Oxford Molecular Genetics Laboratory
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PYRUVATE DEHYDROGENASE (PDH) DEFICIENCY

INTRODUCTION

Genetic defects in the pyruvate dehydrogenase (PDH) complex are among the most common causes of primary lactic acidosis and neurological dysfunction in infants and young children. Hence, PDH deficiency is one of the main causes of Leigh syndrome. Primary PDH deficiency is caused by mutation(s) in genes encoding subunits of the PDH complex, most commonly *PDHA1*. PDH deficiency has also been associated with defects in the PDH phosphatase, thiamine homeostasis, lipoic acid biosynthesis, and iron-sulphur cluster biosynthesis.

SERVICE

Dr Garry Brown leads a biochemical and genetic service for this group of disorders within our laboratory. Analysis of PDH enzyme activity in fibroblasts is typically the first step.

Dr Garry Brown can be contacted directly for further information about the service:
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Details of the main genetic testing options are also summarised under “Strategy” below.

This service is provided alongside our other mitochondrial disease services, and is NHS Highly Specialised Services (HSS) funded for NHS referrals from England and Scotland.

TESTING

Diagnostic:	Clinically affected patients
Carrier or Presymptomatic:	Relatives of clinically affected patients
Prenatal:	At risk of having an affected child

REFERRALS

- From Hospital Consultants, mainly Clinical Genetics, Neurology, Paediatrics, Metabolic Medicine
- Prenatal referrals are only accepted from Clinical Genetics and / or Prenatal Diagnosis. They must be discussed with the laboratory and arranged in advance.

STRATEGY

- PDH enzyme activity in cultured fibroblasts
- Appropriate genetic testing dependant on PDH enzyme activity and clinical information:
  - Sanger sequencing of *PDHA1*
  - Sanger sequencing of subunits of the PDH complex (*PDHA1*, *PDHB*, *DLAT*, *DLD* & *PDHX*)
  - Sanger sequencing of PDH regulation and co-factor biosynthesis genes (*BOLA3, GLRX5, IBA57, LIAS, LIPT1, LIPT2, NFU1, PDP1, PDP2, SLC19A2, SLC19A3, SLC25A19, SLC25A26, TPK1*)
  - Next generation sequencing (NGS) of all the above 19 genes

TARGET REPORTING TIMES

Routine diagnostic tests (high priority tests will be reported more quickly):

112 calendar days	NGS panel of 19 genes
56 calendar days	Sanger sequencing of specific genes

Carrier/Presymptomatic tests:
14 calendar days
Prenatal testing (includes maternal contamination check): 3 calendar days

N.B. Details are correct for the date of printing only – last updated 14/07/2016