

## 4. GENETIC STUDIES

### 4.1. Malaria susceptibility and SNPs among the primitive tribes

Single nucleotide polymorphisms at two functionally coding regions *i.e.* regions coding for TNF- $\alpha$  and ICAM-1 studied among Onges, a primitive tribe settled on the island of Little Andaman. Three new SNPs on TNF- $\alpha$  locus and on ICAM-1 locus four biallelic variant sites were identified. Two of the SNPs identified on TNF- $\alpha$  locus were also shared by Jarawas, another primitive tribe of Andaman Islands.

Genetic variants are powerful tools for reconstructing human evolution and for understanding the genetic basis of disease susceptibility / resistance. The most common sequence variations are single-nucleotide polymorphisms (SNPs), which provide the most comprehensive resource for ascertaining genetic diversity. The variation occurs in both coding and non-coding sequences at a frequency of approximately 1 per 1000 base pairs. A database documenting these SNPs in global populations is dbSNP. Analysis of the data in dbSNP revealed that many populations from Indian subcontinent remain undersampled. The identification of SNPs across geographically and ethnically diverse populations is important because the frequency of SNPs can vary substantially between populations, as will their usefulness as

markers for gene-mapping studies. A study on SNPs on two functionally coding regions was conducted among Onges, a hunter-gatherer tribe of Andaman and Nicobar Islands.

The target DNA regions- tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and intercellular adhesion molecule 1 (ICAM-1) - play important roles in a variety of human diseases. Blood samples were processed and the genomic DNA sequences including 1000 bp upstream region of TNF- $\alpha$  (3085 bp) and ICAM-1 (15 kb) were assembled from UCSC Genome Browser. The genes map to the chromosomal region 6p21.3 and 19p13.2-p13.3 respectively. The TNF- $\alpha$  gene contains four and ICAM-1 gene contains seven exons. The ICAM-1 genomic region was repeat-masked using the Repeat-Masker2 program.

Primers for PCR were designed by using the Primer Express 2.0 software package. The 5' and 3' UTRs, exons and introns were completely sequenced. A total of 3 SNPs were detected and none of which is reported in the NCBI's dbSNP database.

On the TNF- $\alpha$  locus three new SNPs were identified, two of which were shared by Jarawa population also as reported earlier. These variant sites lie either in the promoter or in the intronic region of the gene. One of these private sites C500T is highly polymorphic. The G-433A SNP found exclusively in the Onges population is highly monomorphic with minor allele frequency ~ 5%. At the ICAM-1 locus, 4 biallelic variant sites were identified,

which have already been reported in the dbSNP. One of these SNPs (rs5030382) harbors a non-synonymous change from amino acid glutamic acid (E) to lysine (K) at position 469 of the CD54 protein, while another SNP (rs3093032) lie in the exon-7 (3'UTR) of the gene. The remaining two variant sites were located in the intron- 2 of the gene. Like the SNPs present in TNF- $\alpha$ , the frequencies of ICAM-1 SNPs are also moderate to high. A total of seven haplotypes were observed among which HT1 and HT7 are the most frequent strings contributing 50% and 20% of the gene pool respectively. HT2 & HT4 and HT5 & HT6 are more or less equally frequent in the Onges population.

#### **4.2. Immunological studies among tribal population of Andaman Islands.**

A project to study the immune status of the primitive tribes of Andaman and Nicobar was initiated. As the first step a sample of Jarawa population was screened for circulating anti-leptospiral antibodies. The study showed that 39% of the Jarawas are exposed to Leptospire.

There are several tribal populations (Jarwas, Onges, Shompens, Nicobaries, Great Andamanese) in Andaman and Nicobar Islands. Out of these tribes Nicobaries are the only

tribe leading a normal lifestyle. Jarwas and Onges have features like Negroid pigmies and the remaining tribes are having mongoloid features. Recently Jarwas have come in contact

with the general population. In the recent past, outbreaks of viral hepatitis have been reported in Jarwas. Considering this fact, it would be worthwhile to determine the background health status of the tribal population, especially of Jarwas. To understand the immunological status of the Jarwas, different health parameters need to be investigated.

The objectives of the study were to determine the basal values of Hb, TLC, DLC, the total T cell number and CD4/CD8 ratio of peripheral

blood, serum antibody levels to various common infections like viral hepatitis, leptospira, candida, tetanus, diphtheria, pertusis, Salmonella, *M. tuberculosis* and estimation of zinc and copper in serum.

A total of 44 jarwas serum sample were collected and tested for leptospiral antibodies. Out of 44 samples tested leptospiral antibodies were seen in 17 sera (39%). Collection of more samples are in progress and other parameters are being investigated.



I am amazed to see the wonderful job done by Dr. Sehgal and his team of scientists in A & N Islands. They need all kinds of encouragement for further valuable achievements. The Centre should be rendered all assistance as it is situated in the midst of Bay of Bengal in these Islands where they have to work in unfriendly and harsh conditions. Congratulations.

**Shri. Manoranjan Bhakta**  
Member of Parliament  
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It is nice to come back to Port Blair after a period of seven years. I am pleasantly surprised and highly impressed by the development of the Regional Medical Research Centre (ICMR), Port Blair and the scientific activities carried out in the Centre, which are not only of national but also of international standards. The Centre has been designated as WHO Collaborating Centre for Diagnosis, Research, Reference and training in Leptospirosis. The dynamic leadership shown by Prof. Sehgal in encouraging the small team of scientists to achieve so much scientifically in the remotest part of India in such a short time is an evidence of commitment and dedication to work.

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