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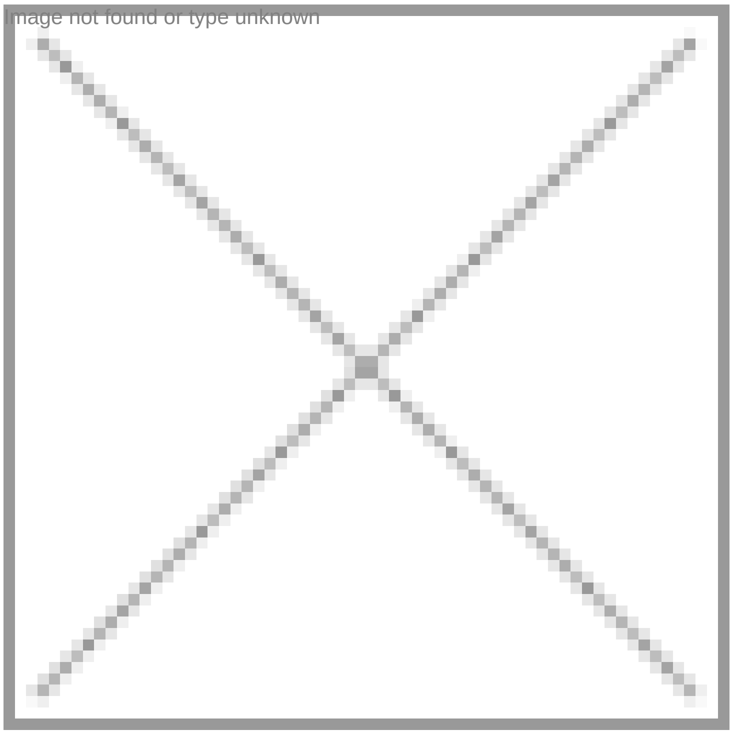
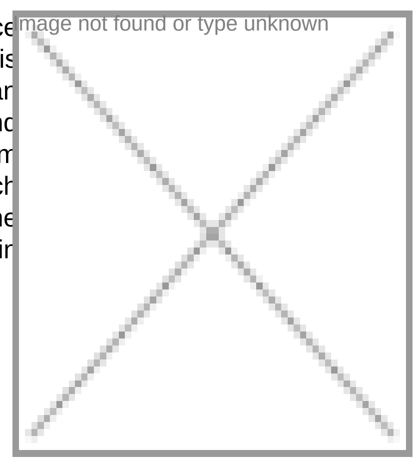
"Biological products difficult to predict and control"

08 January 2004 | News





"Understanding how a seed germinates is rather difficult, than to understand how a space shuttle lands on moon," believes Dr Rakesh Tuli, senior scientist, NBRI, Lucknow. This quote gives an insight into the person who has many firsts to his creditâ€"cloning an agriculturally important gene 12 years ago, synthesizing two new Bt genes recently and then developing an innovative technology transfer method for the industry. It was a room full of research documents, a table full with papers, some samples of on-going research work and amidst all these Dr Rakesh Tuli shared his views with BioSpectrum about the science he delivered to the industry and the challenges and future of agribiotechnology in India.

You were responsible for cloning an agriculturally important gene for the first time in India, while you were with Bhabha Atomic Research Centre, almost about 12 years ago. And now your team has synthesized two new Bt genesâ€"Cry1Ac and Cry1EC. Can you share your experience with us from then to now?

Our first research paper on cloning of an insecticidal gene (cry1Ac) from the soil bacterium Bacillus thuringiensis (Bt) was published in 1989 (Tuli et al., J. Genetics, 68, 147-160). This is to be seen against the backdrop that the first ever, full length Bt gene had been cloned in Madison only four years earlier. The cry1Ac gene was cloned by my group, when I was working at Bhabha Atomic Research Centre, Mumbai. It indeed was the first agriculturally important gene cloned in India. Research groups in the USA developed the first transgenic plants with the Bt gene in 1987. The technology was not properly developed at the stage. Such plants showed poor protection against insect pests. The bacterial gene expressed at a very low level in the engineered plants. Since then, the technology has made a marathon progress. Scientists have learnt why a bacterial gene expresses poorly in plants. They learnt how to design and synthesize long genes artificially and ensure a high level of expression in plants. As a result, in spite of the project concept having been in mind during the mid eighties, it took ten years for even a multinational giant like Monsanto Co., St. Louis to release their first Bt crop for cultivation in 1995.

I decided to move to National Botanical Research Institute, Lucknow, in September 1992 because the laboratory-to-field type of research in a competitive area as this needed larger field space, bigger laboratory and project team than what could have been possible at BARC. Luckily, Dr. CR Bhatia, the then Secretary and Dr (Mrs) Manju Sharma, then Senior Advisor in the Department of Biotechnology were both very enthusiastic about developing indigenous capabilities in this area. A task force was set up, which in 1994 entrusted me to develop Bt cotton. It took me another two years to set up a laboratory in Lucknow. I wish, this period was shorter. The first transgenic Bt cotton was finally ready at NBRI by 1999. This was also the first case of designing and synthesis of such a long gene in India.

How do you look at the limitations and opportunities in the biotech field now compared to that a decade back?

Ten to 15 years back, the managers of biological sciences in India were passing through the learning curve at a much lower level. Purchase procedures regarding the import of quality chemicals and equipments were nearly blind to the urgency and needs of competition faced by Indian science and industry. The realization that competitive biological research also required functioning in teams was beginning to emerge. The need to give opportunity to well trained (and not gray haired or politically connected) scientists to steer research institutes and to monitor research projects in modern biology had begun to be felt. Since then, a change has happened, though still not in pace with the increasing technology divide.

Appreciation for knowledgeâ€“based national planning has increased in recent years. The CSIR, DBT and ICAR, besides other science departments have made higher investments in agribiotechnology. As a result, at least a few centers of excellence have developed in the country. Even non-biologists now support investments in biological sciences. They have realized that it is much more difficult to understand how a seed germinates than to understand how a space shuttle lands on moon. Understanding of seed germination is important for global sustainability. As recently as 1998, when I went back to the DBT with a request to continue the Bt project at NBRI beyond its first, fourâ€“year term, it was felt that the project was taking too long. In fact, our science management systems were not sufficiently experienced to realize the complexities of modern biology. The last five years have made more difference. It is no more perceived as a fly-by-night science. In fact, biological products are more difficult to predict and control than engineering products. Hence, responsible release of an indigenously developed agribiotech product, like saltâ€“tolerant or insectâ€“resistant engineered crop is an achievement, at least as big as launching a geostationery satellite.

What are your expectations from the Bt genes, Cry1Ac and Cry1EC, in the market?

The availability of the two genes designed and synthesized at NBRI and introduced in cotton is only the beginning of successful examples that will be put to the service of nation in the coming years. In cotton alone, an estimated Rs 1000 crore worth of insecticides are annually used in India to control bollworms. But there are other pests, including herbivores, jassids, white flies etc. They damage several crops and spread plant viruses in field and in other cases spoil stored grains. The cry1Ac and cry1EC can be equally good for crops like cotton, rice, pulses, sugarcane, groundnut, vegetable crops, etc. However, long-term success of Bt crops can be assured only if more genes are discovered that kill insects through independent mechanisms. Use of a given gene in too many crops can lead to failure of the gene in long run and the breakdown of resistance. Therefore, continued efforts to find new genes and develop several different transgenic crops improved for insect resistance is essential.

Indian cottonseed market already has genes from the Monsanto technology. The Chinese products are also under field and biosafety evaluation. The NBRI Bt technology, taken by the Hyderabad based consortiumâ€“SBBPL is a test case in agribiotech experience in India. It needs several of us to think together in the national interest both from the government and industry. Success of indigenous Bt cotton can be converted into a successful national experience by closer networking between seed industry and public supported research institutes. I hope that the NBRI Bt cotton network with SBBPL can be developed into a role model to take the confidence and vision of Indian seed industry to a higher pedestal. I have no doubt that its success can open way to global leadership for India in agri-business. However, this needs continued effort in developing new transgenic crops, establishing mechanisms for their safe and responsible release, encouraging a national alliance between public and private sector and at the same time, instilling a feeling of urgency and efficiency in decision making at all levels. This is not easy and requires a well-coordinated teamwork. This must happen at a faster pace if India is to become a leader in agribusiness.

How did you hit upon the novel way of transfer of technology to the consortium?

The cost of developing modern technologies is very high. The complete process of developing transgenic Bt crops involves the use of advanced techniques and managering complex stages. In spite of the first release in 1995 in the USA, it took Monsantoâ€“Mahyco, seven more years and (hearsay) Rs 50 crore to release Bt cotton in India. Indigenisation may make it ten fold less expensive for the Indian seed industry. This was clearly in the minds of Dr Y Yogeshwar Rao of Vikki's Agrotech Ltd, Hyderabad, who visited me in 2001 to discuss the Bt work at NBRI. Several other seed companies including Mahyco, JK Seeds, Nuziveedu Seeds, Ganga Kaveri Seeds, Vibha Agrotech and ProAgro have held discussions with me. I was clearly told that Monsanto does not permit partnership to share Indian technologies in cotton carrying 'their' Bt genes. Considering the costs involved in the development of transgenic varieties and the technical effort required in their release, it was clear that Indian seed companies needed to raise their vision, ambition and infrastructure. This is where Nuziveedu Seeds along with Ganga Kaveri Seeds, Vibha Agrotech and Vikki's Agrotech felt they could work together. Each company has its own market share in cotton seeds. The Bt technology from NBRI would add equal value to their proprietary seeds. That appeared like a winâ€“ win situation to the partners. The seven partners in SBBPL are owner-managed seed companies, with outstanding plant breeders as heads of the R&D units. They could appreciate the merit in the argument and also see that Bt was only the beginning of the road. Indian agriculture will have endless opportunities to become global provided they learn to work together. This is how SBBPL was born.

Beyond the licensing agreement, the real challenge lies in transferring the technology quickly. Would you also look beyond lab research to help get Bt cotton into the field?

Moving the genes into cultivars of highest agronomic potential and then obtaining regulatory clearances are the two major stages to be crossed now. Luckily, the partners or R&D Director's in SBBPL are outstanding plant breeders. They are used to think ahead of time. Since transgenic technologies are expensive, they have to think harder. Selection of their choicest cotton lines will be the key to their success. Each of them has identified his best germplasm. I have also been reminding that we need to think of cotton in context of the changing climate, agricultural zones, disease and pest forecast, fiber and ginning quality. Efficiency in moving the genes into their touchstone breeding lines that would succeed 5 to 10 years from now will be the essence of their success. Public institutes must help them in this challenge. Some aspects are technologically demanding. NBRI, APAU, CCMB, CDFD, CFTRI, ITRC can work with them. To cite an example, immunological tests can be developed for rapid screening of high Bt expressing plants in the field. The Bt strips used currently by Mahyco are imported from a US company. In principle, this is not complicated. It is like one of those kits used commonly by Indian women for the detection of pregnancy. With some guidance, low cost Bt kits can be developed by several of our laboratories experienced in monoclonal antibodies. This has an opportunity for another industryâ€“institute tie up. Further, biosafety tests need similar tie-ups with laboratories with expertise in toxicity, allergenicity, plant biodiversity, soil flora, GMO detection, etc. That is why I see it as a national case for learning to team up. Luckily, we have a consortium willing to trust the Indian public funded systems and work with them. Who spends money at a given point of time should not be important. This is a national need and we must succeed against multinational corporations. We need to use this opportunity to build a role model for agri-business in the country. Money will flow back to the partner institutes, primarily in form of royalty. There is need to develop visionary and efficient systems in the country to steer such alliances to their logical success. The current mindset is still very archaic. Each country has to develop its own strategy. Our model must fit an agricultural economy, disorganized agro industry, small farm holdings, large population, increasing soil infertility, poor agricultural inputs but high ambitions faced with competition on an unleveled playing field. Hence, national partnership is required urgently.

Bt Cotton has been engulfed in a lot of controversies. What was lacking and what are the challenges ahead?

Bt cotton is a global reality now. Enthusiastic farmer's response in all the countries of release speaks volumes in favor of the technology. This is the first global agribiotech experiment happening in real life. The scientific community is still learning from it. By now, some 150 million acres have been grown with single Bt gene carrying crops. According to a USDA funded study at the University of Arizona and Cornell University, quite remarkably, there has not been a single case of break down of the Bt crop resistance. Thanks to the knowledgeâ€“based management of pests in Bt crops through refuge crops and IPM. Nevertheless, possibility of the resistance breakdown in say, ten years can be scientifically argued. As a solution, Bt crops with multiple insecticidal genes is a highly assuring approach. That's what is happening now. Monsanto is understood to be getting ready with Bollgard II that would carry two Bt genes. This takes care of one major controversy related to the fear of breakdown of resistance. It is the first time in the history of agriculture that safety of improved (genetically engineered) cultivars is to be demonstrated before their release. Responsible, safe and informed release of genetically modified organisms is mandatory. This illustrates how the scientific community has learnt to regulate itself in use of the new technologies.

In spite of the best intentions, certain things did go wrong in the past. It was primarily because of difficulties in implementation of the technology. For example, if sufficient refugia is not provided in Bt crops, the frequency of resistance can increase in future. Seasonal variations, crop history or poor expression of the Bt protein can lead to transient escape of insectsâ€“the way it happened in Texas in 1995. A possibly allergenic Bt protein, like Cry9C, permitted for animals may reach human food-stores, the way it happened in the US. Unauthorized and untested Bt varieties may be clandestinely released, the way it happened in Gujarat. Bt gene may be in cultivars that fail to withstand a long dry spell, followed by late rainfall, the way it happened in India last year. But these should not make the technology or science controversial. Such examples should prepare us to devise ways for responsible use of this powerful technology. Infact, all new technologies have to address such issuesâ€”be it drugs for health or atomic energy for power. Agribiotech is no different. In due course, public awareness and confidence in the needs and virtues of biotechnology will increase further and I am sure public support will become available in plenty.

So what are the lessons learnt from Bt cotton and how can agribiotech be further developed in the country?

As I mentioned earlier, the challenges that lie ahead in taking Bt cotton successfully into market are several. Good science must keep flowing into the project. SBBPL must select germplasm that would out perform that of their competitors. Backcrosses, efficient selection on field, regulatory data related to safety as well as yield advantage over local checks must be developed without loss of time. The RCGM and GEAC also need to become more efficient.

Against MNCs, this is not a leveled playing field. Discovery of new matching genes must go on, not only against bollworms but also against sucking pests, white flies and drought tolerance. This requires a larger network and funds. Besides SBBPL and NBRI, other institutes need to join. A well-orchestrated "Dragon Dance" needs to be played to ensure a lasting success in market. This cannot be done by a single Rakesh Tuli at NBRI, assisted simply by three research fellows. I would like to acknowledge their dedication--Dr PK Singh, Mithilesh Kumar and CP Chaturvedi. But a sustainable success against global challenges can happen only when systems are put in place to ensure that every bit of our time and capability is utilized most fruitfully, and especially the young researchers get rewarded for their tireless effort that has brought us as far as this.

By Faiz Askari