Partial isodisomy for maternal chromosome 7 and short stature in an individual with a mutation at the COL1A2 locus


This article describes a third case of maternal isodisomy for the long arm of chromosome 7. The way that the case was identified is intriguing. His mother was included in a study of collagen in women with post-menopausal osteoporosis. A mutation was identified in the β2 chain of type I collagen causing a serine for glycine substitution at position 661. Relatives were screened for the mutation as part of the study and her 30 year old son was found to be homozygous for the mutation. He had features of osteogenesis imperfecta but was disproportionately short and his birth weight at term had been 4.5 lbs. On further investigation maternal isodisomy was confirmed. The previous cases of maternal isodisomy for chromosome 7 both had cystic fibrosis but were investigated further because they also had short stature out of keeping with the diagnosis.

JUDITH GOODSHIP

Complete characterization of a large marker chromosome by reverse and forward chromosome painting


The introduction of aliphid centromere probes has allowed additional marker chromosomes to be typed on the basis of the origin of their centromeres, but these authors show how unwise it is to assume that the origin of the centromere indicates the origin of a whole marker chromosome. In the subject of this report, the marker chromosome was separated from the rest of the chromosomes by flow sorting and a library of probes specific to the separated marker created by the degenerate oligonucleotide primed PCR (DOP-PCR) technique. This library was then hybridised to the patient’s metaphases and painted the whole of the marker chromosome, the pericentromeric area of chromosome 7, the distal long arm of chromosome 5, and the distal short arm of the X. Libraries for chromosomes 5, 7, and X were then used to discover which part of the marker was derived from each of the three constituent chromosomes, and a cosmid used to determine the orientation of the pericentromeric region. The technique requires that the marker be large and distinct enough to sort from the normal chromosomes but this case beautifully illustrates the potential of the reverse painting technique for characterising regions of unknown origin.

J. C. K. BARBER

Association between polymorphism of the glycogen synthase gene and non-insulin-dependent diabetes mellitus


There is strong evidence that non-insulin dependent diabetes mellitus (NIDDM) is a genetic disorder. Concordance in monzygotic twins nears 90%, and the lifetime risk for offspring of one parent with NIDDM is about 40%. The storage of glucose as glycogen in skeletal muscle is frequently impaired in patients with NIDDM and their relatives, suggesting the gene for glycogen synthase, a key enzyme in this pathway, as a candidate gene. The cDNA for glycogen synthase identifies two polymorphic alleles, A, and A1, with XbaI. The gene is on chromosome 19. The A, or A1, genotype was found in 30% of 107 patients with NIDDM, but in only 8% of 164 non-diabetic subjects without a family history of NIDDM (p < 0.001). The diabetic patients with the A1 allele had a stronger than normal family history of NIDDM (p = 0.019), a higher prevalence of hypertension (p = 0.008), and a more severe defect in insulin stimulated glucose storage (p = 0.001) than the diabetic patients with the A allele. However, the concentration of the enzyme in biopsy specimens of skeletal muscle from the patients with the A allele was normal, and the mutation responsible for the XbaI polymorphism is intrinsic and well downstream of the stop codon, suggesting that these results are an example of allelic association and that mutations in the glycogen synthase gene are unlikely to be a direct cause of NIDDM.

ANDREW NORMAN

Abnormal expression of dystrophin-associated proteins in Fukuyama-type congenital muscular dystrophy


The exciting identification of dystrophin as the abnormal gene product in Duchenne muscular dystrophy has now given way to studies of the complex cellular interactions of this protein in both the normal and pathological states. Several sarcolemmal glycoproteins have been observed to participate in these interactions, collectively known as dystrophin associated proteins, part of whose function is to provide a link to laminin in the extracellular matrix. Disruption of this link is thought to underlie sarcolemmal instability and consequent muscle necrosis. In this elegant report, the authors show, by immuno-histochemical methods, that dystrophin expression is normal in Fukuyama-type congenital muscular dystrophy (FCMD) but that the expression of dystrophin related protein, notably 43 DAG, is greatly reduced. These authors have already identified a similar deficiency of 50 DAG in severe childhood autosomal recessive muscular dystrophy (SCARMD). It is intriguing to observe abnormalities of related sarcolemmal proteins as the underlying basis in diseases which are phenotypically similar to DMD and SCARMD and so distinct (DMD and FCMD). In practical terms, the observed deficiency appears to be pathognomonic and will be of value diagnostically. Moreover, clinical practice and counselling will be aided by further studies of this nature aimed at defining the relationship between FCMD and the other forms of congenital muscular dystrophy, classification of which is currently based on clinical criteria for want of better.

W REARDON

Rearrangement of the PAX3 paired box gene in the paediatric solid tumour alveolar rhabdomyosarcoma


The human PAX3 gene maps to chromosome band 2q35 and belongs to the paired box family of DNA binding proteins, originally isolated by homology with Drosophila.