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ABSTRACTS

HGM2008 special plenary abstracts

001: Genetic diversity in Indian populations and its implications in health and disease

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India represents one of the largest source of human biodiversity, consisting of 4,635 culturally and anthropologically well-defined populations with little or no gene flow between them. Hence, study on Indian populations, who are known for their cultural and genetic diversity, not only provides insight into their complex origin, history and relatedness, but also helps in understanding molecular pathology of genetic diseases. Therefore, our interest has been to study both population history and molecular mechanism of diseases among Indian populations. Our study on nearly <10,000 individuals belonging to more than 200 ethnic populations of India, using Y chromosome and mtDNA markers, revealed that the tribal populations of Andaman Islands are probably the descendants of the first modern humans migrated out of Africa about 65,000–70,000 years ago. Our very recent study using 1 million autosomal SNPs further confirms that the Andamanese are very unique, and possibly contributed to the origin of Australian aboriginal and Southeast Asian populations. Further, we have also found that several novel mtDNA haplogroups have originated within India and some of them might be the source of mtDNA and Y chromosome lineages found in Southeast Asia. As each Indian population is unique in their genetic composition, etiologies of genetic diseases are often different from other global populations. For example, in Indian population, we identified an ancient deletion of 25 bp in the cardiac myosin-binding protein-C gene (*MYBPC3*) that is associated with heritable cardiomyopathies as well as with an increased risk of heart failure. Its prevalence was found to be high (~4%) in the general population from the Indian subcontinent. However, this mutation is completely absent among the people from the rest of the world. Mutations in *SRY* and *SOX9* were found to be the main cause for the sex-reversals, but when we analysed several familial cases of sex-reversals, we found a novel region on Xp11 involved in the etiology of the disease. Similarly, we have observed novel variations in *DAZ*, *SPINK1* and *CYP1A1* genes in individuals associated with infertility, fibrocalculous pancreatic diabetes, and recurrent early pregnancy loss, respectively. These studies suggest that the Indian populations are unique in their genetic origin as well as in the mutations underlying in the susceptibility to disease. Therefore, what is true for other global populations, in terms of their genetic basis for disease susceptibility, may not be true for Indian populations.

002: Mapping human genetic history in Asia

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Asia, as the largest and most populous continent, harbors significant cultural and linguistic diversity, but the geographic structure of genetic variation across the continent remains enigmatic. Here, we report a large-scale survey of autosomal variation from a broad geographic sample of Asian populations: more than 50,000 single nucleotide polymorphisms (SNPs) typed in 1,808 DNA samples representing 73 Asian populations. Our results show considerable relatedness amongst all Asian populations and suggest a predominantly south-to-north migration of East Asian populations. Analyses suggest a common ancestral origin for all East and Southeast Asian populations studied, implying that the majority of the gene pool in Asia was derived from a single initial entry of modern humans into the continent.

003: The first sequenced Asian genome

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We have finished a Han Chinese male individual genome with 21X single-ended and 13X pair-ended reads generated by Illumina Genome Analyzer. The sequence has 99.97% coverage of NCBI v36.1 reference, over 90% of which are unique. About 3M SNPs and 417,016 novel ones were discovered in highly confidence, meeting 99.9% coincidence with Illumina Human 1M Genotyping result. 215,982 indels as well as 1,602 structural variations were also found. In addition, comparing the sequence with three previous European genomes had resulted in a better understanding of human evolution.

The project is the first huge genome completed by "Now-Gen" sequencing technology. It demonstrated the powerful capability of the new generation sequencer on whole genome resequencing and shed light on a promising future era of personal genomics and personalized health care.

004: The Indian genome Variation project: Clues and cues for pharmaco-genomics and disease association studies

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The Indian Genome Variation (IGV) project has been evolved to enable genotype-phenotype correlations in complex disorders and pharmacogenomic studies in diverse populations of India. Since India houses nearly one-sixth of the world's population and is a global melting pot of human diversity, the first major challenge was to identify a representative set of populations which captures the genetic spectrum of India. This was carried out through a grid sampling approach wherein genetic relatedness amongst 55 populations encompassing four major linguistic lineages i.e. Indo-European, Tibeto-Burman, Austro-siatic and Dravidian of contrasting ethnicity from different geographical zones was analysed using a subset of 75 genes representing nearly all the chromosomes. The analysis revealed the existence of a population sub-structure. These 55 populations however, could be classified into four genetically distinct and near homogeneous clusters and one bridged population group. Variation data on over 1,000 disease and drug candidate loci from diverse functional categories including validated functional polymorphisms with reported associations in different populations is now available from 26 representative populations of the clusters in the Indian Genome Variation database (http://www.igvdb.res.in/). Additionally it houses genotype data on ~58K neutral markers from Affy 50K array. Analysis of this data has (1) revealed clusters of populations which are related to different HapMap as well as Pan-Asian populations. Indian populations form a continuum of genetic spectrum bridging CEU and JPT/CHB, the two most distinct HAPMAP populations. (2) It has also enabled estimation of the extent of genetic heterogeneity within Indian populations and thus provided pointers for cohort pooling and validation studies (3) hinted at genes/variations which are preferentially targeted by natural/balancing selection and would thus be important disease/drug response candidates. (4) predicted at risk/protected populations for various diseases. This would be enormously useful for epidemiological and pharmacogenomic studies (5) enabled identification of common CNV regions and their frequency in various Indian populations (6) provided guidelines for more effective LD based mutation mapping, founder identification and use of IGVdb data as controls for association studies.

References

1. Hum Genet. 2005; Oct 118(1):1–11.
2. J Genet. 2008 April 87(1):3–20.