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France Médecine Génomique 2025

Jean-François Deleuze, Ph.D, HDR
Head CNRGH
Head CREFIX

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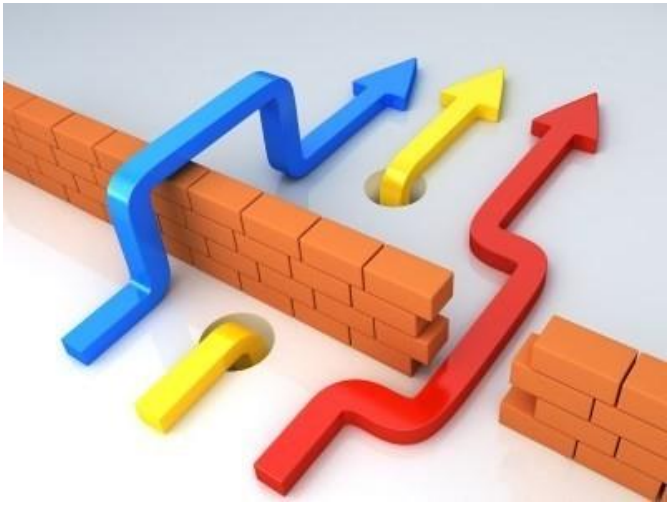
Innovations technologiques en médecine génomique dans le cadre du PFMG 2025

Journées de l'Innovation en Biologie

Palais des congrès
Paris, France
2 Décembre 2022

CNRGH
CENTRE NATIONAL DE RECHERCHE EN GÉNOMIQUE HUMAINE

Centre de **REF**érence, d'**I**nnovation, d'e**X**pertise et de transfert (CRefIX)



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Des succès …. et des besoins d'évolution

« Les Centeuro-nnials »

MGI

- **DNBSEQ Tx**
- 100 $
- 700 génomes per run
- 2020

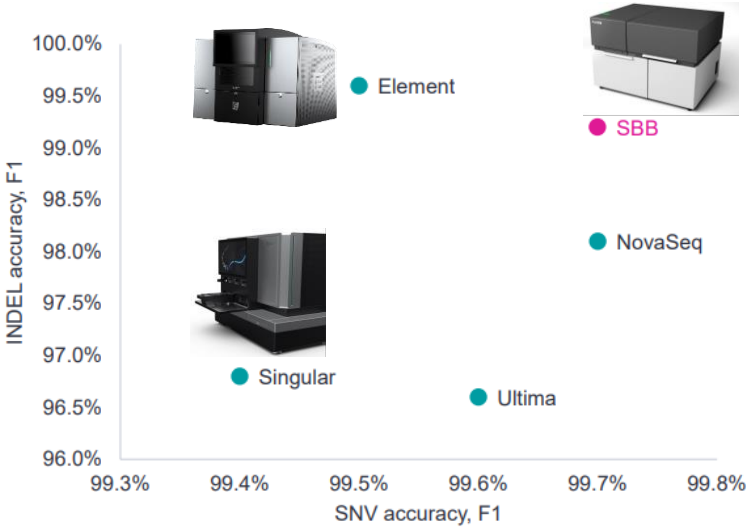
ULTIMA GENOMICS

- **UG 100TM**
- 100 $
- génomes per run ?
- 2023

illumina®

- **Novaseq X**
- 200 $
- 128 génomes per run
- 2023

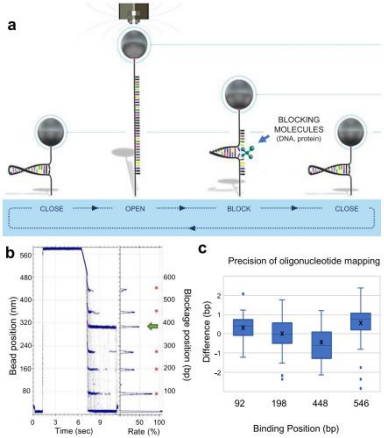
Les fast followers



**Omniome*

Et la France dans tout ca?

Depixus®



Pour vivre heureux vivons cachés…?

Le diable se cache dans les détails

CRefIX France Médecine Génomique 2025 — CNRGH Centre National de Recherche en Génomique Humaine — France Génomique — EASI Genomics — ...

Discussions > Choix > Evaluation > Implémentation

Une profusion de technologies qui impose la mise en place de standards dans les "genomic profiling workflows"

European Partnership on Metrology
Call 2022 – Digital Transformation, Health, Integrated European Metrology, Normative and Research Potential

Selected Research Topic number: **SRT-h01**
Version: 1.0

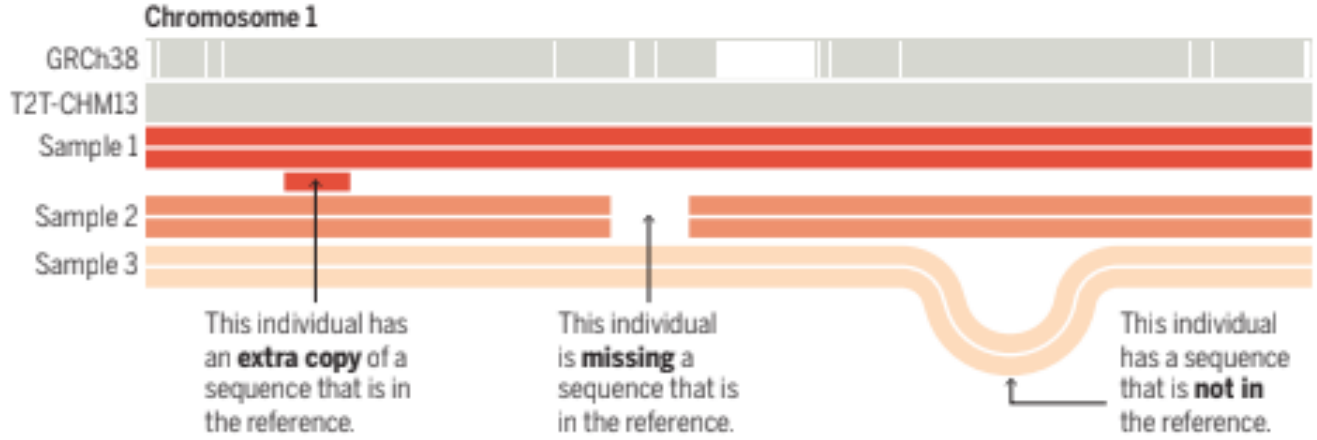
Title: Metrology for genomic profiling to support early cancer detection and precision medicine

Abstract

Advances in genomics are transforming cancer care, enabling earlier detection, and driving development of targeted diagnostics and therapies (personalised medicine), improving patient outcomes and effectiveness of health systems. The quality and comparability of tumour genomic profiling currently varies significantly and development of the standards and metrology to support the field is in its infancy. Therefore, there is a need for the application of metrological principles and development of methods and materials to improve quality and reproducibility of critical processes within genomic profiling workflows, and reference measurement systems for high accuracy SI-traceable cancer gene measurement to improve comparability and support assay validation as required by the In Vitro Diagnostic Regulation (IVDR).

A more complete reference

The new human genome assembly, T2T-CHM13, from the Telomere-to-Telomere Consortium now includes complex and repetitive regions of chromosomes that had not been included in previous versions of the human genome assembly (GRCh38). Although the Y chromosome remains to be completed, this new reference could be annotated with regulatory regions, variants, and sequence diversity to give a fuller picture of human genomic variation.



SVs, régions complexes, haplotypes: Long comment?

- **Short read sequencing**
  Tens of millions of pieces

- **Long read sequencing**
  Hundreds of thousands of pieces

Critical length in long-read resequencing

Wouter De Coster, Mojca Strazisar and Peter De Rijk

VIB-UAntwerp Center for Molecular Neurology, 2610 Antwerp, Belgium

Received May 13, 2019; Revised December 06, 2019; Editorial Decision December 17, 2019; Accepted January 02, 2020

ABSTRACT

Long-read sequencing has substantial advantages for structural variant discovery and phasing of variants compared to short-read technologies, but the required and optimal read length has not been assessed. In this work, we used long reads simulated from human genomes and evaluated structural variant discovery and variant phasing using current best practice bioinformatics methods. We determined that optimal discovery of structural variants from human genomes can be obtained with reads of minimally 20 kb. Haplotyping variants across genes only reaches its optimum from reads of 100 kb. These findings are important for the design of future long-read sequencing projects.

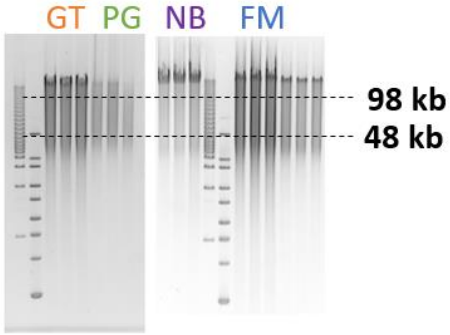
mining the pathogenicity of pairs of compound heterozygous variants and the effect of cis-regulation (12).

To our knowledge, the dependence of SV detection and variant phasing on the read length has not been formally assessed. In this work, we evaluated the influence of the read length on the accuracy and sensitivity of SV detection and on the length of contiguous stretches of phased nucleotides based on simulated long-read data from recent human genome assemblies.

MATERIALS AND METHODS

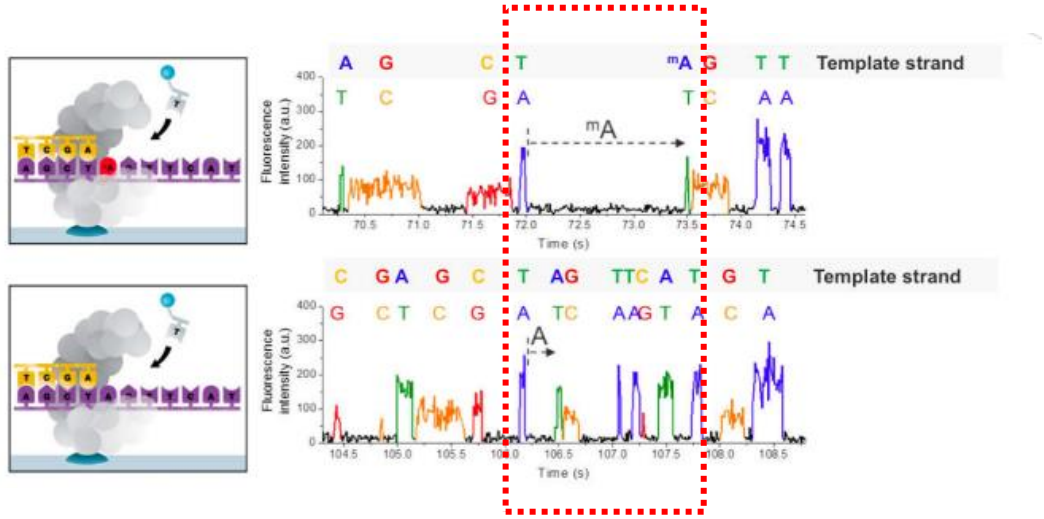
Commands for processing and analysis are included in the Supplementary Data. All scripts and commands are available at https://github.com/wdecoster/read_length_SV_discovery.

We include a high-quality phased genome assem-

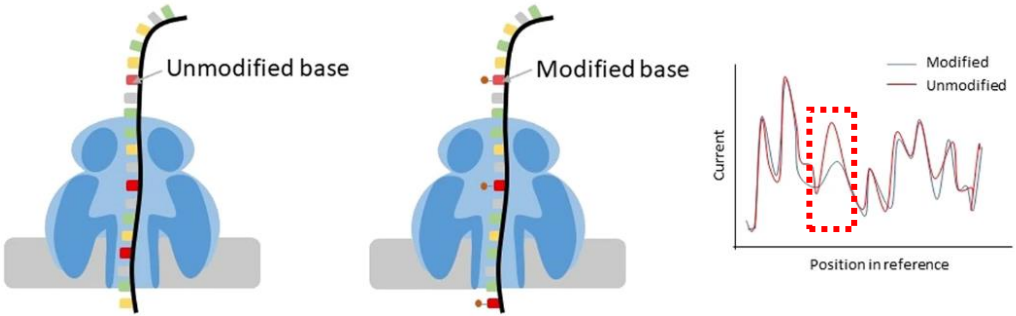


Vers le tout en un…

PacBio



Oxford NANOPORE Technologies



Defidiag long fragment

Sélection des échantillons / critères:

- Cibler les patients atteints de DI sévères (avec bilan neuropsy) à profondes, avec malformations associées, non concluants via analyse initiale WGS short read (absent totale de variants causaux, y compris de classe 3)

- **analyse trio : 20 échantillons** (cas index), soit 60 échantillons totaux

Caractéristiques des échantillons pour le long read:

- ADN de haut poids moléculaire: > 20/30 kb (50 kb optimal)

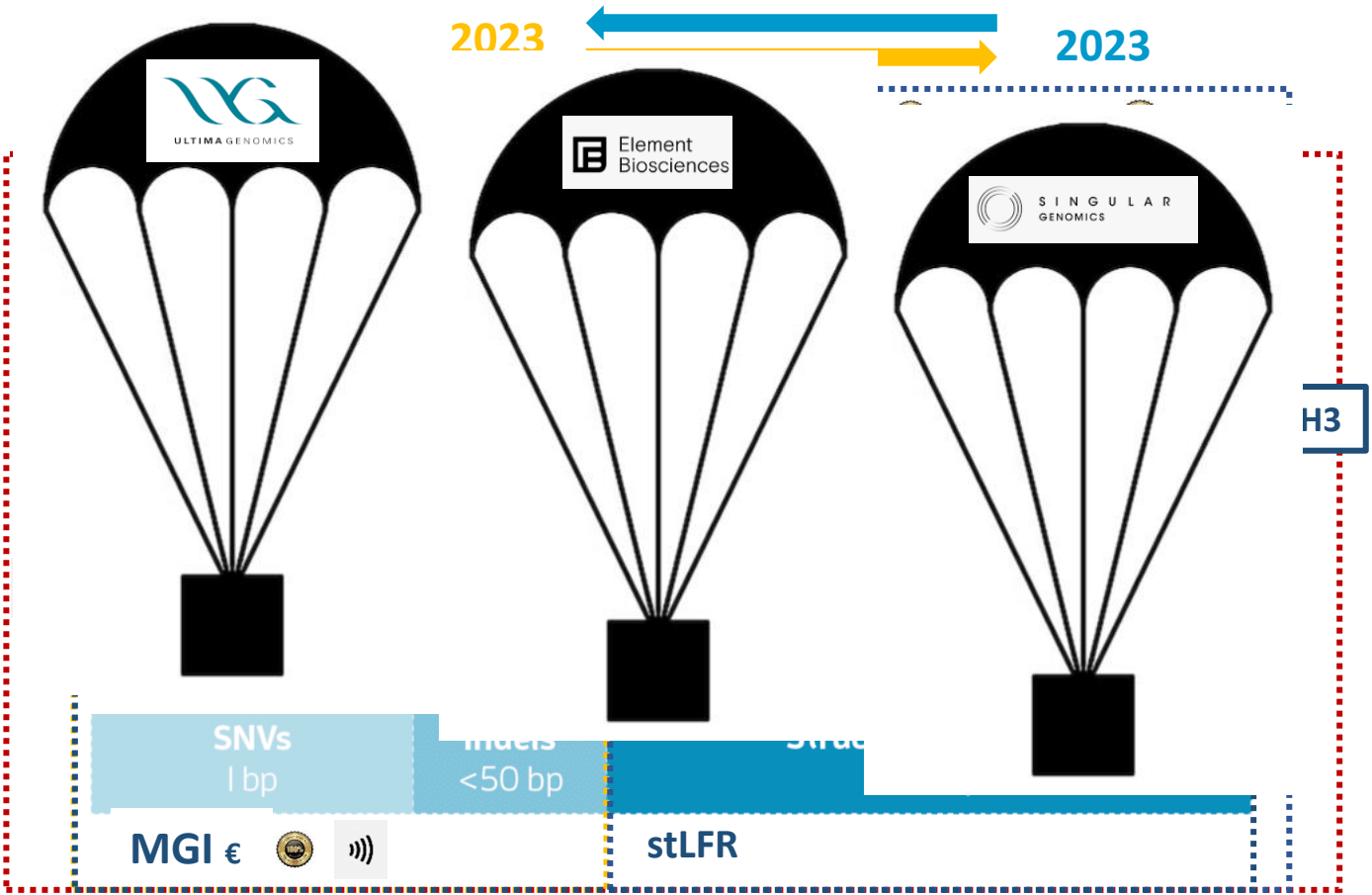
- sang congelé (obtention ADN de qualité) (kit Nanobinds de Circulomics) - *3 x 300µL de sang congelé*

Données complémentaires nécessaires:

- données cliniques (sexe)

- données de séquençage WGS en short read (1ère analyse DEFIDIAG)

La compétition s'accélère…



Exemples d'impact du CREFIX/CNRGH sur les évolutions

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ARTICLE

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Accelerated genome sequencing with controlled costs for infants in intensive care units: a feasibility study in a French hospital network

Anne-Sophie Denommé-Pichon[1,2,3,21], Antonio Vitobello[1,2,21], Robert Olaso[4,5], Alban Ziegler[6], Médéric Jeanne[7,8], Frédéric Tran Mau-Them[1,2], Victor Couturier[2], Caroline Racine[1,2,3], Bertrand Isidor[9,10], Charlotte Poë[2], Thibaud Jouan[2], Anne Boland[4], Bertrand Fin[4], Delphine Bacq-Daian[4], Céline Besse[4], Aurore Garde[1,2,3], Adeline Prost[1,2], Philippine Garret[2], Émilie Tisserant[1,2], Julian Delanne[2,3], Sophie Nambot[2,3], Aurélien Juven[1,2], Magali Gorce[3], Mathilde Nizon[9,10], Marie Vincent[9,10], Sébastien Moutton[2,3], Mélanie Fradin[11,12], Alinoë Lavillaureix[11], Paul Rollier[11], Yline Capri[13], Julien Van-Gils[14], Tiffany Busa[13], Sabine Sigaudy[15], Laurent Pasquier[11], Magalie Barth[6], Ange-Line Bruel[1,2], Cyril Flamant[16], Clément Prouteau[6], Dominique Bonneau[6], Annick Toutain[7,8], Corinne Chantegret[17], Patrick Callier[2,18], Christophe Philippe[1,2], Yannis Duffourd[1,2], Jean-François Deleuze[4,19], Arthur Sorlin[1,2,3], Laurence Faivre[2,3,21] and Christel Thauvin-Robinet[1,2,20,21]

Obtaining a rapid etiological diagnosis for infants with early-onset rare diseases remains a major challenge. These diseases often have a severe presentation and unknown prognosis, and the genetic causes are very heterogeneous. In a French hospital network, we assessed the feasibility of performing accelerated trio-genome sequencing (GS) with limited additional costs by integrating urgent requests into the routine workflow. In addition to evaluating our capacity for such an approach, this prospective multicentre pilot study was designed to identify pitfalls encountered during its implementation. Over 14 months, we included newborns and infants hospitalized in neonatal or paediatric intensive care units with probable genetic disease and in urgent need for etiological diagnosis to guide medical care. The duration of each step and the pitfalls were recorded. We analysed any deviation from the planned schedule and identified obstacles. Trio-GS was performed for 37 individuals, leading to a molecular diagnosis in 18/37 (49%), and 21/37 (57%) after reanalysis. Corrective measures and protocol adaptations resulted in a median duration of 42 days from blood sampling to report. Accelerated trio-GS is undeniably valuable for individuals in an urgent care context. Such a circuit should coexist with a rapid or ultra-rapid circuit, which, although more expensive, can be used in particularly urgent cases. The drop in GS costs should result in its generalized use for diagnostic purposes and lead to a reduction of the costs of rapid GS.

European Journal of Human Genetics (2022) 30:567–576; https://doi.org/10.1038/s41431-021-00998-4

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OMIXCARE: OMICS technologies solved about 33% of the patients with heterogeneous rare neuro-developmental disorders and negative exome sequencing results and identified 13% additional candidate variants

Estelle Colin[1,2*†], Yannis Duffourd[2,3†], Emilie Tisserant[2], Raissa Relator[4], Ange-Line Bruel[2,3], Frédéric Tran Mau-Them[2,3], Anne-Sophie Denommé-Pichon[2,3], Hana Safraou[2,3], Julian Delanne[2,5], Nolwenn Jean-Marçais[5], Boris Keren[6], Bertrand Isidor[7], Marie Vincent[7], Cyril Mignot[8,9], Delphine Heron[10], Alexandra Afenjar[11], Solveig Heide[10], Anne Faudet[10], Perrine Charles[10], Sylvie Odent[12,13], Yvan Herenger[14], Arthur Sorlin[5], Sébastien Moutton[5], Jennifer Kerkhof[4], Haley McConkey[4], Martin Chevarin[2,3], Charlotte Poë[2,3], Victor Couturier[2,3], Valentin Bourgeois[2,3], Patrick Callier[2], Anne Boland[15], Robert Olaso[15,16], Christophe Philippe[2,3], Bekim Sadikovic[4,17], Christel Thauvin-Robinet[2,3,18†], Laurence Faivre[2,5†], Jean-François Deleuze[15,16†] and Antonio Vitobello[2,3*†]

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Merci de votre attention