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Surmounting the speed barriers: the protein NMR episode

Nuclear magnetic resonance (NMR) spectroscopy has emerged during the last three decades as a powerful alternative and complementary technique to X-ray crystallography for determination of protein structures at atomic resolution. Besides, NMR is also invaluable for elucidation of internal dynamics characteristics of the protein molecules under study. While these successes have been commendable, the technique continues to undergo rapid development, both in terms of new concepts and new hardware. With the parallel developments occurring in biology, especially structural genomics and proteomics initiatives, there has been a great demand for high-throughput determination of protein structures, and accordingly, attention towards enhancing the speed of data acquisition and analysis is continuously on the rise.

In late 1970s and early 1980s when two-dimensional (2D) NMR appeared on the scene, Nuclear Overhauser Effect (NOE) made crucial strides in the elucidation of protein structures. This involved assignment of individual resonances to different hydrogen atoms in the protein molecule using a battery of 2D NMR techniques for which data collection had to be done for several weeks, quantifying the J-coupling and NOE correlations between pairs of assigned atoms, and finally, computation of the structure from these inputs. Each of these steps took several months and often it took 1–2 years to arrive at a reliable structure. In the 1990s hetero-nuclear multidimensional NMR experiments with isotopically (^{13}C, ^{15}N) labelled proteins created a new strategy for resonance assignments and also enabled study of larger proteins than could be done before. However, data acquisition and analysis still took a long time. Subsequently, some of the steps of analysis were automated, but still the entire exercise would take about 6–12 months.

Against this backdrop, Dinesh Kumar and Ramakrishna V. Hosur present (**page 1581**) a strategy based on experiments designed by them previously, which enables backbone resonance assignment in small, well-folded proteins in less than a day. A few (2–4) 2D experiments, each of which can be recorded in 1–2 h, are adequate, and the analysis is extremely simple because of the special characteristics of these spectra, and assignments can be established in a few hours. The success of the strategy has been demonstrated with two protein systems. This indeed represents a big leap forward in the practice of protein NMR. It paves the way for structure determination also in less than a day using algorithms based on chemical shift alone for calculation of protein structures, several of which have been reported in the literature.

Gene and cell therapy in India

Novel gene and stem cell-based therapies are promising therapies for diseases where current treatment modalities have failed. In India, a number of groups are carrying out basic research on gene delivery vector development as well as strategies for cancer gene therapy, and adult and embryonic stem cell development. With the establishment of human embryonic stem cell (hESC) lines in a few centres, India is now geared to become one of the major contributors to the emerging field of hESC. Although a few cell-based therapies are underway, a great deal of regulatory measures needs to be in place for both – gene and cell-based therapies. Keeping in mind that a combination of gene therapy and cell therapy will be most effective, India has to gear up to gene therapy product development and clinical trials. Rita Mulherkar (**page 1542**) reviews some of the published and unpublished work with potential to be translated into clinical trials, and discusses the possible hurdles in carrying out clinical trials in the country.

Bt-cotton: not-so-good news

Bt-cotton plants contain gene(s) from a soil bacterium, *Bacillus thuringiensis*, which enables the plant to produce proteins that are toxic to caterpillars feeding on it. Ranjith *et al.* (**page 1602**) show that individuals of a certain population of *Helicoverpa armigera* in Raichur, India are able to survive and successfully breed on the commercial *Bt*-cotton hybrids. In fact, they show that many characteristics of *H. armigera* on *Bt*-hybrids are approximately comparable with those on non-*Bt* hybrids. More interesting is the result that performance of caterpillars on the hybrids containing single toxic gene (*Cry*1Ac) is no different from those containing two toxic genes (*Cry*1Ac and *Cry*2Ab) in their genome. The study, which principally assesses current-field situations of *H. armigera* on some of the commercial cotton hybrids, expresses caution over a potential onset of resistant populations of this dreaded species to *Bt*-cotton.

Field surviving caterpillars of *H. armigera* on *Bt*-cotton (Bollgard^{TM}, Bollgard-II^{TM} and non-*Bt*) were reared in the laboratory on the same plants from which they were collected. Several developmental and reproductive characteristics of the pest were recorded and compared across the test hybrids for the current generation. Survival and development was also assessed for the subsequent generation when reared on the same *Bt* plants. There was no definite trend among the *Bt* and non-*Bt* cotton hybrids with respect to the measured characteristics of the pest insect, and comparable numbers of the test individuals were successful. Previously, several laboratory studies in India and abroad have revealed the possible development of resistance in *Helicoverpa* populations against *Bt* toxins. Also, these laboratory studies have been severally supplemented by occurrence of field populations on *Bt*-cotton hybrids. The present study goes further ahead to demonstrate not only survival but also reproduction among the individuals occurring naturally on commercial *Bt*-cotton hybrids in India.