



Using national data from 10,061 people patch-tested for allergens, a DHMC resident found that children and adults show allergic reactions at similar rates—but to different substances.

## Brain wave: New insight into development

This has been an extremely humbling experience,” marvels physiologist Val Galton, Ph.D., a member of the DMS faculty since 1961. She’s referring to a recent finding that challenges a piece of conventional wisdom in the field she’s worked in for nearly 50 years. Galton began her career by studying thyroid hormone (TH) in the frog—an ideal model for TH studies because of its simplicity; the sole purpose of TH in frog development is to trigger the differentiation that turns tadpoles into frogs. If they lack TH, tadpoles neither grow limbs nor absorb their tails.

Since then, she’s developed a long-term collaboration with endocrinologist Donald St. Germain, M.D. They now work with more complex animal models, primarily looking at how TH regulates brain development in mice. “We went from studying shrinking tails to [studying] growing brains,” observes St. Germain.

**Poor:** As a clinician, he has long sought to develop better treatments for hypothyroidism—a TH deficiency in humans. Children who grow up lacking TH develop cretinism, a condition characterized by mental retardation, short stature, and other features of poor development.

There are two thyroid hormones, T4 and T3; the latter is the active form. It is

the job of enzymes called deiodinases to maintain the right ratio of the two. Proper development requires “receiving the right amount of thyroid hormone at the right time,” says St. Germain. Recognizing TH’s apparent role in brain development, he and Galton began using genetic techniques to wipe out deiodinases in mice, to see the effect of their absence.

Deiodinases are like switches that can be turned on and off to ensure the right balance of T3 and T4 during critical stages of development. The accepted view of TH regulation has been that T3 in the brain is produced there from T4 by a deiodinase known as type 2 (D2).

For their latest study, published in *Endocrinology*, Galton and St. Germain used a mouse model lacking D2; such mice are known as D2KO (the “KO” stands for knockout). The results strongly imply that the current view of TH homeostasis in the brain is incomplete. According to that view, D2KO mice should suffer from severe developmental problems. However, they exhibited only relatively mild functional impairment, plus some difficulties hearing and regulating their body temperature. But infants born with an untreated TH deficiency develop cretinism.

**Role:** So Galton and St. Germain have proposed the existence of important compensatory mechanisms that may minimize functional abnormalities in the absence of D2. “The more we learn about the role of the thyroid hormone in the developing brain, the more optimal a treatment we can offer pregnant mothers and infants suffering from hypothyroidism,” explains St. Germain.

Now, armed with mouse models deficient in various combinations of deiodinases, he and Galton are determined to unveil more of the mystery surrounding thyroid hormone regulation during brain development. **TINA TING-LAN CHANG**



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St. Germain and Galton have collaborated for years.

### Making the cut

Surgery trumps physical therapy, steroid injections, and drugs in relieving pain from a slipped vertebra and a narrowing spinal canal, according to the latest paper from the seven-year, \$21-million Spine Patient Outcomes Research Trial. “We suspected surgery produced better results, but we had little objective data to support that,” said James Weinstein, D.O., M.S., chair of orthopaedics at Dartmouth and lead author of the study, published in the



*New England Journal of Medicine*. “We can now discuss much more fully the surgical and non-surgical options available to our patients so that they can make an informed choice.”

### Function junction

Hunting for better ways to combat cancer, a DMS team examined the expression patterns of 241 microRNAs (miRNAs) in 59 cancer cell lines. Since miRNAs regulate gene expression and protein production, knowing how they function is “essential . . .

for designing effective strategies for cancer prevention and treatment,” note Arti Gaur, Ph.D., and her coauthors in *Cancer Research*. Understanding miRNAs may also offer insight into how a “limited number of genetic alterations . . . result in the profound physiologic changes that characterize all malignant tissues.”

