MEETING REPORT

Cell transplantation and stem cell research*

Although embryonic stem cells have taken their place beside the human genome project as one of the most discussed biomedical issues of the day, India's position in this field is still not very clear. In recognition of the growing excitement and potential of cell transplantation and embryonic cells as models for both the advancement of basic science and future clinical applications, it was felt necessary to organize a workshop to discuss the *status of* cell transplantation in India. The broad aim of this brain-storming workshop was to bring under one roof scientists working and/or interested in this 'thrust and challenging' area of biomedical research.

The workshop consisted of 17 invited lectures by renowned scientists from all over India. There were mainly four categories of talks organized in four sessions: (a) Pancreatic islet cell transplantation; (b) Cell transplantation in other organs; (c) Stem cell research, and (d) Regulatory aspects of stem cell research.

The scientific programme started with a lecture by S. Gunasekaran (CMC, Vellore) discussing that monkey islet grafts in rats maintained structural and functional integrity and inducted reversal of diabetes (45 days) in rats made diabetic with streptozotocin. He also pointed out how his work has run into problems due to recent regulations on animal research, particularly on primates. V. Mohan (MDRF), next reviewed the current status of human islet cell transplantation highlighting success of the Edmonton Trial, where near 100% success had been achieved in a small number of Type-1 diabetic patients. The emerging importance of regenerative biology and tissue engineering in islet cell research was emphasized by R. Bhonde (NCCS, Pune) as his laboratory is involved in large-scale cultivation of islets, their cryopreservation, encapsulation and transplantation. It was interesting to note that Bhonde's group has developed models for *in vitro* generation of the islets from the ductal precursor cells as well as intra islet precursor cells. J. S. Melo (BARC, Mumbai) showed how entrapment or encapsulation has the potential to become one of the important techniques in immobilization of biomolecules. He highlighted the use of 'immunobarrier' strategy, wherein artificial membranes are selectively impermeable to immunoglobulin attack and other immune effector's mechanisms. At the end of this session, Darryl M. Nomura (Life Scan Inc., USA) discussed in detail the use of self-monitoring of blood glucose data algorithms to predict HbA1c values that can be used to improve results of islet cell transplantation.

In the second session, the success and constraints of experimental liver cell transplantation were delineated by V. Bhatnagar (AIIMS, New Delhi) who called for further work in studying the long-term functional analysis of transplanted hepatocytes. T. R. Raju and Sunil Thomas (NIMHANS, Bangalore) talked about the future of cell therapy in neurological disorders and emphasized the basic research studies on the identification of factors, which will govern differentiation and transdifferentiation of stem cells into specific neuronal types. Geeta Kashyap Vemuganti (L.V. Prasad Eye Institute, Hyderabad) demonstrated how limbal stem cells can be exploited to generate the cultured corneal epithelium for reconstruction of ocular surface in patients with advanced corneal diseases. V. Thiagarajan (TANUVAS, Chennai) elaborated the use of hybridoma technique in cell-based therapies.

The third session was entirely an update on stem cell research. N. Pandiyan (Apollo Hospitals, Chennai) emphasized that spare embryos from infertility clinics should be used for research without any hesitation or ethical concerns. Extending optimism, he hoped that India would soon become a major partner in stem cell research. The next two talks were from the two institutes identified and recognized as stem cell working stations in India by the National Institutes of Health, USA. M. Panicker (NCBS, Bangalore) stressed the need for more basic studies in characterization of stem cells, subjecting them to differentiation protocols and selection schemes using cell surface antigens, transcription factors and marker enzymes. He expressed concern on differentiation protocols that drive oncogenes and favoured the approach of conditional immortalization of tissue-specific cells. The Mission Programme of Reliance Lifesciences was projected by Satish Totey (Reliance Lifesciences, Mumbai), which is concerned with ways and means to develop human embryonic stem cell-based therapies for diabetes, neurodegenerative disorders, cardiac diseases and retinal disorders. It was intriguing to note that the embryonic stem cell programme of Reliance Lifesciences is now hosting 45 embryos, 27 inner cell masses and 7 well-characterized cell lines, including insulin-secreting beta-cell line where considerable progress has already been made.

The last session of the workshop was devoted to regulatory aspects of stem cell research. V. K. Vinayak (DBT, New Delhi) projected DBT's initiatives on 'stem cell biology research' and highlighted the centres working in stem cell-related work in India, other than Reliance Lifesciences and NCBS. He also summarized the views of different countries on stem cell research. While highlighting the importance of stem cell research and its clinical applications, Vasantha Muthuswamy (ICMR, New Delhi) warned that embryos should not be generated for the sole purpose of obtaining stem cells. While stressing prohibition for export of cell lines *per se*, Vasantha advised the scientists to adhere to the 'Ethical Guidelines for Biomedical Research on Human Subjects' issued by the ICMR. Rita Bannerjee (DST, New Delhi) informed that the DST is considering establishing a National Facility for research in stem cell biology and stated that stem cell research is one of the priority areas of their research support agenda. In the last session, M. D. Nair (Pharma Consultant, Chennai) outlined the legal, ethical and other issues regarding stem cell transplantation.

The workshop noted that:

(a) Although the source of embryonic stem cells presents ethical concerns, their use may lead to many clinical benefits if differentiated cell types can be derived from them and used to assemble func-

*A report on the Workshop on Cell Transplantation held on 3 and 4 March 2002 and organized by the Madras Diabetes Research Foundation (MDRF), Chennai under the auspices of Department of Science and Technology, New Delhi.

tional organs/tissues. Successful completion of clinical trials will provide a basis for introduction of cell transplantation as a treatment option for people with various diseases like Type-1 diabetes, neurodegenerative disorders and cardiomyopathies.

(b) Basic research studies should look into the following questions and come up with appropriate solutions: (i) Would stem cells do the job we want them to do *in vivo*? (ii) Would the cells get immortalized, fail to undergo apoptosis and lead to malignancy? (iii) Are there other unknown risks? More basic research is needed in the area of embryonic stem cell isolation, culturing, maintenance and controlled fate selection by way of conditional differentiation protocols and modulation of gene expression.

(c) Establishment of repository cell lines for studying diabetes, heart and neuronal diseases should be encouraged.

(d) The National Academy of Sciences, USA has recommended that the terminology 'therapeutic cloning' should be appropriately replaced with 'nuclear transplantation' – to describe stem cells made for research in regenerative medicine using somatic cell nuclear transfer. It appears that this new terminology would clearly articulate the differences between stem cell research and human cloning. We hope that for many activist groups who want a ban on cloning, the term nuclear transplantation may be more acceptable.

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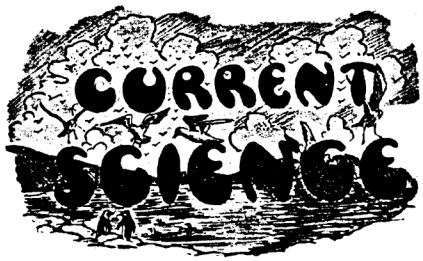

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The changing outlook of engineering science*

As engineering knowledge and the requirements of industry are rapidly changing, planning of engineering education is necessary. Practical and academic sides of engineering should be regarded as one undivided whole. Engineering science is defined as the academic aspect of engineering and the author discusses it under three heads.

Teaching

Industrialists have lost their old time contempt for the engineering graduate but the qualities demanded now are new. The college curriculum tends to overcrowding, each enthusiast desiring to include a little more of his subject. The final result is a syllabus which the average student cannot assimilate. The industrialist now engages specialists for his special problems and demands from the graduate, ability to take wide views, to think, to negotiate and to control; qualities which can be developed only in their undergraduate years given sufficient leisure for original thinking. The knowledge of engineering principles required is such as an average student should be able to acquire and can be tested by easy papers. The timetable should not therefore be overcrowded. There is however need to co-ordinate the three years' college instruction with the two years practical training so as to form a connected five years' training carried out with a single objective.

Research

Engineering research has become specialised and a tendency is observed to leave everything to the pure scientist. The attitude of the engineer to his problems is however entirely different from that of the pure scientist. The latter requires ideal conditions and materials. He is free to choose his path or alter it at his will. His shapes are not dictated by constructional or manufacturing requirements; nor his materials by considerations of strength or cost. The engineer, on the other hand, has to solve a problem as it is presented and some solution he must have, even though it is only approximate. Engineering research requires the gift of visualisation and this must be fostered deliberately. The inevitable factor of safety must be reduced as improved methods are evolved. Owing to a margin of error being ever present in the engineer's data, he cannot copy exactly the scientist's methods, but must develop a method of his own. The 'Relaxation method' devised by the author has been able to solve many problems hitherto regarded as difficult. It is not to be imagined that engineering does not aim at accurate calculations. On the contrary, correct calculations are more important for them as the real check, viz. test to destruction, is both costly and dangerous. Engineering research should aim to point out the 'disturbing factors' in the scientist's solutions and to leave the scientists to solve the new problems thus presented.

Relations to community

The accusation is sometimes levelled against scientists and engineers that they are responsible for the modern wars and their horrors. This is entirely groundless. Wars have always been made by communities and not by engineers; nor is the horror peculiar to modern wars. By their search for knowledge, scientists and engineers have opened up vast sources of power. Knowledge is non-moral. Poisons and deadly weapons may be used for the happiness of a community in preventing disease, etc. It is not the fault of the scientist if these powers are used for evil objects. The engineer has been silent in the past. As a member of the community he has a duty to perform. He can instil into the mind of the public a clearer notion of the real aim of scientific work, which is to seek the truth, believing that the gifts of science hold potential good.

*Summary of address by R. V. Southwell, President, Section of Engineering, British Association for the Advancement of Science, Cambridge, 1938.