01.01
Family study of isolated glycerol kinase deficiency
Kidd, A; Sargent, C; White, I; Auchterlonie, I; Kirk, J; Moore, S; Dean, J
(1) Department of Medical Genetics, Aberdeen Royal Infirmary, Aberdeen
(2) Dept of Pathology, Cambridge University, Tennis Court Road, Cambridge
(3) Dept of Biochemistry, Aberdeen Royal Infirmary, Aberdeen
(4) Dept of Paediatrics, Aberdeen Royal Infirmary, Aberdeen
(5) Dept of Paediatric Biochemistry, Edinburgh Sick Children's Hospital, Edinburgh

Isolated glycerol kinase deficiency is a very rare X-linked condition. Classically the juvenile form is associated with episodic vomiting, encephalopathy and acidemia and the benign form is usually detected incidentally in asymptomatic adults with pseudohypertriglyceridaemia. The gene on Xp21 was cloned in 1993. We present the clinical, biochemical and molecular findings in three affected males and three obligate carrier females in a family ascertained through a two year old boy presenting with ketoacidic comas. A 17 hour fast he was found comatose in the early morning with a blood glucose of 1.1 mmol/L. He rapidly responded to intravenous glucose. Glycerol levels in blood and urine were very high. Glycerol kinase activity in fibroblasts were 12% of normal. He has remained well since then on a high carbohydrate diet and avoiding fasts. His maternal grandfather aged 66 years and maternal great uncle aged 62 years were also found to have very raised urine and plasma glycerol levels but had been asymptomatic throughout life. The uncle was being treated for "hypertriglyceridaemia". A point mutation in exon 9A causing a cystine to arginine aminoacid change at position 256 in the G6K protein is segregating in affected males and obligate carriers but is absent in two male relatives with normal glycerol levels. Hypoglycaemia has only been reported once before in this condition. This is the first report of benign and juvenile forms of glycerol kinase occurring in the same pedigree.

01.11
The use of tissue specific promoters in the correction of OTC deficiency in mouse models
Trainer, A; Akhurst, R.J.
Duncan Gunn Institute of Medical Genetics, Yorlith NHS Trust, Glasgow

Oxime transcarbamylase deficiency is an X-linked urea cycle disorder with high mortality and morbidity. There are two naturally occurring OTC deficient mouse models; sparse fur and sparse fur ASH. Correction of both the biochemical and phenotypic abnormalities in these mice have been previously demonstrated by means of either hepatic-targeted OTC expression using viral vectors or transgenic approaches utilising the endogenous OTC promoter. The aim of this work was to investigate the feasibility of correcting the metabolic abnormality using tissue specific promoters targeting OTC expression, by transgenic technology, not only to the liver but also to non-hepatic tissues, namely skin and muscle. As a mitochondrial enzyme, OTC will have its effect within the target organ and hence in this system success will depend on the ability of the target organ to act as a 'metabolic sink'. Results show that, despite transgene expression, phenotypic correction of the murine models was not achieved although partial metabolic correction was achieved.