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FRAGILE X PRENATAL STUDIES: MOLECULAR ANALYSES OF 890 PREGNANCIES

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We have performed fragile X prenatal studies for 890 pregnancies of 646 women with intermediate (45-54 repeats), premutation (55-200 repeats), or full mutation (>200 repeats) alleles. The studies included 156 amniotic fluid and 742 chorionic villus samples. For 8 pregnancies, both amniocytes and chorionic villi were analyzed due to: unusual findings (3), maternal cell contamination (1), or other technical difficulties (4). Of the 890 pregnancies, the expanded allele was transmitted in 457 (51.3%) instances and was inherited as a full mutation in 209 (45.7%) of them. Twelve (15.8%) of 76 intermediate alleles were unstably transmitted with most size changes increasing from 1 to 4 repeats. Notable exceptions were an expansion of 31 repeats (54 to 85) and a contraction of 20 repeats (53 to 33). Contractions in repeat size were observed in a total of 13 (3.1%) pregnancies in women carrying alleles of 52 to 115 repeats. To confirm the prenatal studies DNA from cord blood was analyzed for 17 amniotic fluid and 65 chorionic villus samples. Analyses of the cord blood confirmed all of the prenatal studies which identified 43 normal, 10 intermediate, 18 premutation and 6 full mutation alleles. Prenatal studies were also performed for two unrelated females who had inherited a revertant allele from their mothers (145 to 43 repeats; 82 to 33 repeats). In both cases the revertant allele was stably transmitted to the offspring. Follow-up information showed that 85/92 (92.4%) pregnancies with full mutation males were terminated as were 69/94 (73.4%) pregnancies with full mutation females. Three pregnancies with males that inherited premutation alleles were terminated: one with 180 repeats and two due to reductions in multiple fetus pregnancies.