罕見病及奇難確診疾病計劃

Rare Diseases and Undiagnosed Diseases Program

林青雲教授
病理學專科醫生
香港大學李嘉誠醫學院病理學系臨床教授
Professor Lam Ching-wan
Specialist in Pathology
Clinical Professor, Department of Pathology
Li Ka Shing Faculty of Medicine, HKU

罕見病

- 罕見病，又名孤兒症 (Orphan disease)
- 全球6,930種罕見病
- 80%遺傳疾病
- 世界衛生組織將罕見病定義為患病人數少於佔總人口千分之0.65-1的疾病。

- 在美國，疾病影響少於二十萬人，則被定義為罕見。
  - 影響兩千五百萬美國人和他們的家庭。
- 在歐洲，當疾病影響少於兩千分之一的人，則被定義為罕見 。
  - 影響三千萬的歐盟公民。
- 50%的患者在出生時或者兒童期發病。
- 罕見病患者都要經過輾轉多次才能找到正確診治途徑。

Rare diseases and legislation in China

First national conference for rare diseases in Beijing, 2009

Public awareness of rare diseases is increasing in China. People with rare diseases and their families, patients' advocacy groups, health-care professionals, lawyers, and representatives of the People's Congress are working together to establish a Rare Diseases Prevention and Treatment Law. On the basis of WHO's definition of a rare disease, at least 10 million people are living with rare diseases in China.[1] This estimate seems conservative for a population of more than 1·3 billion in China.

improving patients' access to health care. These groups include the Home of Babies of the Moon—the China Albinism Association, the Haemophilia Home of China (HHC), the Neuro-Muscular Disease Association of China, the China Organisation of Lymphangioleiomyomatosis (LAM-China), and the China-Dolls Care and Support Association. Some organisations have collaborated nationally and internationally, and the disease-specific groups are planning to form an alliance in China.

Lancet. 2010

http://www.chinadolls.org.cn/

GazetteNet
Maryland Community News Online

Families seek to raise awareness at local Rare Disease Day event

Few resources available for some ill children

By Rebecca J. Barnabi Staff Writer

Abby Weinberg was 3 and a half months old when her parents were told she had severe brain damage and probably would not survive to her first birthday.

In 2007, Abby was diagnosed with Aicardi-Goutieres syndrome, an illness so rare that her mother, Stephanie Weinberg, said genetic testing for the disease is not available in the U.S.

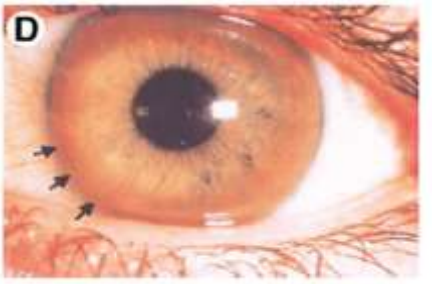
"There's so many things that they don't know yet [about AGS]," Weinberg said. Abby was diagnosed in England while participating in a study on AGS. Weinberg said she thinks the reason why AGS is often undiagnosed or misdiagnosed is because U.S. doctors do not know what to look for.

http://www.somdnews.com/article/20150227/NEWS/150229390/0/families-seek-to-raise-awareness-at-local-rare-disease-day-event&template=gazette

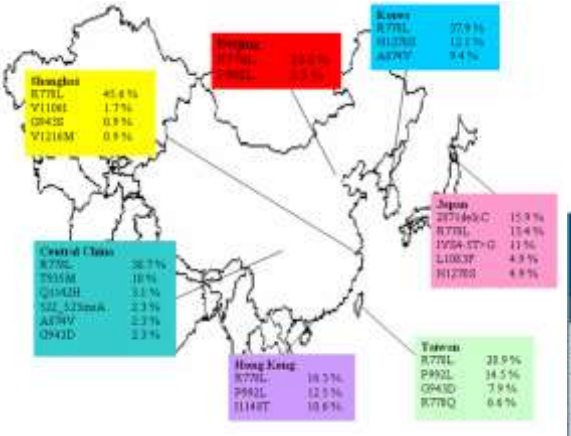
Genetic analysis for *IFIH1* gene

NM_002168.3:c.1178A>T; NP_71451.2:p.Asp393Val

罕見肝病：威爾森氏症 (Wilson Disease)



Geographical Distribution of Common ATP7B Mutations in Various Populations in East Asia



奇難確診疾病 (Undiagnosed Disease)

香港電台 －窗外有藍天

日期： 2014 年 12 月 6 日

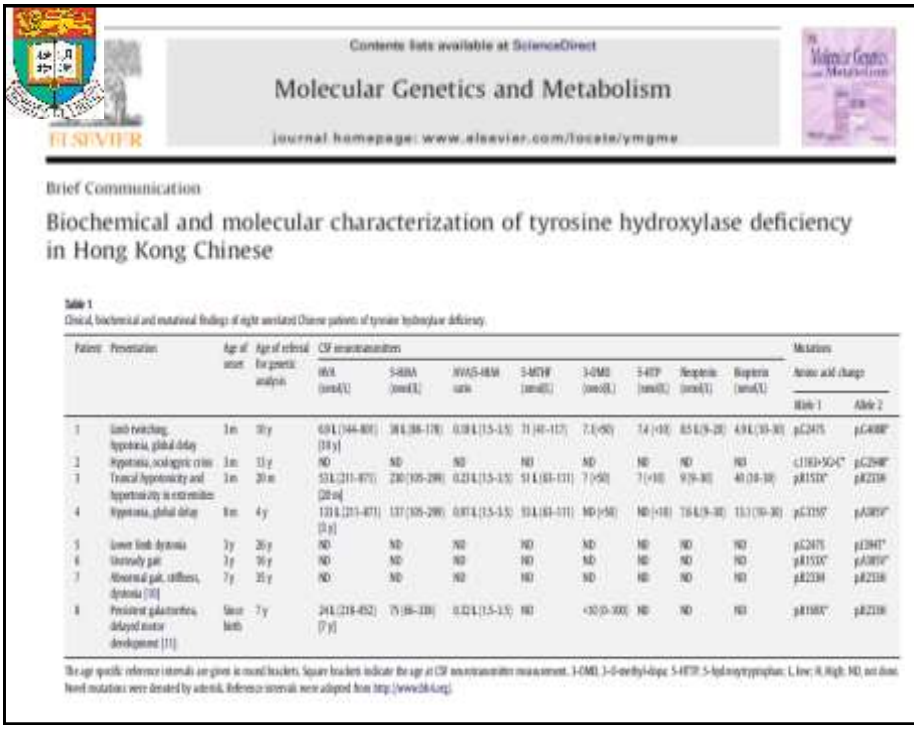
受訪者： 香港大學李嘉誠醫學院病理學系臨床教授林青雲教授

內容： 你是我的夢想

連結： http://programme.rthk.hk/rthk/tv/programme.php?name=tv/underthesamesky2014&d=2014-12-06&p=6383&e=283115&m=episode

Esther(陳秀芳)的大女兒陳思行今年十四歲，在她四個月大的時候，Esther 發現思行與其他同齡嬰兒有明顯差別：全身發軟，對她說話沒有反應，沒有正常的眼神接觸，即使 Esther 帶思行照超聲波、驗血驗尿等，得出的結果都是正常，可惜，隨著思行慢慢成長，症狀愈來愈明顯，現在連行路都有困難，但醫生只能根據思行的基因進行剖析，還未能確診她到底患上什麼病。

Esther 為了能貼身照顧女兒，不得放棄工作做全職媽媽，面對將來的眾多未知數，Esther 依然抱著樂觀的心態應對，相信總有一日，會實現女兒能靠自己走路的夢想。



Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

Brief Communication

Biochemical and molecular characterization of tyrosine hydroxylase deficiency in Hong Kong Chinese

Table 1
Clinical, biochemical and mutational findings of eight unrelated Chinese patients of tyrosine hydroxylase deficiency.

Patient	Presentation	Age of onset	Age of referral for genetic analysis	CSF neurotransmitters								Mutations	
				HVA (nmol/L)	5-HIAA (nmol/L)	HVA/5-HIAA ratio	5-MTHF (nmol/L)	3-OMD (nmol/L)	5-HTP (nmol/L)	Neopterin (nmol/L)	Biopterin (nmol/L)	Amino acid change	
												Allele 1	Allele 2
1	Limb twitching, hypotonia, global delay	3 m	10 y	6.9 L (144-801) [10 y]	38 L (88-178)	0.18 L (1.5-3.5)	71 (41-117)	7.1 (<50)	7.4 (<10)	8.5 L (9-28)	4.9 L (10-30)	p.G247S	p.G408R*
2	Hypotonia, oculogyric crisis	1 m	13 y	ND	ND	ND	ND	ND	ND	ND	ND	c.[18]+5G>C*	p.G294R*
3	Truncal hypotonicity and hypertonicity in extremities	1 m	20 m	53 L (211-871) [20 m]	230 (105-298)	0.23 L (1.5-3.5)	51 L (83-131)	7 (<50)	7 (<10)	9 (9-30)	40 (10-30)	p.R155X*	p.R233H
4	Hypotonia, global delay	9 m	4 y	133 L (211-871) [3 y]	137 (105-298)	0.97 L (1.5-3.5)	53 L (83-131)	ND (<50)	ND (<10)	7.6 L (9-30)	15.1 (10-30)	p.G335V*	p.A385V*
5	Lower limb dystonia	1 y	26 y	ND	ND	ND	ND	ND	ND	ND	ND	p.G247S	p.E394T*
6	Unsteady gait	1 y	16 y	ND	ND	ND	ND	ND	ND	ND	ND	p.R155X*	p.A385V*
7	Abnormal gait, stiffness, dystonia [10]	7 y	35 y	ND	ND	ND	ND	ND	ND	ND	ND	p.R233H	p.R233H
8	Persistent galactorrhea, delayed motor development [11]	Since birth	7 y	24 L (218-852) [7 y]	75 (88-338)	0.32 L (1.5-3.5)	ND	<50 (0-300)	ND	ND	ND	p.R168H*	p.R233H

The age specific reference intervals are given in round brackets. Square brackets indicate the age at CSF neurotransmitter measurement. 3-OMD, 3-O-methyl-dopa; 5-HTP, 5-hydroxytryptophan; L, low; H, High; ND, not done. Novel mutations were denoted by asterisk. Reference intervals were adopted from http://www.bbk4.org.

香港大學奇難確診疾病計劃

- **首個計劃為未能確診的奇難確診疾病患者：**
  - 找出致病基因及基因變異
- **改善疾病管理：**
  - 有效提高罕見基因疾病診斷率
  - 改變治療方法
  - 提供精準遺傳諮詢服務
- **增進醫學知識：**
  - 發現更多罕見病例和新致病基因
- **建立罕見病例患者基因數據庫**

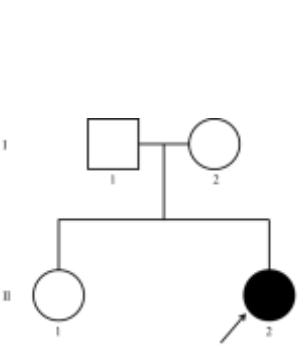
香港大學奇難確診疾病計劃

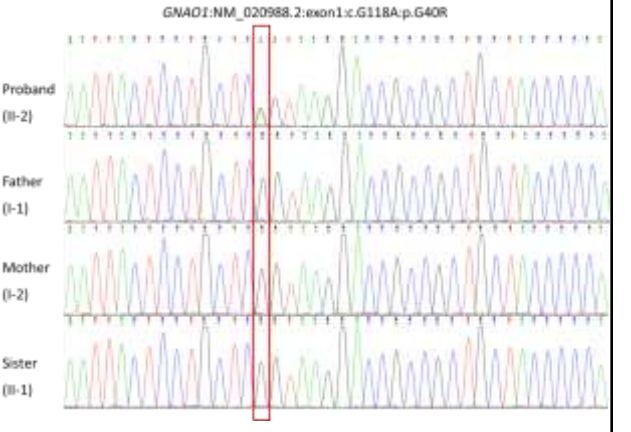
- 10個月大女嬰
- 無癲癇家族史
- 出生後呈現異常抽搐，出生第四天出院
- 雙側上肢反覆抽搐發作及出院後顫動增強
- 體檢：低肌張力，發展遲緩
- 無電解質紊亂或低血糖。尿液代謝篩檢、乾血紙片代謝篩檢及尿液亞硫酸鹽測試皆無異常
- 大腦電腦斷層掃描及磁力共振成像正常

錯義突變 (missense mutation)

***GNAO1*:NM_020988.2:c.118G>A; NP_066268.1:p.Gly40Arg**

新生變異 (*De novo* mutation)





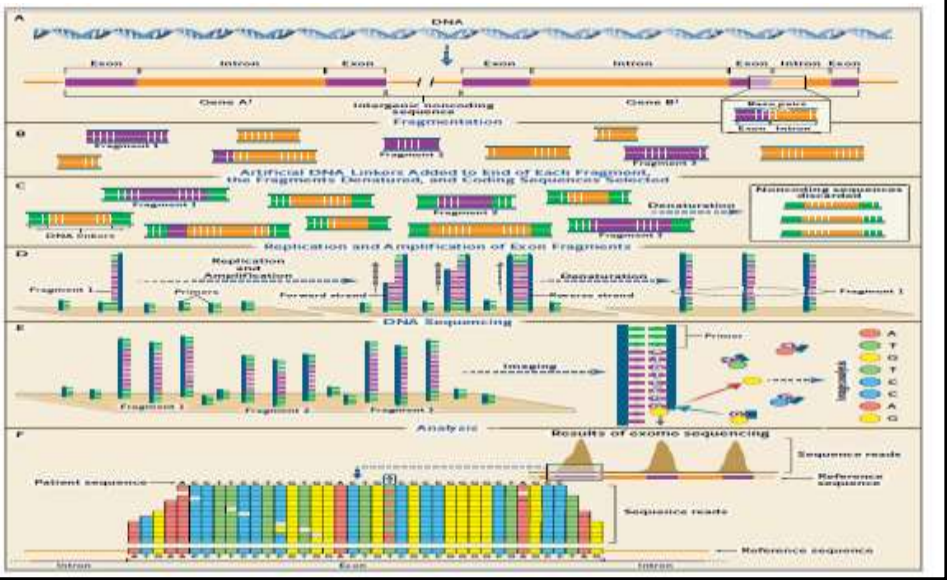
香港大學奇難確診疾病計劃

- 4 歲男童
- 產前無異常
- 表現：
  - 普瑞德威利症候群
  - 整體發展遲緩
  - 低肌張力
  - 呼吸系統問題

串聯基因檢測

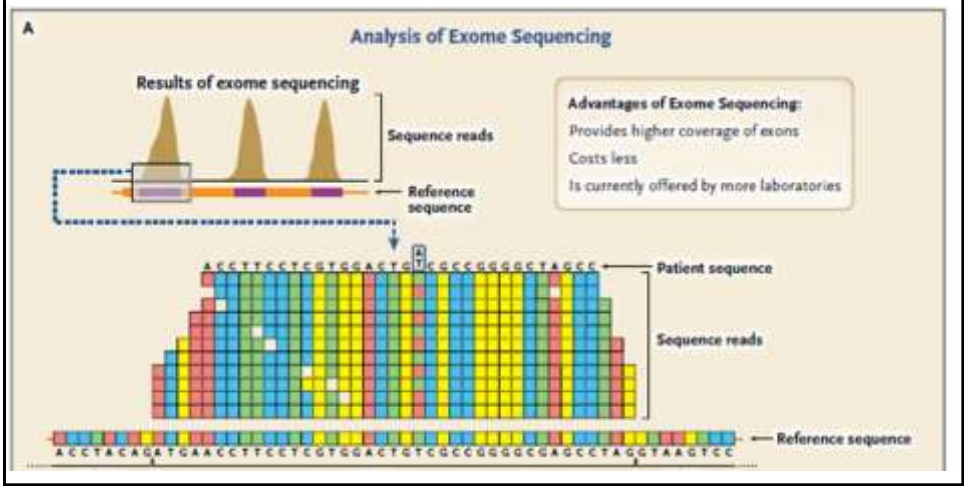
- 普瑞德威利症候群基因甲基化檢測：
  – 陰性
- *PHOX2b*基因檢測(中樞性換氣不足症候群)：
  – 陰性
- 強直型肌肉萎縮症 CTG三聯核酸重複檢測
  – 陰性

並聯基因定序檢測：
可同時檢測2萬個基因



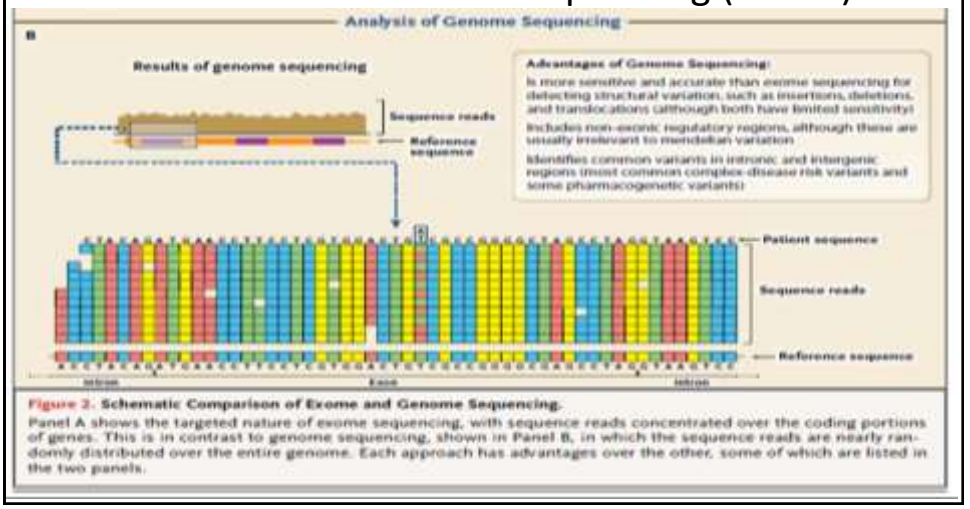
臨床全外顯子基因組定序檢測

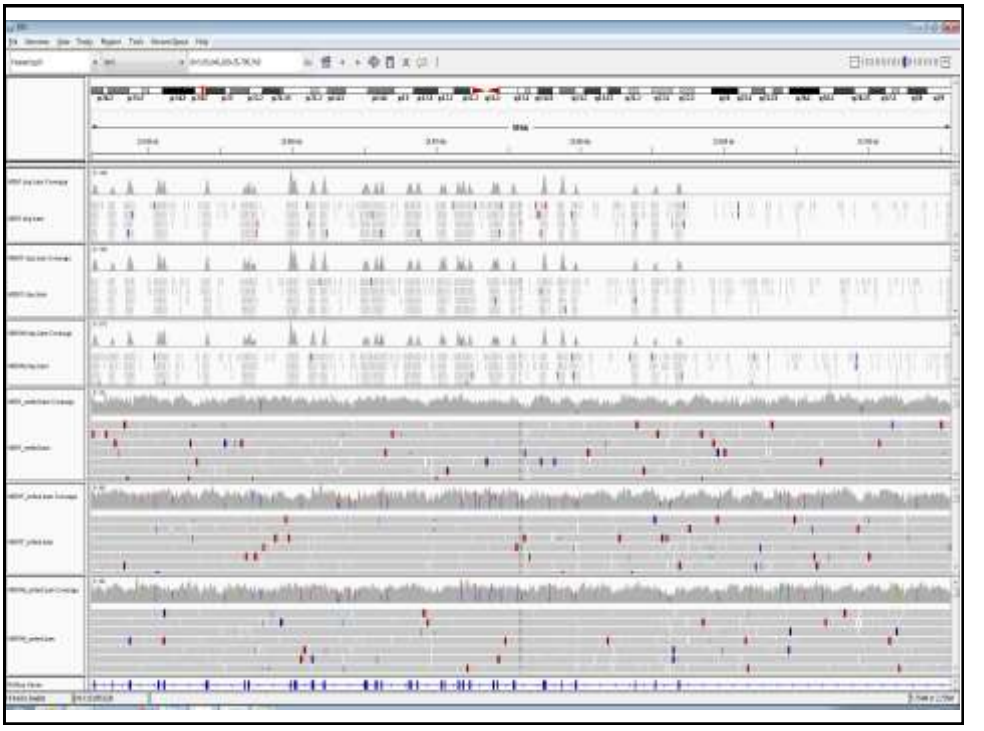
- Clinical Whole Exome Sequencing (CWES)



臨床全基因組定序檢測

- Clinical Whole Genome Sequencing (CWGS)





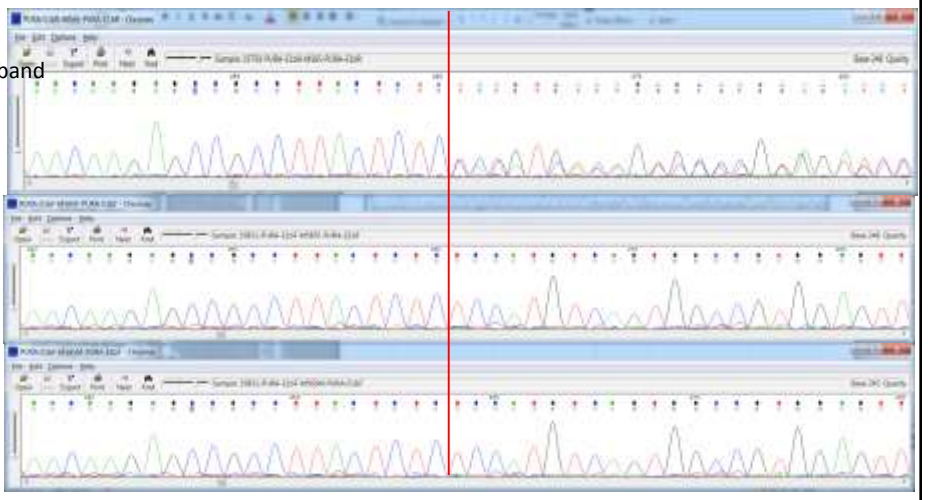
CWES 找出基因變異

移碼突變 (frameshift mutation)

Proband

F

M



REPORT

Mutations in *PURA* Cause Profound Neonatal Hypotonia, Seizures, and Encephalopathy in 5q31.3 Microdeletion Syndrome

Seema R. Lalani,[1,17,*] Jing Zhang,[1,17] Christian P. Schaaf,[1,3,17] Chester W. Brown,[1,11,17] Pilar Magoulas,[1] Anne Chun-Hui Tsai,[4] Areeg El-Gharbawy,[5] Klaas J. Wierenga,[6] Dennis Bartholomew,[7] Chin-To Fong,[8] Tina Barbaro-Dieber,[9] Mary K. Kukolich,[9] Lindsay C. Burrage,[1] Elise Austin,[1] Kory Keller,[4] Matthew Pastore,[7] Fabio Fernandez,[10,11] Timothy Lotze,[10,11] Angus Wilfong,[10,11] Gabriela Purcarin,[11] Wenmiao Zhu,[1] William J. Craigen,[1] Marianne McGuire,[1] Mahim Jain,[1] Erin Cooney,[1] Mahshid Azamian,[1] Matthew N. Bainbridge,[2] Donna M. Muzny,[2,14] Eric Boerwinkle,[2,13] Richard E. Person,[1,14] Zhiyv Niu,[1,14] Christine M. Eng,[1,14] James R. Lupski,[1,2,11,12] Richard A. Gibbs,[1,2] Arthur L. Beaudet,[1] Yaping Yang,[1,14] Meng C. Wang,[1,16] and Fan Xia[1,14,*]

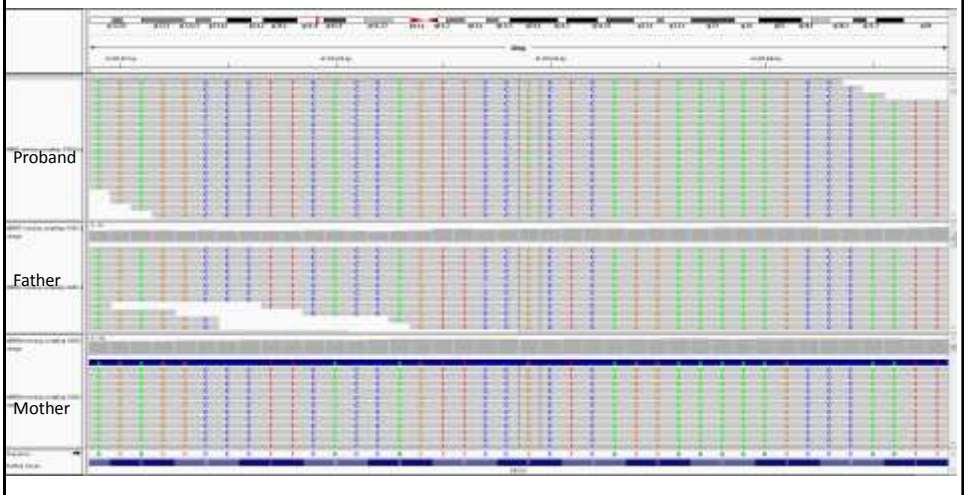
5q31.3 microdeletion syndrome is characterized by neonatal hypotonia, encephalopathy with or without epilepsy, and severe developmental delay, and the minimal critical deletion interval harbors three genes. We describe 11 individuals with clinical features of 5q31.3 microdeletion syndrome and de novo mutations in *PURA*, encoding transcriptional activator protein Pur-α, within the critical region. These data implicate causative *PURA* mutations responsible for the severe neurological phenotypes observed in this syndrome.

Am J Hum Genet. 2014;95:579-83.

香港大學奇難確診疾病計劃

- 1 歲女童
- 整體發展遲緩
- 腦部磁力共振：
  - 後顱窩容量過小畸形及腦室過大
- 神經肌肉型脊柱側彎

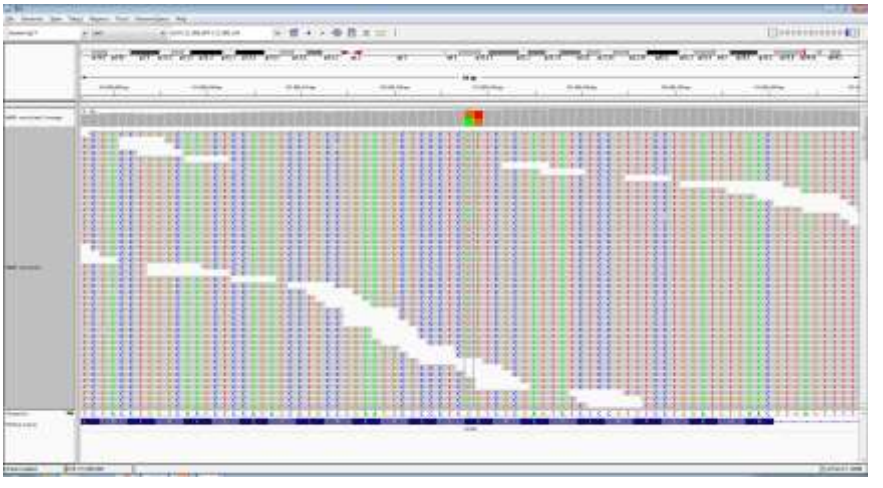
三重 (Trio) CWES
(患者+父+母)



香港大學奇難確診疾病計劃

- 6個月大女嬰
- 發育遲緩
- 疑似視覺及聽覺障礙
- 產前檢查無異常
- 頭圍低於3%
- 無外觀異常
- 輕微肌張力減退
- 及後出現嬰兒痙攣症，獲處方高劑量類固醇。
- 尿液和血液測試沒有異常

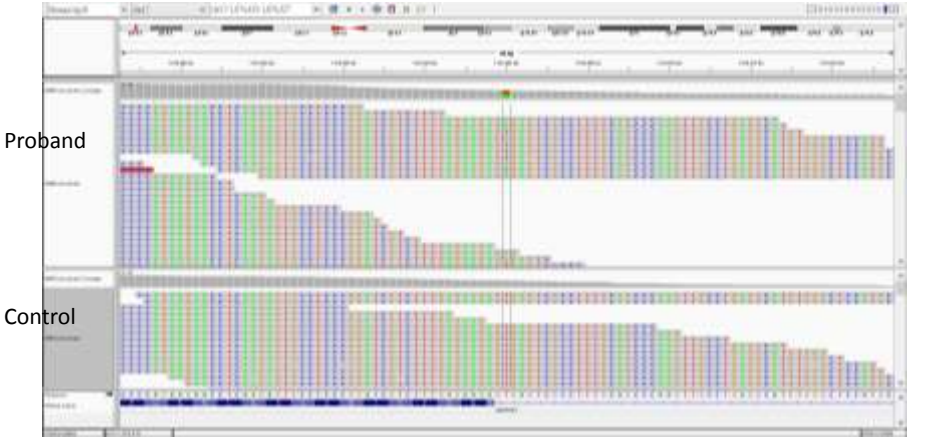
COQ4 (輔酶Q4)



香港大學奇難確診疾病計劃

- 男性
- 成骨不全症 (Osteogenesis Imperfecta)
- 又稱脆骨症、俗稱「瓷娃娃」。

SERPINF1 (成骨不全症六型)



成骨不全症六型治療突破

Two years' experience with denosumab for children with Osteogenesis imperfecta type VI

Heike Hoyer-Kuhn[1*], Christian Netzer[2], Friederike Koerber[3], Eckhard Schoenau[1] and Oliver Semler[1]

Abstract

Background: Osteogenesis imperfecta (OI) is a hereditary disease causing reduced bone mass, increased fracture rate, long bone deformities and vertebral compressions. Additional non skeletal findings are caused by impaired collagen function and include hyperlaxity of joints and blue sclera. Most OI cases are caused by dominant mutations in *COL1A1/2* affecting bone formation. During the last years, recessive forms of OI have been identified, mostly affecting posttranslational modification of collagen. In 2011, mutations in *SERPINF1* were identified as the molecular cause of OI type VI, and thereby a novel pathophysiology of the disease was elucidated. The subgroup of patients with OI type VI are affected by an increased bone resorption, leading to the same symptoms as observed in patients with an impaired bone formation. Severely affected children are currently treated with intravenous bisphosphonates regardless of the underlying mutation and pathophysiology. Patients with OI type VI are known to have a poor response to such a bisphosphonate treatment.

Method: Deciphering the genetic cause of OI type VI in our 4 patients (three children and one adolescent) led to an immediate translational approach in the form of a treatment with the monoclonal RANKL antibody Denosumab (1 mg/kg body weight every 12 weeks).

Results: Short-term biochemical response to this treatment was reported previously. We now present the results after 2 years of treatment and demonstrate a long term benefit as well as an increase of bone mineral density, a normalization of vertebral shape, an increase of mobility, and a reduced fracture rate.

Conclusion: This report presents the first two-year data of denosumab treatment in patients with Osteogenesis imperfecta type VI and in Osteogenesis imperfecta in general as an effective and apparently safe treatment option.

Keywords: Osteogenesis imperfecta VI, SERPINF1, RANKL Antibody, Denosumab, Bone mineral density

罕見病轉診診所 (*C*Rare*DR*)

- 首個罕見病轉診診所
  (Clinics for Rare Disease Referrals; *C*Rare*DR*)
- 奇難確診患者特徵：
  – 3個月內無法確診，治療後病情惡化
  – 發育遲緩，學業成績惡化
  – 做過多個(侵入性)檢測及看過多個專科無果。
- 檢驗醫學(Laboratory Medicine)確診方法：
  – 臨床全外顯子 (CWES)/全基因組定序(CWGS)
  – 香港病理學專科醫生撰寫遺傳檢驗報告

千禧年發現首個
非綜合徵型自閉症致病基因

#300496

AUTISM, SUSCEPTIBILITY TO, X-LINKED 3; AUTSX3

Phenotype Gene Relationships

Location	Phenotype	Phenotype MIM number	Gene/Locus	Gene/Locus MIM number
Xq28	[Autism, susceptibility, X-linked 3]	311990	MECP2	300005

Mapping

Lam et al. (2000) and Carney et al. (2003) identified mutations in the MECP2 gene in sporadic cases of autism, whereas no mutations in the MECP2 gene were found in a sample of 59 autistic individuals by Vourc'h et al. (2003). In 2 of 69 females with autism, Carney et al. (2003) identified 2 different de novo mutations in the MECP2 gene (300005.0011; 300005.0012).

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2. Carney, R. M., Welpert, C. M., Ravan, S. A., Shahbazian, M., Ashley-Koch, A., Cuccaro, M. L., Vance, J. M., Pericak-Vance, M. A. **Identification of MeCP2 mutations in a series of females with autistic disorder.** Pediat. Neurol. 28: 205-211, 2003. [PubMed: 12770674, related citations] [Full Text: Elsevier Science, Pubget]

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http://omim.org/entry/300496?search=%23300496&highlight=300496

April 2008 · Vol. 10 · No. 4

ACMG Practice Guidelines

Clinical genetics evaluation in identifying the etiology of autism spectrum disorders

G. Bradley Schaefer, MD[1], Nancy J. Mendelsohn, MD[2], and the Professional Practice and Guidelines Committee

A synthesis of the published literature suggests that the following diagnostic yields would be projected in the genetic evaluation of ASDs:

- High-resolution chromosome studies (5%)
- aCGH—beyond what would be detected by chromosomal analysis (10%)
- Fragile X (5%)
- *MECP2* (5%—women only)
- *PTEN* (3%—if head circumference >2.5 SDs)
- Other (10%)

Thus, using current knowledge and technology, a thorough clinical genetics evaluation of persons with ASDs will result in a positive answer in up to 40% of individuals.

Research report

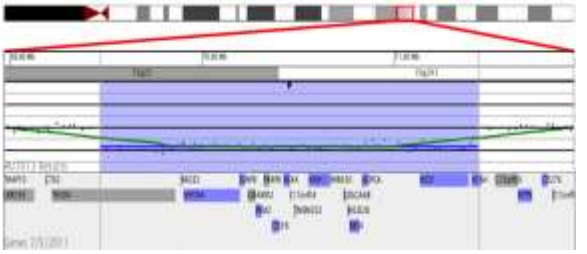
Unmasking a novel disease gene *NEO1* associated with autism spectrum disorders by a hemizygous deletion on chromosome 15 and a functional polymorphism

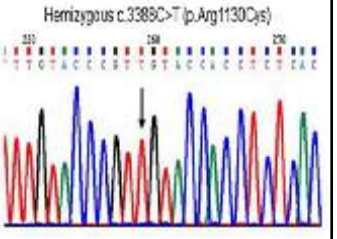
Wai-Kwan Siu[a,b], Ching-Wan Lam[a,*], Wei-Wei Gao[c], Hei-Man Vincent Tang[c], Dong-Yan Jin[c], Chloe Miu Mak[b]

[a] Department of Pathology, The University of Hong Kong, Hong Kong, China
[b] Kowloon West Cluster Laboratory Genetics Service, Department of Pathology, Princess Margaret Hospital, Hong Kong, China
[c] School of Biomedical Sciences, The University of Hong Kong, Hong Kong, China

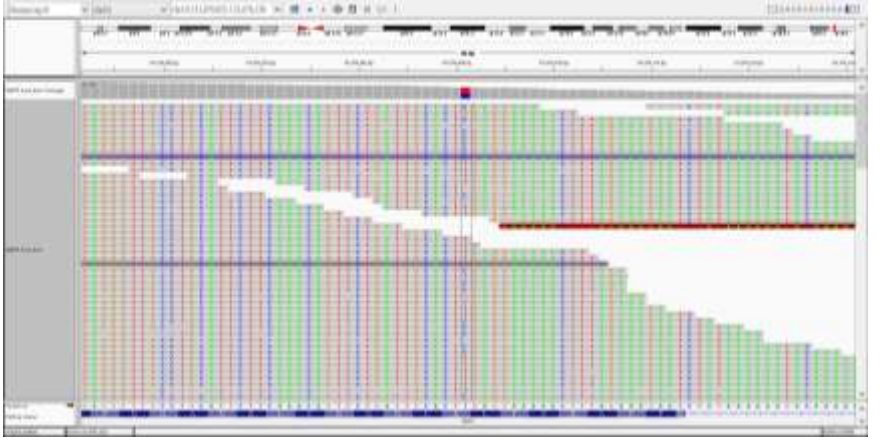
HIGHLIGHTS

- Two *NEO1* missense mutations were identified in autism spectrum disorders (ASD).
- *In silico* analyses predicted both missense mutations as pathogenic.
- Defective nuclear translocation of the neogenin intracellular domain was shown.
- *NEO1*-associated autism is inherited in an autosomal recessive manner.
- *NEO1* is important in axon guidance of neuronal migration.





2016年發現罕見病新致病基因：*EBF3*



香港電台 鏗鏘集

日期： 2014 年 10 月 20 日

連結： http://programme.rthk.org.l 10-20&p=858&e=2809678

內容： 罕有病

受訪者： 香港大學李嘉誠醫學院病理學系臨床教授林青雲教授

無綫電視 － 星期五檔案

日期: 2015 年 9 月 25 日

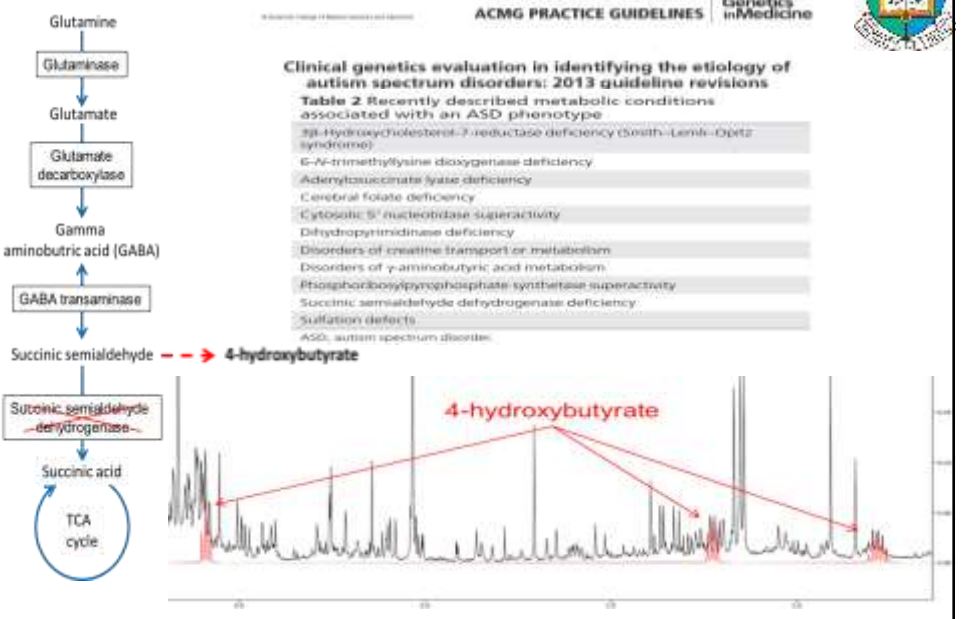
受訪者: 香港大學李嘉誠醫學院病理學系臨床教授林青雲教

內容: 天使的微笑

連結: http://mytv.tvb.com/tc/cat_news/fridayreport/218880

一個都不能少

Succinic semialdehyde dehydrogenase deficiency



罕見病篩查：
香港大學新生兒代謝疾病篩查試驗計劃

- 發病前確診
- 治療後，可如常人一樣。
- 無併發症

CME

CME Activity for Pathologists and Paediatricians

EARLY DIAGNOSIS AND MANAGEMENT OF METABOLIC DISEASES

Speakers:

Dr. Yuen Kar Ngai Robert
MBBS(HK), FRCP(UK, FRCP, FRCP(Edin), FRCP(Glasg), FHKCPaed, FHKAM(Paed), DCH(Lond), DCH(Glasg)
Specialist in Paediatrics

Prof. Lam Ching Wan
MBChB, PhD, MAACB, FRCP(Glasg), FRCPA, FAACB, FHKCPath, FHKAM(Pathology)
Specialist in Pathology
Diplomate of American Board of Toxicology
Professor, Department of Pathology, The University of Hong Kong

Moderator:

Dr. Li Kwok Hung
MBBS, FRCP(C), FHKCPath, FHKAM(Pathology)
Specialist in Pathology
Chief of Service, Pathology Department, Hong Kong Baptist Hospital

Date:
7 December 2012

Time:
6:30 p.m. to 7 p.m. Registration
(Light meal would be provided)
7 p.m. to 8 p.m. Seminar

Venue:
Chapel, 9/F, Block D, Hong Kong Baptist Hospital

Continue Medical Education 2012

CME

Hong Kong Baptist Hospital

Registration & Enquiries:
2339 8885 (Ms. Phoebe Pang)

Continue Medical Education Accreditation: Pending:
Hong Kong College of Community Medicine, Hong Kong College of Paediatricians, HKAM,
Hong Kong College of Pathologists, Hong Kong College of Surgeons, Hong Kong College of Family Physicians,
Hong Kong College of Physicians, Hong Kong College of Obstetricians and Gynaecologists

14 January 2015

191. The DH and the HA have set up a working group to study the feasibility of trying out in the public healthcare system a screening programme for newborn babies for inborn errors of metabolism. The working group will study the types of disease to be screened, scientific evidence on the effectiveness of screening, actual arrangements and related recommendations.

感謝

兒童先天性代謝異常疾病
Management of Inborn Errors of Metabolism in Children

郭美均醫生
香港大學李嘉誠醫學院
兒童及青少年科學系
名譽臨床助理教授

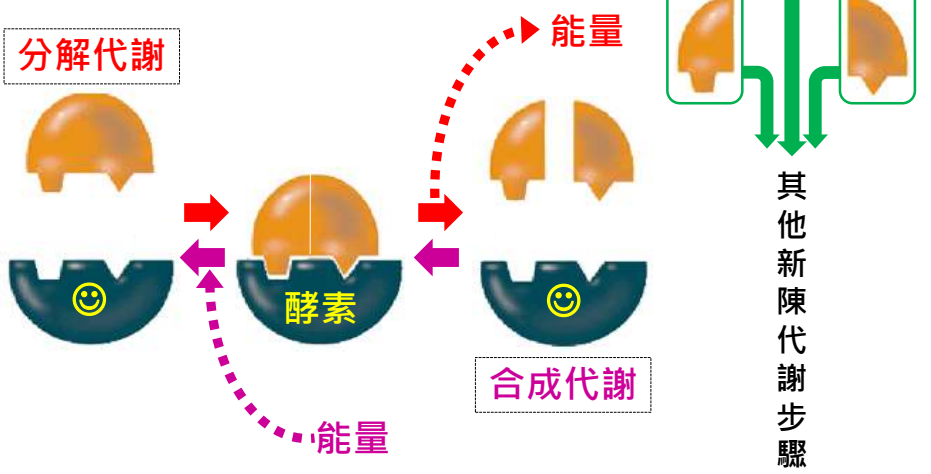
Dr Kwok Mei-Kwun Anne
Honorary Clinical Assistant Professor
Department of Paediatrics & Adolescent Medicine
Li Ka Shing Faculty of Medicine, HKU

12-March-2016

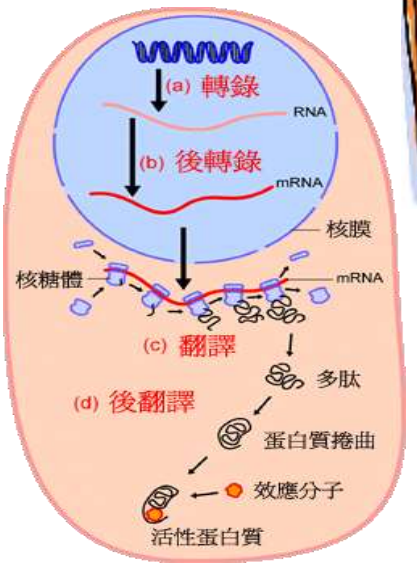
是甚麼？
十分罕有？
有甚麼症狀？
有沒有治療方法？
如何診斷？
如何預防？
可以怎樣做？！

先天性代謝異常疾病
是甚麼？？

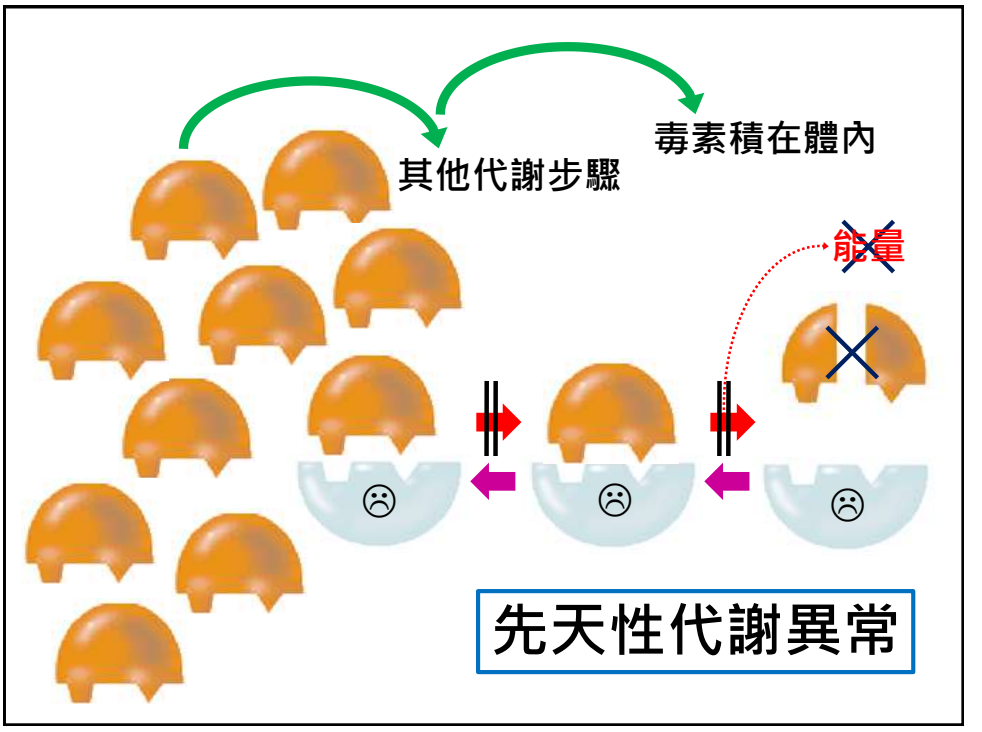
甚麼是新陳代謝？



人體有~35,000個基因



人體有超過一百萬種蛋白質


其他代謝步驟
毒素積在體內
能量
先天性代謝異常

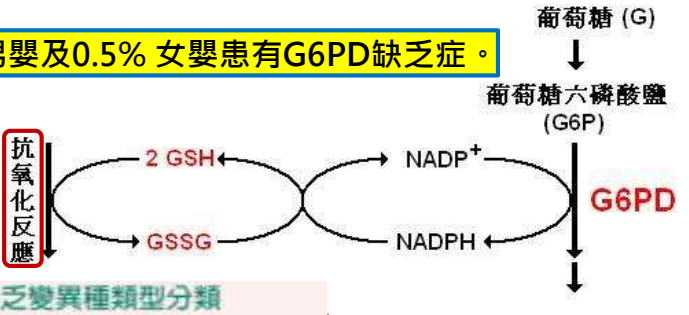

先天性代謝異常疾病
十分罕有？？

先天性代謝異常病的分類

- 碳水化合物代謝異常
- 胺基酸代謝異常
- 脂肪酸代謝異常
- 溶小體儲積症
- 線粒體病
- 過氧化物酶體症
- 代謝物質輸送系統異常
- 有機酸血症
- 先天性糖基化缺陷
- 磷脂代謝缺陷
- 稀有金屬代謝異常
- 紫質代謝異常
- 嘌呤或嘧啶代謝異常
- 先天性膽酸合成障礙
- 等等
- (未計那些只影響單一器官的病)

G6PD缺乏症 (蠶豆症)

在香港，4.5% 男嬰及0.5% 女嬰患有G6PD缺乏症。



世界衛生組織G6PD缺乏變異種類型分類

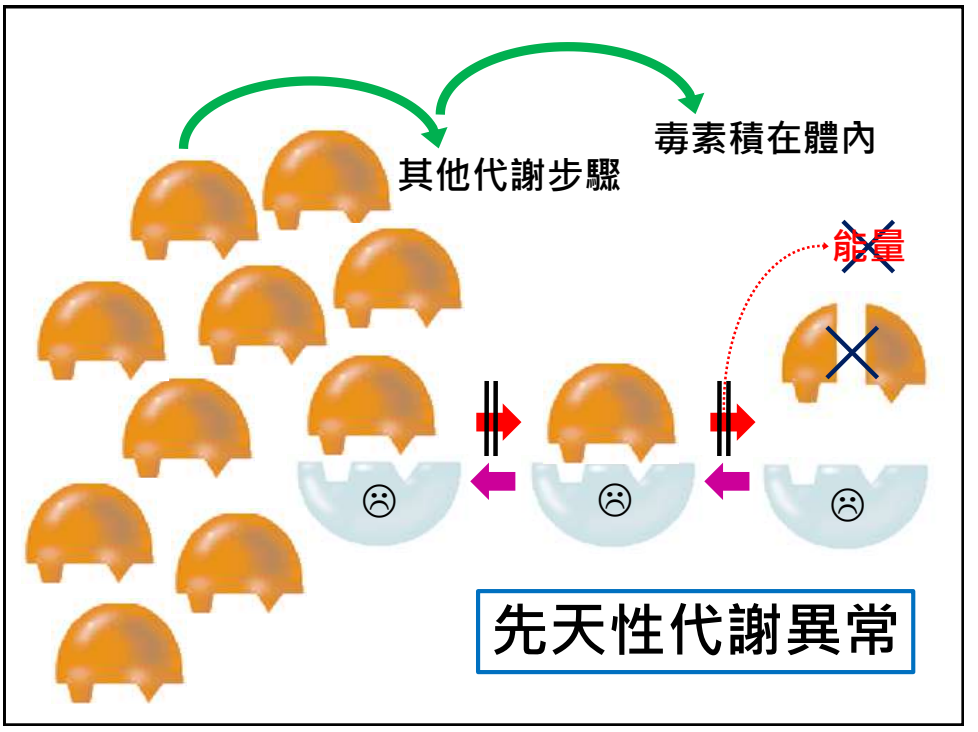
變異種類型	嚴重度	症狀	酵素量
第一型	嚴重酵素缺乏	合併有慢性溶血性貧血	< 10%
第二型	嚴重酵素缺乏	通常只在受感染、藥物或化學物質影響下產生間歇性的溶血	NA
第三型	中度酵素缺乏	在受感染、藥物或化學物質影響下產生間歇性的溶血	10-60%
第四型	酵素活性正常	無溶血情形	NA

不同的酵素缺乏/錯體
→影響不同的代謝步驟
→不同種類的代謝病

先天性代謝異常病種類繁多
每種代謝病的發生率極低

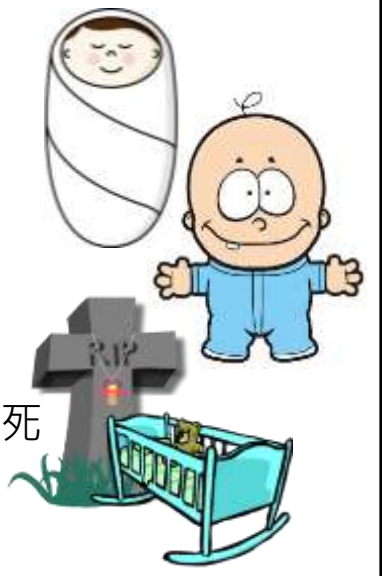
估計最少每3,000 – 4,000個香港BB就有一名患有先天性代謝病

先天性代謝異常病
有甚麼症狀？


其他代謝步驟
毒素積在體內
能量
先天性代謝異常

先天性代謝異常病症狀

- 出世時無明顯症狀
  →症狀之後慢慢出現
  →不可逆轉的損傷及破壞
- 平日無任何症狀
  →突然病發
  →甚至於第一次發作時猝死



先天性代謝異常對身體的影響

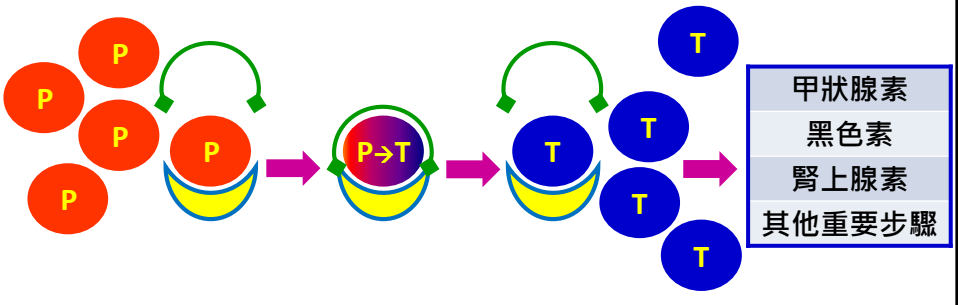
- 影響身體生長發育
  →生長發育遲緩
- 影響腦神經
  →腦部發展遲緩/倒退
  →肌張力低/僵硬
  →行動不便
  →抽搐、嗜睡、昏迷
- 影響其他內臟
  →器官畸形/衰竭
  (心、肝、肌肉、腎、眼、耳、骨等)

先天性代謝異常 – 特殊症狀

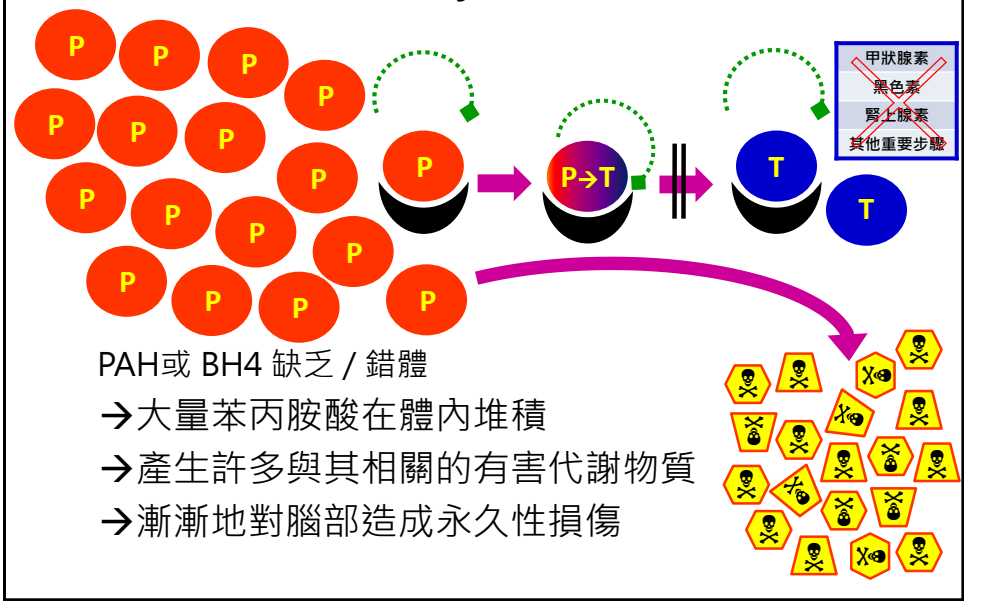
- 低血糖
- 高血氨 (阿摩尼亞)
- 酮酸中毒
- 特殊異味 (楓糖漿甜味、魚腥味、臭老鼠味、臭腳汗味等)

苯酮尿症
Phenylketonuria, PKU

- 胺基酸代謝：
  - 蛋白質被分解成胺基酸 → 胺基酸經各種酵素再作轉化
  - 苯丙胺酸(phenylalanine)由一個酵素 (PAH) 和一個輔酵素 (BH4)負責轉化成另一個胺基酸 – 酪胺酸 (tyrosine)



苯酮尿症 (Phenylketonuria, PKU)

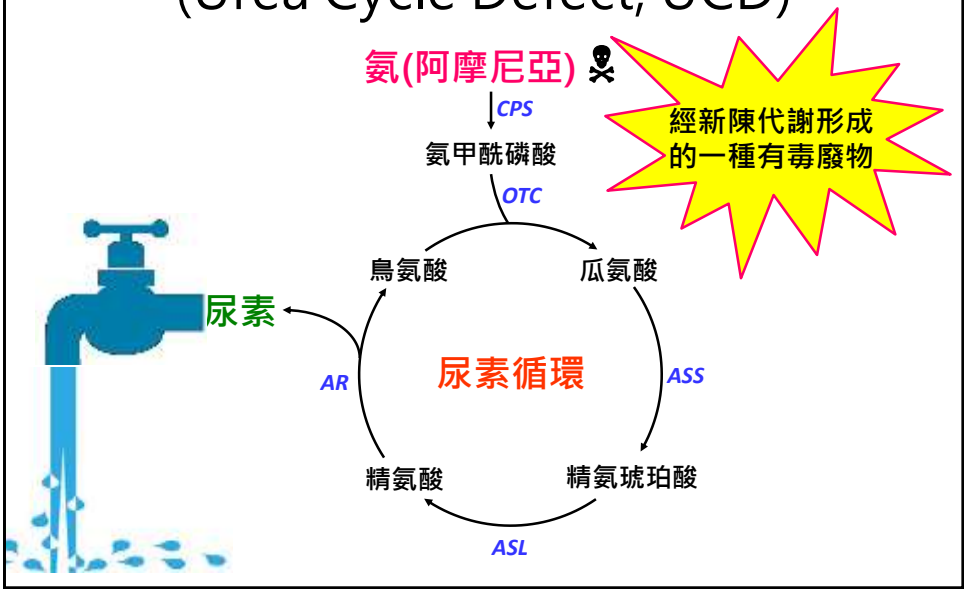


PAH或 BH4 缺乏 / 錯體
→大量苯丙胺酸在體內堆積
→產生許多與其相關的有害代謝物質
→漸漸地對腦部造成永久性損傷

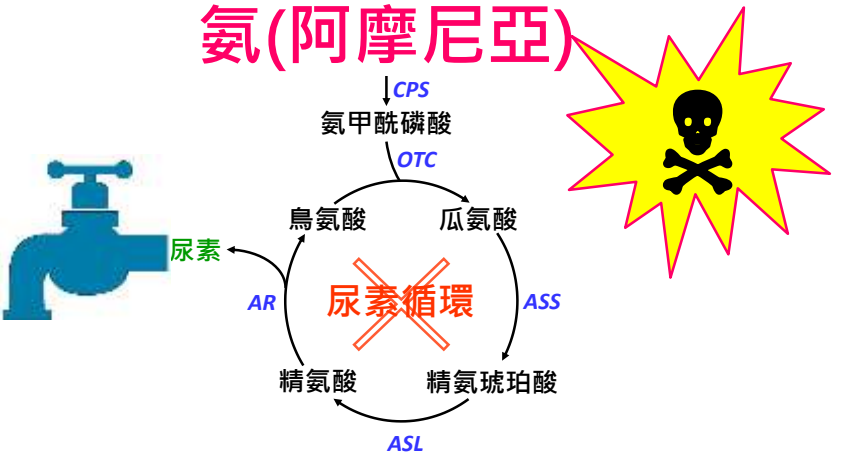
苯酮尿症 (Phenylketonuria, PKU)

- 身體及尿液有臭老鼠味
- 頭圍較小
- 生長發育障礙
- 肌張力降低
- 抽搐、嘔吐
- 影響智能發展
- 皮膚蒼白乾燥
- 金髮、藍眼

先天性尿素循環代謝障礙
(Urea Cycle Defect, UCD)



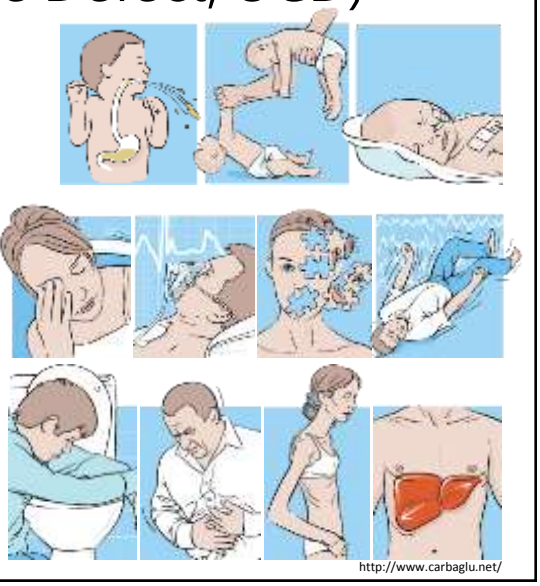
先天性尿素循環代謝障礙
(Urea Cycle Defect, UCD)



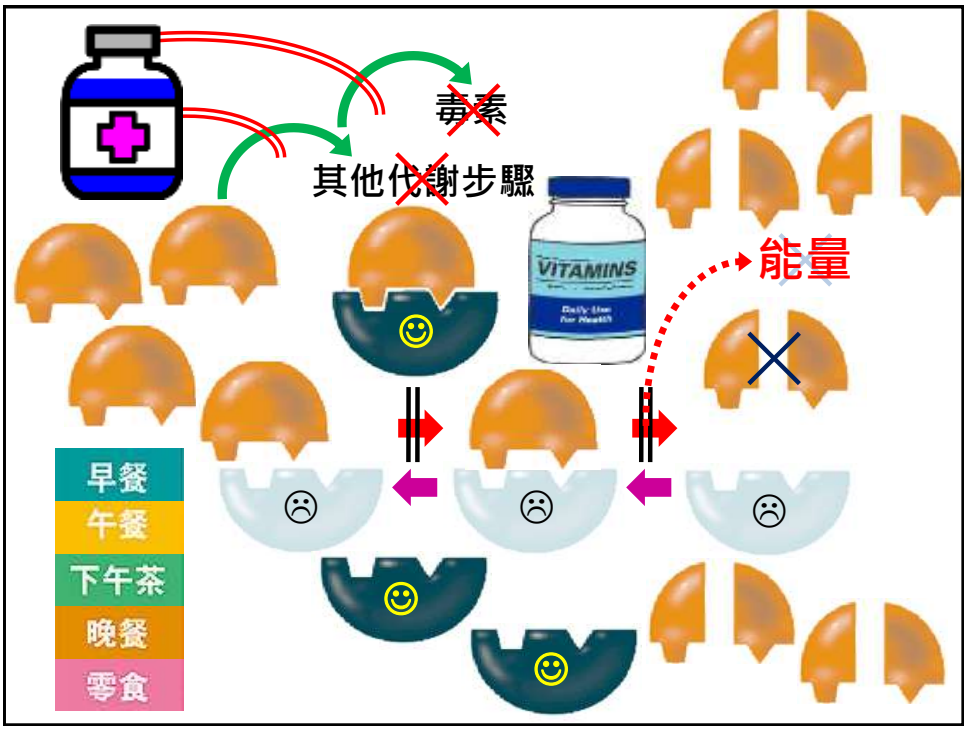
先天性尿素循環代謝障礙
(Urea Cycle Defect, UCD)

- 出生時無症狀
- 發病時身體嚴重惡化
  - 急性代償失調
- 嘔吐、呼吸急促
- 昏迷、抽搐、痙攣
- 死亡

- 後遺症
  – 永久中樞神經損壞
  →嚴重殘障



那先天性代謝病有沒有治療方法？！



先天性尿素循環代謝障礙 (Urea Cycle Defect, UCD)

急救

- 停止蛋白質攝取
- 高能量飲食 / 靜脈營養
- 靜脈注射的排氨解藥
- 靜脈注射特定胺基酸
- 血液透析 (洗血)
- 處理併發症 (如腦水腫)

日常治療

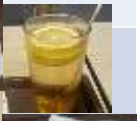
- 低蛋白飲食
- 攝取均衡營養及適當熱量
- 口服排氨解藥
- 口服特定胺基酸
- 於高危期前作預防措施
- 肝臟移植

10歲男孩的低蛋白餐單示範

	蛋白質	2000卡路里, 27克蛋白質
早餐	4克	蜜糖水 ***麵包***2片+ 塗牛油/花生醬/果醬/三文治醬
茶點		果汁飲品
午餐	7克	***蝦仁***炒銀針粉 (1兩) 雜菜 例湯/ 羅宋湯(不吃肉) 熱檸檬蜜
茶點	2克	***克力架***2片+ ***忌廉芝士***1湯匙
晚餐	4克 10克	***飯1碗*** 番茄 煎***三文魚*** 翠玉瓜雲耳洋蔥炒***雞柳*** 炒菜心 青紅蘿蔔南北杏瘦肉湯(不吃肉)
茶點		雪葩 /水果

總共不多於1兩半肉





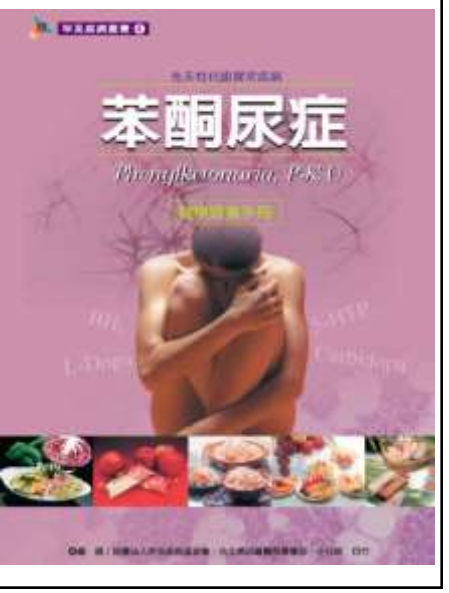



治療之黃金時機：出生後1個月內

- 限制苯丙胺酸攝取
- 確保足夠熱量及蛋白質等營養的均衡攝取
- 特殊低苯丙胺酸配方和副食品
- BH4

苯酮尿症 (Phenylketonuria, PKU)

開始飲食治療	平均智商
1個月內	95
1~2個月大	85
3-4個月或以後	53-45



先天性代謝病的處理

- 有些代謝病只要及早發現，便可透過適當治療控制病情，減低對身體的損害：
  - **飲食調節、藥物**
  - **靜脈酵素替代療法、器官移植**
- 部分代謝病目前尚無治愈方法
- 對患者提供完整的醫療照顧
  - **給予訓練，盡量發揮潛能**
  - **定期監察，紓緩症狀，及早處理併發症**
- 對家庭提供支援及輔導

如何診斷及防治先天性代謝病?

診斷先天性代謝病

- 由兒科專家作臨床評估
- 血液、尿液、組織檢查
  - 代謝物分析 : 如胺基酸、有機酸檢查
  - 細胞酵素檢查 (e.g. G6PD)
  - 基因檢查

預防和及早診治先天性代謝病

- 遺傳諮詢
- 產前診斷
  - 在懷孕期13-18週內進行絨毛細胞抽檢
- 輔助生殖 + 植入前診斷

- 新生兒代謝病篩查
  - 衞生署和醫管局已成立專責小組，研究在香港執行新生兒代謝病篩查之可行性，並於2015年10月在兩家公立醫院推行「先導計劃」。
  - 期望香港兒童醫院在2018年落成後，新生兒代謝病篩查可全面推行。