perhaps unfortunate characteristic of colliding-beam storage rings that they can simultaneously serve only a few long-running (and hence large) experiments rather than the many that fixed-target accelerators such as synchrotrons can handle at once. Phase I of LEP, in particular, will have four experiments.

The issue in competition for space at LEP is what to do with losing proposals. An entire CERN member state could lose out on LEP if its physicists were in the wrong group. CERN's solution, which is being implemented in the experimental selection process now going on, is in essence to have no losers; every European physicist who wants to work at LEP will find a place. The mechanism to achieve this is to allow a regroupment period between the preliminary approval of favored letters of intent and the call for final proposals during which those physicists on weaker teams would find places on stronger ones.

How well will the huge experimental collaborations that result work together? The UA-1 group, headed by Carlo Rubbia of CERN, which is looking for the W and Z particles when the SPS is working in its proton-antiproton collider mode, is often singled out as a model of future LEP teams. UA-1, which has about 125 active physicists, built a 2000-ton detector that cost $20 million. Based on the letters of intent, one can conclude that each LEP detector will weigh 2500 tons or more, cost $30 million, and be built by a group of 200 or more physicists.

For starters, the physics community has been pleasantly surprised that UA-1 (and also its competitor UA-2) has managed to build such a complex instrument in so short a time—3 years from approval to first data. So, the LEP collaborations will have an ambitious but attackable task. But it will not be easy. Members of UA-1 credit Rubbia's strong personality as the force that held the group together during a difficult time.

And there are many questions. How do you train students to be physicists in such large groups where specialization reaches an extreme? During the years-long construction period, physicists will have few or no publications on the subject on which their careers depend. Finally, an old question but one exacerbated by the complexity of the new detectors is, Who is to run and maintain the instrument once it is built? The natural tendency, already in evidence in UA-1, is for collaboration members to retreat to their home laboratories for more or less independent data analysis.

It is too early to tell if all this pain is only the outcome expected of any big change, or something more. One possibility is that elementary particle accelerators have reached their natural limit and that the era of ever larger machines is drawing to a close.

—ARTHUR L. ROBINSON

Can Genes Jump Between Eukaryotic Species?

Biologists are beginning to take seriously the heterodox idea that genes can jump across the species barrier in higher organisms

Molecular biologists are now thoroughly comfortable with the idea that genes and other genetic elements have a certain mobility within a genome. Although it came as a considerable surprise initially, research of recent years has now firmly established the existence of a range of mechanisms, beyond classic recombination, that can cause heritable rearrangements of genetic material. Just as researchers are beginning to ponder on the mechanistic and evolutionary implications of dynamic DNA within a species' genome, there come the first strong indications that genetic mobility might extend across species barriers in higher organisms. If true, gene transfer between species will add yet another evolutionary dimension to the phenomenon of jumping genes in eukaryotic organisms.

Gene transfer between species is well known in prokaryotic organisms; it is the basis of transduction, transformation, and sexduction in bacteria. The current interest in interspecific gene transfer is, however, very much focused on eukaryotic organisms. "The theory of horizontal gene transfer is a salutary challenge to received views of a totally coherent evolution and orderly transmission of genes in eukaryotes." With this clear statement of the issue, Meinrad Busslinger, Sandro Rusconi, and Max Birnstiel, of the University of Zurich, concluded a recent paper on one of the most closely analyzed candidates for eukaryotic horizontal gene transfer (*1*).

The investigation of something as apparently fanciful and certainly unorthodox as gene transfer involving higher organisms must proceed in two stages. First, does it occur at all? Second, if it does occur, how common and how important is it? Current work is very much at the beginning of the first stage, but is directed with a keen eye on truly intriguing answers to the second.

Until recently there were just a few examples of apparent eukaryotic gene transfer. One clear case is that between *Agrobacter tumefaciens* and host plants in the etiology of crown gall tumor. A possible example of transfer in the reverse—eukaryote to prokaryote—direction involves *Progenitor cryptocides* and humans. This microorganism is found in close association with certain tumors and in culture secretes a protein apparently produced by the gene for human chorionic gonadotropin. Both these instances involve pathologies and might therefore be set aside as aberrant events. In any case they are generally not included in the small catalog of solid candidates currently being considered.

As Birnstiel and his colleagues point out, the advent of rapid DNA sequencing and gene cloning now allows the systematic search for transferred genes. This is certain to apply in the future, but the current list of four putative transferred genes came as fortuitous discoveries. These are the genes for the enzyme superoxide dismutase in *Photobacter leiognathi*, the symbiotic bacterium of the ponyfish; a family of histone genes in sea urchin; a subfamily of repeated sequences in sea urchin; and the leghemoglobin gene in legumes.

Superoxide dismutase is a widely distributed enzyme that appears to mop up harmful oxygen radicals. In eukaryotes the enzyme contains copper and zinc, in prokaryotes it contains iron, and a third form found in prokaryotes and mitochondria contains manganese.

When, in 1974, two French researchers, K. Puget and A. M. Michelson, reported the existence of a copper-zinc enzyme in the bioluminescent bacterium *P. leiognathi*, the anomaly quickly caught the attention of Irwin Fridovich of Duke University. Although Fridovich

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immediately suggested that there might have been a transfer of a superoxide dismutase gene from the ponyfish to its symbiotic bacterium, he didn't pursue the proposal further until Joseph Martin joined him in 1979.

The result of the collaboration was a comparison of the amino acid composition of the bacterial enzyme with a range of eukaryotic and prokaryotic species. The result was clear-cut. The enzyme from *P. leiognathi* fell unequivocally in the eukaryotic category and by a number of criteria resembles closely the enzyme from the ponyfish.

Martin and Fridovich conclude that the intimacy of the symbiotic relation between fish and bacterium might reasonably be assumed to have facilitated transfer of the copper-zinc–containing superoxide dismutase gene from eukaryote to prokaryote. They also note, however, that "it is difficult to imagine what selective advantage could have caused this gene to be retained by the bacterium."

When they published their paper in June 1981 Martin and Fridovich (*2*) reported that a survey of 93 strains of enterobacteria isolated from both land and sea organisms failed to yield a second example of a copper-zinc–containing enzyme in prokaryotes. Since then, Howard Steinman of the Albert Einstein College of Medicine, New York, has found a second case in *Caulobacter crescentus*, a free-living bacterium that inhabits pond waters; this organism is not part of a symbiotic relationship with a eukaryotic organism, and neither is any of its relatives. Does this seriously weaken the case made for *P. leiognathi*? Or does it betoken a long-dissolved symbiosis, as Fridovich speculates?

According to Steinman, the *C. crescentus* enzyme is reminiscent of the eukaryotic enzyme, but less closely so than that in the ponyfish symbiont. The second possibility, that of a long-dissolved symbiosis of which *C. crescentus* was a part, is therefore tenable. Steinman plans to use DNA hybridization techniques to determine whether other bacteria possess the copper-zinc superoxide dismutase gene, but simply do not express it.

Superoxide dismutase is, incidentally, the subject of a possible gene transfer in the reverse—prokaryote to eukaryote—direction. Marvin Salin and Susan Bridges, of Mississippi State University, surveyed 43 plant families and found the iron-containing, prokaryotic, enzyme in three of them, the Gingkoaceae, Nymphaceae, and Cruciferae (*3*). The three enzymes are significantly different from each other, a fact that Salin interprets to imply three separate gene transfer events.

The second of the four principal candidates for horizontal gene transfer is leghemoglobin, a myoglobin-like protein in legumes that combines with oxygen. The subject of prolonged controversy, leghemoglobin bears an uncanny resemblance to vertebrate globin, and contains heme. And earlier this year Kjeld Marcker and his colleagues at the University of Aarhus, Denmark, reported that the structure of the leghemoglobin gene is very similar to that of the vertebrate globin gene, including the precise location of two of its introns (*4*).

It has been suggested that the leghemoglobin gene might have come from the plant symbiont bacterium *Rhizobium*, but the presence of introns in the gene leads Marker and his colleagues to reject this hypothesis. They favor the notion that the gene might have been transferred from another eukaryote to legumes recently in evolution, possibly as a passenger on a virus. "Such a mechanism circumvents the rules of classical Mendelian genetics with rather important implications for our understanding of the mechanism of evolution," they note.

> ". . . it might occur and be unimportant. Or it might occur and be of overwhelming importance."

The sea urchin is a highly popular experimental organism in molecular biology, and therefore it is perhaps not surprising that the last two rather detailed examples of putative gene transfer come from this source. Roy Britten, Eric Davidson, and four co-workers at the California Institute of Technology reported last year on the homologies in a superfamily (denoted 2108) of repeated sequences in several species of sea urchin (*5*). One of their most puzzling findings was the very close homology in one subfamily of 2108 between sea urchin species that had diverged almost 200 million years ago. The unique sequence DNA in these species, *Strongylocentrotus purpuratus* and *Tripneustes gratilla* for example, had only little homology.

The Caltech group mentioned horizontal gene transfer as a possible explanation of this anomoly, but then dismissed it as "a very unlikely proposition." Since the publication of Birnstiel's work, Britten has been willing to take the idea more seriously. "I think it is interesting enough for us to continue looking at it," he says. Davidson is less sanguine.

Birnstiel and his colleagues have been sequencing clones of histone genes from species of sea urchin so as to determine the mutation rate through evolutionary time. During their work they were surprised to find that a minor clone, h19, from the North Atlantic species *Psammechinus miliaris* differed, on the average, by only 1.3 percent of its bases from a homologous clone from *Stronglyocentrotus purpuratus*, a Pacific species from which it diverged some 65 million years ago. The unusual homology could be explained, they suggested, by either extreme and unusual conservation of sequences, including nontranscribed sequences, or by horizontal gene transfer.

In support of horizontal transfer Birnstiel and his colleagues eventually found a clone equivalent to the h19 clone in *Strongylocentrotus dröbachiensis*, a species that had migrated to the North Atlantic during the last 5 million years. "We must consider the possibility of horizontal gene transfer of an h19-like gene cluster from *S. dröbachiensis* to *P. miliaris* within the last million years," they conclude.

Nothing definitive can be reported yet about the mechanism of gene transfer in these cases, if indeed that is what they represent. Of several possible mechanisms, however, the involvement of a viral vector is a clear favorite and one for which there are precedents in other systems. Birnstiel and his colleagues plan to look for evidence of viral translocation in the flanking regions of the putative transferred gene cluster in the h19 clone.

Birnstiel says he is sufficiently interested in the heterodox phenomenon to devote more effort to studying it. But, like Britten, he cautions that as yet there is insufficient data to make a judgment on its reality. "People will be looking for more possible examples," says Britten. "In any case, it might occur and be unimportant. Or it might occur and be of overwhelming importance." The prospects are tantalizing.—ROGER LEWIN

Additional Readings

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