

Live, fast, die old

Cutting calories quickly alters genes

HELEN PEARSON 5 September 2001



Calorie counting could give you more than a good figure

Photodisc

It's never too late to diet. Cutting calories for only a few weeks late in life causes anti-aging changes in mouse genes. Even those averse to weight watching might have their cake and eat it if researchers can find drugs that mimic dieting's effects.

Cutting calories is known to increase lifespan and reduce age-related disease in experimental mammals. Stephen Spindler and colleagues of the University of California, Riverside probed how gene activity changes when an elderly mouse diets.

Over half the changes that usually occur with aging were absent from mice that were given 44% fewer calories, the team found¹. To their surprise, cutting calories for only four weeks in old mice mimicked most of the genetic effects of a lifetime of calorific abstinence.

"Even old people may be able to benefit rapidly from switching to a calorie-restricted diet," speculates Spindler.

Then again, who wants to diet, he adds, if there's a "magic pill" that can mimic the benefits. Drugs could be rapidly screened for those that reproduce the gene-expression profile of calorie restriction, the team hopes.

Calorie restriction has been known to extend lifespan since the 1930s. "Why is an open question," says age researcher Brian Merry of the University of Liverpool, UK. These findings "put meat on the skeleton," he adds.

A quick diet may initiate changes in gene activity "but you haven't got the time to accumulate the benefits," to lifespan or health, he warns. Spindler's group have not yet shown how long the effects of their crash diet last.

Keep the change

The team looked at the activity of 11,000 mouse-liver genes on a gene chip, adding to previous work on aging brain and muscle. Stress and inflammation genes become more active with age, the team showed, and those that kill off potentially cancerous cells decrease in activity. Long- and short-term calorie cuts reduced these and other changes.

Such genes are the cell's defence against the cumulative damage that causes aging, says Tom Kirkwood of the University of Newcastle, UK, who studies how the response evolved. Starving animals divert energy from reproduction into cell repair and maintenance, he explains, "boosting the systems that stave off damage".

In the study, control mice gorged on 95 kilocalories a week. Dieters ate a mere 53 kilocalories, equivalent to cutting a standard human intake of 2,500 kilocalories a day to a hungry 1,395.

Applying such research to humans is a long way off, the researchers warn. Eternal life might be some egotists' dream, but more important is making old age healthier, by delaying the onset of age-related conditions such as cancer and heart disease.

References

Cao, S.X., Dhahbi, J.M., Mote, P.L., & Spindler, S.R. Genomic profiling of short and long-term caloric restriction effects in the liver of aging mice. *Proceedings of the National Academies of Science*, **98**, 10630 - 10635, (2001).

© Nature News Service / Macmillan Magazines Ltd 2001