The brain grows while the body starves

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When developing babies are growth restricted in the womb, they are typically born with heads that are large relative to their bodies. The growing brain is protected at the expense of other, less critical organs. Now, researchers reporting in the August 5th issue of *Cell*, a Cell Press publication, unearth new molecular evidence that explains just how the brain is spared.

In studies of rapidly growing fruit fly larvae, they've traced this developmental phenomenon to the activity of a gene called Anaplastic Lymphoma Kinase (ALK).

"ALK breaks the link between dietary nutrients and neural growth," said Alex Gould of the Medical Research Council's National Institute for Medical Research in London.

The first step for Gould's team was to find out if they could reproduce the same kind of brain sparing known to occur in humans in the lab. They looked at fruit flies in their larval stages because that's when they do most of their growing.

"If you restrict dietary nutrients at the late larval stage, body tissues shut down growth completely yet the neural stem cells in the brain continue growing at close to 100 percent," Gould said. The question is how.

The researchers got their first surprise when they disabled the nutrient sensing pathways that respond to amino acids and insulin, both of which were known to be essential for the growth of many different tissues.

Without those pathways in working order, most parts of the fly body did indeed stop growing, but brain neural stem cells "just kept on going."

Further investigation revealed that activation of ALK in the brain allows neural stem cells to grow without the usual need for insulin and amino acid signals. In other words, ALK converts cells from their usual nutrient-sensitive state to a nutrient-responsive one, Gould explained.

As the name suggests, ALK was first identified for its role in lymphomas and has since been found in many other forms of human cancer. The new findings uncover a previously unknown molecular link between stem cell growth and cancer.

"It's interesting. We think of cancer cells as being able to outgrow normal healthy cells," Gould said. "So it appears that ALK can give cells a growth advantage in contexts as diverse as human cancers and developing fruit flies."

The fruit flies now offer an experimental model for intra-uterine growth restriction (IUGR) in humans, which may lead to a greater understanding of the genes and pathways involved. "I don't want to over-speculate," Gould said, "but, in the future, this genetic model may also shed light on the related issue of why IUGR predisposes individuals to metabolic disease later on in adult life."

Provided by Cell Press