Spotlight on...

Turkey’s Hacettepe School of Medicine DNA/Cell Bank furthers understanding of rare diseases

Due to its high rate of consanguinity, Turkey has an opportunity to offer scientific contributions in the field of genomics of autosomal recessive diseases by defining new phenotypes and identifying new genes and relevant pathways. The DNA/Cell Bank at Hacettepe Medical Center has been instrumental in creating a working environment that is in line with international guidelines of governance and ethics for biological repositories. Since its foundation, the repository of the DNA/Cell Bank has facilitated collaborations leading to the identification of new disease genes, including: Megalencephalic leukoencephalopathy with subcortical cysts, MLC (MIM 604004); Ceroid Lipofuscinosis, neuronal, 7, CLN7 (MIM 610951); Heterotopia, periventricular, autosomal recessive (MIM 608097); Chanarin-Dorfman syndrome, CDS (MIM 275630); Arachidonate 12-Lipoxygenase, R type, ALOX12B (MIM 603741); L-2-Hydroxyglutarate dehydrogenase L2HGDH (MIM 609584).

The DNA/Cell Bank was established at Hacettepe School of Medicine in 1995 to facilitate biomedical research into rare genetic diseases including identification of new genes, diagnosis, prevention and new treatment modalities. Another mission is to provide training for good laboratory practice and ethical guidelines for those who wish to establish biobanks at their institutions. Biological samples, along with personal and medical information from patients and families, serve to create a database that facilitates national and international partnerships in the area of rare diseases.

Turkey has a population of about 71 million, of which 28% is below the age of 15 years. Consanguinity in the general population is 21%, a figure which rises to 39% in the southern and south-eastern parts of the country. Hacettepe University Medical School was established in 1967 on the foundations of a paediatric hospital that began operating in 1957. The Medical Center hospital complex consists of the Children’s Hospital (241 beds, 163,835 outpatients/year, 4694 inpatients/year), the Adult Hospital (808 beds, 435,438 outpatients/year, 23,465 inpatients/year), and the Oncology Hospital (180 beds, 30,000 outpatients/year). Since 2007, the Adult Hospital has been accredited by the Joint
Commission International. The high in/out-patient capacity and location in Central Anatolia makes Hacettepe Medical Centre a large reference centre for patients from eastern, south-eastern, northern and southern Anatolia, serving a population of about 30 million - almost half of the total population of Turkey.

Serving a large population from different geographic regions has been instrumental in establishing large patient registries and a bio-repository for genetic disorders that creates unique opportunities for genomics research. Demographic data indicate that the child bearing age runs quite long, especially in rural areas, and if a family has a rare disease, it is likely that there will be multiple affected siblings. Moreover, in rural areas, multiple generations live in one habitat, creating a favourable environment for genetic investigations, from which sampling from the complete family is easier to achieve. Homozygosity mapping technique is thus a favourable algorithm for genomics research.

Establishment and funding
Against this background, funding was obtained from the Technological Development Fund of Turkey (TTGV) in 1995 with financial support through a grant from the World Bank (project no: TTGV 113/S). Between 1995 and 2006, the Bank was supported by the Scientific and Technological Research Council of Turkey. As the biobank is a public facility at a government university, there is no charge demanded from families for deposition of samples.

The repository
Families are referred to the biobank after clinical examination by respective departments. A document of medical and personal information together with the informed consent form accompanies samples, signed by the medical attendee and the principle medical doctor responsible for the unit. As of December 2010, the total number of DNA samples was 21,100 from 5500 families and 1200 cells/tissues (lymphoblastoid cell lines, fibroblast, muscle, brain and other biopsy specimens). The main contributions to the DNA registry are neurological (46%), metabolic (19%), nephrological (15%), gastroenterological (9%), immunological/haematological (5%), chest diseases (3%) and dermatological disorders (3%). The medical and personal data from the families are maintained via the Oracle Database Server System. The system is encrypted with codes open to only the IT personnel. Retrievable anonymization of the data complies with basic ethical norms.

Ethics and governance
There is no specific national law for biobanking in Turkey. Thus, the following are used for
ethical guidance of the working principle of the Biobank.
UNESCO - *The Universal Declaration on Human Genome and Human Rights, 1999*
UNESCO - *International Declaration on Human Genetic Data, 2003*
Turkish Penal Code (article 90), 2005
Ministry of Health (MoH), Regulations Regarding Clinical Trials, 2008
Turkish Medical Association, Declaration on Protection of Genetic Data, 2009

Every new research project involving the samples is reviewed by the Ethics Committee of the Hacettepe Medical School. If the samples are to be used for national collaborations, the signature of the depositing medical doctor is obtained. If the samples are to be used in international collaborations, a “material transfer agreement” is required, signed by the depositing medical doctor, the DNA Bank director and the international collaborator.

**Infrastructure and management**
The physical infrastructure is as follows: cryopreservation unit, tissue culture laboratory, general laboratory, IT facility and molecular biology laboratory. The total capacity of the cryopreservation unit is: -20°C, 15,000 samples; -80°C, 200,000 samples; -196°C, 15,000 samples. The system is run by security CO2 Back up system, Uninterrupted Power Supply (UPS) Systems, and Alarm System linked to telephones. The Bank is managed by a director (PhD, professor of Medical Biology); one biologist (MS) responsible for sample preparation and quality assurance; one medical biologist (PhD) responsible for daily operations and best practice guidelines; and a data manager responsible for data entry and retrievable anonymization of samples.

**Training**
The bank is also responsible for training researchers from other institutions who wish to establish their own facilities. A grant was obtained from the State Planning Agency for collaboration with four different institutions and training was given in ethical guidelines and GLP in tissue acquisition and processing and quality assurance in biosample preservation. There are also education materials prepared for national audiences: *Biobanks and Ethics, Good Clinical Practice, no 22, 2009*.

The DNA/Cell Bank at Hacettepe Medical Center hopes to continue facilitating scientific collaborations culminating in new discoveries and to play an instrumental role in the creation of networks of biobanks and governance through which the cross-border sharing of databases and samples can be facilitated.

For further information