

teraction in plant diseases, role of rhizosphere organisms in plant health and appreciation of plant defence strategies is a relevant publication serving to integrate information available in different fields. Hence, it is a very important reference source to researchers in plant pathology.

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Gene Therapy – Principles and Applications. Thomas Blankenstein (ed.). Birkhauser Verlag AG, P.O. Box 133, CH-4010, Basel, Switzerland. 1999. 392 pp. Price: DM 198/SFr 168.

The hype about gene therapy stems from the fact that for the first time in medical history, hope is held out that there could be a cure for genetic disorders. The pressure from the population that is afflicted directly or indirectly to share the burden of a suffering closest kith and kin, has given a tremendous purpose to pursue this field. The scope of gene therapy has been broadened to treat cancers and HIV and in fact the major emphasis in recent years has shifted to studying cancer therapy using this approach. The growing clinical trials have indicated that the major problems with the approach are in terms of getting an ideal vector to introduce the gene followed by optimal and durable expression of the gene product in the recipient, besides consideration of safety. While a dramatic success of a cure is yet to be reported, the information made available on the subject is exploding. Therefore, any book that gives a comprehensive account of the field is welcome and the present title fits the bill.

The book is organized into four major sections – Gene transfer methods, gene therapy of single gene defects, gene marking and gene therapy of cancer. Each section has several articles written by different authors working in the field.

The section on gene transfer methods encompasses six articles, three on biological gene transfer and three on physical approaches to gene targeting. Retroviral, adeno and recombinant adeno associated viral (γ AAV) vectors have been described in detail. Despite the limitation of retroviruses to infect only dividing cells, these constitute the most widely used system for *ex vivo* gene therapy. A few examples of *in vitro* delivery of 'suicide genes' are also available. Adenovirus can express the transgene in the nucleus of both replicating and non-replicating cells. Replication-deficient recombinant adenovirus carrying the transgene of choice has been studied for use in cystic fibrosis, the Ad2 and Ad5 subtypes having tropism for the lung. More recently, γ AAV is being seriously considered as a future gene therapy vector. Attempts to obtain a high titre (3×10^{11} particles/ml) seem to be successful and the vector has unique potential for targeted integration into the chromosome. Three other articles deal with liposome and receptor-mediated gene delivery as well as particle bombardment as another tool. While these physical methods would be ideal from safety point of view, in general their efficiency of gene transfer is low.

The section on gene therapy of single gene defects has four articles covering information on severe combined immuno deficiency (SCID), lysosomal storage disorders, familial hypercholesterolemia and cystic fibrosis. Adenosine deaminase deficient SCID is the first genetic disorder to be treated with retroviral-mediated gene transfer and the studies have demonstrated the feasibility of introducing functional genes into peripheral blood lymphocytes and hematopoietic stem cells to restore normal immune function in this disease. The article on lysosomal storage disorders highlights the point that natural animal models provide a powerful investigative tool, when the animal phenotype closely matches the symptoms in the human, as is the case with mucopolysaccharidosis Type VII in mouse. However, gene-targeted mouse models of certain other lysosomal disorders, do not mimic the human condition, but manifest changes rendering certain facets of disease pathology not manifest in humans. Cystic fibrosis has been the

disease of choice to study the efficacy of various vector systems and routes of administration to the airway epithelium. The results reported in early clinical trials are equivocal and with several strategies available for improvement, the development of therapy protocols is likely to be incremental. Familial hypercholesterolemia is due to a defect in LDL receptor and the first clinical trial has demonstrated the general feasibility using retroviral-mediated *ex vivo* gene transfer.

The section on gene marking consists of three articles dealing with gene marking in bone marrow cells, peripheral blood cells and T lymphocytes used in transplantation as well as MDR gene transfer to hematopoietic cells. Gene marking studies provide crucial information on feasibility, safety and efficacy of genetically modified cells, a prerequisite for gene therapy trials. The marker with retroviral vectors as such does not modify the cells, but allows them to be detected. The results suggest that autologous transplanted cells contribute to long-term hematopoiesis. The marking studies also establish the contribution of unpurged autologous bone marrow to disease relapse following bone marrow transplantation. The lymphocytic target cells for gene marking include tumour infiltrating lymphocytes (TILS), virus specific cytotoxic T cells and donor derived lymphocytes. *MDR1* gene transfer studies have shown that the expression of P-glycoprotein in hematopoietic tissues can protect progenitor cells from cytotoxicity of anticancer drugs. Transformed cells have a selective advantage over non-transformed cells in terms of protecting bone marrow cells from myelosuppression following chemotherapy. The approach permits to introduce and over-express otherwise non-selectable genes that can correct genetic disorders.

The section on gene therapy of cancer has eight articles. The first one elaborates on antisense oligonucleotide therapy using *c-myc* proto-oncogene as the target. The article on thymidine kinases discusses the prospects of tk-mediated 'suicide' gene therapy. Tumour cells transduced with HSVtk become sensitive to Gancyclovir and the approach has attracted attention in view of the 'Bystander' effect. The characterization of tumour associated antigens, the

availability of many immunostimulatory molecules to improve the immunogenicity of the tumour vaccine and improved methods of gene transfer of mammalian cells have revived the long-standing interest in cancer immunotherapy and the rest of the articles in this section are devoted to this subject. Immune memory may be able to suppress recurrence from the few neoplastic cells that are left behind following surgery and chemotherapy. The 'autologous vaccine' derived from a genetically modified patient's own tumour and the allogenic tumour vaccine based on genetically modified tumour cell line established from one or more patients – are under consideration.

Since T-cell activation involves specific processing of antigenic peptides, precise knowledge of tumour peptides needs to be obtained. The peptide vaccine itself is relevant, although it has drawbacks in terms of down regulating T-cell response. Finally, a combined immuno and chemotherapy is illustrated by the efficacy of administering low dose cyclophosphamide with cytokine gene-modified tumour vaccine to treat murine tumour.

This book has comprehensively brought out the status of the field, the lacunae and the future directions. Data from clinical trials have been analysed, although many trials are still under progress. The book establishes the sound

scientific basis behind gene therapy and gives the feeling that it is a matter of time before consistent success with the cure of atleast some of the cancers becomes a reality. It is a bit surprising that a book of this high technical standard has many errors of language and spelling. I guess Queen's English is not needed to describe gene therapy! The book should be of significant use to researchers in the field of gene therapy.

G. PADMANABAN

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Errata

Probing fundamental problems with lasers and cold atoms: An Indo-French workshop

C. S. Unnikrishnan

[*Curr. Sci.*, 1999, 76, 1523–1526]

On page 1525, paragraph 1, in the line ... experiment on parity violation pioneered and pursued by Helene Bouchiat..., Helene Bouchiat should read as Madome Marie Anne Bouchiat.

New elements discovered and the island of stability

K. R. Rao

[*Curr. Sci.*, 1999, 77, 328–330]

Ref (4b) should read: Ninov, V. *et al.*, *Phys. Rev. Lett.*, 1999, 83, 1104.

In addition, the following references pertain to recent work at Dubna:

- (i) Oganessian, Yu.Ts. *et al.*, *Phys. Rev. Lett.* (submitted).
JINR preprint E7-99-53 (JINR, Dubna, 1999)
- (ii) Oganessian, Yu. Ts. *et al.*, *Nature*, 1999, 400, 242.

Quantum signature of the classical chaos in the field-induced barrier crossing in a quartic potential

P. K. Chattaraj, S. Sengupta and A. Poddar

[*Curr. Sci.*, 1999, 76, 1371–1376]

Equations (1), (2) and (9) should read as

$$\mathcal{H} = \frac{p^2}{2m} + ax^4 - bx^2 + cx \cos(\omega_0 t). \quad (1)$$

$$\hat{\mathcal{H}}\psi(x, t) = \left[-\frac{1}{2} \frac{d^2}{dx^2} + ax^4 - bx^2 + cx \cos(\omega_0 t) \right] \psi(x, t) = i \frac{\partial \psi(x, t)}{\partial t}. \quad (2)$$

and

$$V(x) = ax^4 - bx^2 + cx \cos(\omega_0 t), \quad (9)$$