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FISH spots microdeletion in heart defects

P. Ferraz-Gameiro* J. Ferrão* C. Mendes* L. M. Pires* E. Matoso* and I.M. Carreira*

* Laboratório de Citogenética, Instituto de Biologia Médica, Faculdade de Medicina de Coimbra, Portugal
icarreira@fmed.uc.pt

The 22q11.2 microdeletion is found in most of DiGeorge and velocardiofacial syndromes. These individuals have a wide range of anomalies including congenital heart disease, palatal abnormalities, characteristic facial features, hypocalcaemia, immune deficiency, and learning difficulties. Congenital heart disease, particularly conotruncal malformations are associated with 29% of deletions. This syndrome may be inherited as an autosomal dominant trait, but the majority of patients (93%) have a *de novo* deletion. To access the presence of the microdeletion in those individuals whose phenotipic changes suggested abnormalities in chromosome 22, a study has been made in several children with congenital heart defects.

In the present study, the screening for the microdeletion 22q11.2 was evaluated in a total of 90 children selected by the presence of specific clinical features associated, such as: congenital heart disease (74%), palatal abnormalities and other dismorfisms without heart defect (26%). The diagnosis of the 22q11.2 deletion was made by *fluorescent in situ hybridization* (FISH) using commercially specific DNA probes (TUPLE1 and D22S75) (Figure 1). This screening was also made by *multiplex ligation-dependent probe amplification* (MLPA) using SALSA KIT P250 DiGeorge. Affected children parents were evaluated to infer familial transmission.

Two microdeletions were found in this study group of 90 children. With data from the laboratory, referring to the years 1994 to 2007, it was detected in a total of 406 cases, 22 microdeletions. All of these cases include at least two anomalies related to the 22q11.2 deletion, in different combinations confirming the high variability of 22q11.2 deletion phenotype. Facial features were present in 20 cases. Congenital heart defect was the major common structural anomaly reported in 19 of the affected probands, 12 of which had a conotruncal defect. The three individuals with the deletion but without cardiac anomaly, showed other phenotypes such as immune deficiency and hypocalcaemia. The parents of the 22 patients with the deletion were also tested with the same DNA probes to evaluate a possible inherited transmission, all shown normal results.

The screening for 22q11.2 microdeletion should always be applied to those who have congenital conotruncal heart defects. However, there are other phenotypic traits associated with the microdeletion like hypocalcaemia, without congenital heart defects, which makes it urgent to consider these non-heart defect phenotipic alterations in order to obtain a more accurate diagnosis when there is suspicion of 22q11.2 deletion. The cases in which there was absence of the microdeletion and the presence of CATCH 22 phenotype (Cardiac, Abnormal facies, Thymic hypoplasia, Cleft palate, Hypocalcaemia) the search in other candidate regions was considered , for example the DiGeorge2 in 10p by FISH and other molecular studies such as MLPA.

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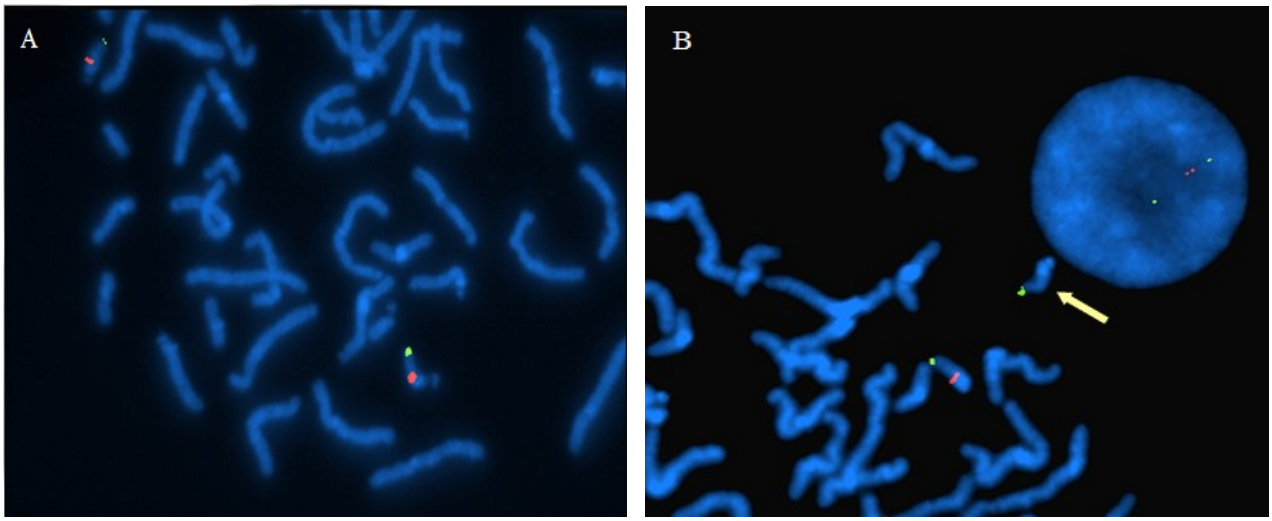

Fig. 1. FISH studies using D22S75 DNA Probe. The green signal shows the telomeric control region 22q13.3 and red signal the DiGeorge critical region 22q11.2.
(A) metaphase cell with two normal chromosomes 22.
(B) metaphase cell and an interphase cell with a normal chromosome 22 and a del(22)(q11.2q11.2). Arrow head indicate a chromosome 22 with q11.2 deletion.

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