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PRENATAL DIAGNOSIS OF PROPIONIC ACIDEMIA AND METHYLMALONIC ACIDEMIA WITH AMNIOCYTES

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Prenatal diagnosis of propionic acidemia(PA) and methylmalonic acidemia(MMA) were performed by analyzing the incorporation of the radiolabel from propionate-1-^{14}C into protein (trichloroacetic acid insoluble material), with ^{3}H-Leu as an internal control, in amniotic cells for detecting defects in propionate metabolism. Recently, a pregnancy at risk of PA was prenatally diagnosed with this method. The family had a child affected with PA and a normal sibling, who was born after prenatally diagnosed with normal PCC activity (574 pmol/min/mg protein) in amniocytes. The PCC activity (28 pmol/min/mg) and propionate incorporation (34 pmol/hr/mg protein) of cultured amniotic cell from this pregnancy were much lower than the reference ranges of 340-570 pmol/min/mg (n=5) and 180-390 pmol/hr/mg (n=20), respectively, and were similar to the results (7 pmol/min/mg and 16 pmol/hr/mg, respectively) of the PA cell line (GM0371 from NIGMS Human Genetic Mutant Cell Repository, USA). After counseling, the pregnancy was terminated at 21 weeks of gestation as requested by the family. Both propionate incorporation and PCC activity in the fibroblast cultured from the abortus confirmed that the fetus was affected with PA as prenatally diagnosed. A normal fetus was predicted for another pregnancy, which was at risk of MMA, with propionate incorporation at 216 pmol/hr/mg in amniocytes. This baby will be born in June 1990. These prenatal diagnosis of PA and MMA were all confirmed with GC/MS determination of methylcitrate in the amniotic fluid by Dr. L. Sweetman (San Diego, USA). The propionate incorporation method is expected to be applied on chorionic villi samples for prenatal diagnosis of PA and MMA at earlier stage (8 wks) of pregnancy.