

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 fontanelles, 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

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The molecular characterization of several rearrangements interpreted as simple duplications led to 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 tracheo-esophageal 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

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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

without dysmorphisms. Until 2007, the analysis of metaphases, obtained from cultured lymphocytes following standard protocols, was performed by fluorescence in situ hybridization (FISH): the first kit to be used was the Chromoprobe Multiprobe-TM (Cytocell) kit (until 2005), which was followed by the TotalVysion Multi-Color FISH Probe (Vysis). In 2007, multiplex ligation-dependent probe amplification (MLPA) was implemented in the laboratory using kits P036 and P070 (MRC, Holland). All the unbalanced cases detected by MLPA were confirmed by FISH.

Of a total of 1,180 individuals, 62 (5.3%) showed chromosomal alterations: 60 in the subtelomeric regions and 2 in the control regions. It was not possible to perform any familial studies in 12 of the 62 cases (1.0%), and therefore the results were considered inconclusive. In the other 50 abnormal cases, the parental investigation allowed us to conclude that 30 (2.5%) of these patients had chromosomal abnormalities “de novo” that might be responsible for the clinical phenotype; the remaining 20 possibly abnormal cases (1.7%) were considered polymorphisms without pathological significance since the apparent deletion or duplication had been inherited from phenotypically normal parents.

The authors compare the results obtained in the individuals in the present study with literature reports and highlight the advantages/disadvantages of each technique.

**Keywords:** Subtelomeric rearrangements, FISH, MLPA

### 3.P6

#### Study of subtelomeric rearrangements in a cohort of 569 pediatric patients with developmental delay

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Submicroscopic telomere imbalances are a significant cause of mental retardation (MR) with or without other phenotypic abnormalities.

Patients were referred to the department of medical genetics by pediatricians, pediatric neurologist and clinical geneticist. We have analysed a population of 569 patients with MR or psychomotor retardation and in some cases with dysmorphic features and/or malformations.

In all cases, we performed a karyotype and studied subtelomeric rearrangements. Subtelomeric rearrangements have mostly been supported by multiplex ligation-dependent probe amplification kits P036 and P070. Fluorescence in situ hybridization analysis was also carried out on the remaining cases using Vysis TM ToTel Vysion Probe Panel. When a subtelomeric rearrangement was detected, the study of the parents was also performed.

We found a pathogenic genomic imbalance in 37 cases (6.5%). In 71.4%, the alteration was “de novo”, and 12 of the remaining cases were inherited from either one of the progenitors. From these 37 cases, six cases were polymorphisms and the rest could be the cause of developmental delay.

Some of these results corresponded with known syndromes, like the 1p36 syndrome, the del22q13p syndrome, or the 3q29 microdeletion syndrome. Other alterations affected a few patients and were to date still quite unknown.

Our results confirm previous findings on the relevance of subtelomeric rearrangements in the etiology of MR. The high proportion of familiar rearrangements emphasizes their importance for genetic counseling.

In the near future, common use of high-resolution microarray system that covers the whole human genome will help identify some genes responsible for genetic disorders, including MR related syndromes.

#### 4. DNA repair deficiency disorders. Chromosomes Mutagenesis

### 4.P1

#### Human lymphocyte micronucleus genotoxicity test with an organophosphorus pesticide diazinon

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In the present study, the genotoxic effects of commercial formulation of an organophosphorus