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New testicular cancer gene found

Scientists have successfully cloned the first known gene linked to heritable testicular cancer, with potentially important implications for future research targeting this disease.

For over a decade now, scientists have linked the *Ter* mutation in mice with the loss of primordial germ cells (PGCs), the precursors of sperm and oocytes. In certain mouse strains, there is also an association between this mutation and significantly elevated susceptibility to testicular germ cell tumor (TGCT), the most common form of cancer affecting human males between the ages of 20 and 40. Now, in a recent article from *Science* (19 May), researchers from Case Western Reserve University (Cleveland, OH) and the MD Anderson Cancer Center (Houston, TX) led by Joseph Nadeau and Angabin Matin, announce the cloning and initial characterization of *Dnd1*, the gene affected by the *Ter* mutation and the first gene yet to be directly linked to heritable testicular cancer.

This mutation seems to consist of a single base change that introduces a premature stop codon into the *Dnd1* RNA transcript; by replacing this mutated allele with the wild-type version, the researchers were able to effect a partial rescue of PGC loss. Structural evidence suggests that this protein may be involved in RNA binding and editing, mechanisms thought to be essential for PGC development; the authors are optimistic that their findings could suggest important new directions for future TGCT research.

Low carb = short life?

Fruit flies fed a diet restricted in fat and protein live significantly longer than those fed a reduced-sugar diet, suggesting that what you eat might matter more than how many calories you consume.

Decades of research involving a variety of animals have indicated that cutting calories promotes longevity. Now, Linda Partridge and her colleagues in the Centre for Research on Ageing, University College London (UK), present a rare challenge to that idea in a report published in *PLoS Biology* (July).

Fruit flies (*Drosophila melanogaster*) fed standard medium get all of their nutrients from sucrose (sugar) and autolyzed yeast powder (fat and protein). Female flies fed a reduced-yeast diet lived more than 60% longer than flies on a control diet. A similar reduction in sugar concentration extended the median life span by no more than ~16%.

While this work suggests that when it comes to longevity all calories may not be created equal, people looking for the fountain of youth shouldn't boost their sugar intake just yet. It remains to be seen what, if any, implications these results have for humans.

Leaky mitochondria clog arteries

A new study in mice shows that inefficient metabolism in blood vessels leads to clogged arteries, possibly explaining why a healthy lifestyle doesn't always ward off heart disease.

Although we know that certain risk factors, such as high cholesterol, increase atherosclerosis, many heart attack victims have normal cholesterol levels. Now, in the 26 May issue of *Nature*, a group at Washington University School of Medicine (St. Louis, MO), led by Clay F. Semenkovich, present a study in mice that helps to clear up this mystery.

The group crossed *Apoe*$^{-/-}$ mice, which are highly susceptible to diet-induced atherosclerosis, with transgenic mice bred to overexpress uncoupling protein 1 (UCP1) in the artery wall. Respiratory uncoupling, in which protons leak across the inner membrane of the mitochondria, leads to the production of reactive oxygen species, which have been implicated in promoting vascular damage. UCP1 expression led to high blood pressure, and when fed a high-fat 'Western' diet, these mice had more atherosclerotic lesions than *Apoe*$^{-/-}$ mice that did not also overexpress UCP1.

If the mitochondria in aging cells in the blood vessel wall begin to leak and produce reactive oxygen species, the resulting oxidative damage may cause an immune response, setting the stage for plaque formation. The link between respiratory uncoupling and atherosclerosis could someday lead to new treatments for this common disease.