

Transgenics – At crossroads

With the development of recombinant DNA technology, breeders have access to a large number of genes that can be integrated into the plant genome. Direct *in vitro* transfer of DNA between or within species is a new branch of biotechnology, which is referred to as genetic modification or genetic engineering. The term 'transgenics' or genetically modified organisms (GMO) is used to describe new strains of organisms in which the DNA has been modified through *in vitro* insertion of genetic material from a foreign organism.

Transgenic or genetically modified plants are being made both in food and cash crops. Several crop plants have been released for commercial cultivation in USA which are herbicide-tolerant, and insect and disease-resistant. Other transgenic traits fall under the categories of nutritional and post-harvest quality improvement. The transgenic tomatoes (Flavr savr, a Calgene product) with delayed ripening genes were first introduced in USA at a commercial level. In 1998, the global area of transgenic crops increased from 16.8 million hectares to 27.8 million hectares¹. The major transgenic crops are soybean, maize, cotton, rapeseed and potato, in descending order of area of cultivation. Although the yields of genetically engineered soybean was found to be 5 to 7 per cent less in the university-based soybean varieties trial in 1998, (USDA), other transgenic crops have resulted in higher yield and profit. Economic benefits to the growers from the transgenic crops were estimated conservatively at \$128 million for *Bt* cotton in 1996 and \$133 million in 1997. Similarly, economic benefits were estimated at \$19 million and \$119 million for *Bt* corn and \$12 million and \$109 million for herbicide-tolerant soybean in 1996 and 1997 respectively, in USA. China, after 1996 has approved commercialization of *Bt* cotton, sweet pepper, CMV-resistant and delayed ripening tomatoes². The Chinese have also accepted genetically modified food. In India, work on transgenic plants is hampered by lack of

trained manpower, finance and infrastructure facilities.

The multiple benefits of transgenic crops include flexibility in terms of crop management, decreased dependency on conventional insecticides and herbicides, higher yields, cleaner and higher quality grain or end product. The economic returns from these transgenic crops have also increased considerably along with consumer acceptability. The benefits to mankind can be many fold, for example the new 'golden rice' which has *b*-carotene gene³ could cure 2 million children from the deadly malaise of blindness. Transgenic bananas containing hepatitis-B vaccine would be of immense help in the immunization programmes for eradicating hepatitis. Nutritionally improved potatoes containing amaranthus albumin gene⁴ (*AmA1*) which is nonallergenic and rich in all essential amino acids would be a great boon to developing countries to alleviate the malnutrition problem.

Despite all the promises that the transgenic technologies hold, the anti-biotechnology environment groups' thinking that GMO are potential threats to public health and environment is harmful to the development of this new technology. Their main argument is genetic engineering is so new that the effects on the environment cannot be predicted. This argument is highly misleading, in fact for hundreds of years virtually all food has been improved genetically by plant breeders. Genetically altered antibiotics, vaccines and vitamins have improved our health, while enzyme-containing detergents and oil-eating bacteria have helped to protect the environment.

The risks of modern genetic engineering have also been studied by technical experts at the National Academy of Sciences and World Bank. They concluded that the environmental effects can be predicted by reviewing past experiences with those plants and animals produced through selective breeding. None of these products of selective breeding has harmed either the environment or bio-

diversity. According to the FAO reports, the per-person-grain-harvest declined from 415 kg in 1965 to 360 kg in 1996. There is a need to reverse this trend for which transgenics have created opportunities for efficient crop improvement. Their rapid adaptation into Indian agriculture will ensure increased crop productivity in future. In addition, adopting a wider application of biotechnology, plant tissue culture and micropropagation technologies are capable of producing high quality plant stock at lower economic costs than the conventional methods. It is important that we should enhance farm productivity, per unit land, water and capital without ecological harm. It is therefore urged that the political and scientific leaders, society and the mass media of our country should promote efforts in mobilizing the tools of biotechnology and genetic engineering for improving productivity, profitability, stability and sustainability of our major cropping system.

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Clinical database network

Narayana Dutt and Krishnan¹ had reported how the power of computing can be used in specialized cardiac care units. We propose that a clinical database network be developed to pool the enormous case material that is available in our country. Such networking can help in refining clinical features, documenting response to treatment and showing geographical or genetic variations.

The database can be initially limited to one or a few specialties (e.g. endocrinology, cardiology², gynaecology, orthopedics³), conditions (e.g. diabetes mellitus, myocardial infarction, caesarean section, fracture of the hip) and locations (one or more hospitals within a geographical area). The scope of the database can be expanded later⁴ to link other local⁵, national and international⁶ physical locations.

We believe that it is easier, though expensive, to set up the infrastructure for such a networking and get the software in place. Access to the Internet through TCP/IP networks allows communication among machines only a local phone call away. It would be more difficult to implement it in day-to-day practice, and capture data. The main reason for this difficulty is that the patient–doctor clinical interaction depends on a face-to-face interview, with generation of clinical data in a non-structured manner. Physicians are trained to fit the clinical information into discrete groups, and comprehend the social and psychological aspects of the patient. A synthesis of all these is ultimately satisfying to both the patient and the physician.

Clinical computerization, which generates data for the proposed network, finds it difficult to develop a bridge across this interaction⁷, especially for doctors who are not used to electronic medical records (EMR). Software may be developed consisting of a structured database incorporating a detailed symptom or sign checklist, but it needs information from the physician, in dovetailing what and how much of data to collect.

It requires a new set of skills for physicians to think in a structured format and not lose social and emotional contact with the patient. To us, this seems to be the major obstacle for using computers to

gather all clinical information. Therefore physicians must first carefully analyse and plan the kind of data, the order, and the details that can be captured without losing focus of the patient.

Newly trained doctors must overcome this difficulty by learning to utilize the awesome power of information technology in subjects with patients.

Once a clinical database network is developed and implemented, two advantages are immediately apparent. Firstly, pattern recognition is improved. At present, fundamental clinical skills are generally based on pattern recognition⁸. History taking, physical findings and laboratory investigations are associated with particular clinical states. With a large database covering a lot more number of subjects than an individual or even an institution can expect to study, a networked clinical database improves pattern recognition. Secondly, the science of medicine is based on statistically significant evidence, which can be generated by networked databases. Over time the practice of clinical medicine would improve on both these counts.

Patients can also be allowed access to their health information, so that a centralized repository (on Internet or private networks) is available irrespective of the geographical location of the patient. Privacy can be ensured by a variety of ways⁹, including an encrypted code, smart cards, finger prints or iris pattern of the eye.

Such access helps patients communicate with their physicians, in seeking appointments or even in obtaining a second medical opinion. It is also possible to eventually send information from related web-sites on conditions or issues related to each person⁹ (e.g. to start exercise in sedentary persons, to stop smoking in the case of smokers, on the use of inhalation for persons with bronchial asthma, etc.)

Moreover, patients can then develop a database of their own experiences with evidence-based information about treatments, the illness and with other useful resources (e.g. Database of Individual Patients' Experience of illness, DIPEX)¹⁰. A database of health-professional experience was proposed as a repository of international case reports¹¹.

The issue of privacy, of being free from commercial and political targetting is undoubtedly a central concern in such networking¹¹.

Down the line, one can expect a 'quantity leap' in technology, or freedom from some of current technical limitations¹². Bandwidth constraint can be relieved to allow sight, sound and perhaps even touch across networks. Videoconferencing with physicians should become a routine. A related 'quality leap' is also possible: the human to human communication on the web can evolve into a 'machine understandable information', in which a global medical knowledge database is ultimately browsable and searchable across languages and continents. All these should ultimately revolutionize discovery and disseminate knowledge in medicine.

Practical advantages of such a clinical database network are already apparent. There is a report that the Centres for Disease Control and Prevention in USA has developed an internet-based system, the CaliciNet, for data on gastroenteritis outbreaks in the country. The network allows submission of data on the common cause of nonbacterial acute gastroenteritis. Exchange of provisional epidemiological information and a sequence comparison database of nucleotides is possible. Automated notification is made to participants once a strain match is identified. The system can help both in tracking outbreaks and in attempting to halt them before they spread.

A recent report from Mexico exemplifies how limited research resources can be harnessed by networked information technology to find a cost-effective way of applying new information from the Human Genome Project¹³. The essential components of the Mexican Network of Molecular Biomedicine were health-oriented, cooperation-based, high quality, patient-centred and nationwide. The thrust areas were health, research and education, with the main focus on medical care.

In summary, a database of clinical networks is invaluable in education, research and ultimately clinical care¹⁴. Not only can text be linked to images, processes and protocols^{15–17}, but there can finally be a seamless fusion of text and

images, along with communication among patients, their health care providers and others¹⁸.

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Ripe time for academia–industry partnership in production of abiotic stress-tolerant crops

The drought period is over with the arrival of the monsoon, but soon it will be the management of floods which will be the cause of worry. High and low temperature stresses are likewise seasonal factors which have detrimental effects on crops. On the other hand, intensity of salt stress in an ever-increasing problem. It is therefore heartening to note that internationally plant scientists are not all that far behind in production of abiotic stress-tolerant transgenic plants. For instance, let us take the case of drought stress which made a significant impact on crops in states like Gujarat and Rajasthan this year. Tarczynski *et al.*¹ from the University of Arizona, USA made a path-breaking contribution in showing that when levels of mannitol are increased in the tobacco plant by introducing a mannitol-synthesizing gene taken from *E. coli*, its osmotic stress tolerance is significantly enhanced. In 1997, it was shown that increasing levels of ononitols (a sugar alcohol) also have a positive effect in increasing water stress tolerance². Holmstrom *et al.*³ from Sweden produced transgenic plants which over-produced

trehalose sugar and there was a marked increase in water stress tolerance of the resulting plants. Pilon-Smits *et al.*⁴ from The Netherlands showed that the transgenic plants over-synthesizing fructans are relatively more drought-tolerant. Hayaishi *et al.*⁵ from Japan have shown that increasing levels of glycinebetaine in transgenic plants increase water stress tolerance, low temperature tolerance, salt tolerance and even high temperature tolerance. Kishore *et al.*⁶ from Ohio State University, USA have shown that over-production of proline increased root biomass and flower development in drought stress conditions. Xu *et al.*⁷ from Cornell University, USA produced transgenic rice plants that over-synthesized a protein which is normally present in seeds. As a result, there was a higher growth rate of the transformed plants than the non-transformed plants. McKersie *et al.*⁸ from the University of Guelph, Canada have shown that if damage to stress cells is mitigated through suitable mechanisms, drought stress tolerance is significantly increased. Admittedly, there are certain relevant reservations on these reports

such as the fact that the above experiments have mostly been conducted in laboratory conditions so far and carried out using certain model plant systems. The level of drought tolerance achieved in these experiments is also not well-quantified. However, the on-going R&D aims at taking care of these shortcomings while extending these findings further to important crops like rice, wheat and maize. Transgenic plants showing high level tolerance to salt stress, temperature stress and flooding stress have also been produced in the laboratory^{9,10}.

However, while genetic engineering of plants for several different agronomic traits (i.e. herbicide resistance, improved nutritional quality, etc.), including resistance against biotic stress factors (i.e. virus resistance, insect resistance, fungus resistance, etc.) has received tremendous support from the private seed companies, there is a notable reluctance on the part of private seed companies in adopting tolerance to abiotic stresses on the same footing. Therefore, research on abiotic stresses has so far been supported through public sector, governmental and other

donor agencies only. The recent success in production of different abiotic stress-tolerant plants warrants that time is ripe for private seed companies to take up this venture too. There will be gains to both sides if the industry-academic heads put their efforts together. Loss of crop yield due to abiotic stresses is tremendous (rice yield is affected more by abiotic stresses than by biotic stresses¹¹). Therefore, agricultural production will get a significant boost, resulting in higher production to meet the demand of the masses as well as higher monetary benefits to the farmers and to the concerned industries. Further, this may give the much-needed impetus to the relevant R&D for the academia. There are several bottlenecks for which solutions need to be searched such as: (i) identification, isolation and cloning of novel genes for abiotic stress tolerance may allow gene pyramiding for higher level stress tolerance, (ii) establishment of gene transfer methods for crops which are grown under stress-prone areas but have been ignored in genetic transformation work, and (iii) regulation of expression of abiotic stress tolerance genes in requisite amounts and tissues so that

growth penalty on transgenics is minimized. More money to academia for basic work on these themes would be of great value. Agriculture is still our main force, driving our economy. Abiotic stresses are more pertinent to the Indian ecosystems than to the West where agriculture is a more organized sector. Thus initiatives to combat abiotic stresses by combining academia and industry must be our priority.

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