上海市儿童医院
CHILDREN'S HOSPITAL OF SHANGHAI, CHINA
上海交通大学附属儿童医院

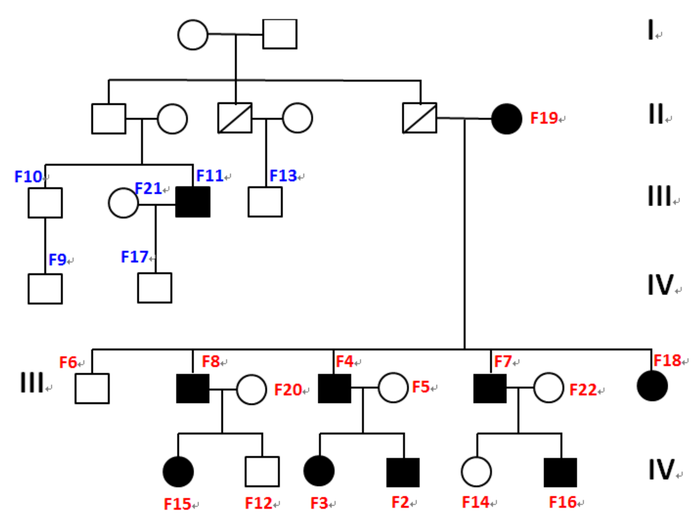
Copy number variation (CNV) sequencing identifies a novel mutation of the glucokinase gene in Maturity-onset diabetes of the young

Author： Yan Li, Pin Li
Institution： Department of Endocrinology, Children's Hospital of Shanghai, Shanghai Jiaotong University, Shanghai, China

Background:
Maturity-onset diabetes of the young (MODY) is a cluster of early-onset, monogenic disorders which is inherited in autosomal dominant form. It is mainly caused by genetic defects in beta-cell, which results in beta-cell dysfunction. Till now, 14 MODY types specified by mutation in respective 14 genes with their etiologies are known. Among them, glucokinase (GCK) gene encodes glucokinase enzyme which plays a crucial role in the regulation of insulin secretion.

Methods:
Clinical features and laboratory data were collected from the patient and her family member 10, and linkage analysis and copy number variation (CNV) detection were performed to screen the mutation of all the 14 MDOY gene.

Results:
The 3-year-old patient was referred to the endocrinology clinic for evaluation of elevated fasting blood glucose (FBG) measurements. Family studies and laboratory review of other families of hers conformed to the clinical features of MODY. Genetic testing showed the autosomal dominant, deletion mutation in the GCK gene, which is correlated with GCK-MODY. Of the candidate CNV regions, one copy deleted respectively in exon 8, exon 9, exon 10 and exon 11 in all the patients of this family, while normal people have no such deletion mutation, which is a novel mutation of GCK gene.



Chr	Exon	Start	End	Type
Chr7	8	4418 4726	4418 4939	HET Loss
Chr7	9	4418 5609	4418 5729	HET Loss
Chr7	10	4418 6097	4418 6261	HET Loss
Chr7	11	4418 7217	4418 7382	HET Loss

Conclusion:
MODY represents a combination of genetic, metabolic, and clinical heterogenicity. MODY has several subtypes depending upon the involvement of genes and their mutations. Our patients likely represented a novel deletion mutation of GCK-MODY. Besides linkage analysis and exon mutation screening, CNV sequencing might be used to identify other novel GCK mutations.

Identify:
Diabetes Mellitus, maturity-onset diabetes of the young, glucokinase