B.M.SANKARATHI
DEPARTMENT OF GENETICS
Dr. ALMPG Institute of Basic Medical Sciences
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AREAS OF INTEREST: Medical Genetics/Human Genetics, cancer genetics, Pediatric genetics field, Clinical genetics, Therapauetic genetics, Molecular biochemistry

OBJECTIVE: To pursue a research as a career in the frontier areas of Genetics, that invokes immense challenge ensuring a continuous process of learning, paving way to efficient research abilities and teamwork.

RESEARCH EXPERIENCE:

Working experience in Genetic toxicology, Animal handling, Analysis of human mutations (PCR, SSCP, RFLP, TGGE, dHPLC, Sequencing).

ACADEMIC PROFILE:

B.SC.	BIO-CHEMISTRY	UNIVERSITY OF MADRAS	1998
M.SC	ENVIRONMENTAL BIOLOGY	UNIVERSITY OF MADRAS	2000
M.PHIL	GENETICS	UNIVERSITY OF MADRAS	2001
PH.D.	GENETICS	UNIVERSITY OF MADRAS	Dec-2005 (submitted)

M.PHIL RESEARCH PROJECT:

'Inhibitory effects of Spirulina fusiformis on Cisplatin and Urethane induced clastogenicity in Swiss albino mice'

Abstract of the work:

Experiments were carried out to test the protective effects of Spirulina fusiformis on the in vivo genotoxicity of Cisplatin (Cis) and Urethane (Ure). For this purpose, Swiss albino mice were pretreated for five consecutive days with 3 doses (1000mg/kg, 500mg/kg, 250mg/kg of body weight) of aqueous extract of Spirulina. Genotoxic effects were studied by observing the chromosomal damage. The results obtained suggest that pretreatment with Spirulina significantly reduces the effects Cisplatin and Urethane in a dose dependent manner. Spirulina reduce the Cisplatin induced mutation rate by about 53-60% and that of Urethane by about 18-43% at the highest dose.

DOCTORAL WORK: (Abstract given in page-6)

"CONNEXIN 26 GENE MUTATIONS AND THEIR CONTRIBUTION TO THE CHILDHOOD HEARING IMPAIRMENT IN TAMILNADU POPULATIONS, SOUTH INDIA"

THESIS ADVISOR: **PROF. A. RAMESH**

PUBLICATIONS: **"**MUTATIONAL ANALYSIS OF GJB2 AMONG SOUTH INDIANS – AN EPIDEMIOLOGICAL REPORT" - under communication

HONORS/AWARDS AND FELLOWSHIPS

- Awarded **S**enior **R**esearch **F**ellowship by **I**ndian **C**ouncil of **M**edical **R**esearch (**ICMR**), New Delhi (2004-till to date)
- Best Poster Award by XXIXth National conference of **I**ndian **S**ociety of **H**uman **G**enetics (**ISHG, 2004**)
- Awarded **J**unior **R**esearch **F**ellowship by Lady TATA Memorial Trust (**LTMT**), Bombay (2002-2003)

- **Third Rank holder** in M.Sc Environmental Biology, University of Madras (2000)

TECHNICAL EXPERIENCE

RAMAN SPECTROSCOPY

CYTOGENETICS

- **ANIMAL HANDLING - intra-peritoneal and oral administration of drug**
- **Chromosomal aberration analysis in mice**

MOLECULAR BIOLOGY:

- **GENOMIC DNA EXTRACTION FROM**

  Human blood cells

  Animal tissues

  Plant cells
- **PRIMER DESIGNING FOR PCR**
- **PCR**

  Allele specific PCR

  Hot start PCR
- **GEL ELECTROPHORESIS**

  Agarose

  Polyacrylamide
- **Single Stranded Conformation Polymorphism (SSCP)**
- **Temperature Gradient Gel Electrophoresis (TGGE)**
- **Restriction Fragment Length Polymorphism (RFLP)**
- **Denaturing High Performance Liquid Chromatography (DHPLC)**
- **Automated sequencer model 3100**

TRAINING AND WORKSHOPS ATTENDED:

- **Indo-UK workshop on "Ethics in Medical Research" at University of Madras, 2004, Chennai**
- **Short training course in "Usage and application of Bioinformatics tools for life sciences" at Anna University-KBC, 2004, Chennai**
- **National workshop on "Genetic Diagnosis and management of congenital hearing impairment" at Osmonia University, 2003, Hyderabad**
- **First CMC winter symposium on "Cell Biology and Molecular Medicine", Vellore, January 2003**

COMPUTER SKILLS

Working knowledge of

- **Microsoft office**
- **Adobe photoshop**

POSTERS AND PAPERS PRESENTED AT:

- **28th All India Cell Biology conference and symposium on Genome Biology – Indian society of cell Biology, Chandigarh, December 2004, entitled "GJB2 mutations in childhood hearing impairment".**
- **XXIX Annual conference of ISHG on "Trends in human Genetics, Biotechnology And Bioinformatics: next 5 years", Bangalore, January 2004, entitled "Screening of connexin 26 mutations in childhood deafness"**

PERSONAL DETAILS:

Father's Name: B. Mehanathan

Date of Birth: 26.5.78

Age: 26

Nationality: Indian

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REFEREES:

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SUMMARY OF THE DOCTORAL WORK:

The present study is to evaluate the contribution of Cx26 gene (DFNB1; 13q11-12) mutations to the childhood hearing impairment with particular reference to Tamilnadu, South India. The study group consists 366 school children who are attending special schools for hearing impaired located in Tamilnadu state. The age of the subjects range from six to twenty years with a mean age, 13.5 years. Audiological information was obtained from the school records. All probands have severe to profound sensorineural hearing impairment. About five ml blood sample was obtained from each subject by venipuncture method after obtaining institutional ethical committee clearance and with due consent from proband's parents and school authorities. DNA was extracted from the blood samples using Miller's protocol (1988).

Bi-directional sequencing was carried out to analyze the coding region of Cx26 gene using ABI 3100 Genetic Analyzer (Applied Biosystems). The carrier frequency for the most common mutations W24X and R127H were analyzed, using PCR/RFLP (*AluI* and *AciI)* on 901 and 100 normal hearing persons respectively.

Of the total 366 subjects with sensorineural hearing impairment (SNHI), 31 percent of the chromosomes (225/732) or about 43 percent of the individuals (156/366) bear mutation in the coding region of the Cx26 gene. Among the 156 individuals with Cx26 gene mutations, homozygous Cx26 gene mutations were observed in 40 individuals (25.6%) and compound heterozygous condition in 16 individuals (10.3%). Three of them are multiple heterozygotes. Ninety-five subjects (60.9%) who have a Cx26 gene mutation are heterozygotes. A majority of the heterozygotes (64/95) carried R127H mutation. The

remaining five individuals (3.2%) carried one mutation in homozygous condition and a second mutation in heterozygous state.

In total, twenty-seven mutations were found. Twenty of these mutations are missense mutations, two non-sense, one frameshift and four silent mutations.

R127H (c.380G→A) is the most common mutation. This mutation was observed in about 11 percent of the chromosomes analyzed (83/732) or about 37 percent of the chromosomes bearing a Cx26 gene mutation (83/225). Seventy-seven of the 156 individuals with Cx26 gene mutations (about 49%) showed R127H mutation: six are homozygotes (R127H/R127H), 64 heterozygotes (R127H/+), four compound heterozygotes (R127H/V153I-2, R127H/F106F-1, R127H/S139R-1) and three multiple heterozygotes (R127H/V153I/R165W-2; R127H/E119K/ V153I-1). One homozygote carried V27F in heterozygous state. R127H was observed in normal hearing persons with a frequency, 0.6.

W24X (c.71G→A) is the second most common mutation. This mutation was observed in about ten percent (72/732) of the chromosomes analyzed. This mutation occurred in homozygous condition in 34 subjects (9.3%); as heterozygote in three subjects and as compound heterozygote (W24X/V91M) in one individual. Two homozygotes have an additional mutation in heterozygous form, Q80Q and T186M (W24X/W24X/Q80Q/+; W24X/W24X/T186M/+). The carrier frequency in normal hearing persons was found to be about two percent (18/901).

W77X (c.231G→A) is another causative mutation observed in about 0.5 percent of the chromosomes analyzed (4/732). This mutation was observed in homozygous state in two individuals and one of them has F83L in heterozygous state.

Twenty-one of the 27 mutations are ‘rare’ in the sense that they occurred in one or two chromosomes. Three of the 27 mutations occurred as homozygotes (I35S, N62N, and R184P), nine as compound heterozygote and rest as heterozygotes. The R75W mutation observed in one familial case was found to be a dominant mutation with variable expression.

Twelve of the 27 mutations (V27F, L28P, V37L, L56L, P70L, V91M, F106F, S139R, F146L, D159Y, T186M, and I196N) are ‘novel’. Except D159Y, all novel mutations were found to be evolutionarily conserved among mammals.

The high frequency of heterozygosity (about 25 percent of the affected) of Cx26 gene mutations among the hearing impaired indicates that the mechanism of hearing may be complex, in the sense that childhood hearing impairment could be caused not only by the homozygosity of the individual genes, but also by the interaction of mutations at more than one locus. Analysis of Cx26 gene mutations based on ethnic populations may be helpful not only in understanding the mechanism of hearing but also in genetic counselling.