

Sister Chromatid Exchange : A Useful Tool for Genetic Screening

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Introduction

Man is continuously exposed to a variety of natural and synthetic pollutants. The aim of upgradation of technology and industrialization is to provide a comfortable lifestyle and hygienic environment, though the plethora of chemicals introduced in man's environment is rising alarmingly. These industrial chemicals have cytotoxic, clastogenic, mutagenic, teratogenic and carcinogenic effects on the health of the industrial workers. These toxic agents may cause mutations of germ cells resulting in accumulation of heritable abnormal genes or may lead to mutations of somatic cells resulting in formation of malignant tumours. Chromosomal damage constitutes a set of efficient and reliable criteria to measure genetic toxicity¹.

There are two types of **cytogenetic test systems** :

1) Classic Chromosome Aberration Measurement and the more recently. 2) Sister Chromatid Exchange.

The cytological features of chromosomal aberrations are too complex to learn and need prolonged training for accurate interpretations.

Sister chromatid exchange (SCE) is preferred as a sensitive and convenient test for routine chemical mutagenicity; it gives objective results². SCE basically represents reciprocal exchanges of homologous segments between sister chromatids, first demonstrated by Taylor³ in autoradiographic studies of plant chromosomes.

Perry and Wolff⁴ developed the staining procedure named Fluorescence plus Giemsa staining which provided permanently stained heteroduplex chromosomes in which SCE's could be counted and scored.

Rationale for analysis of SCE in Humans

Being well aware that various natural and synthetic agents can modify the genetic material leading to mutational changes, determination of SCE frequency attains paramount importance in detecting these early changes. SCE is the cytological manifestation of a four strand exchange in the DNA, where one exchange is counted as two breaks. Thus formation of SCE involves breakage of genetic material and subsequent recombination of the four DNA strands. The exchanges are visible through differential staining which is brought about by incorporation of a thymidine analog-Bromodeoxyuridine.

Significance of SCE

Elevated SCE frequencies can be produced in response to environmentally induced DNA damage or spontaneously i.e. in the absence of external inducing agents. The induction of SCE is dose dependent i.e. the more the number of years of exposure to the mutagen the more will be the SCE frequency⁵.

The Peripheral Blood Lymphocyte as a Cell used to determine SCE Frequency

The following features of *lymphocytes* make them suitable for SCE analysis: 1) accessibility, 2) capable of proliferation in vitro, 3) representative of cell population.

The peripheral blood circulates to every organ carrying nutrients, metabolites and chemicals to and from the cells of the body. Thus, the peripheral blood lymphocyte serves as a useful indicator of exposure.

Factors affecting SCE analysis in Human population

- (1) Inherent factors
- (2) External Factors-Genotype, lifestyle, physiological state of the individual.

Agents known to induce SCE

- (1) UV Light, (2) alkylating agents like nitrosoureas and alkyl sulphates, (3) anti cancer drugs like mitomycin-C and cyclophosphamide, (4) smoking, (5) metals like copper, iron dust, nickel, cadmium, (6) oral contraceptives, (7) caffeine, saccharin, (8) medication, drugs

Methodology

Blood Culture is performed taking peripheral blood of the patient through a venepuncture. A suitable serum should be added in the blood culture tube along with a mitogen-phytohemagglutinin, and a thymidine analog-bromodeoxyuridine. The blood is incubated at 37°C for 72 hours and at the 69th hour a metaphase arresting agent colchicine is added. The solution is centrifuged and then the cell pellet is treated with 3:1 ratio of methanol and acetic acid.

Several slides can be prepared from each culture. The slides can be stained for analysis by fluorescence or fluorescence plus Giemsa⁴ method, using Hoechst dye 33258. Well differentiated metaphases should be accepted for scoring. The slides can be reviewed under low magnification (100-200x) and selected for scoring on the basis of good staining and chromosome number.

Conclusions

Several studies on SCE frequency as a diagnostic tool for genetic monitoring have done in the past to study the influence of chemical mutagens on the health of industrial workers^{6,7,8,9}. A latent period i.e. time period between the exposure to the agent and clinical manifestations of the disease has been described by Vogel⁹.

Early intervention in this period may prevent the industry related diseases. SCE therefore is useful in monitoring ensuing genetic damage in persons at risk. It is imperative to determine the margin of safety in person exposed to environmental or industrial mutagens and provide timely measures before it is too late. Such an assessment test will be of great help in forecasting, preventing and monitoring oncogenic hazards in persons at risk. There is a uniform consensus that Sister Chromatid Exchange is a simple, sensitive and objective test for routine mutagenicity testing. (Anwar, Yang, Kukura).

Recent Advances

Chromosomal analysis incorporating SCE is being used in a variety of clinical conditions..... e.g. leukaemias, lymphomas, choriocarcinoma, hydatiform mole, ovarian tumours.

Although newer techniques like FISH, genomic hybridizations are developing to characterize certain tumours, baseline cytogenetic bio-markers such as SCE Frequency cannot be replaced and are of utmost importance in correlation of the extent of the disease and genetic damage.

Man's most precious possession is his genetic heritage. If we carelessly squander our resources and poison our germ plasm with mutations produced as a result of environmental pollution, then our heirs will be the losers.

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IMSA News

IMSA Chapter Activities (July - Sept. 2005)

Tamil Naidu Chapter

- 10-7-2005 : Prof. G. Ravindran: 'Application of Robot in Medical Science.'
- 14-8-2005 : Prof. G. Sivakumar: 'Current Management of Diabetic foot Disease - Role of Preventive Strategy.'
- 11-9-2005 : Dr. M. Chandrasekaran: 'Management of Thyromegaly'.

Rural CMEs conducted by Tamil Nadu Chapter

- 21-8-2005 : Dr. M. Itambara Thi, Prof. Madras Medical College and ENT Surgeon Govt. General Hospital Chennai. Topic: 'Common ENT problems in general practice and their management.'

- 5-9-2005 : Dr. M. Rajkumar, Prof. of Vascular Surgery, Madras Medical College, Chennai. Topic: 'Deep vein thrombosis'.
- 18-9-2005 : Dr. Namitha Bhuvaneshwari Raj Kumar, Prof. Ophthalmology : Kilpauk Medical College. Topic: 'Childhood blindness'.

Rural CME - Tamil Nadu Chapter (Chennai)
CME Programme conducted by IMSA Branch Unit at Annamalai Nagar, Chidambaram.

- 16-7-2005 : Dr. N. Muragan: 'End stage liver disease - current concept and management.'
- 31-7-2005 : Dr. G. Santhanam: Type II diabetes Mellitus - Erectile Dysfunction.
- : Dr. S.V. Raghunathan: Type II Diabetes Mellitus - Problems and Management.

IMSA WORKSHOP International Medical Sciences Academy (IMSA), in collaboration with Kundan Laser Centre is organizing a workshop '6th Hands-on-Laser Workshop' Basic Orientation' Course and Workshop (Aesthetic Laser Surgery and Hair Removal) on 5th and 6th November 2005 at Kundan Laser Centre (Institute of Laser and Research Centre) 4771/23, Bharat Ram Road, Daryaganj, New Delhi-110002, India.

For registration contact : Dr. S.S. Sethi, President - IAALS, Convenor and Chairman at above address under intimation to IMSA Headquarter.

Election of Fellows

Fellows & Members elected during the quarter July-Sept. 2005

Dr. M. Bhaskar	Chennai	Dr. Patel Hemant	USA
Mr. Zinobia Mahiar Madan	Mumbai	Dr. Birinder Jeet Kaur	USA
Dr. N. Mohan	Salem	Dr. Sanjiv Kumar	Switzerland
Dr. D.P. Singh Toor	New Delhi	Dr. (Mrs.) Neeta Kumar	Switzerland
Dr. S. Anuradha	New Delhi	Dr. Nabendu Bhattacharjee	Kolkata
Dr. Ravi Ramalingam	Chennai	Dr. Deepa Sachdeva Passi	Noida
Dr. N.D. Ramanujam	Chennai	Dr. Navtej S. Butter	USA
Dr. D. Sachithanandam	Vellore	Dr. Ajay Sharma	New Delhi
Dr. R.N. Srivastava	New Delhi	Dr. Usha Gupta	New Delhi
Dr. S.V.S.R. Krishna	New Delhi	Members	
		Dr. Harish Pathak	New Delhi

HONOURS

Prof. S.C. Sahgal FIMSA, Director WHO collaborating Centre for Leptospirosis, Regional Medical Research Centre (ICMR) Port Blair, has been bestowed '**Fellowship of Royal College of Pathologists, UK**', in recognition of his contribution in medical science, for his work carried out especially in Andoman Nicobar Island.

Dr. T.D. Chugh has been awarded '**Genl. Amir Chand Oration**' by National Academy of Medical Sciences' for the year 2005' and has been appointed National Emeritus Professor by the Academy.

Dr. SNA Rizvi FIMSA has been awarded the prestigious '**Netaji Oration Award 2007**' in recognition of his significant work on Metabolic Bone disease by the association of Physicians of India.

Dr. (Mrs.) S. Sachdev, Founder Fellow of IMSA has been awarded '**Helpage India Golden Award**' for the year 2005 by Helpage India, on Oct. 1st, 2005.

IMSACON 2006

Annual Conference '**IMSACON 2006**' will be held on 3-4-5 November 2006 at Lahore (Pakistan) **Dr. Shaheena Asif**, Surgimed Hospital Lahore will be the Organising Secretary.

Theme : 'Update in Medical and Dental Sciences'

Venue : Lahore Medical & Dental College, Canal Bank North, Tulspura, Lahore-53400, Pakistan

Visa : Visa is required for Pakistan and must be obtained before travel. Please allow 3 months before conference date for application to be processed.