



# Le long-read en cytogénétique : réelle utilité ou fake news

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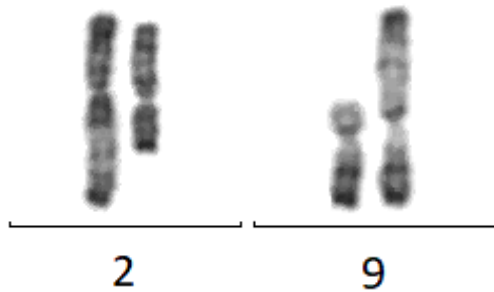
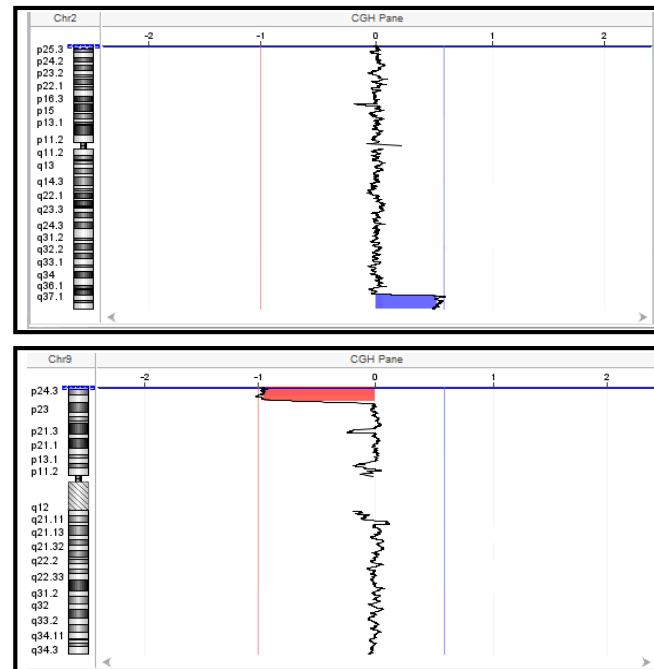
ATC 2026

*Benjamin GANNE – AHU*

# Pourquoi s'embêter ?

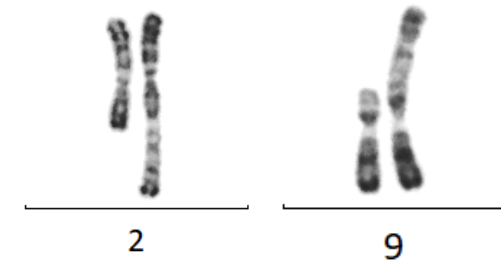
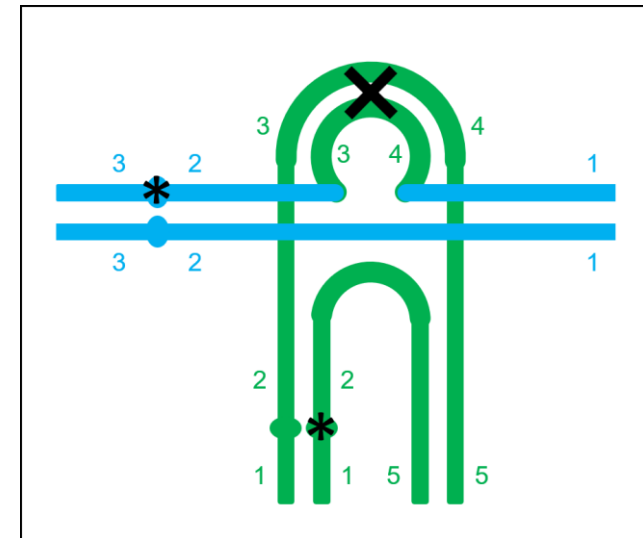
## Cytogénétique

Foetus

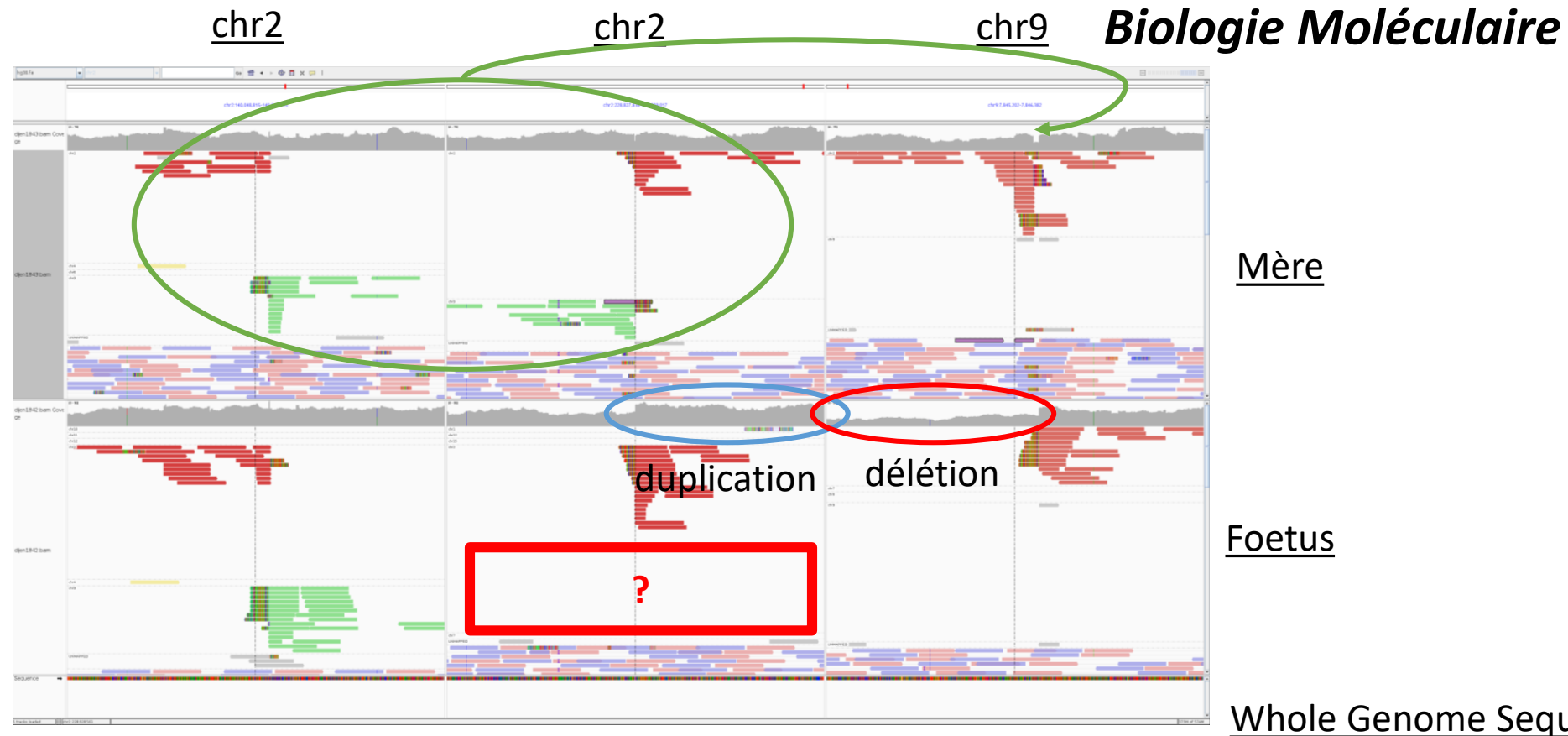
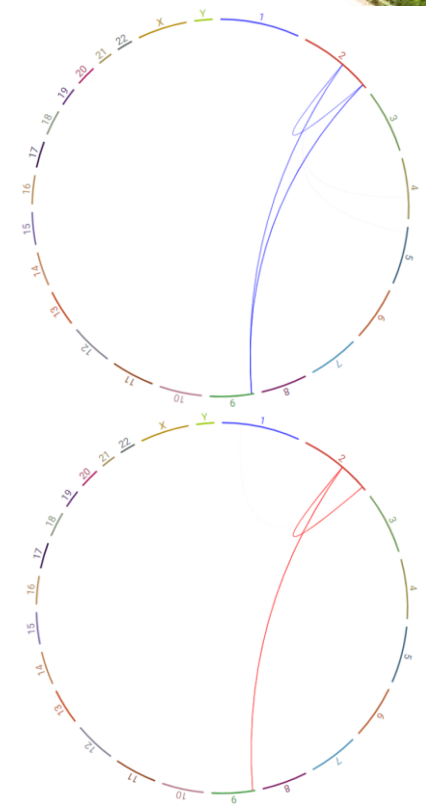


Caryotype + 2-3 FISH + ACPA

Mère

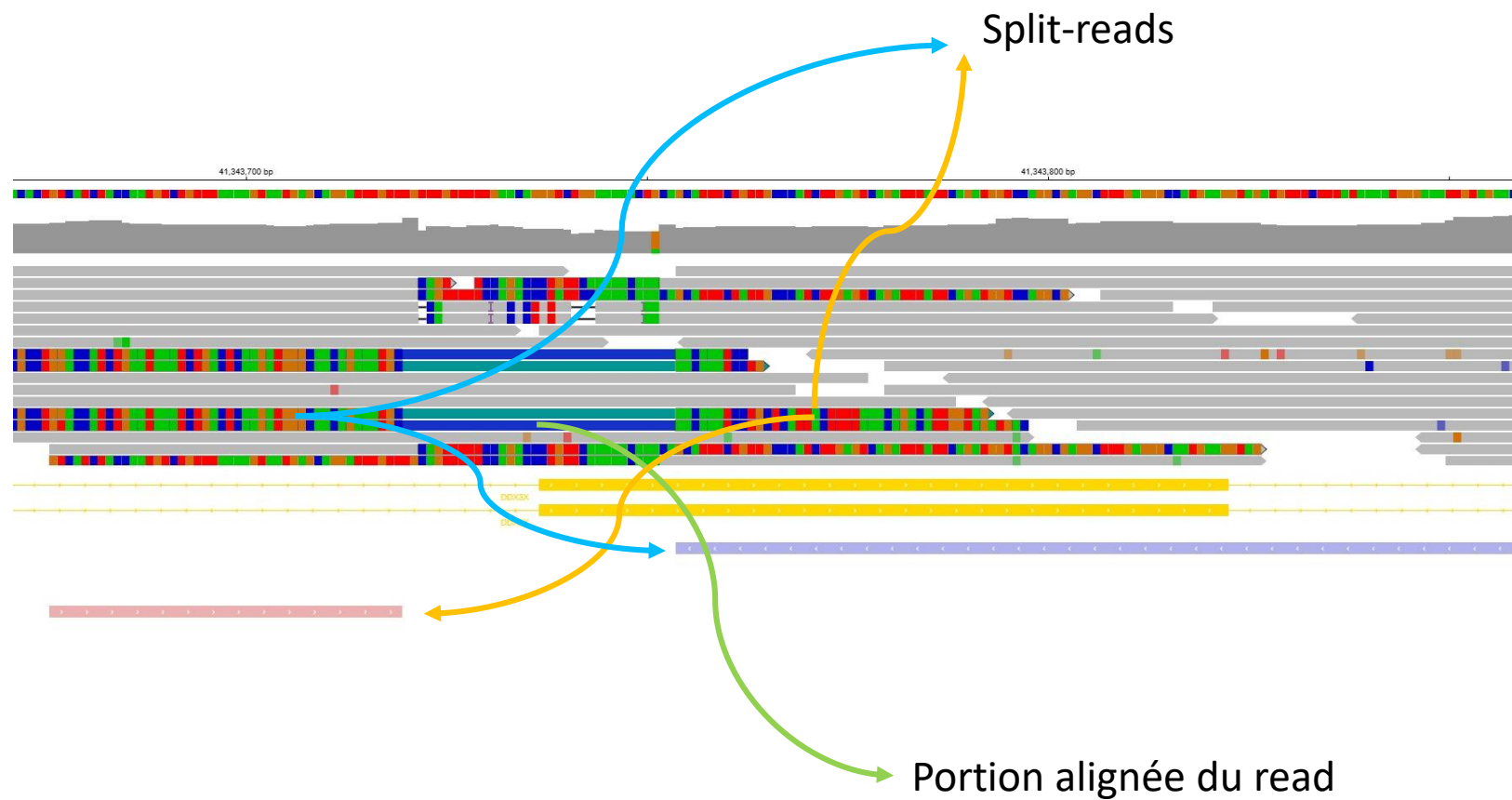


# Pourquoi s'embêter ?



Whole Genome Sequencing

# Principe du split-read





# La réalité de la biologie moléculaire

## Délétion/Duplication

| SV classes               | Read pair | Read depth | Split read |
|--------------------------|-----------|------------|------------|
| Deletion                 |           |            |            |
| Interspersed duplication |           |            |            |
| Tandem duplication       |           |            |            |

Visibles en Panels + Exomes + Génomes

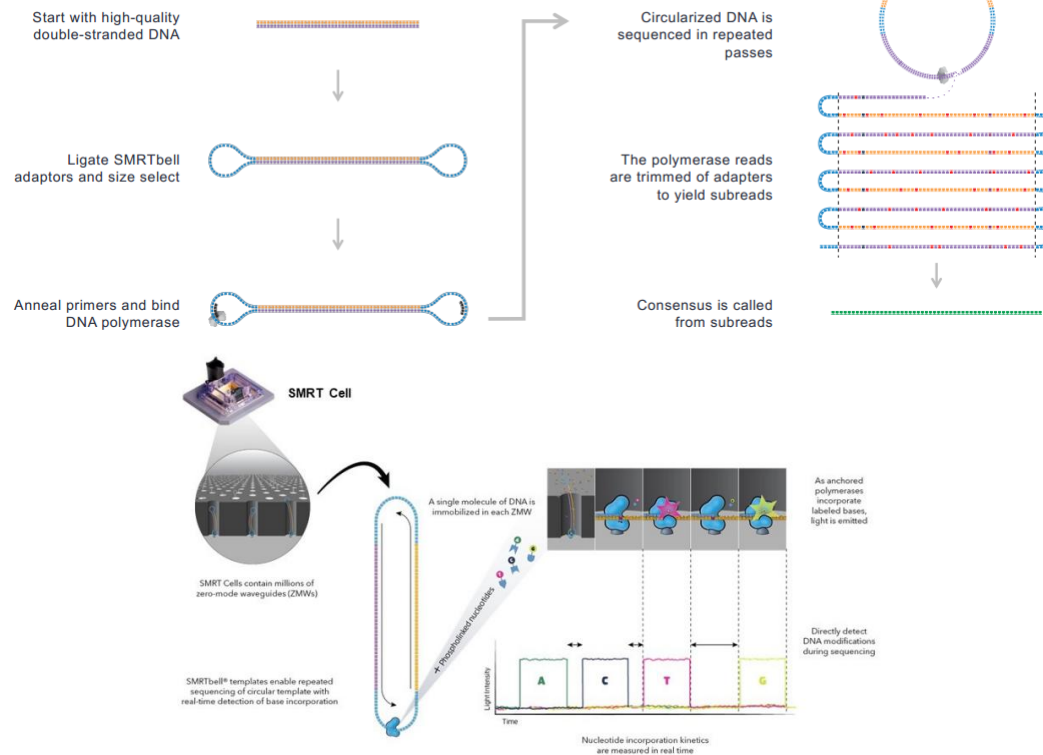
## Inversion/Insertion/Translocation

| SV classes               | Read pair | Read depth     | Split read |
|--------------------------|-----------|----------------|------------|
| Novel sequence insertion |           | Not applicable |            |
| Mobile-element insertion |           | Not applicable |            |
| Inversion                |           | Not applicable |            |

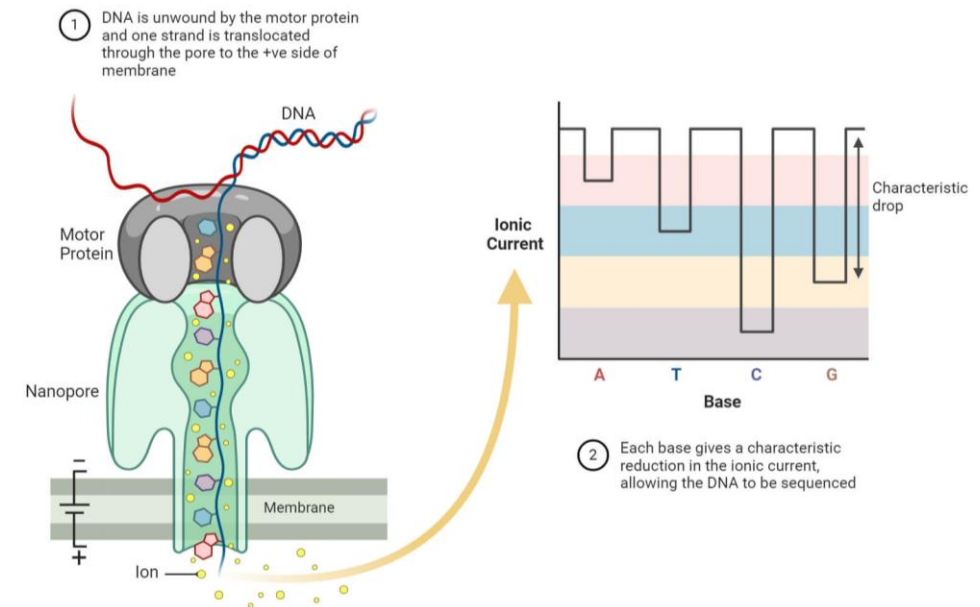
Visibles en Génomes

# Quelles technologies ?

## PacBio



## Oxford Nanopore Technologies



# Quelles technologies ?

PacBio  
VEGA



Priced at USD \$189,000<sup>1</sup> and \$995 per run

Environ 300-400€ /  
génom à 20X

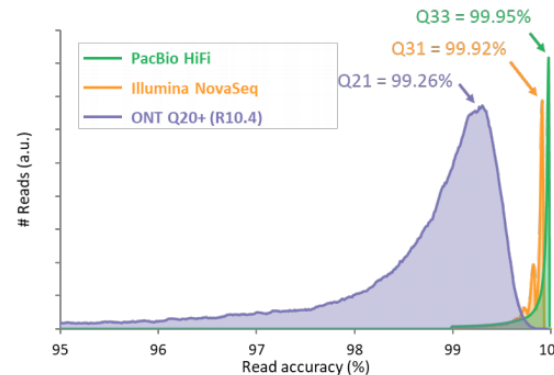
\$779,000



## Oxford Nanopore Technologies



€2,940.00



Environ 400€ / génome à 10X

1 puce = 4 génomes 10X

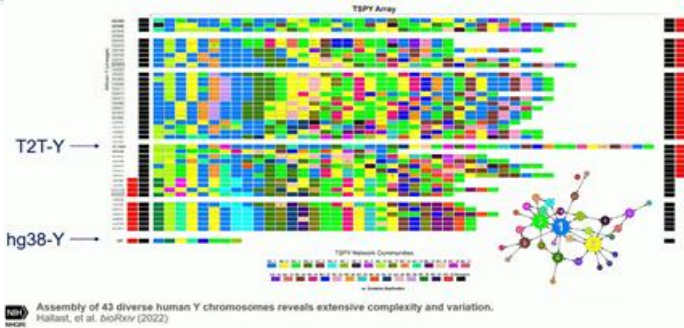
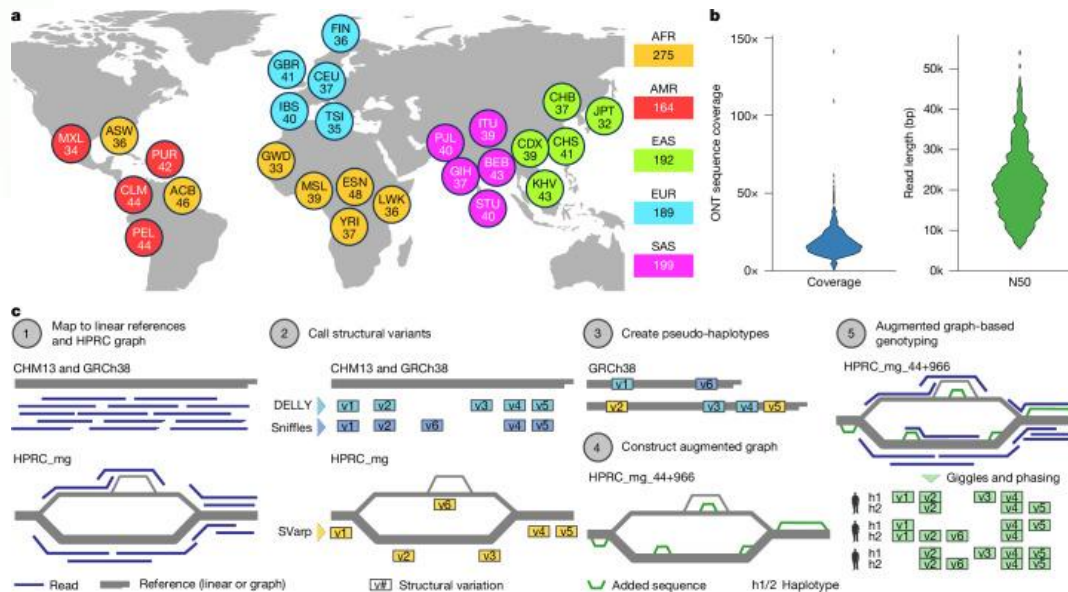
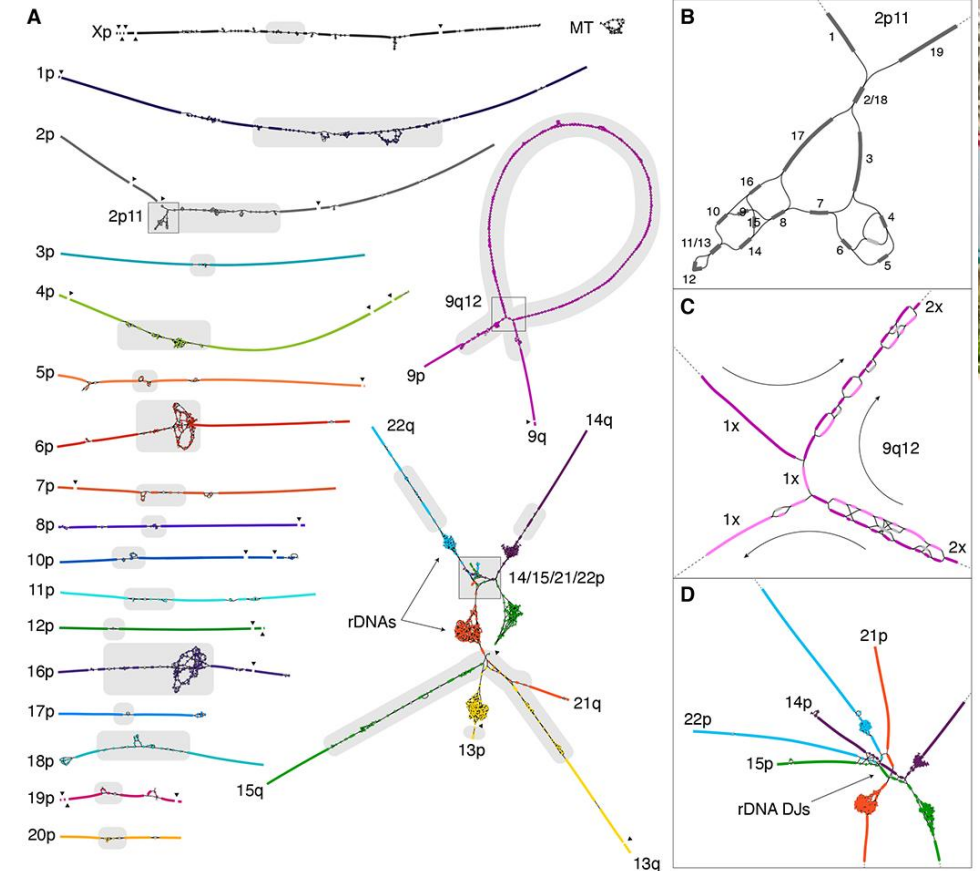
Ligation : 3-4h de technique  
Multiplex : 10-12h de technique



**Facile à technique**

Pacbio : gros coût d'entrée, gros volume // Nanopore : faible coût d'entrée, petit volumes

# Nouvelles ressources



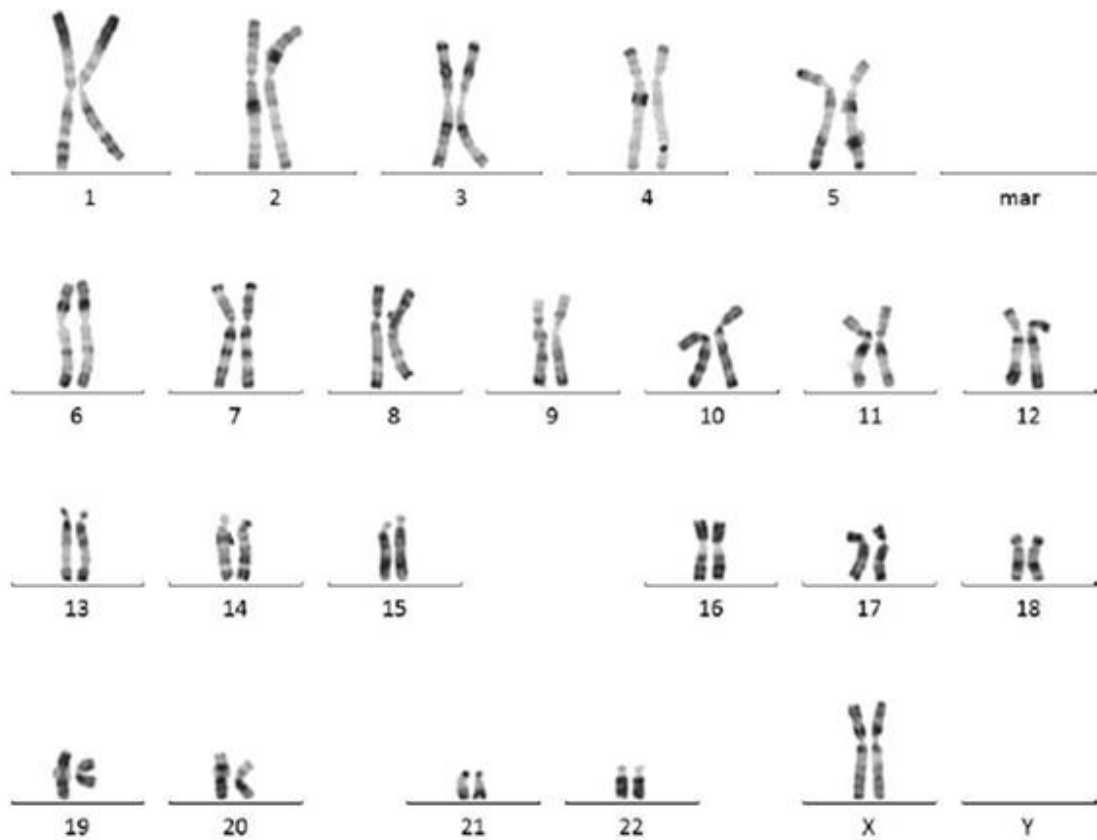
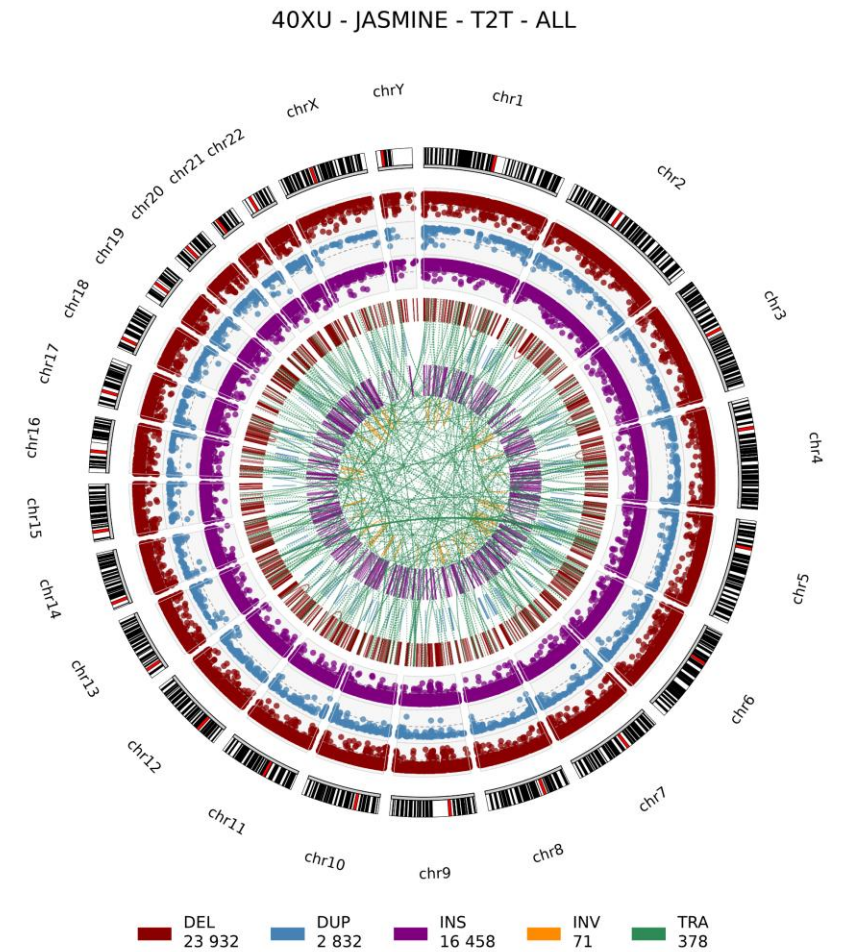
**On détecte concrètement 3-6 fois plus de variants de structure en LRS**

Schloissnig S, Pani S, Ebler J, et al. Structural variation in 1,019 diverse humans based on long-read sequencing. *Nature*. 2025;644(8076):442-452. doi:10.1038/s41586-025-09290-7

Nurk S, Koren S, Rhie A, et al. The complete sequence of a human genome. *Science*. 2022;376(6588):44-53. doi:10.1126/science.abj6987

Moustakli E, Christopoulos P, Potiris A, et al. Long-Read Sequencing and Structural Variant Detection: Unlocking the Hidden Genome in Rare Genetic Disorders. *Diagnostics (Basel)*. 2025;15(14):1803. Published 2025 Jul 17. doi:10.3390/diagnostics15141803

# Gros changement visuel



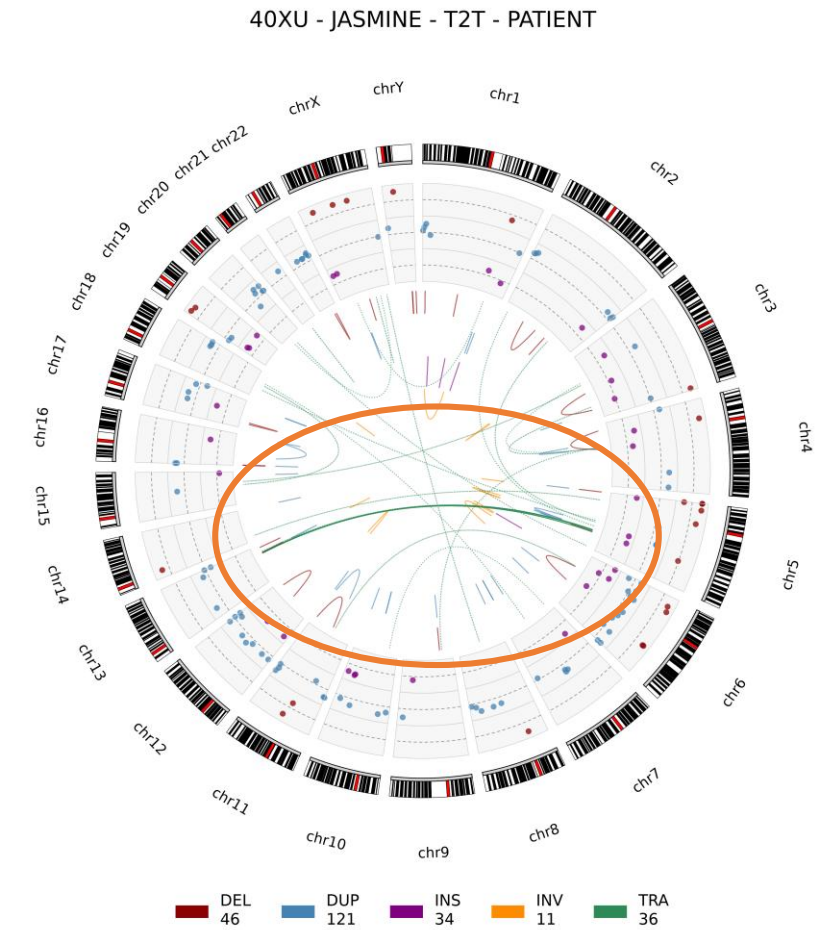
[illegible]

# La bioinformatique, un outil essentiel

Population Générale (gnomAD, dbvar, ColorSDB, 1kgv, Lin ...)

Elements répétés (Alu, Tandem repeat, duplications segmentaires ...)

**Beaucoup  
d'éléments mobiles  
et d'insertion de  
population encore  
non connues**

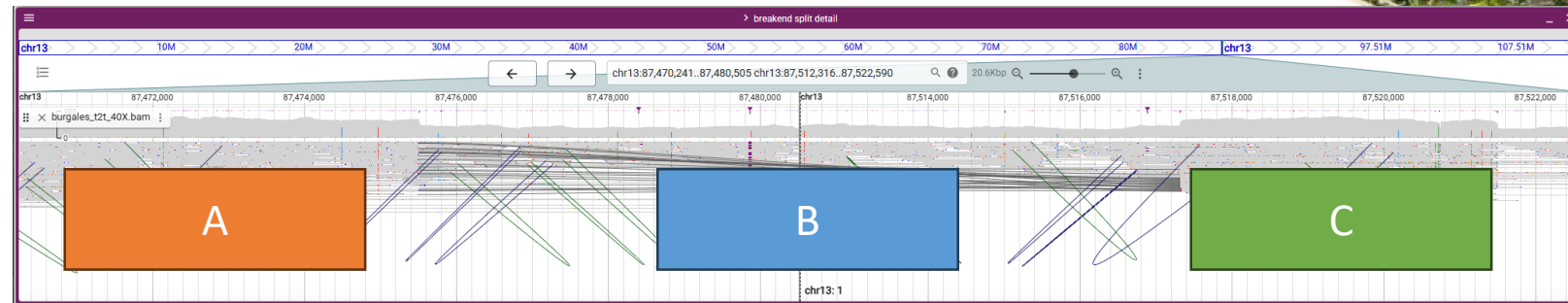


# Le LRS et ses défauts

| CHR   | START     | END       | CHR2  | START2    | END2      | SVTYPE | STRAND | SVLEN   | FOUNE |
|-------|-----------|-----------|-------|-----------|-----------|--------|--------|---------|-------|
| chr5  | 107895436 | 107929455 |       |           |           | DEL    |        | 34019   | MID   |
| chr5  | 107895436 | 107895437 | chr5  | 124831127 | 124831128 | TRA    | +-     |         | YES   |
| chr5  | 107929455 | 107929456 | chr5  | 125535930 | 125535931 | TRA    | ++     |         | YES   |
| chr5  | 123773208 | 123807570 |       |           |           | DEL    |        | 34362   | MID   |
| chr5  | 123807570 | 123807571 | chr5  | 129976695 | 129976696 | TRA    | ++     |         | MID   |
| chr5  | 124831127 | 124883981 |       |           |           | DEL    |        | 52854   | NO    |
| chr5  | 124883981 | 124883982 | chr13 | 85946079  | 85946080  | TRA    | ++     |         | YES   |
| chr5  | 125535930 | 125571429 |       |           |           | DEL    |        | 35499   | NO    |
| chr5  | 125571429 | 125571430 | chr13 | 90864802  | 90864803  | TRA    | ++     |         | YES   |
| chr5  | 125649762 | 125655863 |       |           |           | DEL    |        | 6101    | NO    |
| chr5  | 125649762 | 125649763 | chr13 | 88087905  | 88087906  | TRA    | +-     |         | YES   |
| chr5  | 125655863 | 125655864 | chr5  | 126054559 | 126054560 | TRA    | +-     |         | MID   |
| chr5  | 125657493 | 126054559 |       |           |           | DEL    |        | 397066  | NO    |
| chr5  | 125657493 | 125657494 | chr13 | 86108996  | 86108997  | TRA    | +-     |         | YES   |
| chr5  | 129442307 | 129612152 |       |           |           | DEL    |        | 169845  | MID   |
| chr5  | 129442307 | 129442308 | chr5  | 130113437 | 130113438 | TRA    | ++     |         | MID   |
| chr5  | 129612152 | 129612153 | chr5  | 130129103 | 130129104 | TRA    | ++     |         | MID   |
| chr5  | 129976695 | 130113437 |       |           |           | DEL    |        | 136742  | NO    |
| chr5  | 130129103 | 131048232 |       |           |           | DEL    |        | 919129  | NO    |
| chr5  | 131048232 | 131048233 | chr13 | 86003690  | 86003691  | TRA    | +-     |         | YES   |
| chr5  | 131105335 | 131132688 |       |           |           | DEL    |        | 27353   | NO    |
| chr5  | 131105335 | 131105336 | chr13 | 87694246  | 87694247  | TRA    | ++     |         | YES   |
| chr5  | 131132688 | 131132689 | chr13 | 87289611  | 87289612  | TRA    | ++     |         | YES   |
| chr13 | 85823483  | 85823484  | chr13 | 87694225  | 87694226  | TRA    | ++     |         | MID   |
| chr13 | 85823483  | 85946079  |       |           |           | DUP    |        | 122596  | MID   |
| chr13 | 86003690  | 86009868  |       |           |           | DUP    |        | 6178    | MID   |
| chr13 | 86071091  | 86071092  | chr5  | 123773208 | 123773209 | TRA    | ++     |         | YES   |
| chr13 | 86071091  | 86108996  |       |           |           | DUP    |        | 37905   | NO    |
| chr13 | 87424130  | 87424131  | chr13 | 88104326  | 88104327  | TRA    | +-     |         | MID   |
| chr13 | 87424130  | 87475516  |       |           |           | DUP    |        | 51386   | MID   |
| chr13 | 87475516  | 87475517  | chr13 | 87517316  | 87517317  | TRA    | ++     |         | MID   |
| chr13 | 87475516  | 87517316  |       |           |           | DUP    |        | 41800   | MID   |
| chr13 | 87517316  | 87521496  |       |           |           | DUP    |        | 4180    | NO    |
| chr13 | 87521496  | 87521497  | chr13 | 87565677  | 87565678  | TRA    | ++     |         | MID   |
| chr13 | 87565677  | 87694225  |       |           |           | DUP    |        | 128548  | NO    |
| chr13 | 87694246  | 87973014  |       |           |           | DUP    |        | 278768  | MID   |
| chr13 | 87973985  | 88087905  |       |           |           | DUP    |        | 113920  | NO    |
| chr13 | 88104326  | 90864802  |       |           |           | DUP    |        | 2760476 | NO    |

## Cas de chromoanagenesis

38 SV → 10 bons, 16 moyens, 12 non callés



## Réalité

Insertion de deux blocs de chr13 dans le chr5



=

2 DUP + 3 TRA

Appel du caller → “Je n’ai pas de bloc B” → 1 DEL + 3 TRA

Compléments → Wakhan, delly, spectre-ont

# Conclusion

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- Le LRS n'est PAS une technique magique
  - Plus de SV détectés → OUI
  - Facile à techniquer → OUI
  - Aussi bon que le reste → OUI
  - Nécessité un.e bioinfo → OUI
  - Fait tout même le café → NON
    - Limité pour les mosaïques
    - Limité pour les clones
- ✓ Le caryotype reste irremplaçable

