for GJB2 mutations (35delG/M34T).
Conclusions: Additional investigation of subtelomeric aberrations in standard karyotype has an important role to play in making a precise diagnosis of the child with developmental delay and in his genetic counseling and subsequent treatment.

Keywords: Subtelomeric chromosome rearrangement, Developmental delay, Congenital anomalies

3.P2

Telomeric fusions and chromosome instability in familial papillary thyroid cancer patients

Milena Pisu[1], Daniela V Frau[2], Paola Caria[2], Silvia Cantara[1], Serena Capuano[1], Marco Capezzone[1], Stefania Marchisotta[1], Giulia Busonero[1], Caterina Formichi[1], Furio Pacini[1], Roberta Vanni[2]
[1]University of Siena Department of Internal Medicine, Endocrinology and Metabolism and Biochemistry, Section of Endocrinology and Metabolism, Cagliari, Italy
[2]University of Cagliari, Department of Biomedical Science and Technology, Cagliari, Italy

Chromosome instability, a genetic condition inducing a large number of genetic and chromosome alterations, is a shared feature of most cancers. Using a molecular approach, recent studies on the telomere–telomerase complex in the peripheral blood of patients with familial papillary thyroid cancer (FPTC) have shown the presence of short telomeres and hTERT gene amplification and expression. To study the phenomenon at the chromosomal level, we investigated the presence of chromosome breakage, telomeric association (TA) and telomeric fusion (TF) in phytohemagglutinin-M-stimulated lymphocytes from FPTC patients, unaffected family members (UFM) and healthy subjects (HS). T lymphocyte cultures were obtained from peripheral blood of 13 FPTC patients, 6 UFM and 10 HS. Spontaneous chromosomal instability was evaluated by scoring for TA and chromosomal breakage (gaps, breaks, centric fissions, acrocentric fragments, rings, min/dmin) Giemsa-stained metaphases (200/sample), whereas TF was studied on PNA-telomeric probe (Q-FISH) hybridized metaphases (50/sample). Q-FISH also fluorescence in situ hybridization (FISH). FPTC patients displayed increased spontaneous chromosome instability, both with conventional (p=0.045) and molecular (p=0.026) cytogenetic analysis as compared with the other categories. FPTC patients showed a higher frequency of telomeric association than UFM (p=0.00034). Q-FISH analysis revealed that FPTC patients have shorter telomeres (dark telomeres, p=0.015) as compared with other groups and have a significantly increased number of non-acrocentric (p=0.039) and acrocentric fusions (p=0.04) and acentric fragments with double telomeric signal (p=0.005) as compared with HS. A few cells from FPTC patients showed three copies of the hTERT gene as compared with UFM and HS cells; however, the result was not statistically significant. Our data confirm the presence of short telomeres in cells from FPTC patients and demonstrate that this phenomenon favours elevated chromosome instability, including telomeric fusion.

Supported by AIRC through a fellowship to M.P, and FIRB.

Keywords: Telomeric fusion, Chromosome instability, Familial papillary thyroid cancer

3.P3

Chromosome 1p36 deletion syndrome: a report on 4 cases

Cristina Candeias[1], Manuela Mota Freitas[1], Joana Ribeiro[1], Fernanda Paula Oliveira[1], Joaquim Aguiar[1], Natália Oliva Teles[1], Gabriela Soares[2], Inês Carrilho[3], Márcia Martins[4], Hildeberto Correia[1], Maria da Luz Fonseca e Silva[1]
[1]Centro de Genética Médica Jacinto de Magalhães, INSA Departamento Genética, Unidade Citogenética, Porto, Portugal
[2]Centro de Genética Médica Jacinto de Magalhães, INSA Departamento de Genética, Unidade de Genética Médica, Portugal
[3]Centro Hospitalar do Porto Hospital Maria Pia, Portugal
[4]Centro Hospitalar do Porto Maternidade Júlio Dinis, Portugal

Chromosome 1p36 deletion syndrome (MIM #607872) was first described in 1997 by Shapira et

al. This condition is compatible with a monosomy of the 1p36 band in the distal region of the short arm of chromosome 1 and is the most common terminal deletion in humans, with an estimated prevalence of approximately 1 in 5,000 live births. This constitutional deletion is associated with mental retardation, developmental delay, seizures, hypotonia and heart defects. The syndrome is also characterized by several distinct dysmorphic features, including large anterior fontanels, microcephaly, brachycephaly, deep-set eyes, flat nose and nasal bridge, and pointed chin. The 1p36 band is not very clearly visible using classical cytogenetics, and it is therefore difficult to detect these deletions in banded karyotypes. Fluorescence in situ hybridization (FISH) and multiplex ligation-dependent probe amplification (MLPA) analysis have increasingly been used, in addition to classical cytogenetic analysis, in children with mental retardation in order to identify this chromosomal abnormality.

The authors present four patients between 1 month and 14 years of age with apparently normal karyotypes. Using molecular cytogenetic techniques, all cases showed a "pure" 1p36 deletion: three were detected by FISH (CEB108/T7, located at 1p36.3, Vysis) and are "de novo"; the fourth was detected by MLPA (P036 and P070, MRC Holland) analysis, and its origin is still unknown.

The phenotypes of these patients are described and compared with other cases having this syndrome, described in the literature. We also emphasize the importance of good clinical characterization in order to establish the best cytogenetic strategy to assure accurate diagnosis

Keywords: Telomere, Deletion, 1p36, Monosomy

3.P4

Subtelomeric deletion syndrome: can easily be overlooked

Oğuz Çilingir, Esra Dikoğlu, Muhsin Özdemir, Beyhan Durak Aras, Ilgin Gizem Bedir, Sevilhan Artan
Eskisehir Osmangazi University, Medical Faculty, Medical Genetic Department, Eskisehir, Turkey

The molecular characterization of several rearrangements interpreted as simple duplications led to the discovery that most of them were in fact inverted duplications associated with the deletion of the portion distal to the duplication. Inverted 8p duplication deletions are one of the rare chromosomal rearrangements in this group. We report on clinical and cytogenetic findings in a case of inverted duplication of region 8p, de novo. A severe mentally retarded girl with kyphoscoliosis, orthopedic abnormalities, congenital heart defect, seizures, agenesis of the corpus callosum, refractory vomiting and minor facial alterations is described. In addition, she had had surgery for vesicoureteral reflux and tracheoesophageal fistula. A telomeric deletion of region 8p was confirmed with fluorescent in situ hybridization using a telomeric probe for chromosome 8p. The mother had a normal karyotype, while the patient's father was deceased. Molecular analysis is planned to confirm the results. This deletion syndrome is more frequent than previously thought. Careful investigation is required to uncover the imbalance derived from this small deletion, which is easily overlooked.

3.P5

Detection of subtelomeric rearrangements in 1180 patients: FISH and MLPA contribution

Manuela Mota Freitas, Joana Ribeiro, Cristina Candeias, Elisa Lopes, Fernanda Paula Oliveira, Joaquim Aguiar, Maria Céu Ribeiro, Silvia Pires, Natalia Oliva Teles, Hildeberto Correia, Maria Luz Fonseca Silva
Centro de Genética Médica Jacinto Magalhães, INSA, I.P. Citogenetica, Porto, Portugal

Mental retardation (MR) is a major social, educational and health problem affecting 3% of the population. Subtelomeric chromosome aberrations are one of the major causes of MR with or without multiple anomalies; previous studies have shown that these rearrangements are responsible for 3–6% of unexplained mental retardation.

Between 2000 and 2010 in the Cytogenetics Unit, Centro de Genética Médica Jacinto de Magalhães, INSA (Portugal), the subtelomeric regions of all the chromosomes were analysed in 1,180 individuals whose karyotype had been considered normal. The reasons for referral included (1) psychomotor developmental delay or (2) mental retardation with or