INTRODUCTION

As we look back on the history of science, the development of new technologies in science has found applications in areas as varied and diverse as sociology, economics, mathematics and statistics. The discovery of the structure of DNA in the first half of this century established the foundation for genetic engineering and DNA technologies with unexpected applications. Although, the impact of these technologies in different countries has been different, globally the unprecedented and unimaginable gains provided by gene technologies have provided several benefits. Keeping in view the large-scale applications of new DNA technologies, India has prepared itself to utilize this knowledge for the benefit of its people. It was therefore, appropriate for the Department of Biotechnology (DBT) of the Ministry of Science & Technology, Government of India to establish the Centre for DNA Fingerprinting and Diagnostics (CDFD) as a unique institution for the social and judicial benefit of its people. This centre is located in Hyderabad, one of the oldest cities of India with a rich historical background. The CDFD, within a short span of less than three years, has acquired an enviable position among the established scientific institutions of the country.

The CDFD represents a synthesis of quality service and state-of-the-art basic research. The major service components of the CDFD involve DNA fingerprinting, diagnostics and bioinformatics. Quality assurance, the guiding principle of the services provided at the CDFD, is based on quality control developed at the centre by its scientists. The CDFD conducts R&D activities in areas of DNA fingerprinting applied to paternity/maternity disputes, immigration, exchange of new born babies in hospitals and crime investigations. It also disseminates information to assist law enforcement agencies, forensic scientists and the judiciary. This knowledge helps to underscore the evidential value of DNA and related techniques in crime investigation matters. Apart from this, the CDFD also trains forensic scientists of other laboratories. Landmark judgements delivered by the high courts of Indian States, based on evidence provided by the CDFD, have today made the centre more or less synonymous with DNA fingerprinting for which it is considered the standard. The CDFD has provided social accountability to biologists and has shattered the myth of they being mere occupants of ivory towers.

Basic research in overlapping frontier areas of modern biology is an integral component of the CDFD. These include proteomics and computational biology, genomics and biodiversity, molecular epidemiology, mechanisms of intervention in the disease process and gene expression.

SERVICES

DNA FINGERPRINTING

To date, the CDFD has received and reported on more than 600 cases, involving about 2500 samples pertaining to paternity/maternity disputes, identification, rape, murder and other cases, without a single case finding having been disputed. Several non-human cases such as authentication....
of seed lines and wildlife identification disputes, have also been successfully reported. Internationally, the CDFD has been able to provide its services to agencies in Australia, New Zealand, USA, Mauritius, Bangladesh and Nepal. In order to disseminate DNA fingerprinting technology and make it available to more and more people, and also to serve the ends of social justice, the CDFD has ventured into agreements with forensic science laboratories of other States of India to provide technical know-how as well as support for DNA fingerprinting of cases referred to those labs.

The tremendous advances in identification by the use of DNA markers have resulted in the development of single locus probes. Scientists from the centre have identified sequences from the human genome which detect polymorphisms at a particular locus. The probe designated as Hps2, contains a 900 bp sequence which repeats along with a variable number of interspersed sequences. Other similar clones are also being characterized not just from the point of their utility as locus-specific probes but also to aid in the understanding of the mechanism(s) involved in the generation of these hypervariable loci.

Application of short tandem repeat (STR) loci analysis has been found to be a useful tool for human identification in forensics. A highly variable set of STR loci is being specifically used for the Indian population. Research is underway to make a high efficiency STR kit indigenously for technical as well as economic reasons. Population studies of the ethnic groups of India are being undertaken. This project would be a prologue for the national database of the Indian population.

**DIAGNOSTICS**

Perhaps, the greatest tragedy befalling human beings is the defective functioning of gene(s) resulting in genetic disorder(s). Today there are more than 4000 known common and rare genetic diseases. Molecular biology has found applications in medicine, thereby creating a new branch of “Detective and Predictive Medicine.” Keeping in view the burden of genetic disorders on the Indian society, the charter of the CDFD includes the establishment of DNA diagnostic methods for detecting genetic disorders and developing probes for such detection, in addition to providing consultancy services to medical institutions/public health agencies, the industry, and also to the affected people.

Until gene therapy becomes a practical solution, identification of genetic disorders, carrier detection, prenatal diagnosis and genetic counseling would be the main thrust of work at the CDFD. Genetic disorders such as fragile X-syndrome, β-thalassemia, sickle cell anemia, Duchenne and Becker muscular dystrophy, Huntington’s disease, neural tube defects and other triplet repeat associated pathologies like Friedrich’s ataxia, myotonic dystrophy, muscular atrophy, Alzheimer’s disease, premature ovarian failure, primary amenorrhea, abnormal sexual development, ambiguous genitalia, etc., are common genetic disorders on which the diagnostic group of the CDFD has been focusing. The CDFD has also directed its diagnostic services to other disorders like hemophilia A and B, male infertility, spinal muscular atrophy and various inborn errors of metabolism. The CDFD has received, analyzed and reported over 650 cases so far.

**BIOINFORMATICS**

Computer technologies are central to applications of DNA technologies. Computers are being used for more objective and precise analysis of results obtained by DNA technologies. Centralized or linked databases containing biological information permits a more rapid and sure method of dissemination of information. Similarly, databanks are being used to store biological information for generation of population genetic database and support data. The CDFD has always been a forerunner in understanding the future implications of databasing and databanking. To this end, the bioinformatics services set up at the CDFD presents another strong feature of the centre, with ORIGIN 2000, as its web server. Besides this Octane 02, RAID several pentium PCs, MACS 14-bay server.
CDROM server are connected over the FDDI network. The bioinformatics group, with several databases and applications software relating to sequences and structure analysis, molecular modeling and visualization also carries out fundamental research on analysis of protein sequences and structures. The European Molecular Biology Network (EMBnet) recognizing the expertise and state-of-art infrastructure of bioinformatics at the CDFD, has chosen it to be the national node of the EMBnet in India for providing bioinformatic services. The CDFD node is one of the 37 nodes drawn from different member countries of the world. The homepage of CDFD (http://salarjung.embnet.org.in) can be accessed from anywhere in the world. The services at CDFD EMBnet node at the centre are updated on a regular basis. The program GLIMMER that is useful for analyzing microbial genomics is available at the CDFD. The Sequences Retrieval System (EBI, U.K), Gene Cards (Weizmann Institute of Science, Israel) and Predict Protein (Columbia, USA) services are also available. A database on the structural motifs in proteins (DSMP) was developed at CDFD, which would be useful for protein structure prediction, modeling and design.

BASIC RESEARCH
SILKWORM GENOMICS

Applied research is always an outcome of basic research. To achieve this goal, the CDFD, apart from providing services, has initiated fundamental research in areas relevant to it. Global efforts to sequence the entire genome of the silkworm Bombyx mori have found an intellectual partner in the CDFD. The work on this at the CDFD led to a search of Bombyx mori sequences in the EMBL and GenBank database which yielded 85 microsatellite motifs providing important landmarks on the silkworm genome. These loci revealed a high degree of allelic length variations among different genotypes of silkworm and are thus also very useful as genetic markers. The molecular genetic analysis of these markers will provide useful information to understand basic and applied problems in saturniid biology.

The CDFD is also investigating other aspects of the silkworm genome such as determination of the structural organization and phylogeny of genes encoding the digestive enzyme alpha amylase from silkworm. In addition to Bombyx mori, the Tassar silk moth A. mylitta is also a focus of attention, with particular reference to the structural and phylogenetic characterization of the mariner transposable element. Analysis of phylogenetic trees show that the silk moth genome harbors different types of mariner elements belonging to different subfamilies of the mariner family. For e.g., P. cynthia ricini contains the mariner elements of the Cecropia subfamily, the Mauritiana subfamily and the Mellifera subfamily. Different genomes were also found to harbor similar types of elements pointing to a horizontal transfer of mariner elements across genera, and their possible vertical inactivation. Based on these studies it is now possible to quickly screen for active mariner elements of insects.

MOLECULAR GENETICS OF MDR TUBERCULOSIS

The CDFD has initiated research in the areas of molecular analysis and genetic epidemiology of multi-drug resistance (MDR) in clinical isolates of M. tuberculosis. A great deal of polymorphism in the MDR-M.t.b. isolates from India was found. Molecular mapping of the loci involved in multi-drug resistance has revealed the presence of
novel mutations conferring drug resistance. These data suggest that the MDR strains in India are different from those of the West, reflecting a separate evolutionary branch of M. tuberculosis in India. The other important area is the development of PCR based probes for rapid detection of M. tuberculosis in clinical samples. These probes are currently under extensive evaluation under field conditions.

With a strong bioinformatics component, the CDFD has initiated a research program synthesizing “dry” computational biology of M. tuberculosis “wet” clinical material based research aimed at unraveling the mysteries of virulence drug resistance and identifying new drug targets.

GENETIC FLUIDITY AND ONCOGENESIS

Genetic fluidity as evidenced by genomic alterations in the human genome leading to meningioma, a form of brain cancer, has been a subject of investigation at the CDFD, in collaboration with clinical researchers at the All India Institute of Medical Sciences, New Delhi. This research has led to the identification of three different novel genetic loci, meng 1, 2 and 3, which are believed to be associated with meningioma. One of these loci shows significant homology with a bacteriophage gene, raising the probability of the association of the bacteriophage gene with human meningiomas and its role in promoting tumorigenesis in humans. Genomic cloning and chromosomal localization of the meng loci, and evaluation of their utility as markers for predisposition, initiation and progression of meningiomas are underway.

GENE EXPRESSION

Research at the CDFD has also been initiated on understanding some basic cellular and molecular processes regulating transcription using gene expression in baculovirus-infected insect cells as a model. The CDFD, in collaboration with the National Institute of Immunology, New Delhi, has been able to contribute to major findings which highlight the importance of host virus interaction(s) in the regulation of transcription from the baculovirus polyhedrin gene promoter. Investigations on the mechanism(s) of action of the baculovirus encoded anti-apoptotic p35 gene have resulted in very interesting findings of an anti-oxidant mode of action of this protein in controlling programmed cell death.

HUMAN SCIENTIFIC RESOURCE DEVELOPMENT

Human scientific resource development at the cutting edge of biological research, is of special interest to the CDFD. On the-bench training in state-of-the-art services in DNA fingerprinting and diagnostics is regularly provided at the national level. Experts from India and abroad visit the centre to impart theoretical as well as laboratory training to the participants in topical areas of diagnostics. Short-term workshops to train forensic scientists in the area of DNA fingerprinting is another mode of disseminating knowledge.

The bioinformatics section of the CDFD is actively involved in promoting and making scientists aware of the strength of information technology. Towards this purpose, the centre conducts workshops focusing on database reference searching, sequence searching, mapping, importing and exporting sequence formats, translation, gene finding, pattern recognition and primer design.

The CDFD believes in the future. Therefore, young and promising scholars at the postgraduate level are selected to undergo a summer training program in areas of research ongoing at the centre. As an affiliate of the University of Hyderabad, the CDFD admits doctoral students to pursue their PhD program.

At the dawn of the new millennium, the CDFD stands at a critical junction. During the earlier part of the millennium, CDFD will be moving to its own new state-of-the-art building complex complete with all infrastructural facilities required for a centre of excellence in modern biotechnology research.