ABSTRACT BOOK

th National Congress on Genetics

'Unravelling the Secrets of the DNA'

5-7 MAY 2007

KOTA BHARU, KELANTAN, MALAYSIA

JOINTLY ORGANISED BY :

Persatuan Genetik Malaysia

Pusat Genom Manusia
Pusat Pengajian Sains Perubatan
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INCIDENCE OF CHROMOSOMAL ABNORMALITIES AND CLINICAL OUTCOME IN MALAYSIAN COUPLES EXPERIENCING REPEATED SPONTANEOUS ABORTIONS

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Parental chromosomes in couples with habitual abortions are usually not studied until other aetiological factors have been excluded. Recent advances in cytogenetic techniques have led to the understanding that couples with a history of more than two first trimester abortions may carry a balanced chromosomal rearrangement leading to foetal aneuploidy and miscarriage. Reportedly, in 5-7% of couples having at least 2 spontaneous abortions, one partner carries a chromosomal rearrangement. We analysed retrospectively the karyotype pattern and patient profiles of 36 couples with history of repeated abortions, referred to Human Genome Centre over the last 5 years. Results revealed chromosomal abnormalities in 4 out of 36 couples (11%), a relatively higher frequency compared to earlier reports. Two patients, one male and one female had balanced translocations namely, 45, XY,t(13;14) and 46,XX,t(5:11). Two other patients had mosaic aneuploid karyotypes namely, 46,XX/47,XX, +1 marker chromosome and 46,XY/47,XY,+21. On analysis of the case files, the average number of spontaneous abortions before the couples were referred for karyotyping was 4.The other investigations were mostly normal. Ectopic pregnancies had occurred in 3 patients who however had normal karyotypes. The prognosis in terms of having a normal baby after repeated abortions was found to be 1 in 3 in couples having no chromosomal abnormality and 1 in 4 among couples having chromosomal abnormality. In conclusion, our study indicates that cytogenetic analysis is an important and necessary investigation in couples with recurrent spontaneous abortions and the possibility of prenatal diagnosis and a fair chance of achieving normal pregnancy outcome can be counseled to them.

A SNP EX3 1209A→G IN PGF2α RECEPTOR GENE AND ITS ASSOCIATION WITH PRESSURE LOWERING EFFECT OF TOPICAL LATANOPROST AMONG GLAUCOMA PATIENTS: A PRELIMINARY REPORT

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Prostanoid FP receptor is encoded by PGF2α receptor gene, and it is believed to be involved in increasing the uveoscleral outflow through unknown mechanism. Its analogue, Latanoprost proved to be a good drug in reducing the intraocular pressure of glaucomatous patients. The polymorphism of PGF2α receptor gene might result in the variation of responsiveness of glaucomatous patients to the drug. A prospective cohort study was conducted with 48 glaucomatous patients and 48 controls. All were planned for treatment with topical Latanoprost 0.005%. Measurements of intraocular pressure (IOP) were taken at 0, 1, 3 and 6 month. Patients were categorized as good responder (more than 30% IOP reduction), moderate responder (between 15% and 30% IOP reduction) and poor responder (less than 15% IOP reduction). DNA was extracted from blood and subjected to PCR amplification. dHPLC was performed and mutation was confirmed by DNA sequencing. Allele frequency in glaucoma patients was A= 0.896; G= 0.104 and in the control group was A= 0.906; G= 0.094. For IOP reduction, 39.5% of homozygous sample wild type (AA) was categorized as good responder, 34.2% moderate responder and 26.3% poor responder while among the heterozygous (A→→G), 80.0% was categorized as good responder, 10.0% moderate responder and another 10.0% poor responder. There was no significant association between a SNP (EX3 1209AG) and responsiveness to Latanoprost (p=0.110) in our population. However, a larger sample size is needed to confirm this association.

CLINICAL AND MOLECULAR GENETIC ANALYSIS OF MALAYSIAN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

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Duchenne Muscular Dystrophy (DMD) is an X-linked recessive genetic disorder characterized by rapidly progressive muscle weakness. The cause of this disease is associated with several types of mutations in the dystrophin gene, located on the X chromosome (Xp21). Dystrophin is a component of the plasma membrane cytoskeleton, which anchors and supports the sarcolemma during exercise. Deletions account for 60% of the mutations within the 79 exons of the dystrophin gene. Seven exons (43, 44, 45, 46, 49, 50 and 51) were found to be the most commonly deleted among Asian patients. To detect the deletion of DMD, we used polymerase chain reaction (PCR) in patients' samples using the 7 selected exons. A total of 20 Malaysian male patients were analysed. The mean age of initial presentation was 60 months (SD 32 months, range 5-120 months). Fourteen patients were found to have at least one deletion in those seven exons; deletion on exons 49, 50 and 51 were the most frequent (71.43%). The remaining six patients did not have any deletion detected on the tested exons. In view of this, both clinical diagnosis and molecular analysis should ideally be performed for the confirmation of DMD. Deletion on exons 49, 50 and 51 are thought to be the 'hot spot' of DMD within the Malaysian population. Since the number of patients analysed in this study is limited, further investigations are essential to confirm whether the major cause of DMD is due to the deletion of exons 49, 50 and 51.

NUCLEOTIDE 153, 104 (A TO G) RB1 SNP AMONG MALAYSIAN RETINOBLASTOMA CHILDREN AND THEIR PARENTS: DISTRIBUTION AND ASSOCIATION

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Retinoblastoma is an early childhood intraocular cancer, associated with the RB1 gene, located at chromosome 13q14. The SNP at 153, 104(A→G) of RB1 gene was previously reported to be common only in Asian populations. This study attempted to determine the distribution of this SNP in Malaysian children with retinoblastoma, their parents and control subjects as well as its association with the laterality and staging of the disease. A total of 36 retinoblastoma patients (29 Malays, 3 Chinese and 4 Indians) and an equal number of ethnic proportions of unrelated healthy controls were recruited. Blood samples were collected and subjected to PCR-RFLP analysis. The presence of the minor allele of this SNP was found in 10 out of 29 Malays patients with a frequency of 0.14. It was absent in all the three Chinese and four Indian patients. For the healthy control subjects, this SNP was found in five out of 36 subjects with an allele frequency of 0.07. There was no significant different between case and control study ($p=0.147$). This RB1 SNP was also found in the parents of the patients with paternal and maternal allele frequencies of 0.125 and 0.16 respectively. There was no significant association of this SNP with laterality ($p=0.468$) or disease staging ($p=0.545$). Our results were in accordance to the previous study done by Kadam Pai *et al.* (2003). A larger study to correlate this SNP with the disease is currently in progress.

THE USM HUMAN GENOME CENTRE EXPERIENCE ON MOLECULAR DIAGNOSTIC TESTING OF SMA CASES

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Spinal Muscular Atrophy (SMA) is an inherited neuromuscular disorder and is one of the most common genetic causes of childhood fatality. SMA is classified into three groups based on age of onset and clinical severity. Currently, SMA is diagnosed based on clinical features and/or muscle biopsy ± electromyography (EMG). Survival Motor Neuron (SMN) gene has been identified as being responsible for SMA. From August 2003 until Feb 2007 we received 93 samples for SMN1 gene deletion analysis from various hospitals in Malaysia. Except 3 patients (Indonesian, Burmese, Indian), the rest were Malaysians (71 Malays, 5 Indians, 9 Chinese and 5 patients are mixed ethnicity). Muscle biopsy was performed in only 5 patients and EMG in 27 patients. DNA were extracted from blood samples using DNA extraction kit and subjected to SMN1 gene deletion analysis. Forty-nine out of 93 samples (20 type I, 21 type II, and 8 type III) were found to have homozygous deletion of at least exon 7 of the SMN1 gene. Twelve patients (7 type I, 4 type II, 1 type III) showed the presence of the SMN1 gene and the rest were excluded as they did not fulfill the criteria of International SMA Consortium. Deletion of exons 7 and 8 of the SMN1 gene were found in 80% of the SMA patients. This molecular genetic test can be an alternative to the existing diagnostic modalities.

IDENTIFICATION OF GENETIC IMBALANCES OF NASOPHARYNGEAL CARCINOMA (NPC) BY COMPARATIVE GENOMIC HYBRIDIZATION (CGH): A PRELIMINARY REPORT

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Comparative Genomic Hybridization (CGH) is a molecular cytogenetic technique that was modified from *in situ* hybridization technique. This technique was designed to compensate the difficulties present in conventional cytogenetic and Fluorescent *In Situ* Hybridization (FISH) and is not dependent on cell culture. CGH can also be performed on archival material and it requires no prior knowledge of the genetic aberrations. This technique can be used to identify imbalanced genetic alterations such as deletions, gains and amplifications. Patients with Nasopharyngeal Carcinoma (NPC), diagnosed clinically and histopathologically were enrolled into this study. This study was conducted to identify the pattern of genetic imbalances in NPC in Malaysia. Tumor DNA was extracted from NPC biopsies while reference DNA was extracted from normal controls peripheral blood. Then, tumor DNA and normal reference DNA were labeled by nick translation method with green and red fluorescent dyes, respectively. Hybridization of red and green fluorescent labeled DNA to metaphase spread was performed. DNA was counterstained with 4',6-diamidino-2-phenylindole (DAPI). Finally, the image was captured and then analyzed. Chromosomal gains that were found in this study were 4q26 (20%) and 11q13- q14 (20%). Chromosomal losses that were observed in this study were 20p12 (40%) and 13q21-q31 (20%). This preliminary study postulates that there may be activation of oncogene in the gain regions and suppression of tumor suppressor gene in the loss regions. Our findings may also, in future, provide a comprehensive profile of chromosomal regions showing losses and gain in NPC within the Malaysian population.

Y-CHROMOSOMAL STR VARIATION IN MALAYS OF KELANTAN AND MINANG

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Malays in Malaysia are a mixture of different races, caused by the history of migrations centuries ago and may consist of 14 sub-ethnic groups. We used the Y-chromosomal STR (Y-STRs) to genotype two of the sub-ethnic groups namely, Kelantan and Minang Malays. The aim of this ongoing study is to investigate the polymorphisms of six Y-STR loci namely, DYS19, DYS388, DYS390, DYS391, DYS392, and DYS393 in the two populations mentioned. Twenty males (10 Kelantanese and 10 Minang) were analyzed by PCR amplifications followed by 8% non-denatured polyacrylamide gel electrophoresis. Randomly selected samples were sequenced for validation. Results revealed a total of 32 alleles, ranging from three (DYS19) to nine alleles (DYS390). Allele frequency distributions ranged from 0.05 (DYS388, DYS391 and DYS393) to 0.65 (DYS388). The highest gene frequency of 0.6 was found in Kelantan Malays [DYS388 (127bp); DYS391 (163bp)] while for Minang it was DYS388 (127bp) with a frequency of 0.7. Although the level of polymorphism of the two populations are similar the number of alleles (4); heterozygosity (0.6) and allelic frequency distributions appeared to be imbalanced. Significant differences of allele frequency distributions were observed in loci DYS390 (199bp), DYS391 (167bp) and DYS393 (132bp). Surprisingly, none of the individuals shared the same haplotypes. However, errors of scoring and factors like small sample sizes should be considered. Preliminary result revealed polymorphisms in the six loci among the two Malay sub-ethnic groups. Significant differences of the allelic frequency distributions were observed, but a further investigation with larger sample sizes is warranted to confirm these findings.

SMN2 COPY NUMBER OF MALAYSIAN SMA PATIENTS WITH HOMOZYGOUS DELETION OF SMN1

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SMA is an inherited neuromuscular disorder caused by homozygous deletion of SMN1 gene. Deficiency of survival motor neuron protein causes the degeneration of anterior horn cells in the spinal cord leading to progressive muscle weakness. SMA has been classified into 3 clinical subtypes based on age of onset and clinical severity. Type I is the most severe while type III is the mildest form. More than 90% of SMA patients have deletion of SMN1 gene irrespective of disease severity. However, patients with homozygous deletion of SMN1 gene retain at least 1 copy of the duplicated gene, SMN2. The copies of the SMN2 gene were reported to be inversely proportional with the severity of the disease. In this study, we performed a quantitative PCR analysis in 35 SMA patients (12 type I, 17 type II and 6 type III) with homozygous deletion of SMN1 gene to determine the copies of SMN2 gene. The DNA was extracted from the blood using GeneAll® DNA extraction kit. CFTR and SMN2 genes were then amplified using LightCyler® real-time PCR machine and SYBR® Green I fluorescent dye. The SMN2 copies were calculated relative to the CFTR of each sample. The majority (83%) of type I patients showed 2 copies, 94% of type II showed 2 and 3 copies and 100% of type III showed 3 and 4 copies of the SMN2 gene. The copy number of SMN2 in our SMA patients indicated a close relationship between the gene and clinical severity of patients.

MUTATIONAL ANALYSIS OF H-RAS GENE IN ORAL CANCER PATIENTS TREATED IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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H-ras gene is a proto-oncogene that encodes for membrane-bound protein known as p21ras, which plays an important role in signal transduction and cell proliferation. Point mutations may convert this proto-oncogene into oncogene, which, in turn leads to the development of cancer through complicated cascade events. Mutated H-ras gene has been identified in various human cancers, including oral cancer, primarily located at the exon 1 (codons 12 and 13) and at low frequency, at the exon 2 (codon 61). This study was conducted to investigate the presence of mutations at exons 1 and 2 of the H-ras gene in 30 cases of oral cancer using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP). DNA was extracted from surgically removed oral cancer tissue and subjected to PCR amplification. Digestion was performed using Msp I and BstN I restriction enzyme for exons 1 and 2 respectively. Two cases (7%) showed mutations at the codon 12 of exon 1, whereas no mutations were detected in codon 61 of exon 2 of the H-ras gene. Compared to the frequency of codon 12 mutations reported in western (<5%), India (35%) and Taiwan (%) populations, these results suggest that H-ras gene may play a role in the oral carcinogenesis. However, larger sample size and sequencing are required to yield more precise results.

APPLICATION OF DHPLC FOR SCREENING OF GJB2 MUTATIONS AMONG MALAYS WITH NON-SYNDROMIC HEARING LOSS: A PRELIMINARY REPORT

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Hearing loss (Hl) is the most common congenital sensory defect in human affecting approximately 1:1000 newborns worldwide. Hl can be caused by environmental and genetic factors. Genetic causes represent 50-70% of Hl of which 80% are autosomal recessive. Many genes are involved in the non-syndromic hearing loss (NSHL). Several of these genes have been identified and mutations in the GJB2 gene (13q11-q12.1), encoding gap junction protein connexin 26 (Cx26) have been confirmed to be responsible in a majority of the patients. The objective of this study was to screen mutations in the coding region of GJB2 gene. A total number of 33 NSHL Malay patients were screened for mutations in the Cx26 coding region. The DNA was extracted from buccal swabs using GeneAll® DNA extraction kit and subjected to PCR. The fragments were then electrophoresed and slow -reannealing was performed, followed by screening using denaturing high performance liquid chromatography. Eight out of the 33 samples showed heterozygous peaks indicative of presence of mutations.

CONSTRUCTION OF GENETICALLY ENGINEERED LIVE ATTENUATED NON TOXIGENIC, AUXOTROPHIC *Vibrio cholerae*

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Cholera is an epidemic, endemic and the only pandemic bacterial disease and is caused by gram negative bacteria, *Vibrio cholerae*. Therapies against cholera are available but the ideal approach is to prevent cholera. Cholera can be prevented by improved sanitations or by vaccination against *V. cholerae*. Since sanitation is not possible on a large scale so oral live attenuated cholera vaccines are the ideal choice for cholera prevention because of ease of administration and their natural; acquired active immunogenic response. This study reflects the construction of genetically engineered live attenuated non toxigenic auxotrophic *V. cholerae* vaccine candidates, VCUSM5 and VCUSM6. These vaccine strains are metabolic auxotrophs of amino levulinic acid (ALA) because of the mutation in the hemA gene. This auxotrophy in VCUSM5 was achieved by the insertion mutation of the aphA cassette into hemA that codes for gutamyl tRNA reductase, an important enzyme of the C5 pathway of ALA biosynthesis. In the case of VCUSM6 auxotrophy was achieved by frame shift mutation in hemA. Colonization assay with infant mice showed that the vaccine candidates are good colonizers of the small intestine. These vaccine candidates were found to be the least reactogenic in the rabbit ileal loop assay and this was confirmed by histopathological examination of the ileal loops. The vaccine candidates are environmentally safe and cannot survive longer than 4-5 days in environmental waters as compared to the wild type which survives more than 15 days in water samples. All the above results show that VCUSM5 and VCUSM6 are the promising least toxic and safe vaccine candidates.

TRISOMY 9 – A CASE REPORT

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Trisomy 9 is a rare chromosomal disorder in which the entire chromosome nine appears three times rather than twice in cells of the body. This can occur either as a mosaic or non-mosaic pattern and may be caused by errors during the division of parental reproductive cells (meiosis) or during the division of body tissue cells (somatic cells) early in the development of the embryo (mitosis). We report a case in which the infant showed the characteristic phenotypes of a small face, wide fontanelle, prominent occiput, micrognathia, low set ears, upslanting palpebral fissures, high arched palate, webbed neck, short sternum, overlapping fingers, limited hip abduction, rocker bottom feet and heart murmurs. Cytogenetic analysis done on the blood of the patient confirmed the presence of non-mosaic trisomy 9. Non-mosaic or complete trisomy 9 is a lethal diagnosis, with most fetuses dying prenatally or during the early postnatal period and most of the cases end in spontaneous abortion in the first trimester. However, in the present case, the infant survived until 20 days after birth. This report adds to the literature of cases of trisomy 9 live-born infants that survived beyond one week.

DUPLICATION 9(Q12Q13): A NEW VARIANT OF DUPLICATION 9Q SYNDROME?

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We report a case of a two year - old Malay boy who presented with facial asymmetry, small and malformed left ear pinna, left hearing impairment and high arched palate. He was born full term with a birth weight of 3.1 kg to non - consanguineous Malay parents. At birth, his mother and father were aged 32 and 39 years respectively. There was no similar family history of note. His developmental milestones were appropriate for age. An initial diagnosis of Goldenhar syndrome was made until cytogenetic analysis revealed a karyotype of 46,XY, dup(9)(q12q13). In our patient, duplication involved only the proximal region (q12q13) of the long arm of chromosome 9. Our patient did not present with features typical of duplication 9q syndrome and appears to have a better prognosis. To the best of our current knowledge, this is the first case report of duplication 9q that solely involved the proximal part of the long arm of chromosome 9 (q12q13) which could be a new variant of duplication 9q syndrome.

DOWN SYNDROME AS A RESULT OF ROBERTSONIAN TRANSLOCATION INVOLVING CHOROMOSOME 14 AND 21: A CASE REPORT

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Generally, the karyotype profile of Down Syndrome has been reported to be full trisomy 21 in 92% of patients, mosaic trisomy 21 in 4% of patients and translocation involving chromosome 21 in 4% of patients in most of the population groups worldwide. But, karyotype analysis of 149 DS patients at the Human Genome Center, USM, during the past five years revealed that free trisomy accounted for 94.6%, mosaic trisomy 21 for 4.7% and translocation involving chromosome 21 in 0.7% of the Down Syndrome etiology in North East Malaysian population, indicating a low frequency of translocation DS in this region. Here, we report one case of translocation Down Syndrome encountered during karyotype analysis of 149 DS cases. The patient was a young male aged 2 months, born as a third child to young parents aged 28(F) and 26(M) years, who were referred to Human Genome Center, USM, for cytogenetic analysis. The child has clinical features like flat facial profile, epicanthic folds, flat nasal bridge, convergent strabismus, single simian crease , etc to be suspected as a case of Down Syndrome. Chromosome analysis was carried out employing short term micro culture of the peripheral blood lymphocytes of the patient at 37°C for 72 hours, harvested by standard cytogenetics procedures and karyotypes from GTG banded metaphases were prepared following standard procedures. Chromosome analyses of the parents were also done similarly. Analysis of 20 GTG banded metaphases of the patient showed 46,XY,+ 21, der (14;21) (q10;q10) karyotype pattern in all the metaphases. Karyotype showed a Robertsonian translocation where an entire extra chromosome 21 was attached to the centromere of one of the chromosome 14, resulting in a derivative chromosome 14 with attached chromosome 21. Karyotype analysis of the parents revealed a normal 46,XY pattern for the father and 46,XX pattern for the mother. Translocation Down Syndrome may arise either de novo or as a result of inheritance from a balanced translocation carrier parent. As the parents of this DS child showed normal karyotypes, it can be concluded that this Robertsonian translocation had arisen de novo either prior to or at conception. In cases of de novo Robertsonian translocation, the risk of DS in a subsequent pregnancy is estimated to be 2-3%. However, in translocation DS, karyotyping of the parents should be done compulsorily to determine the origin of the translocation and for proper genetic counseling.

CYTOGENETIC AND MOLECULAR GENETIC ANALYSIS IN ACUTE MYELOID LEUKEMIA (AML) PATIENTS

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It has been well established that Acute Myeloid Leukemia (AML) is a very heterogeneous disease at both the cytogenetic and molecular genetic levels. Some of the FAB subtypes are associated with specific genetic alterations, which can be detected at the cytogenetic level as consistent chromosome abnormalities or at the molecular level as consistent fusion gene transcripts. Because cytogenetic findings are among the most important prognostic factors, cytogenetic analysis of bone marrow samples is now mandatory in the diagnostic workup of newly diagnosed patients with AML. The presence of fusion genes associated with specific chromosome translocations can be detected by molecular techniques. At the Hospital Universiti Sains Malaysia (HUSM), cytogenetic and molecular genetic investigations are undertaken routinely for the diagnostic workup of AML patients. During the period from 2003 to 2006, bone marrow samples of 104 AML patients were analyzed at the Human Genom Center, USM , for the presence of specific and nonspecific numerical and structural chromosome abnormalities. Among these 104, 50 samples were analyzed for the presence of AML1/ETO, PML/RARα and CBFß/MHY11 fusion genes at the Haematology Department, HUSM, employing RT PCR. Out of the 104 samples analyzed cytogenetically, 54 (52 %) showed normal karyotypes, 30 (29 %) showed abnormal karyotypes and 20 samples (19 %) failed to give satisfactory chromosome preparations. FAB subtype specific as well as nonspecific chromosome abnormalities were observed. Out of the 50 samples analyzed for molecular genetic alterations, 22 (44 %) were negative, 15 (30 %) were AML/ETO positive, 12 (24 %) were PML/RARα positive and 1 (2 %) was CBFß/MYH11 positive. In few cases which failed to give satisfactory cytogenetic results, molecular genetic analysis could provide data on the underlying molecular genetic alteration. Through cytogenetic analysis, both specific chromosome abnormalities associated with specific FAB subtypes of AML as well as other random chromosome abnormalities present in the leukemic cells could be detected. So both cytogenetic analysis as well as molecular genetic analysis are important for the diagnostic and prognostic workup of AML patients.

TWO DIFFERENT, THREE WAY COMPLEX, VARIANT PHILADELPHIA CHROMOSOME TRANSLOCATION IN TWO PATIENTS WITH CHRONIC MYELOID LEUKEMIA

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Chronic Myeloid Leukemia (CML), is a clinical myeloprol liferative disorder involving the pluripotent stem cell. The hallmark of CML is a karyotypic marker, the Philadelphia (Ph) Chromosome, originating from a reciprocal t(9 ; 22) (q34 ; q11) translocation between chromosome 9 and 22 and genetically resulting in a fusion BCR –ABL gene. Variant Ph translocations derived through other rearrangements rarely occur. Here we present two cases of Chronic Myeloid Leukemia with variant Ph translocations. Both cases have been diagnosed clinically and haematologically as CML. Karyotype analysis employing GTG banded metaphases of the bone marrow samples of these 2 patients showed complex translocations involving 3 chromosomes. Case 1, a female aged 32 years, showed 46 , XX, der (21) t (9; 21; 22) (q34; q13; q11) karyotype pattern. The second case, also a female, aged 39 years, showed 46 , XX, der (22) t (5 ; 9 ; 22) (q11; q34 ; q11) karyotype pattern. Both karyotypes were suggestive of variant Philadelphia translocation cytogenetically, which was later confirmed through molecular analysis for bcr-abl fusion gene transcripts. Complex chromosome translocations usually involving exchanges between three or more chromosomes, may be formed by multiple simultaneous breaks or some may arise as a result of two or even more, genetic events in close association. Both conventional cytogenetic techniques and molecular genetic techniques are important in identifying variant Philadelphia chromosome translocations in chronic myeloid leukemias.

SCREENING FOR BETA-GLOBIN MUTATIONS BY PCR-RFLP AMONG KELANTAN MALAYS WITH BETA-THALASSEMIA MAJOR

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Beta-thalassemia major is an autosomal recessive disorder characterized by severe hypochromic microcytic anemia. Beta-thalassemia occurs as a result of mutation in the β-globin gene (HBB) which is located on chromosome 11. Over 200 mutations have been reported in association with thalassemia. Six common mutations in the Malay population were studied which were IVS-1 nt5 (G→C), IVS-1 nt1 (G→T), codon 26 (G→A), codon 19 (A→G), codon 15 (G→A) and codon 41-42 (4 bp del). A cross sectional study was conducted in 35 Kelantan Malay β-thalassemic patients who attended the Hospital Universiti Sains Malaysia. DNA was extracted from blood and subjected to PCR amplification. The amplicons were then digested with six restriction enzymes, Cac8I, BslI, AluI, SfcI, MnlI and TaqI to detect the presence of these mutations. Five mutations were detected namely, IVS-1 nt5 (G→C), IVS-1 nt1 (G→T), codon 26 (G→A), codon 41-42 (4 bp del) and codon 19 (A→G). One mutation in codon 15 (G→A) was not detected. Among these, the two most common mutations were codon 26 (G→A) and IVS-1 nt5 (G→C), which accounted for 74.3% and 48.6% respectively. None of the six mutations were detected in two patients. Our results add to the existing data on the common β-globin gene mutations among the Kelantan Malays. A larger sample size is needed to confirm the spectrum of β-thalassemia mutations and its clinical implications among this Malay ethnic group.