Soy foods not good for every body?

A soy-based diet exacerbates a heart condition in a transgenic mouse model of hypertrophic cardiomyopathy (HCM). These results may have important implications for the interactive relationship between diet and heart disease in humans and the choice of diets fed to animal models used in research.

HCM is a relatively common genetic cardiac disorder resulting from a defect in one of several genes; the condition affects as many as 1 in every 500 people. Thickening of the heart muscle characterizes HCM, which results in shortness of breath, chest pain, palpitations, fainting, and in some cases, sudden cardiac death.

There is considerable evidence that diets rich in soy provide numerous health benefits, including reduced cancer and cardiovascular risk, probably because of their phytoestrogen content. However, little information is available about the effects of soy consumption on people (and animals) with specific genetic disorders.

Leslie A. Leinwand at the University of Colorado at Boulder and her colleagues created a transgenic mouse model of HCM, carrying a mutated α-myosin heavy chain gene. Male HCM mice have enlarged heart muscles that contract poorly, eventually leading to heart failure. Female HCM mice, in contrast, maintain cardiac contractile function and do not develop heart failure.

Leinwand's group proposed that the sex-dependent phenotypic characteristics of HCM mice result from exposure to phytoestrogens, which in turn leads to a series of biochemical reactions that culminate in apoptosis of cells in the myocardium. To test this idea, they fed a group of HCM animals a casein-based diet and compared the results to that of mice fed a standard soy-based rodent diet. Although the dietary change showed little effect in females, male mice on the casein diet had improved cardiac function and did not progress to heart failure; indeed, they were almost indistinguishable from wild-type males (*J. Clin. Invest.*, January).

The authors speculate that the dramatic sex-related difference in response to the soy diet may arise from the issue that, because "female animals have higher endogenous estrogen levels, the proportional increase in estrogenic compounds via diet is less in females compared with males, who are chronically exposed to significantly lower levels of estrogenic compounds."

Although the present results certainly do not suggest that healthy individuals should shun soy, they do highlight the need to study the interaction of diet and genetics. Likewise, these results underscore the importance of considering diet when characterizing transgenic animal models.

Tanja Schub

UNCOVERING THE ROOTS OF PAIN

New research may have uncovered a 'master switch' protein for the development of a broad variety of pain-sensing neurons.

Nociception, the transmission of pain signals in response to potentially harmful stimuli, is under the control of a diverse array of neuron subtypes expressing receptors activated by a wide range of triggers, including temperature, noxious chemicals and mechanical injury. However, the developmental process by which this diversity is attained has remained largely unclear.

Dana-Farber Cancer Institute (Boston, MA) investigator Qiufu Ma and his colleagues were interested in identifying proteins that manage these processes; they began by investigating the importance of *Runx1*, a transcription factor gene for which expression is restricted to nociceptive neurons. They generated mice in which *Runx1* expression had been inactivated in the peripheral nervous system, and they observed a number of clear deficits in nociceptor development (*Neuron*, 2 February).

The absence of *Runx1* expression seems to block the development of at least one key population of nociceptor precursors in the dorsal root ganglia, the structure in which somatosensory neurons reside. This has apparently serious implications for downstream developmental steps, for Ma's team found that these mice showed eliminated or markedly reduced levels of a variety of nociceptive receptors, including a number of heat- and cold-responsive receptors. They also observed marked alterations in the targeting of afferent processes from *Runx1*$^{-/-}$ neurons to the spinal cord, where pain signals are processed before transmission to the brain.

The *Runx1*$^{-/-}$ mice showed significantly delayed responses to cold or heat stimuli relative to wild-type animals, as well as reduced sensitivity to the hot pepper-derived compound capsaicin. However, their responses to pinprick discomfort did not change, suggesting that not all modes of pain detection were impaired. Ma's team also tested the animals' response to neuropathic pain—the perception of typically nonpainful stimuli as painful, often a result of nerve damage. Unlike wild-type animals, nerve-damaged *Runx1*$^{-/-}$ mice showed no neuropathic pain response, suggesting an important role for the gene in this particular pathology.

The action of *Runx1* seems to govern the development of a wide variety of classes of nociceptive neurons, and the authors conclude: "The identification of a core transcriptional control program for many of the ion channels and receptors known to transduce noxious stimuli has intriguing implications for the design of more effective pain therapies."

Michael Eisenstein