid concentrations.

"During the first year of life, babies go through big changes in their diet, from exclusive milk or formula to complementary feeding, with milk and solid food," said Dr. Nancy E. Moran, associate professor of pediatrics at Baylor College of Medicine and member of the USDA/ARS Children's Nutrition Research Center. "Our team is interested in understanding the role of carotenoids in children's health, and we've known for a while that skin carotenoid measurements could be a good read-out of adults' carotenoid fruit and vegetable intake. What we didn't know was if this measurement could be used with infants."

The study compared infant's skin carotenoid scores with their blood carotenoid concentrations and carotenoid intake calculated from food records.

First, the participants visited the research team three separate times to have their skin carotenoid scores measured using a portable reflection spectroscopy device. At each visit, measurements were taken on both the index finger and the heel of the infant's foot. This process took less than two minutes. The average scores of the heel and finger were analyzed.

Caregivers were asked to record a detailed food diary for seven days around each visit. This diary listed what their infant ate and drank, including brand names, amounts, recipes and times and locations of consumption. This information was used to calculate daily intake of various carotenoids. Since infant formula and human milk carotenoid levels can vary, the team measured samples for each infant in the study to customize their food diary analysis.

Finally, infant plasma samples were collected and analyzed to record their carotenoid levels.

To validate skin carotenoid scores as a biomarker, the research team compared the average skin carotenoid score from each visit to the total dietary carotenoid intake and total plasma carotenoid concentration. At both 4- and 8-months of age, skin carotenoid score was strongly correlated with total carotenoid intake, although no correlation was observed at 6-months.

"We were happy to see that when children were in a stable dietary pattern, like at 4-months during primarily milk feeding, and at 8-months during complementary feeding, their skin carotenoid measurements agreed with their blood carotenoid concentrations and with what their parents reported that they were eating," Moran said.

"We were surprised that at 6-months of age, the skin carotenoid scores didn't agree as well with the food records," Moran said. "We think this is because babies at 6-months are just starting to try many solid foods, so there is a big, big change in their diet and their skin carotenoids haven't had a chance to 'catch up' to that change."

"Right now, it is hard for pediatricians to monitor the amount of fruits and vegetables young children are getting in their diet. Without reliable information, they cannot connect families with resources or support to get young children on the right track," Moran said. "Local, state and national groups interested in supporting children's nutritional health may like to use this type of measurement as a quick way to get a snapshot of what children's fruit and vegetable intake is at a population level."

Moran's team is currently conducting a larger study, called the Baylor Infant and Toddler Biomarker of Nutrition Study, that seeks to better understand how and when the skin carotenoid measurements work best in infants and toddlers. Families interested in learning more and volunteering for the BITBON Study can learn more or learn more online or by email.

By Aaron Nieto, communications associate
at Baylor College of Medicine

BEDTIME SLEEP ROUTINES ASSOCIATED WITH HEALTHIER WEIGHT GAIN IN CHILDREN

Compared to the school year, parents likely notice a difference in their child's behaviors during the summer months, including eating, interactions with others, and sleeping. In a study published in *Sleep Health*, researchers at the USDA/ARS Children's Nutrition Research Center at Baylor College of Medicine and Texas Children's Hospital examined how differences in a child's sleep and sleep hygiene (i.e., behaviors that support healthy sleep) between the school year and the summer break relate to their body mass index (BMI), which is a commonly-used measure of body fatness.

"Our sample included 197 children between the ages of 5 and 8. We measured their height and weight at the end of the school year and after the summer break," said Dr. Jennette Moreno, assistant professor of pediatrics at Baylor College of Medicine. "Parents also reported their child's sleep patterns (what time they wake up and go to bed) and their sleep hygiene practices. We then looked at how their sleep hygiene practices related to their reported sleep patterns and BMI during these times."

Researchers found that during the school year, children who engaged in more sleep-preventing behaviors before bed (i.e., using electronics, drinking caffeine, roughhousing) reported sleeping fewer hours or less soundful than children who did not engage in sleep-preventing behaviors or, at least, did fewer of them.

"Children went to bed later during the summer compared to the school year – the difference being about 12 minutes, so not a big shift," Moreno said. "Compared to the school year, children in the summer spent about 38 minutes more using screen devices (e.g., TV, tablets, video games) and drank less caffeine."

They also discovered that children who engaged in better sleep hygiene practices during the school year and had fewer sleep-preventing behaviors had a healthier (i.e., lower) BMI.

"For parents, promoting good sleep hygiene practices, like maintaining a consistent bedtime routine and engaging in calming activities before

bed, may be part of a lifestyle that supports a healthier weight status in children," Moreno said.

The next step for Moreno and other researchers is to learn how these data can inform obesity prevention interventions for children.

"There is a push to incorporate healthy sleep behaviors into obesity prevention practices," she said. "These data will help us understand what to focus on when we promote healthy sleep patterns in children."

Currently, researchers are recruiting 4-year-old children to participate in The Goodnight Screen Media Study, which seeks to understand how children's use of tablet devices before bed is related to their sleep, learning and memory. To learn more, visit https://redcap.link/goodnight.

The team also plans to recruit children between 8 and 11 to participate in the upcoming SCREENS study. This study will test how children's use of tablet devices before bed is related to their sleep, learning and emotion regulation. To learn more about this study, email Screens_Study@bcm.edu.

By Taylor Barnes, senior communications associate at Baylor College of Medicine

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The findings suggest that patients who develop obesity because of mutations in this gene might benefit someday from medications that can bypass the communication block when the receptor is mutated. Further studies must be carried out to test if this approach would work.

"Even though we don't have specific treatments yet for each of the different genetic causes of obesity, in my experience, families who are able to find genetic causes often feel more empowered to support their child and optimize their child's health," Sisley said. The findings from this study, of a gene that is not functioning properly, can also help scientists and doctors understand how cells in the brain should usually communicate to maintain a healthy weight.

By Ana María Rodríguez, Ph.D., lead science writer at Baylor College of Medicine

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JOIN A CNRC NUTRITION STUDY!

Houston-area residents are invited to participate in the following nutrition research projects designed to help CNRC scientists learn more about the nutritional needs of children. Free parking is provided. For most studies, financial compensation is provided. **For questions on becoming a CNRC research volunteer, call Noemi Islam at 713.798.7002 or email nislam@bcm.edu**

Baylor Infant and Toddler Biomarker of Nutrition Study (BITBONS) H-52929 Infants are needed for a free study of whether a rapid, skin sensor measurement is as good as surveys and blood measurements at determining what a child eats. The study involves six visits to the CNRC from 4-24 months of age for length and weight; blood and milk samples; surveys on health and food; optical skin measurements; and vision testing. Participants must meet health criteria and will receive refreshments and up to $300 in pre-paid credit cards. To see if your child qualifies, complete the Prescreening Eligibility Questionnaire, contact us at **713.798.0517** or e-mail BITBONStudy@bcm.edu.

Technology Effects on Child Health (TECH) Study H-52282 Parents with a child age 3-4 years in the Greater Houston area are needed for a 12-month TECH Study testing new technology to measure screen use and evaluate screen-time effects on children's sleep quality, development and problem-solving skills. Up to $410 in compensation. For more information, go to https://redcap.link/techstudy, call **713-798-0388** or email screentimesleep@bcm.edu.

Screens Study Sleep, Circadian Rhythm, Electronic Devices in the Evening: Screens Study H-53533 Do you have an child age 8-11? Help us learn about their sleep and screen media use. Your child does not need to use electronic screens regularly in order to participate. Up to $500 compensation. Learn more at https://redcap.link/SCREENS or email us at Screens_Study@bcm.edu

Papás Saludables, Niños Saludables H-50011 Hispanic dads with children ages 5-11 are invited to participate in a test of the Papás Saludables, Niños Saludables program to promote healthy eating and active lifestyles. The program is run by Baylor College of Medicine at a local YMCA. Up to $180 in compensation. If interested, call **713.798.0503** or email healthydads@bcm.edu; https://redcap.link/PSNS

Super Chef: Family Fun in the Kitchen H-51143 Parents and their 10-12 year-olds are needed for a study to help us evaluate an online program to help families adopt the Mediterranean Diet. Family must qualify for or participate in free/reduced priced school lunch. Stipend. Contact Chishinga Callender, **chishinga.callender@bcm.edu 713.798.0506** or Noemi Islam at **nislam@bcm.edu 713.798.7002.**

Fit24+ H-50331 We're looking for Hispanic youth, age 12-16, who struggle with weight and have a cell phone. You'll receive a Fitbit watch and text messages to help you move more and improve sleep. The 12-week study offers weekly nutrition and health classes. Compensation up to $140. Call **713.798.7138** or **713.798.7067** or email Marbelly.Partida@bcm.edu or Callie.Lopez@bcm.edu