Acromesomelic dysplasia Maroteaux type (AMDM) (OMIM 602875) is a rare autosomal recessive skeletal dysplasia with an estimated prevalence of 1/1,000,000. It is characterised by severe dwarfism with shortening of the middle and distal segments of the limbs. Although the patients have normal length and weight at birth, a skeletal disorder can be suspected by one year of age. Mutations in the NPR2 gene which encodes for the natriuretic peptide receptor B (NPR-B) is the underlying genetic cause of this disorder.

Objective: Genetic confirmation of AMDM and the identification of the causal mutations in NRP2 gene

Methods: A total of 8 individuals, belonging to 7 families, diagnosed of AMDM plus relatives were referred from UK, France, India and Spain for genetic analysis. The patients fulfilled clinical and radiological criteria of AMDM and the informed consent was obtained. Molecular genetic study: DNA was extracted from peripheral blood leukocytes by standard techniques. All the coding exons as well as intro-exon boundaries of NRP2 gene were amplified and directly sequenced by Sanger method.

Results: The clinical diagnosis was genetically confirmed in all the patients. Ten novel mutations were identified and each mutation was unique for each patient (P) or family (F). For the description of the genotypes of the patients see the table 1. Electrophorograms of mutations from families 1, 2, 3 & 4; see figures 1, 2, 3, 4.

Conclusions:

1) We have identified ten novel mutations in NRP2 as the cause of AMDM, which broadens the spectrum of inactivating mutations in this gene.

2) These NRP2 mutations are “private”: unique to individuals and/or families.

3) The identification of the causal mutation in AMDM is important not only to confirm the clinical and radiological diagnosis but to enable a proper genetic counseling and an eventual prenatal diagnosis.

*The authors declare that there are no conflicts of interest.