Molecular biology

A new protein in petunia

from J.E. Varner and G.I. Cassab

CAROL Condit and Rich Meagher, on page 178 of this issue[1], report the discovery of a gene in petunia plants that is predicted to encode a protein containing 67% glycine residues with a sequence mainly conforming to the formula $(\text{glycine-X})_n$, where X is frequently glycine. The product of the gene is presumably secreted because it begins with a transit peptide sequence. Condit and Meagher propose that the protein is secreted into the cell-wall compartment where it forms part of the extracellular matrix.

Speak of glycine-rich proteins and one calls to mind structural proteins made up of short repeating units, for example collagen $(\text{X-proline-glycine})_n$; the cocoon silks *Bombyx mori* $(\text{X-glycine})_n$ and *Antheraea paphia* (25% glycine); and spider-web silks (41–52% glycine)[2]. In collagen the presence of glycine at every third position in the peptide chain, together with the presence of proline or hydroxyproline at every second position, allows three peptide chains to form the triple-helical structure that gives collagen its unique and useful properties. The occurrence of glycine at every fourth or second residue in silks allows the formation of parallel and antiparallel β-sheets. These glycine-rich conformations meet the structural and architectural needs of many species.

As its happens there are several known instances in plant tissues in which glycine is a major fraction of the total protein nitrogen. These include the soybean (*Glycine max*) seed coat (21% glycine)[3], the gourd (*Cucurbita ficifolia*) seed coat (21% glycine)[4], the pumpkin (*Curcurbita pepo*) seed coat (the major protein of the cell walls contains more than 47% glycine; our own unpublished observations), milkweed (*Periploca graeca*) stem (cell walls, 31% glycine)[5], moisture-stressed soybean hypocotyls (cell walls, the major soluble protein contains 25% glycine; C.S. Bozarth, J.E. Mullett and J.S. Boyer, personal communication) and oat (*Avena sativa*) coleoptiles (epidermal cell walls, 27% glycine; D. Pope, personal communication). Because cell walls contain several enzymes with normal content of glycine (8–12%) and a hydroxyproline-rich structural glycoprotein that contains no glycine, we are certain that for the tissues mentioned the glycine-rich proteins, when purified and characterized, will be found to be two to three times as rich in glycine as the cell walls they are extracted from. To cite another example of the importance of glycine richness in structural proteins, one of the glycoproteins which makes up *Clamydomonas reinhardtii* cell walls is glycine-rich (23%)[6]. And, finally, to illustrate the usefulness of glycine-rich proteins in cell-wall architecture, *Thermomicrobium roseum*, a Gram-negative, obligately thermophilic bacterium, possesses a cell wall that is composed predominantly of a protein with a monomeric relative molecular mass of 75,000 that is 34% glycine[7].

In the past few years there has been a general and belated realization that the hydroxyproline-rich glycoproteins of plant cell walls discovered by Lamport and Northcote[8] in 1960 are of considerable importance in cell-wall structure (particularly in dicotyledons), not only with respect to growth and development[9] but also in the response of the plant to injury and infection[10]. The discovery and characterization of a gene encoding a protein remarkably rich in glycine that is probably localized in the wall is likely to increase further our awareness of cell-wall proteins. Perhaps we should now ask whether the plant cell wall contains other kinds of structural proteins. □

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Immunology

Bone marrow grafts and tolerance

from E. Donnall Thomas

BONE marrow transplantation is now widely used in human beings as a treatment for both acquired and genetically determined diseases. However, transplantation between individuals who are not genetically identical may give rise to an immunological reaction of host cells against donor cells resulting in graft rejection, or of graft cells against the host resulting in graft-versus-host disease. T lymphocytes, or T-cell subsets, are thought to mediate these reactions. Graft rejection is uncommon in recipients receiving intensive chemoradiotherapy before grafting but the problems of graft-versus-host disease remain and may be severe even if donor and recipient are matched for the antigens of the major histocompatibility system, HLA. In this issue (*Nature* **323**, 164; 1986) Cobbold *et al.* describe the use of monoclonal antibodies against T cells in mice that may point the way to the resolution of these problems.

Immunosuppressive drugs or drug combinations have been developed to prevent graft-versus-host disease in most patients with matched or partially matched donors (Storb *et al. N. Engl. J. Med.* **314**, 729; 1986) but they are not always effective and are associated with significant toxicity. For this reason, investigators have studied various methods of removing T cells from the donor marrow before the marrow is given to the patient. These approaches have resulted in a decreased incidence and severity of graft-versus-host disease, but a new problem has arisen, the problem of graft failure within a few weeks or months after the transplant.

The reasons for graft failure are not understood but include the possibility of damage to haematopoietic stem cells during the T-cell depletion; the possibility that T cells are in some way essential to normal haematopoiesis; and the possibility that the absence of donor T cells permits an immunological reaction of residual host T cells resulting in graft rejection. The last possibility is supported by the demonstration of small numbers of residual host T cells after treatment by the use of cytogenetics and analysis of restriction fragment length polymorphisms.

The study by Cobbold *et al.* in a murine model of bone marrow transplantation across the major histocompatibility barrier shows clearly that an immunological reaction by T cells is the mechanism of graft rejection and that it involves more than one subset of T cells. The authors administered monoclonal antibodies reacting with both the L3/T4$^+$ and Lyt-2$^+$ T-cell subsets (equivalent to the CD4$^+$ and CD8$^+$ subsets in man) that prevented graft rejection even after sublethal irradiation exposure. Surprisingly, and of greatest interest, many of these animals became long-lived chimaeras, specifically accepting a donor's skin graft, that is, they were operationally tolerant.

A preliminary study by Fisher *et al.* (*Bone Marrow Transplantn* **1**, 167; 1986)