Joshua Hellmann Foundation - Newborn Metabolic Screening Program

Centre of Inborn Errors of Metabolism

The Chinese University of Hong Kong

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Target inborn errors of metabolism (IEM) in this program

	Inborn Errors of Metabolism	**Disease OMIM**	**ACMG[¶] classification**	**Key metabolites**	**Incidence in Chinese[$]**	**Confirmation test(s)[§]**	**Outcome if not diagnosed and treated on time**	**Treatment**	**Causative gene(s) (Gene OMIM)**
	Amino Acid Disorders								
1	*****Phenylketonuria (PKU) (苯丙酮尿症)	#261600	Core	↑ Phe	1 in 14,515[ψ]	1, 2, 4, 5	MR	Diet, drugs	*PAH* (*612349)
2	*****Maple syrup urine disease (MSUD) (楓糖尿病)	#248600	Core	↑ Leu/Ile	1 in 101,624	1, 2, 5 ± 6	MR, early death	Diet, drugs	*BCKDHA* (*608348) *BCKDHB* (*248611) *DBT* (*248610)
3	*****Citrullinaemia type 1 (瓜氨酸血症 1 型)	#215700	Core	↑ Cit	1 in 118,543	1, 5	MR, early death	Diet, drugs	*ASS1* (*603470)

4	*****Argininosuccinic aciduria (精胺丁二酸酶缺乏症)	#207900	Core	↑ Cit	1 in 592,717	1, 2, 5	MR, early death	Diet, drugs	*ASL* (*608310)
5	*****Homocystinuria (高胱氨酸尿症)	#236200	Core	↑ Met	NA	1, 2, 5 ± 6	MR, neuromuscular disability	Diet, drugs	*CBS* (*613381)
6	*****Tyrosinaemia Type 1 (酪氨酸血症 1 型)	#276700, #276600, #276710	Core	↑ Tyr, SA	NA	1, 2, 5	MR, early death	Drugs, liver transplantation	*FAH* (*613871)
7	Arginase deficiency (精氨酸血症)	#207800	2°	↑ Arg	NA	1, 5	MR, neuromuscular disability	Diet, drugs	*ARG1* (*608313)
8 (Group)	*****Defects of biopterin cofactor biosynthesis and regeneration (生物喋呤合成或再生缺陷引起的苯丙酮尿症)	#233910 #261640 #261630 #264070	2°	↑ Phe	1 in 14,515#	1, 2, 4, 5	MR	Diet, drugs	*GCH1* (*600225) *PTS* (*612719) *QDRP* (*612676) *PCBD1* (*126090)
9	*****Citrullinaemia type 2 (Citrin deficiency) (瓜氨酸血症 2 型)	#605814	2°	↑ Cit	1 in 20,000	1, 2, 5	Neonatal hepatitis	Diet	*SLC25A13* (*603859)
10 (Group)	Hypermethioninaemia (甲硫胺酸上升相關疾病)	#250850 #606664	2°	↑ Met	NA	1, 2, 5	MR, neuromuscular disability	Diet, drugs	*MAT1A* (*610550) *GNMT*

									(*606628)
	Organic Acid Disorders								
11	*Propionic acidaemia (PA) (丙酸血症)	#606054	Core	↑ C3	1 in 600,562	2, 3, 5	MR, early death	Diet, drugs	*PCCA* (*232000) *PCCB* (*232050)
12 (Group)	*Methylmalonic aciduria (MUT, cblA/B) (甲基丙二酸血症)	#251000, #251100, #251110	Core	↑ C3	1 in 101,625	2, 3, 4, 5	MR, early death	Diet, drugs	*MUT* (*609058) *MMAA* (*607481) *MMAB* (*607568)
13	*Isovaleric acidaemia (IVA) (異戊酸血症)	#243500	Core	↑ C5	1 in 660,562	2, 3, 5	MR, early death	Diet, drugs	*IVD* (*607036)
14	*ß-ketothiolase deficiency (BKT) (酮硫解酶缺乏症)	#203750	Core	↑ C5OH, C5:1	NA	2, 3, 5	MR, early death	Diet, drugs	*ACAT1* (*607809)
15	*Glutaric acidaemia type 1 (GA1) (戊二酸血症第 1 型)	#231670	Core	↑ C5DC	1 in 101,625	2, 3, 5	MR, early death	Diet, drugs	*GCDH* (*608801)
16	*3-Hydroxy-3-methylglutaryl-CoA lyase deficiency (HMG) (白胺酸代谢異常症 or 三羥基三甲基戊二酸血症)	#246450	Core	↑ C5OH	NA	2, 3, 5	Sudden/early death	Diet	*HMGCL* (*613898)
17	*Multiple carboxylase deficiency (MCD) (多發性羧化酶缺乏症)	#253270, #253260	Core	↑ C5OH	1 in 296,359	2, 3, 4, 5	MR, early death	Drugs	*HLCS* (*609018) *BTD*

									(*609019)
18	3-Methylcrotonyl-CoA carboxylase deficiency (3MCC) (3-甲基巴豆醯輔酵素羧化酵素缺乏症)	#210200, #210210	Core	↑ C5OH	1 in 18,522	2, 3, 5	MR, early death	Diet, drugs	*MCCC1* (*609010) *MCCC2* (*609014)
19	2-Methyl-3-hydroxybutyric aciduria (2M3HBA) (2-甲基 3-羥基丙二酸尿症)	#300438	2°	↑ C5OH	NA	2, 3, 5	Asymptomatic to MR	Diet	*HSD17B10* (*300256)
20	Malonic aciduria (丙二酸尿症)	#248360	2°	↑ C3DC	NA	2, 3, 5	MR	Diet, drugs	*MLYCD* (*606761)
21	3-Methylglutaconic aciduria type I (3MGA) (3 型 3-甲基戊二酸尿症)	#250950	2°	↑ C5OH	NA	2, 3, 5	MR, early death	Diet, drugs	*AUH* (*600529)
22	Isobutyryl-CoA dehydrogenase deficiency (IBG) (異丁酰輔酶 A 脫氫酶缺乏症)	#611283	2°	↑ C4	NA	2, 3, 5	MR, early death	Diet, drugs	*ACAD8* (*604773)
23	2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG) (2-甲基丁酰輔酶 A 脫氫酶缺乏症)	#610006	2°	↑ C5	1 in 330,281	2, 3, 5	Asymptomatic to MR	Nil specific	*ACADSB* (*600301)
24 (Group)	Cbl C/D (甲基丙二酸血症)	#277400, #277410	2°	↑ C3	NA	2, 3, 5 ± 6	MR, early death	Diet, drugs	*MMACHC* (*609831) *C2ORF25* (*611935)
	Fatty Acid Oxidation Disorders								
25	*****Primary carnitine deficiency /	#212140	Core	↓ C0	1 in	3, 5	Sudden	Drugs	*SLC22A5*

	carnitine update defect (CUD) (卡尼丁吸收障礙)				118,543		death/early death		(*603377)
26	*****Medium-chain acyl-CoA dehydrogenase deficiency (MCAD) (中鏈醯輔酶 A 去氫酶缺乏症)	#201450	Core	↑ C8	1 in 660,562	2, 3, 5	Sudden death/early death	Diet, drugs	*ACADM* (*607008)
27	*****Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD) (極長鏈醯輔酶 A 去氫酶缺乏症)	#201475	Core	↑ C14:1	NA	3, 5	Sudden death/early death	Diet, drugs	*ACADVL* (*609575)
28	Long-chain 3-hydroxyl-acyl-CoA dehydrogenase deficiency (LCHAD) (長鏈醯輔酶 A 去氫酶缺乏症)	#609016	Core	↑ C16OH	NA	3, 5	Sudden/early death	Diet	*HADHA* (*600890)
29	Trifunctional protein deficiency (TFP) (三種功能蛋白缺乏症)	#609015	Core	↑ C16OH	NA	3, 5	Sudden/early death	Diet	*HADHA* (*600890) *HADHB* (*143450)
30	*****Short-chain acyl-CoA dehydrogenase deficiency (SCAD) (短鏈醯輔酶 A 去氫酶缺乏症)	#201470	2°	↑ C4	1 in 118,543	2, 3, 5	MR	Nil specific	*ACADS* (*606885)
31	*****Carnitine palmitoyltransferase I deficiency (CPT1) (卡尼丁結合酵素一缺乏)	#255120	2°	↑ C0	NA	3, 5	MR, early death	Diet	*CTP1A* (*600528)
32	*****Carnitine palmitoyltransferase II deficiency (CPT2)	#608836, #600649	2°	↑ C16	NA	3, 5	MR, early death	Diet	*CPT2* (*600650)

	(卡尼丁結合酵素二缺乏)								
33	*****Carnitine-acylcarnitine translocase deficiency (CACT) (卡尼丁穿透障礙)	#212138	2°	↑ C16	NA	3, 5	Sudden death/early death	Diet, drugs	*SLC25A20* (*613698)
34	*****Multiple acyl-CoA dehydrogenase deficiency **(**Glutaric aciduria type 2, GA 2) (戊二酸血症第 2 型)	#231680	2°	↑ C4, C5	NA	2, 3, 5	Sudden death/early death	Diet, drugs	*ETFA* (*608053) *ETFB* (*130410) *ETFDH* (*231675)
35	Medium/short-chain hydroxyl-acyl-CoA dehydrogenase deficiency (M/SCHAD) (中/短鏈羥酰基輔酶 A 脫氫酶缺乏症)	#231530	2°	↑ C4OH	NA	3, 5	Asymptomatic to neuromuscular disability	Nil specific	*HADH* (*601609)

*Conditions with an asterisk have been diagnosed and reported locally.

NA: not available

¶ACMG: American College of Medical Genetics (Ref 1 – 2). Core conditions: newborn screening for these disorders are mandated in the United States. 2° conditions: they are part of the differential diagnosis of a core condition, they are clinically significant and revealed with the screening technology but lack an efficacious treatment, or they represent incidental findings for which there is potential clinical significance.

ψThe combined incidence for phenylketonuria and biopterin cofactor biosynthesis and regeneration defects.

§Confirmation tests: 1 – plasma amino acid analysis, 2 – urine organic acid analysis, 3 – plasma free carnitine and acylcarnitine analysis, 4 – other locally available laboratory tests, 5 – genetic analysis, 6 – overseas send out tests (e.g. enzyme study)

$Total incidence of all IEM covered in this program is estimated to be 1 in 4,122 to 1 in 5,882.(Ref 3 – 4).