At the International Conference on Alzheimer's and Parkinson's Diseases, DMS's Tracie Caller, M.D., made a presentation about selecting the optimal site of deep brain stimulation to treat Parkinson's.

Researcher builds a better microarray

Why do muscle cells contract, or neurons transmit signals, or cancer cells grow out of control? Every cell in a body has the same DNA, but which genes are turned on and which are turned off determines how a given cell acts.

Genes: The way scientists study gene expression has been revolutionized by a technique called a microarray. It used to be that only a few genes in a cell could be studied at once, but for the past few decades microarrays have allowed scientists to look at the behavior of tens of thousands of genes at once. Now, Dartmouth cancer researcher Craig Tomlinson, Ph.D., may have come up with a better way to do microarrays.

How a cell acts is controlled by the proteins it produces. Genes that are turned on send messages called RNAs that the cell then uses to make proteins. So scientists can tell from RNAs which genes are turned on. Microarrays let scientists look at the levels of virtually all RNAs in a cell on one small chip. "So one can essentially look at what a cell is producing to be that kind of cell," says Tomlinson.

Not all RNAs end up being made into protein, however. RNAs are made in a cell's nucleus and then move to the cytoplasm, where they are translated into protein. But, says Tomlinson, only about 5% of RNAs actually make it to the cytoplasm to become protein. Nevertheless, scientists have always done microarrays on all the RNAs in a cell, assuming the nuclear RNA wouldn't affect the results. Recently, Tomlinson posed a simple yet never-before-asked question: "Does the nuclear RNA matter?"

Their findings show that results using total RNA are very different.

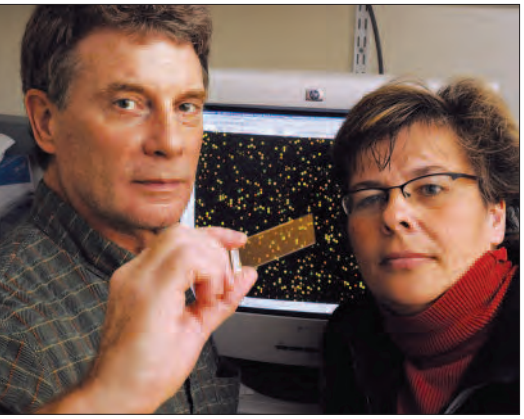
He and colleagues found it matters quite a bit. Their findings, published in the journal *RNA*, show that results using total RNA are very different from those using just cytoplasmic RNA. The difference is so profound, he believes it is imperative to get rid of nuclear RNA.

Test: Cancer researchers, explains Tomlinson, study "the different message RNAs made in a cancer cell versus a normal cell." Sometimes they find genes that, according to the microarray, appear to be expressed at different levels in a cancer cell than a normal cell—but further studies show there really isn't a significant difference. Tomlinson thinks many of these false positives may be caused by nuclear RNA. So if they test only cytoplasmic RNA, scientists may not have to chase after as many false positives.

The process of looking for a few differences out of many, many possible genes is sometimes referred to among scientists as "fishing." So, says Tomlinson, by including nuclear RNA in microarrays, "we've been fishing in the wrong pond."

But he's not stopping there. He thinks microarray results can be made better still by using RNA from just the polysome, the actual machinery in the cytoplasm that makes protein. So if his recent finding directed scientists to the right pond, his next one may show them what part of the pond to look in.

KRISTEN GARNER



JON GILBERT FOX

Tomlinson, left, and his lab manager, Heidi Trask, examine the RNA levels on a microarray chip.

Bubble trouble

Exercising right before undergoing a rapid change in air pressure may raise the risk of acquiring decompression sickness. Exercise causes tiny bubbles called micronuclei to form, but they had never been conclusively detected—until recently. DMS researchers had subjects exercise strenuously for 30 minutes. They then used a form of ultrasound to spot bubbles in subjects' legs. "The ability to measure micronuclei could offer a way to examine how and where they form, and their relationship to decompression sickness risk," they wrote in the *Journal of Applied Physiology*.

Benefits of breast-feeding

A team of DMS and DHMC researchers have made an intriguing finding with regard to breast-feeding and ovarian cancer. They studied hundreds of women with and without ovarian cancer and concluded that breast-feeding offers some protection against ovarian cancer—but only if the woman breast-fed her youngest child. There was no protective effect if a woman breast-fed some of her children but not her final child. "These findings," the authors wrote in the journal *Cancer Causes Control*, "which require confirmation by future studies, imply that breast-feeding resets pregnancy-related states that mediate ovarian cancer risk."