transplantation, either by cellular dissociation or by selective elimination of specific cell types. By transplantation of tissue cultures that contain immunocytochemically defined cell populations, the tissue specific for the expression of rhythmicity in the host may be defined. Genetic alteration prior to transplantation of the cultured SCN cells using replication-deficient viral vectors, is a novel approach which might throw light on mammalian pacemaker function at a cellular and molecular level.

Stumbling block to clinical application. The hindrance to wide clinical application of neural transplantation in humans is the absence of long-term survival of functionally competent grafted tissue. The failure of grafts is attributed to the immunological response of the host to neural grafts.

Central nervous tissue is different from the majority of peripheral tissue with respect to immune status. Though brain was considered as a privileged tissue as far as immune response is concerned, observations such as rapid rejection of neural tissue transplanted beneath host kidney capsule, suggested that neural tissue behaves like an orthotopic skin graft and that it is immunogenic, though there may be differences of degree[8]. Experiments also show that there is no prior deficiency of immune response in the efferent arch, but the afferent arch might rather be compromised in some way. Recent studies have shown that there is a higher rate of failure of take up of foetal nervous tissue transplant in rhesus monkeys compared to rats. The graft in monkeys was found in these studies to be invaded by both T and B lymphocytes and macrophages. MHC type II molecules were demonstrated not only in the endothelial cells of blood vessels of the grafts and the surrounding brain but also in astrocytes and microglial cells. Grafted neurones were found to undergo progressive degenerative changes after an initial healthy survival period of several months. This premature ageing of the graft has been attributed to immune rejection[9, 10].

Review of available data reveals that CNS may represent an immunologically privileged site indeed but the privilege is far from absolute[1, 9, 11]. Some form of immunosuppression has been advocated in the therapeutic regimen when allografts are used. While solid tissue fragments and cell suspensions of neural tissue are immunogenic as a whole, the individual cell types within the graft themselves could be immunogenic to different degree. There are claims that neural allograft rejection can be completely surmounted by preselecting a subpopulation of embryonic epithelial cells for grafting. This can be achieved with the use of immunobead separation on the basis of major histocompatibility (MHC) expression. The neuronal precursor cells which did not express MHC class I antigen *in vitro* when treated with interferon-r (IFN-r) were successfully maintained in the brain parenchyma in a mouse model where whole neural grafts were normally rejected. This observation obviously offers the possibility of grafting enriched neuronal cells population across allogenic and perhaps even xenogenic histocompatibility barriers, without the need to immunosuppress the recipients.

Use of neuronal stem cells. Yet another novel pursuit in transplantation research focuses on the identification and manipulation of neuronal stem cells. Techniques that allow the culture of primary foetal cells and their expansion *in vitro* prior to grafting promise greater versatility compared with fresh tissue in two ways. Firstly, they might allow an increase in the number of cells available for transplantation. Secondly, during the short period in culture the graft cells might be manipulated to express genes with useful functional effects[1, 12].

To conclude, in neural transplantation, the game is just beginning.

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Complete nucleotide sequence

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Several laboratories in the world have begun the ambitious project to sequence the entire human genome. The magnitude of the task can be judged from the fact that the longest sequence – on *one* of the yeast chromosomes consisting of 315×10^3 bases – has recently been published (*Nature*, 1992, **357**, 38) and has been hailed as a landmark in the sequencing of entire genomes. Yeast has 16 pairs of chromosomes and the sequencing of the smallest of them is the result of the collaboration of 35 laboratories in 17 countries. Compare this achievement with what has to be done with regard to the human genome which consists of 23 pairs of chromosomes, the smallest of which – chromosome 21 – has 150×10^6 bases. Daniel Cohen at CE PH, Paris is in the final stages of sequencing this chromosome.

In March 1992, 121×10^3 bases from three contiguous stretches of the genome of the nematode *Caenorhabditis elegans* was published in *Nature*. Within the next four years the nucleotide sequence of *C. elegans* and the bacterium *Escherichia coli* should be complete as well as a few of yeast (*Saccharomyces cerevisiae*) chromosomes and one or two

chromosomes – probably chromosome 21 and X chromosome – of the human genome.

Most of the sequencing of the yeast chromosome has been done 'by hand', and though hereafter automatic sequencing machines will undoubtedly be used, this gives hopes to Indian laboratories, which are not richly equipped, to participate in future sequencing programmes. On the other hand, these long sequences will have to be stored in computers and searched automatically. As Maddox points out in *Nature*, the sequence of the smallest of the yeast chromosomes would have occupied 45 pages of *Nature*.

The results of sequencing *C. elegans* genome and yeast chromosome reveal some unexpected information. With both there are more genes in the regions sequenced than had been expected. In *C. elegans*, for example, the number of predicted genes in the three cosmids sequenced is higher than that would have been expected on the basis of genetic estimates of essential gene numbers and on a previous transcript analysis around the vitellogenin gene. The high gene density (one over 3–4 kb) may arise in part because the sample comes from the gene-rich cluster on chromosome 3. But each chromosome contains a central gene-rich cluster, and the physical map shows that about half the genome is contained in such clusters. Extrapolations indicate that *C. elegans* will have about 15,000 genes in the clusters alone. The other half of the DNA is not devoid of genes, but there is no accurate estimate of the gene density there.

Chromosome III of yeast is also replete with previously unknown genes, or at least with open reading frames from which mRNA molecules can be transcribed when there are appropriately placed regulatory elements to turn them on. Indeed, the genetic map of the chromosome contained only 34 genes before the complete sequence was assembled, but now there are 182, not counting tRNA genes, transposable elements and genes with fewer than 300 bases. Allowing for a small handful of genes previously sequenced but not mapped, the result is that chromosome III has now 145 new genes, or that its gene content is five times greater than previously believed.

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Erratum

Seismotectonics of Himalaya

Umesh Chandra

(*Curr. Sci.*, 1992, **62**, 40)

In Figure 1 on page 59, the boundary of the NW parts of India was wrongly indicated. The correct map is given below.