How do organisms make dietary choices?

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When given a choice, organisms will choose a diet that maintains a nutritional balance in tune with their needs. That choice, studied in fruit flies for the first time, is regulated by activity in a molecular pathway involved in aging, cancer and diabetes. The research undertaken in fruit flies at the Buck Institute for Age Research has implications for humans, who share the same molecular pathway. The study, the first to be done in a genetically tractable lab animal, provides a way to begin the development of treatments that could "reboot" metabolic pathways in individuals who are obese or suffer from diabetes. The study appears in the May 13, 2010 online edition of the journal *Current Biology*.

"How an organism balances its intake of nutrients has a great impact on its health and survival," said Buck faculty member Pankaj Kapahi, PhD, the lead author on the study, who said that an imbalance of protein and carbohydrates has been implicated as a cause for both diabetes and obesity and influences the aging process, "In this study we've established a model using the fruit fly to address the question of how an organism chooses between protein and carbohydrate."

The study revealed that fruit flies deprived of either carbohydrates or protein (yeast) in their diet show a strong preference for the nutrient they were previously deficient in. In addition, the researchers discovered that the gender and the mating status of the species alters its dietary choices. They found that S6 Kinase, a key protein in the TOR (target of rapamycin) pathway which is involved in nutrient sensing in all species ranging from plants to humans, also influences dietary choices. TOR is well established as playing an important role in cancer, diabetes and

aging. The study also found that changes in levels of serotonin influence the choice between protein and carbohydrate. Serotonin is a key neurotransmitter found in the gut and in the brain and is involved in the regulation of mood, appetite, sleep and cognitive functions.

Kapahi emphasized that this study opens the doors to study the phenomenon of dietary choices in a genetically tractable animal, something new in a laboratory environment where animals are generally put on fixed diets. "This study allows us to begin to ask the question of whether changes in metabolism and aging are influenced by dietary choices," said Kapahi. "These studies will have great relevance for humans who share these nutritional signaling pathways with flies." Kapahi said the issue of choice becomes vital as treatments are developed for obesity and diabetes. "This adds a crucial dimension to the research, one that takes into account the reality of human experience which involves food choice," he said.

"Dietary choices in humans play a critical role in the development of obesity and diabetes," said Kapahi. "This research can help us develop treatments that correct nutritional imbalances." As examples, Kapahi mentioned possible treatments for those genetically predisposed to diabetes or obesity. He also said it may be possible to develop treatments that would "reboot" the metabolism of people who have become accustomed to eating excess sugar and carbohydrates.

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