and evolved with them. In Mattick's scheme, the prokaryotes couldn't put up with the introns, because their cells lack nuclei and, as a result, the transcription of DNA into messenger RNA and the translation of messenger RNA into protein occur simultaneously. Hence if introns were introduced into a prokaryotic cell's genes, there would be no opportunity to remove them before the protein is made, and the result would be "nonsense" nonfunctional proteins. As Mattick puts it, for prokaryotes, "the selection pressures against carrying parasitic RNA elements would be enormous."

In eukaryotic cells, on the other hand, transcription takes place within the nucleus, and translation in the surrounding cytoplasm. If introns are present in the genes, they can be snipped out before translation takes place. And once the introns had set up shop in eukaryotic genes, argues Mattick, they got co-opted into providing a second mechanism for regulating the genome—one that may explain the enormous evolutionary success of eukaryotes. This system works according to a quite different mechanism from its protein-based counterpart: In the second system Mattick is proposing, genes are regulated by intron-encoded RNAs that bind either the DNA or RNA.

"[Mattick's] idea is very interesting indeed," says evolutionary geneticist Laurence Hurst of Cambridge University, England. "And it's perfectly testable." For example, he says, Mattick's model predicts that certain genes, like regulatory developmental genes, that must be finely controlled, will likely bear intron-encoded regulatory RNAs.

In fact, surprising new results point to the existence of just such regulatory RNAs. In the fall of 1992, researchers found that the XIST gene, which shuts down one of the two X chromosomes in female mammalian cells, performs its function without ever making a protein. Now, a team led by Jeanne Lawrence of the University of Massachusetts Medical School in Worcester has evidence suggesting that XIST makes an RNA that remains stuck to the chromosome, blocking its further activity.

That intriguing finding provides support for Mattick's revolutionary idea. Late last year, Rosalind Lee, Rhonda Feinbaum, and Victor Ambros of Harvard University offered up another example of a regulatory RNA. The Harvard group found that *lin-4*, a developmental control gene from the roundworm *Caenorhabditis elegans*, encodes a small RNA that binds to the messenger RNA of another gene called *lin-14*, blocking its ability to make a protein. This discovery was particularly dramatic, given Mattick's gene regulation hypothesis, because *lin-4* sits in the intron of another gene.

That was an interesting bit of confirmation for a novel—and not yet widely accepted—theory. But it doesn't exhaust the junk DNA connections with *lin-4*. The binding site of the lin-4 RNA on the *lin-14* RNA is the so-called 3′ untranslated region (3′UTR)—a region that until very recently was dismissed as deadly dull junk. The 3′UTR, which lies at the end of each gene's messenger RNA, is not translated into protein, and for that reason it had been classified as functionless.

This "nonfunctional" region, however, seems to provide the site for some important regulatory activities, since it may not just be *lin-14*'s activity that is regulated via interactions with its 3′UTR end. Over the past few years, a swarm of discoveries has revealed that mutations in the 3′UTR region of at least 10 different genes from worms, fruit flies, and vertebrates can suppress the activities of those genes, by suppressing translation or by hastening degradation of their messenger RNAs. Indeed, one of those mutations, which occurs in the 3′UTR region of the gene for the enzyme myotonin kinase, triggers myotonic dystrophy, a hereditary muscle-wasting disease.

What's more, *lin-4*, *XIST*, and the few other regulatory RNAs that are identified may be just the tip of the iceberg. "There's too many cases of odd RNAs," says molecular geneticist Marvin Wickens of the University of Wisconsin, Madison. "It smells like there might be a whole family of regulatory RNAs." And if that suspicion proves correct, it would be a big boost for Mattick's new theory, as well as for the status of junk DNA—a status that is likely to keep on rising over the next couple of years. Enough gems have already been uncovered in the genetic midden to show that what was once thought to be waste is definitely being transmuted into scientific gold.

–Rachel Nowak

Additional Reading

J.W. Bodnar, "Telephone Book of Life," *Nature* **361**, 580 (1993).

M. Wickens and K. Takayama, "Deviants—or Emissaries," *Nature* **367**, 17.

EMBRYOLOGY

Watching New Developments—Live

In the Golden Age of television—its embryonic years—most shows were broadcast live. That often made them more exciting than today's taped shows, since the audience could delight in watching the performers respond to the inevitable surprises on the set.

Today, an anxious new group is awaiting the unexpected developments that come with live broadcasts: embryologists. On page 681, Russell Jacobs and Scott Fraser of the California Institute of Technology describe a new magnetic resonance imaging (MRI) technique that may allow researchers to watch the movements of all the cells of developing embryos—live. "They have done something that is very, very difficult and done it exquisitely. They have taken [microscopic MRI] into a discipline where it will show a lot of promise," says G. Allan Johnson of Duke University's Center for *In Vivo* Microscopy, one of the pioneering centers of microscopic MRI.

The new technique uses a souped-up MRI machine that has a magnetic field 10 times stronger than those of clinical instruments and can therefore provide a million times better resolution—enough to see even individual cells provided they are labeled with a suitable contrast agent. After the Caltech team injected such an agent into a single cell of a live, 16-cell frog embryo, they watched what happened to that cell and its progeny as the organism developed. "We can look at the whole embryo, inside and outside, and watch how sheets of cells move in relation to each other," Jacobs says.

Such cellular movements and interactions are critical for normal development of complex organisms, and even though biologists have already been remarkably successful in tracing the cellular choreography in embryos, their conclusions have been limited by the available techniques. Following the fate of cells inside an embryo usually requires the examination of many different embryos, each halted at a different stage of development, fixed, and then analyzed microscopically.

Microscopic MRI has changed that, say Jacobs and Fraser, and its newfound capacity for imaging all the cells of the embryo is bound to bring new insights. In fact, Jacobs and Fraser have already made one observation that challenges the received wisdom. They noticed that movements of two key early layers of cells, the mesoderm (which gives rise to blood and muscles) and the ectoderm (which produces skin and nerves) may not be as well coordinated as had been assumed. The promise of new insights is heightened by Jacobs and Fraser's more recent finding that the technique can even be used on mouse embryos within the uterus.

Despite its promise, don't expect microscopic MRI to become a staple in every lab. Richard Harland, a developmental biologist at the University of California, Berkeley, notes that the technology is expensive and there's skepticism about exactly what new biological questions it can address. Yet Harland says he's intrigued. "There's undoubtedly a tremendous advantage to watching it happen live. There might be a host of surprises," says Harland. Expect embryologists to be glued to their monitors in the future.

–John Travis