香港中文大學 婦產科學系

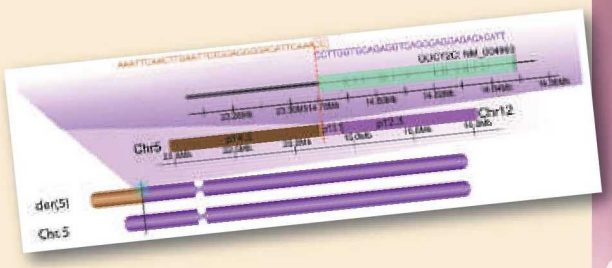
# ChromoSeq

## 染 色 體 測 序

..ATCGAATTCG..
..GAATTCGAATT..
..GACGGATTCG..

### 甚麼是 ChromoSeq 染色體測序?

ChromoSeq 染色體測序是一種基於DNA長片段的全基因組測序技術。與胎兒測序（FetalSeq）相比,此嶄新技術同時能檢測染色體結構異常和雜合性缺失。





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### 選擇此項技術的好處及其檢測範圍

ChromoSeq能夠全面、精準地檢測基因組變異。相比傳統核型分析技術、胎兒DNA芯片以及胎兒測序技術，ChromoSeq 技術尚能額外檢測的遺傳學變異類型包括：

1. 染色體結構異常：包括平衡易位、插入及染色體複雜重排。[1,2]
2. 全基因組範圍內5Mb以上的雜合性缺失（包括單親二倍體）。

[1] PMID: 31679651, [2] PMID: 31173071.

### 檢測流程

檢測前遺傳諮詢

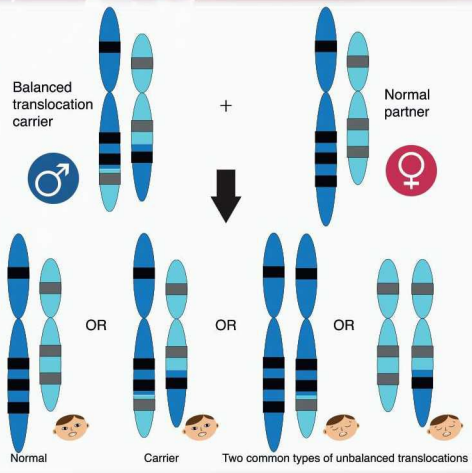
樣本類型
（例如絨毛、羊水、流產組織、外周血）

ChromoSeq 染色體測序檢測

報告（3個星期內）

### 平衡易位如何導致疾病

圖一
(Figure 1)




### 病例分享

圖一展示，當夫婦其中一方是染色體平衡易位携帶者時，他們的後代可能出現染色體不平衡。該結果會導致流產，先天性結構異常以及其他臨床表型。

圖二（背面）展示的是一對患有5號染色體和14號染色體平衡易位的夫婦的案例，該易位很難被傳統的核型分析檢驗到。（A）圖展示的是正常的染色體，衍生染色體和染色體G顯帶模型圖，箭頭指示的是重排的段裂點。（B）ChromoSeq通過跨越重排的異常序列來檢測易位。（C）圖中展示該對夫婦的植入前遺傳學檢測（PGT）結果，顯示部分胚胎患有非平衡易位。證明PGT能協助排除受影響的胚胎，幫助夫婦成功受孕。

### 誰有需要做此項檢測？

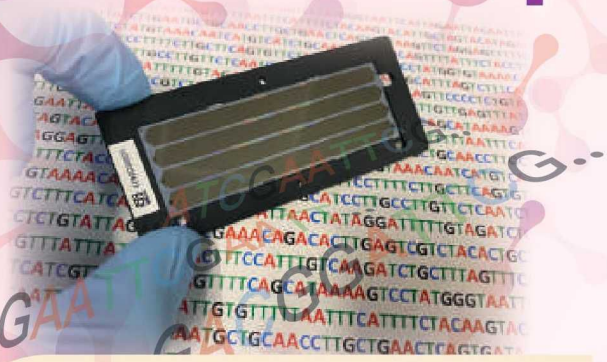
1. 曾出現流產或死胎的夫婦；
2. 所有需要進行侵入性產前檢測的孕婦，如超聲檢測胎兒存在結構異常、唐氏綜合症篩查或胎兒無創DNA檢測屬高風險、高齡妊娠等；
3. 患有發育和智力遲緩，自閉症譜系障礙或先天性多發性畸形的兒童。

### 選擇此服務需要注意的事項

1. 技術限制：本技術不可檢測的變異類型包括：因較長重複序列引起的染色體重組事件（如羅伯遜易位）、低比例嵌合體（低於30%）及單核苷酸突變；
2. 即使報告結果正常，胎兒或患者亦有機會患有其他此技術沒有覆蓋的基因變異。

Department of Obstetrics and Gynaecology
The Chinese University of Hong Kong

# ChromoSeq



## What is ChromoSeq?

ChromoSeq is a genetic test which utilizes large DNA fragments genome-sequencing technology. Superior to FetalSeq, it can also identify chromosomal structural rearrangements and absence of heterozygosity (AOH).

## Test workflow

- Pre-test Genetic Counseling
- DNA Sampling
  (e.g. chorionic villus sampling, amniocentesis, products of gestation, peripheral blood)
- ChromoSeq Analysis
- Report (within 3 weeks)

## ChromoSeq's scope of detection

ChromoSeq enables comprehensive and precise detection of genomic variants and detects additional genetic abnormalities over conventional karyotyping, FetalChip and FetalSeq including:

1. **Chromosomal structural rearrangements** including balanced translocations, inversions, insertions and complex rearrangements.[1,2]
2. **Absence of heterozygosity (and/or uniparental disomy)** on a genome-wide scale at a 5Mb resolution.

[1] PMID: 31679651, [2] PMID: 31173071.

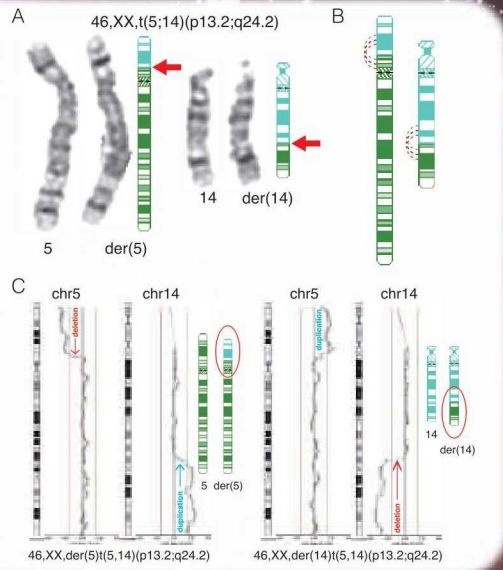
## Case illustration

Figure 1 (back page) shows one of the couple is a carrier of a balanced translocation (upper panel). The blue and teal chromosome segments at the lower terminal ends are rearranged. The couple is at risk of transmitting an unbalanced chromosome to their offspring (lower panel). Unbalanced genetic content could result in miscarriage, congenital abnormalities or other clinical features.

Figure 2 illustrates a case example of an individual with a balanced translocation involving chromosomes 5 and 14. This is difficult to detect by karyotyping. (A) shows the normal and the abnormal chromosomes. The red arrow shows the rearrangement breakpoints. (B) ChromoSeq identifies the translocation by detecting chimeric sequence reads spanning the rearrangements. (C) Preimplantation genetic testing (PGT) can be utilized to help the couple achieve an unaffected pregnancy. PGT identified embryos with unbalanced chromosomes that are inherited from the carrier parent.

## Case illustration
(chromosomal insertion in patients with recurrent miscarriages)

Figure 2
(圖二)




## Who will benefit from this test?

1. Couples with infertility, miscarriage or a history of stillbirth;
2. Women who are indicated for invasive prenatal testing due to fetal ultrasound anomalies, high risk from Down's Syndrome Screening/ non-invasive prenatal testing or advanced maternal age;
3. Children with developmental delay, intellectual disability, autism spectrum disorders or multiple congenital anomalies.

## Important notes for this test

1. Limitations: ChromoSeq is unable to detect chromosomal rearrangements mediated by large repetitive elements (e.g. robertsonian translocations), low-level mosaicisms (<30%) and single-nucleotide variants;
2. Normal test results do not exclude other genetic causes that are undetectable by ChromoSeq.