ANALYSIS: RUBISCO GENE CLONED

The nuclear genomes of plants are typical of eukaryotes generally: large, complex, containing a variety of repeating sequences, probably transposons, and other elements. Genes, or at least cDNAs, for most of the major storage proteins, have been isolated, cloned, and mapped. These genes typically contain introns and code for multiple subunits that are processed by proteolytic cleavage and glycosylation. The genetics of seed proteins form a scientifically rich lode and are of enormous economic importance.

Nuclei also code for those chloroplast proteins that are not provided by the chloroplast itself. These proteins are synthesized on free cytoplasmic ribosomes as precursors, transported across the chloroplast envelope, and there cleaved into the mature proteins. The chlorophyll a/b-binding protein is one such protein. Its genes have been isolated from nuclear DNA.

Another kind of nuclear gene is the subject of an article by Broglie, Coruzzi, Lamppa, Keith, and Chua in this issue of Bio/Technology (see p. 55). To appreciate the significance of this work, we should say something more about RUBISCO. It is the doorman of photosynthesis that provides entry for carbon dioxide to the Calvin-Benson cycle of carbon reduction. The higher plant version of RUBISCO contains eight large and eight small subunits. The large subunits are synthesized in the chloroplast itself; the smaller subunits are synthesized on free ribosomes in the cytoplasm as a precursor, transported into the chloroplast, and processed into the mature subunit[5]. RUBISCO is therefore a genetic hybrid, analogous to the cytochrome oxidases of animal and fungal mitochondria. Another chloroplast protein, the coupling factor for photophosphorylation, is also a genetic hybrid. Because RUBISCO is essential to photosynthesis and because RUBISCO is so inefficient, plants are obliged to synthesize prodigious quantities of it. Considering both the functional importance of RUBISCO and the large investment that its synthesis represents to the economy of the plant, we can understand why it has been eyed as a prime target for genetic manipulation.

Broglie *et al.* have studied the organization of the gene for the small subunit of RUBISCO in wheat. They have located the gene in the nucleus, determined that it is part of a multigene family, that it contains an intron between exons coding for a transit peptide and the mature subunit, and that its 5′- and 3′-flanking sequences are similar to those seen in other eukaryotes. Part of the significance of these results lies in their generality. Broglie *et al.*'s finding of multiple copies of the gene for the small subunit of RUBISCO fits exactly with the conclusions drawn for all of the nuclear genes thus far analyzed in plants. These include genes for seed proteins, such as zein, the chlorophyll a/b-binding protein.

The existence of a number of multigene families coding for important plant proteins presents both a complication and an opportunity for genetic manipulation. It complicates the problem of replacing one function with another, but it also provides a rich array of genetic variation to choose from. Some members of these gene families vary within the coding region and others within non-coding regions. The geneticist may be in a position, therefore, to select among genes that produce slightly different proteins or which have different promoters.

The presence of transit peptides on cytoplasmically synthesized chloroplast proteins also appears to occur generally, as does the location of introns at or near the point where proteolytic processing occurs. These regions could be a fruitful target for genetic manipulation in altering the way processing occurs or in introducing new proteins into the chloroplast.

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BIOTECHNOLOGY PATENTS OF 1983

AN INTERNATIONAL PERSPECTIVE

Although patents are well recognized by the general public and considered to be "good," it is amazing to see their aversion by research scientists and, in particular, by the academic community. However, the latter group's attitude is changing quickly as more and more universities adopt the policy of patenting the inventions of their faculty. Last year, 32 U.S. academic institutions were granted 76 U.S. patents on biotechnology.

A patent is a document which describes an invention, i.e., a new product or process that is novel, not obvious and useful, in sufficient detail so that any person skilled in the "art" is able to make and use that invention. In return for this public disclosure, which is intended to foster the promotion of science and technology, a government grants the inventor (or the assigned owner) a monopoly for a certain time period. Thus, the owner of a patent has the right to exclude others from making the product or using the process for the specified time period, which is 17 years for U.S. patents. Patents are only valid in the countries issued.

This paper surveys U.S. and international aspects of biotechnology patents and not legal issues or procedural matters raised by last year's events. For the present purpose, biotechnology refers to the *controlled* use of intact biological organisms or isolated cellular components to solve problems or obtain benefits. With organisms, the term is usually restricted to the use of microorganisms—bacteria, yeast, algae, fungi, and protozoa. Not included in the data base is the use of microbes for testing biocides or antibiotics in which the emphasis was on the synthesis or characterization of the compound; however, antibiotics produced by microbes are indeed included. Major areas encompassed by this definition of biotechnology are analytical biochemistry, immunology, clinical biochemistry, and microbiology, medicine, enzymology, genetic engineering, fermentation, biological separation processes, foods, pharmaceuticals, chemicals, minerals, and animal health products.

Although a world perspective on biotechnology patents is desirable and would include patents issued in other countries, such a data base is far too complex, incomplete, and incon-