Análisis del transcriptoma mediante RNA-seq: Aplicaciones actuales y perspectivas

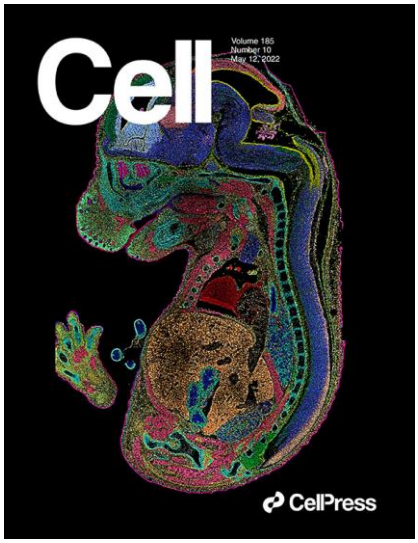
Oscar Ortega-Recalde, MD, PhD
Profesor Asistente | Facultad de Medicina
Universidad Nacional de Colombia

1

Conflictos de Interés

No existe ningún conflicto de interés para participar en este evento.

2



"Computers do not just scale up biology… they bring with them completely new tools and questions"
Stevens Hallam

Chen *et al*, Cell, 2022

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Contenido

- Introducción
- Flujos de análisis de RNA-seq
- Ejemplos de aplicaciones actuales
- Perspectivas

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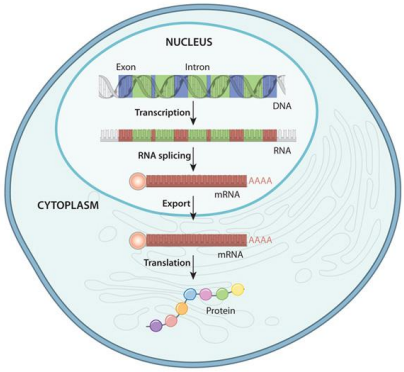
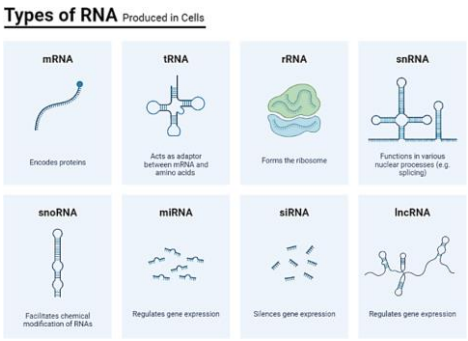
Introducción

El transcriptoma constituye el **conjunto total de moléculas de ARN** presentes en una célula o grupo de células en un momento determinado.





An overview of the flow of information from DNA to protein in a eukaryote, Nature; Jabbar *et al*, Molecular Biology Reports 2024

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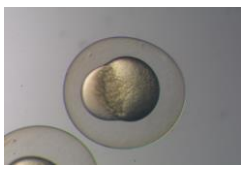
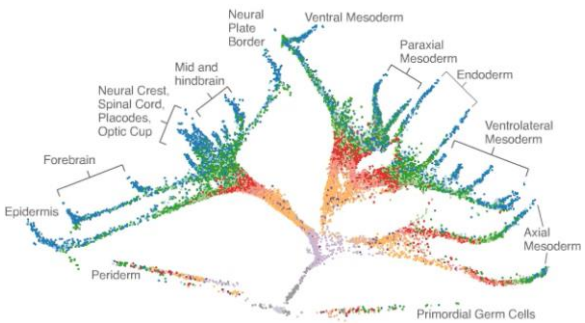
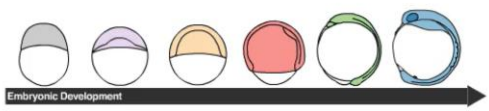
Introducción



A diferencia del genoma, el transcriptoma es **variable** en **lugar, tiempo** y respuesta a **estímulos**.





Farrell *et al*, Science, 2018

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Introducción

Existen **diversas técnicas** para el análisis de expresión génica / transcritos.

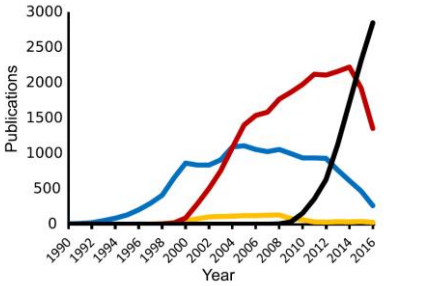

Fig 1. Transcriptomics method use over time. Published papers since 1990, referring to RNA sequencing (black), RNA microarray (red), expressed sequence tag (blue), and serial/cap analysis of gene expression (yellow)[12].

https://doi.org/10.1371/journal.pcbi.1005457.g001

Table 1. Comparison of contemporary methods [23] [24] [10].

Method	RNA-Seq	Microarray
Throughput	High [10]	Higher [10]
Input RNA amount	Low ~ 1 ng total RNA [25]	High ~ 1 μg mRNA [26]
Labour intensity	High (sample preparation and data analysis) [10][23]	Low [10][23]
Prior knowledge	None required, though genome sequence useful [23]	Reference transcripts required for probes [23]
Quantitation accuracy	~90% (limited by sequence coverage) [27]	>90% (limited by fluorescence detection accuracy) [27]
Sequence resolution	Can detect SNPs and splice variants (limited by sequencing accuracy of ~99%) [27]	Dedicated arrays can detect splice variants (limited by probe design and cross-hybridisation) [27]
Sensitivity	10^{-6} (limited by sequence coverage) [27]	10^{-9} (limited by fluorescence detection) [27]
Dynamic range	$>10^5$ (limited by sequence coverage) [28]	10^3–10^4 (limited by fluorescence saturation) [28]
Technical reproducibility	>99% [29][30]	>99% [31][32]

RNA-Seq, RNA Sequencing

- EST
- RNA microarrays
- SAGE/CAGE
- RNA-seq

Lowe *et al*, PLOS Comp Biol, 2016

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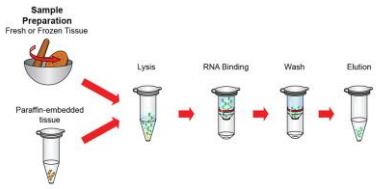
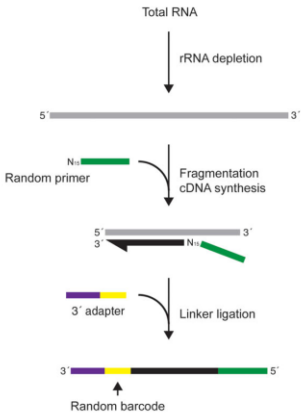
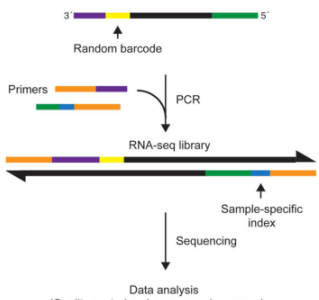
Introducción

Preparación de librerías para RNA-seq







Poulsen *et al*, Curr Protoc Nucleic Acid Chem, 2018

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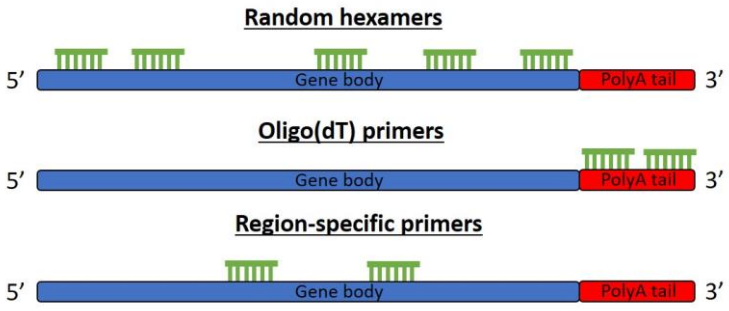
Introducción

Preparación de librerías para RNA-seq



https://toptipbio.com/cdna-synthesis-primers/

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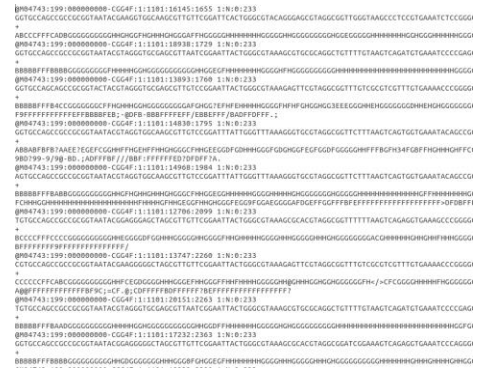
Introducción

Secuenciación de siguiente generación y llamado de bases

Plataformas de NGS



Archivos FASTQ

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Flujos de análisis de RNA-seq

- **No existe un pipeline óptimo para todas** las diferentes aplicaciones y escenarios de análisis de RNA-seq.
- Los experimentos y las estrategias de análisis deben ser **adaptados** dependiendo del **organismo** a ser estudiado y los **objetivos** del estudio.
- RNA-seq puede ser utilizado de **manera aislada o en combinación** con otros métodos de genómica funcional para analizar expresión génica.

Conesa *et al*, Genome Biology, 2016

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Flujos de análisis de RNA-seq

RNA-seq: Basic Bioinformatics Analysis

Fei Ji[1,2] and Ruslan I. Sadreyev[1,3,4]

[1]Department of Molecular Biology, Massachusetts General Hospital, Boston, Massachusetts
[2]Department of Genetics, Harvard Medical School, Boston, Massachusetts
[3]Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts
[4]Corresponding author: *sadreyev@molbio.mgh.harvard.edu*

CURRENT PROTOCOLS
Current Protocols in Molecular Biology e68
Published in Wiley Online Library (wileyonlinelibrary.com).
doi: 10.1002/cpmb.68

Conesa et al. Genome Biology (2016) 17:13
DOI 10.1186/s13059-016-0881-8

Genome Biology

REVIEW Open Access

A survey of best practices for RNA-seq data analysis

Ana Conesa[1,2*], Pedro Madrigal[3,4*], Sonia Tarazona[2,5], David Gomez-Cabrero[6,7,8,9], Alejandra Cervera[10], Andrew McPherson[11], Michał Wojciech Szcześniak[12], Daniel J. Gaffney[3], Laura L. Elo[13], Xuegong Zhang[14,15] and Ali Mortazavi[16,17*]

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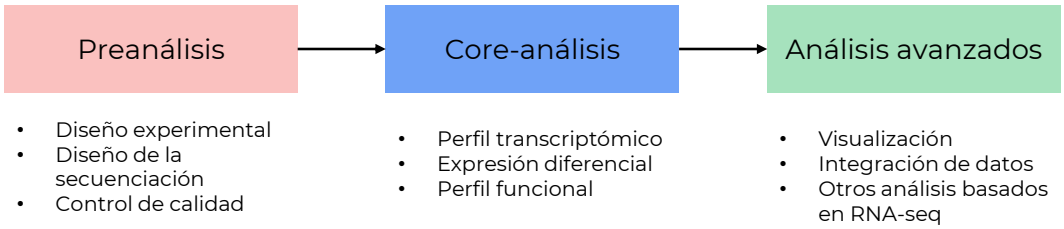
Flujos de análisis de RNA-seq



Conesa *et al*, Genome Biology, 2016

Flujos de análisis de RNA-seq

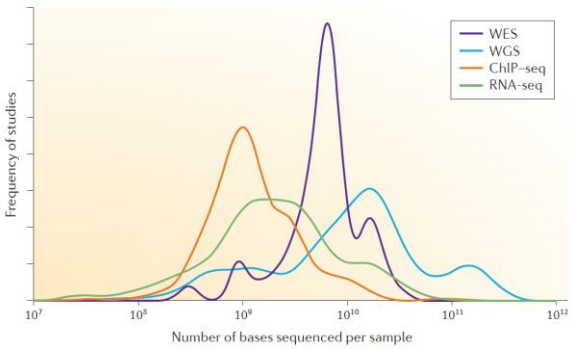
Preanálisis

- Las fases de diseño experimental y de secuenciación son **claves para evitar dificultades en los análisis posteriores.**
- Puntos para tener en cuenta:
  - Tipo de librería (single-end vs paired end)
  - Longitud de las lecturas
  - Numero de replicas y numero de lecturas.
  - Spike-in
  - Aleatorización

Conesa *et al*, Genome Biology, 2016

Flujos de análisis de RNA-seq

Número de lecturas



5m 50m

Los requerimientos de secuenciación dependen del **tamaño, complejidad del transcriptoma y objetivo de investigación**.

30-50m = Permite la cuantificación de genes con expresión > 10 FPKM (80% con 36m)

> 80m = Alta profundidad, cuantificación de genes con niveles de expresión más bajas.

> 200m = Detección del rango completo de transcritos

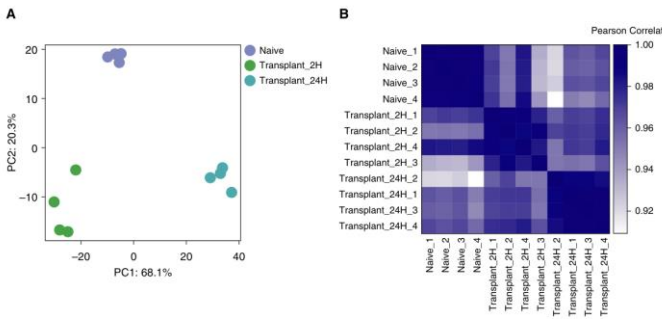
Sims *et al*, Nat Rev Genet, 2014

Flujos de análisis de RNA-seq

Control de calidad

Se recomienda realizarse en los **diferentes niveles de procesamiento**

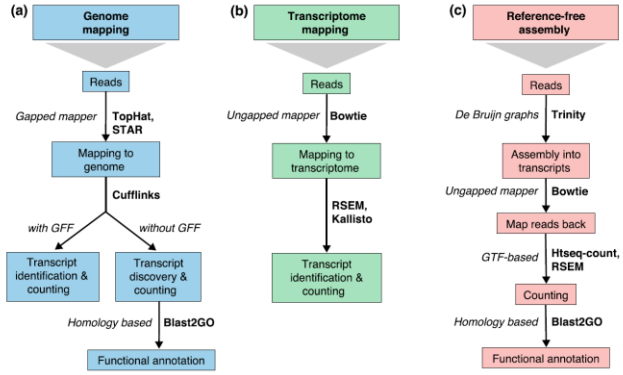
- Lecturas crudas
- Alineamiento de lecturas
- Cuantificación
- Reproducibilidad(e.g. R2 > 0.9)



Koch *et al*, Translational Review, 2018

Flujos de análisis de RNA-seq

Estrategias de mapeo e identificación de transcritos



Conesa *et al*, Genome Biology, 2016??

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Flujos de análisis de RNA-seq

Cuantificación de transcritos

Matriz de conteo

Gene Name	Rep1 Counts	Rep2 Counts	Rep3 Counts
A (2kb)	10	12	30
B (4kb)	20	25	60
C (1kb)	5	8	15
D (10kb)	0	0	1

RPKM (Reads per kilo base per million mapped reads)

Gene Name	Rep1 RPKM	Rep2 RPKM	Rep3 RPKM
A (2kb)	1.43	1.33	1.42
B (4kb)	1.43	1.39	1.42
C (1kb)	1.43	1.78	1.42
D (10kb)	0	0	0.009

RPM (Reads per million mapped reads)

Gene Name	Rep1 RPM	Rep2 RPM	Rep3 RPM
A (2kb)	2.86	2.67	2.83
B (4kb)	5.71	5.56	5.66
C (1kb)	1.43	1.78	1.42
D (10kb)	0	0	0.09

FPKM (Fragments per kilo base per million mapped reads) – PE

https://www.youtube.com/watch?v=TTUrtCY2k-w

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Flujos de análisis de RNA-seq

Análisis de expresión diferencial

Table 4. RNA-Seq differential gene expression software.

Software	Environment	Specialisation
Cuffdiff2 [111]	Unix-based	Transcript analysis at isoform-level
EdgeR [112]	R/Bioconductor	Any count-based genomic data
DEseq2 [113]	R/Bioconductor	Flexible data types, low replication
Limma/Voom [114]	R/Bioconductor	Microarray or RNA-Seq data, isoform analysis, flexible experiment design

RNA-Seq, RNA sequencing.

https://doi.org/10.1371/journal.pcbi.1005457.t004

La normalización es crítica en el proceso de análisis bioinformático

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Flujos de análisis de RNA-seq

Análisis de expresión diferencial

Love et al. Genome Biology (2014) 15:550
DOI 10.1186/s13059-014-0550-8

Genome Biology

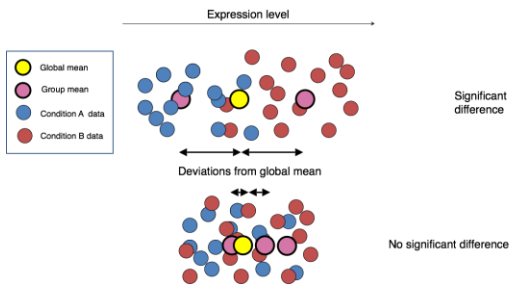
METHOD Open Access

Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2

Michael I Love[1,2,3], Wolfgang Huber[2] and Simon Anders[2*]

Abstract

In comparative high-throughput sequencing assays, a fundamental task is the analysis of count data, such as read counts per gene in RNA-seq, for evidence of systematic changes across experimental conditions. Small replicate numbers, discreteness, large dynamic range and the presence of outliers require a suitable statistical approach. We present *DESeq2*, a method for differential analysis of count data, using shrinkage estimation for dispersions and fold changes to improve stability and interpretability of estimates. This enables a more quantitative analysis focused on the strength rather than the mere presence of differential expression. The *DESeq2* package is available at http://www.bioconductor.org/packages/release/bioc/html/DESeq2.html.



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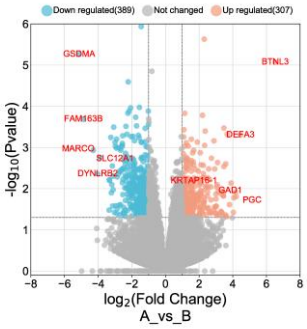
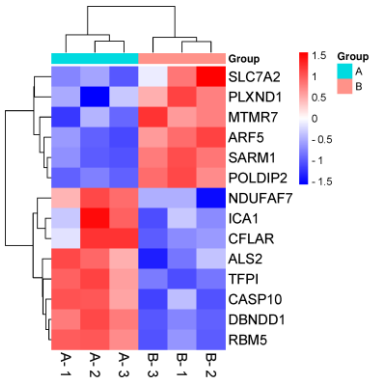
Flujos de análisis de RNA-seq

Visualización de expresión diferencial



Volcano plots



Heatmaps
(mapa de calor)

https://www.bioinformatics.com.cn/plot_basic_3_color_volcano_plot_086_en

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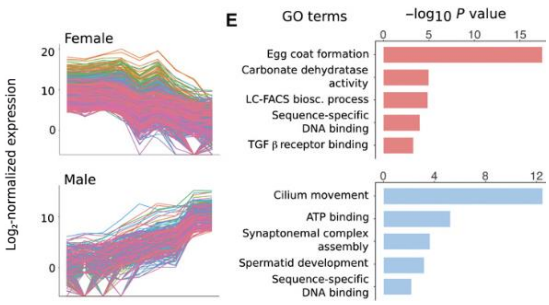
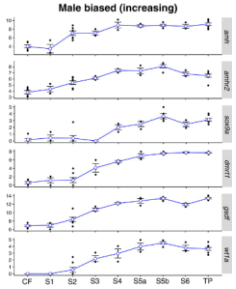
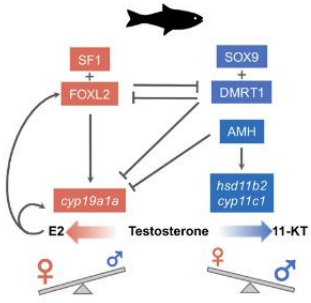
Flujos de análisis de RNA-seq

Perfiles funcionales







Co-expresión y
Enriquecimiento funcional

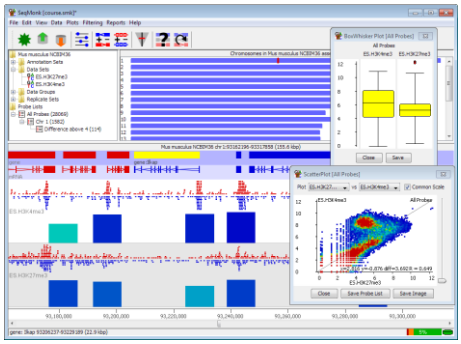
Análisis de vías
moleculares

Todd *et al*, Science Advances, 2019

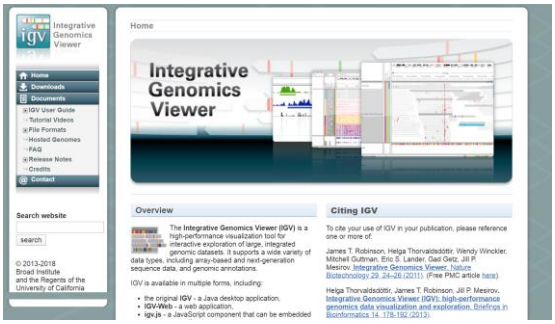
22

Flujos de análisis de RNA-seq

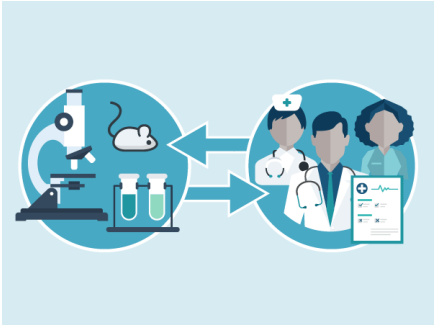
Visualización y análisis



SeqMonk



IGV



¿Qué utilidad tienen estas técnicas en investigación biomédica y contexto clínico?

Ejemplos de aplicaciones actuales

Análisis basados en RNA-seq son actualmente utilizados en el **contexto biomédico y clínico** para mejorar nuestra comprensión de los fenotipos.

"Fenotipos transcriptómicos"

- Detección de expresión diferencial
- Detección de SNVs
- Detección de fusiones génicas
- Detección de expresión aberrante
- Expresión monoalelica
- Detección de splicing aberrante

Peymani *et al*, Pediat Investig, 2022; Smirnov *et al*, Human Mutation, 2022

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Ejemplos de aplicaciones actuales

Received: 1 July 2021 | Revised: 15 May 2022 | Accepted: 25 May 2022
DOI: 10.1002/humu.24416

SPECIAL ARTICLE

Human Mutation HGVS WILEY

Guidelines for clinical interpretation of variant pathogenicity using RNA phenotypes

Dmitrii Smirnov[1,2] | Lea D. Schlieben[1,2] | Fatemeh Peymani[1,2] | Riccardo Berutti[1,2] | Holger Prokisch[1,2]

GG25_Art02_Montgomery ARjats.cls January 17, 2024 9:25

ANNUAL REVIEWS

Annual Review of Genomics and Human Genetics

RNA Sequencing in Disease Diagnosis

Craig Smail[1] and Stephen B. Montgomery[2]

[1]Genomic Medicine Center, Children's Mercy Research Institute, Children's Mercy Kansas City, Kansas City, Missouri, USA; email: csmail@cmh.edu

[2]Department of Biomedical Data Science, Department of Genetics, and Department of Pathology, Stanford University School of Medicine, Stanford, California, USA; email: smontgom@stanford.edu

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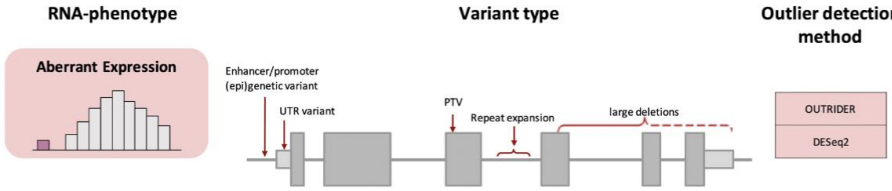
Detección de expresión aberrante

Expresión génica por fuera del rango fisiológico, a menudo asociada con niveles bajos de expresión génica.



Peymani *et al*, Pediat Investig, 2022; Smirnov *et al*, Human Mutation, 2022

Detección de expresión aberrante

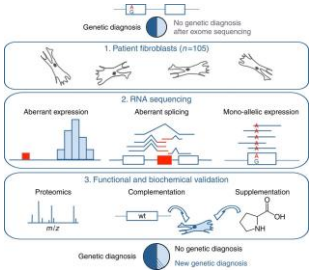
ARTICLE

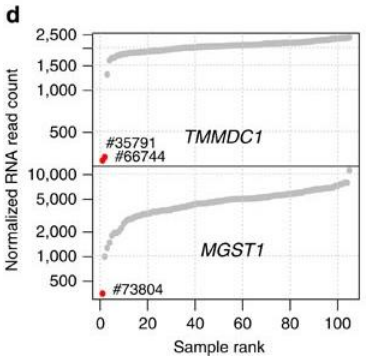
Received 29 Dec 2016 | Accepted 28 Apr 2017 | Published 12 Jun 2017 OPEN

Genetic diagnosis of Mendelian disorders via RNA sequencing

Laura S. Kremer[1,2,*], Daniel M. Bader[3,4,*], Christian Mertes[3], Robert Kopajtich[1,2], Garwin Pichler[5], Arcangela Iuso[1,2], Tobias B. Haack[1,2,†], Elisabeth Graf[1,2], Thomas Schwarzmayr[1,2], Caterina Terrile[1], Eliška Koňaříková[1,2], Birgit Repp[1,2], Gabi Kastenmüller[6], Jerzy Adamski[7], Peter Lichtner[1], Christoph Leonhardt[8], Benoit Funalot[9], Alice Donati[10], Valeria Tiranti[11], Anne Lombes[12,13,14], Claude Jardel[12,15], Dieter Gläser[16], Robert W. Taylor[17], Daniele Ghezzi[11], Johannes A. Mayr[18], Agnes Rötig[9], Peter Freisinger[19], Felix Distelmaier[20], Tim M. Strom[1,2], Thomas Meitinger[1,2], Julien Gagneur[3,4] & Holger Prokisch[1,2]

DESeq2





48 pacientes con enfermedades mitocondriales sin etiología molecular

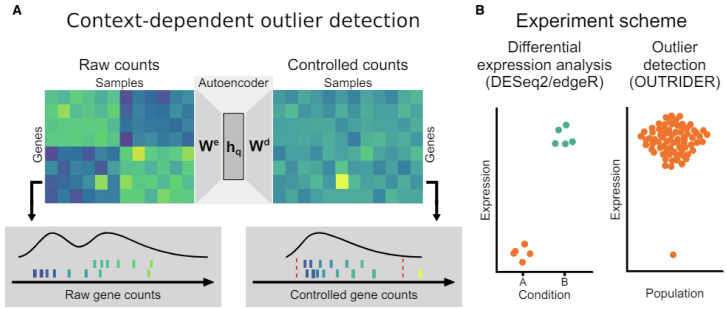
Detección de expresión aberrante

ARTICLE

OUTRIDER: A Statistical Method for Detecting Aberrantly Expressed Genes in RNA Sequencing Data

Felix Brechtmann,[1,3] Christian Mertes,[1,3] Agnė Matusevičiūtė,[1,3] Vicente A. Yépez,[1,2] Žiga Avsec,[1,2] Maximilian Herzog,[1] Daniel M. Bader,[1] Holger Prokisch,[1,4] and Julien Gagneur[1,2,*]

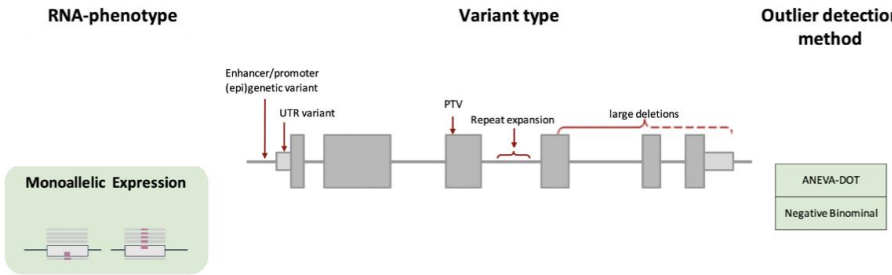
The American Journal of Human Genetics *103*, 907–917, December 6, 2018 907



29

Expresión monoalélica

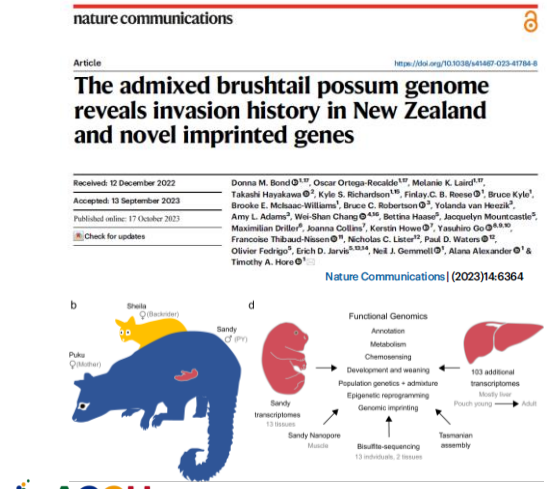
Condición en la cual solo uno de los alelos es expresado principalmente (>80%). Puede ser resultado de silenciamiento epigenético, variantes en promotores o que un alelo sea degradado.



Peymani *et al*, Pediat Investig, 2022; Smirnov *et al*, Human Mutation, 2022

30

Expresión monoalélica



nature communications

Article

https://doi.org/10.1038/s41467-023-41784-8

The admixed brushtail possum genome reveals invasion history in New Zealand and novel imprinted genes

Received: 12 December 2022

Accepted: 13 September 2023

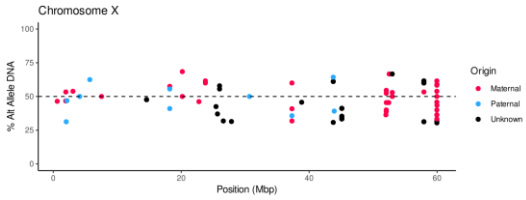
Published online: 17 October 2023

Check for updates

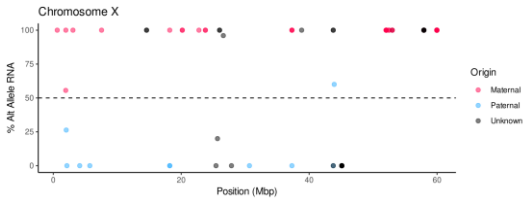
Donna M. Bond, Oscar Ortega-Recalde, Melanie K. Laird, Takashi Hayakawa, Kyle S. Richardson, Finlay C. B. Reese, Bruce Kyle, Brooke E. McIsaac-Williams, Bruce C. Robertson, Yolanda van Heezik, Amy L. Adams, Wei-Shan Chang, Bettina Haase, Jacquelyn Mountcastle, Maximilian Driller, Joanna Collins, Kerstin Howe, Yasuhiro Go, Francoise Thibaud-Nissen, Nicholas C. Lister, Paul D. Waters, Olivier Fedrigo, Erich D. Jarvis, Neil J. Gemmell, Alana Alexander & Timothy A. Hore

Nature Communications | (2023)14:6364

ADN cría Trio 1



ARN cría Trio 1



31

Expresión monoalélica

nature COMMUNICATIONS

ARTICLE

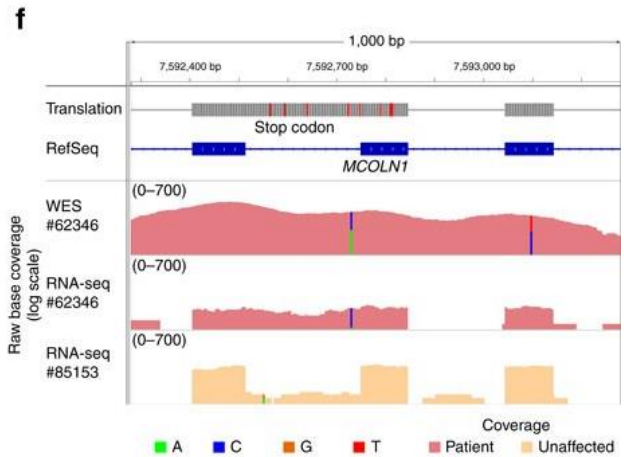
Received 29 Dec 2016 | Accepted 28 Apr 2017 | Published 12 Jun 2017

OPEN

Genetic diagnosis of Mendelian disorders via RNA sequencing

Laura S. Kremer, Daniel M. Bader, Christian Mertes, Robert Kopajtich, Garwin Pichler, Arcangela Iuso, Tobias B. Haack, Elisabeth Graf, Thomas Schwarzmayr, Caterina Terrile, Eliška Koňaříková, Birgit Repp, Gabi Kastenmüller, Jerzy Adamski, Peter Lichtner, Christoph Leonhardt, Benoit Funalot, Alice Donati, Valeria Tiranti, Anne Lombes, Claude Jardel, Dieter Gläser, Robert W. Taylor, Daniele Ghezzi, Johannes A. Mayr, Agnes Rötig, Peter Freisinger, Felix Distelmaier, Tim M. Strom, Thomas Meitinger, Julien Gagneur & Holger Prokisch

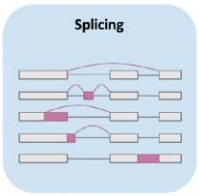
Test de distribución binomial negativa

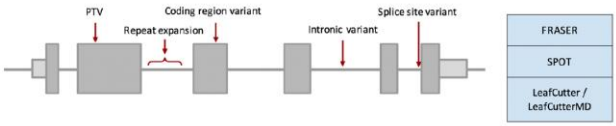


32

Detección de splicing aberrante

Las alteraciones de splicing son una causa conocida e importante de patologías humanas hereditarias (15%).
Técnicas basadas en RNA-seq pueden permitir la identificación y cuantificación del defecto subyacente.

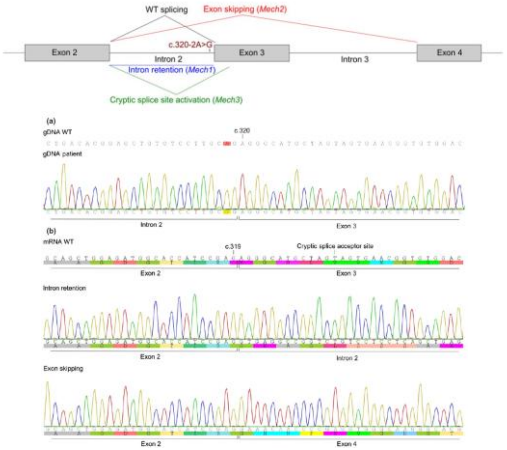


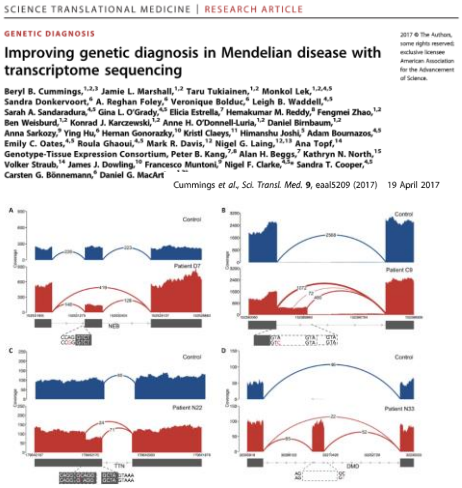


Peymani *et al*, Pediat Investig, 2022; Smirnov *et al*, Human Mutation, 2022

33

Detección de splicing aberrante





SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

GENETIC DIAGNOSIS

Improving genetic diagnosis in Mendelian disease with transcriptome sequencing

Beryl B. Cummings,[1,2,3] Jamie L. Marshall,[1,2] Taru Tukiainen,[1,2] Monkol Lek,[1,2,4,5] Sandra Donkervoort,[6] A. Reghan Foley,[6] Veronique Bolduc,[6] Leigh B. Waddell,[4,5] Sarah A. Sandaradura,[4,5] Gina L. O'Grady,[4,5] Elicia Estrella,[7] Hemakumar M. Reddy,[8] Fengmei Zhao,[1,2] Ben Weisburd,[1,2] Konrad J. Karczewski,[1,2] Anne H. O'Donnell-Luria,[1,2] Daniel Birnbaum,[1,2] Anna Sarkozy,[9] Ying Hu,[6] Hernan Gonorazky,[10] Kristl Claeys,[11] Himanshu Joshi,[3] Adam Bournazos,[4,5] Emily C. Oates,[4,5] Roula Ghaoui,[4,5] Mark R. Davis,[12] Nigel G. Laing,[12,13] Ana Topf,[14] Genotype-Tissue Expression Consortium, Peter B. Kang,[7,8] Alan H. Beggs,[7] Kathryn N. North,[15] Volker Straub,[16] James J. Dowling,[10] Francesco Muntoni,[9] Nigel F. Clarke,[4,5] Sandra T. Cooper,[4,5] Carsten G. Bönnemann,[6] Daniel G. MacArt

Cummings *et al*., *Sci. Transl. Med.* 9, eaal5209 (2017) 19 April 2017

Ortega-Recalde *et al*, Clinical Dermatology, 2016

34

Detección de splicing aberrante

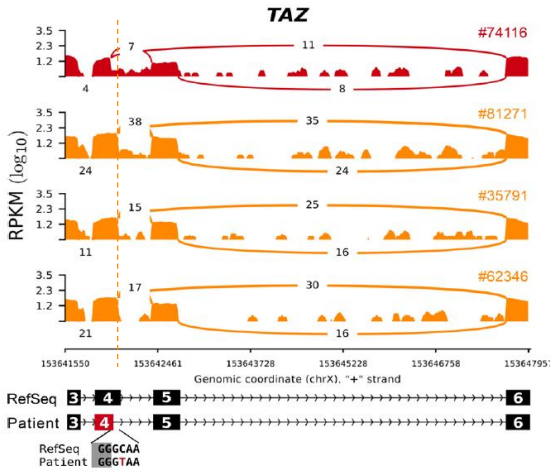
ARTICLE

https://doi.org/10.1038/s41467-020-20573-7 OPEN

Detection of aberrant splicing events in RNA-seq data using FRASER

Christian Mertes[1,6], Ines F. Scheller[1,2,6], Vicente A. Yépez[1,3], Muhammed H. Celik[1], Yingjiqiong Liang[1], Laura S. Kremer[4,5], Mirjana Gusic[4,5], Holger Prokisch[4,5] & Julien Gagneur[1,2,5]✉

NATURE COMMUNICATIONS | (2021)12:529 | https://doi.org/10.1038/s41467-020-20573-7 | www.nature.com/naturecommunications



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Perspectivas

El desarrollo de **nuevos métodos y aplicaciones** basadas en RNA-seq es un área activa de investigación biomédica.

- Single cell RNA-seq
- Transcriptómica espacial
- Secuenciación de ARN nativo
- Secuenciación de ARN no codificante
- Integración a ciencias multiómicas

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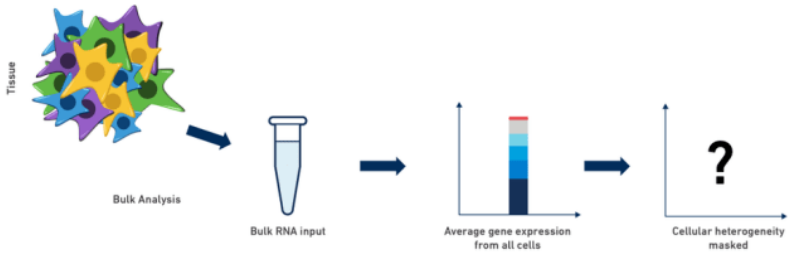
Single-cell RNA-seq

¿Por qué es útil la secuenciación de células únicas?

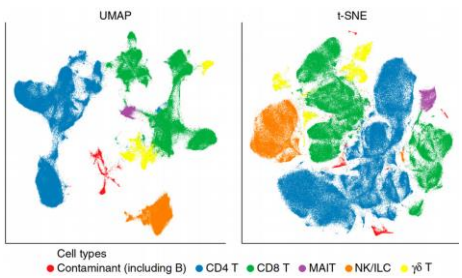


https://www.10xgenomics.com/blog/single-cell-rna-seq-an-introductory-overview-and-tools-for-getting-started

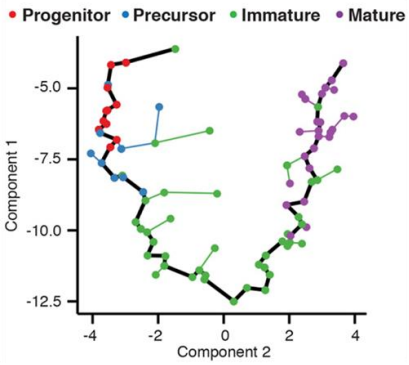
37

Single-cell RNA-seq

Análisis de datos



Reducción de la dimensionalidad
(e.g. UMAP, t-SNE)



Pseudotiempos
(análisis de trayectorias celulares)

https://cole-trapnell-lab.github.io/projects/sc-trajectories/

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Single-cell RNA-seq

nature reviews genetics
https://doi.org/10.1038/s41576-023-00613-w

Perspective
Check for updates

Transitioning single-cell genomics into the clinic

Jennifer Lim[1,2,3,4,10], Venessa Chin[1,3,4,10], Kirsten Fairfax[5], Catia Moutinho[1], Dan Suan[1,6], Hanlee Ji[7,8] & Joseph E. Powell[1,4,9]

Nature Reviews Genetics | Volume 24 | August 2023 | 573–584

nature medicine

Perspective
https://doi.org/10.1038/s41591-022-02104-7

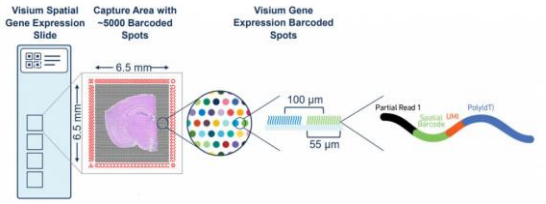
Impact of the Human Cell Atlas on medicine

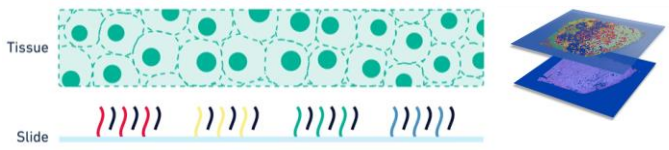
Received: 24 August 2022
Accepted: 24 October 2022
Published online: 8 December 2022
Check for updates

Jennifer E. Rood[1,4], Aidan Maartens[2,4], Anna Hupalowska[1], Sarah A. Teichmann[2,3] & Aviv Regev[1]

Single-cell atlases promise to provide a 'missing link' between genes, diseases and therapies. By identifying the specific cell types, states, programs and contexts where disease-implicated genes act, we will understand the mechanisms of disease at the cellular and tissue levels and can use this understanding to develop powerful disease diagnostics; identify promising new drug targets; predict their efficacy, toxicity and resistance mechanisms; and empower new kinds of therapies, from cancer therapies to regenerative medicine. Here, we lay out a vision for the potential of cell atlases to impact the future of medicine, and describe how advances over the past decade have begun to realize this potential in common complex diseases, infectious diseases (including COVID-19), rare diseases and cancer.

Transcriptómica espacial





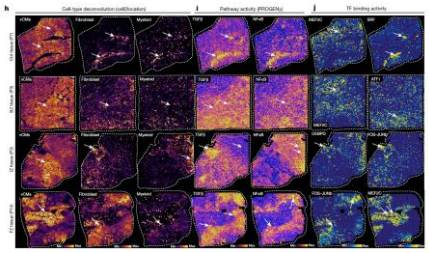
Article

Spatial multi-omic map of human myocardial infarction

https://doi.org/10.1038/s41586-022-05060-x
Received: 30 November 2020
Accepted: 29 June 2022
Published online: 10 August 2022
Check for updates

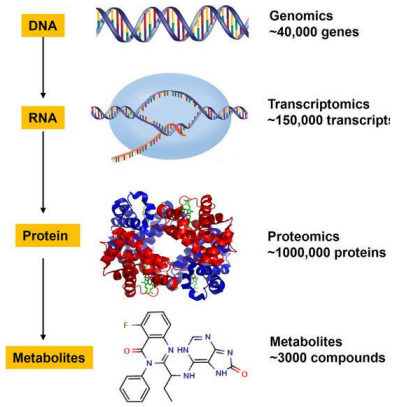
Christoph Kuppe[1,2,34], Ricardo O. Ramirez Flores[3,4,34], Zhijian Li[5,6,34], Sikander Hayat[1], Rebecca T. Levinson[3,4,7], Xian Liao[1], Monica T. Hannani[1,2], Jovan Tanevski[3,8], Florian Wünnemann[1], James S. Nagai[3,9], Maurice Halder[1], David Schumacher[1], Sylvia Menzel[1], Gideon Schäfer[1], Konrad Hoeft[1], Mingbo Cheng[10], Susanne Ziegler[1], Xiaoting Zhang[1], Fabian Peisker[1], Nadine Kaesler[1,2], Turgay Saritas[1,2], Yaoxian Xu[1], Astrid Kassner[1], Jan Gummert[11], Michiel Morshuis[11], Junedh Amrute[12], Rogier J. A. Veltrop[13,14], Peter Boor[1,15], Karin Klingel[16], Linda W. Van Laake[14], Aryan Vink[17], Remco M. Hoogenboezem[18], Eric M. J. Bindels[18], Leon Schurgers[19,20], Susanne Sattler[20], Denis Schapiro[2,20], Rebekka K. Schneider[21,22], Kory Lavine[10], Hendrik Milting[5,23], Ivan G. Costa[3,8,24], Julio Saez-Rodriguez[4,8,25,26] & Rafael Kramann[1,2,25,26,27]

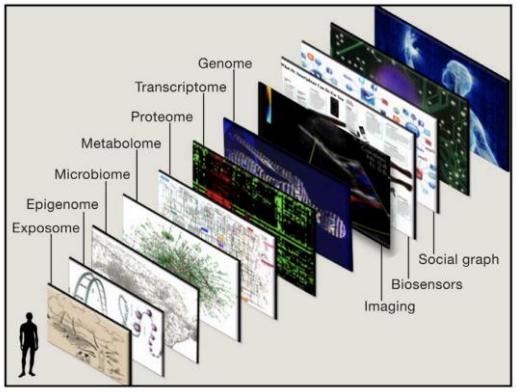
766 | Nature | Vol 608 | 25 August 2022



Kuppe *et al*, Nature, 2020

Integración a ciencias multiomicas





Yu *et al*, Oncotarget, 2017; Topol, Cell, 2014;

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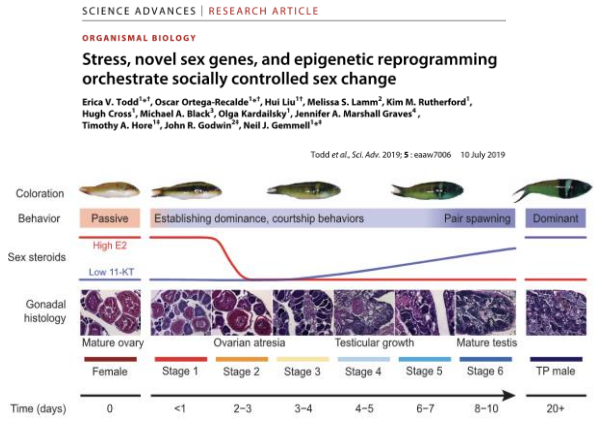
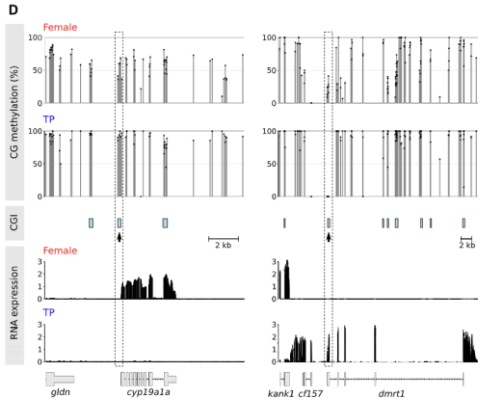
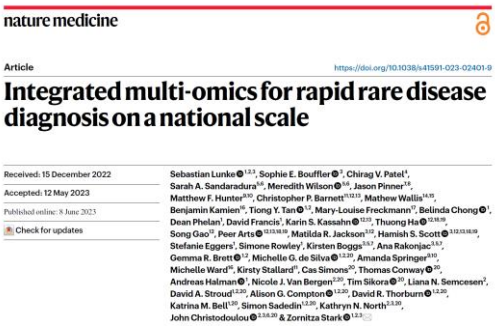
Integración a ciencias multiomicas





42

Integración a ciencias multiomicas



nature medicine

Article

https://doi.org/10.1038/s41591-023-02401-9

Integrated multi-omics for rapid rare disease diagnosis on a national scale

Received: 15 December 2022

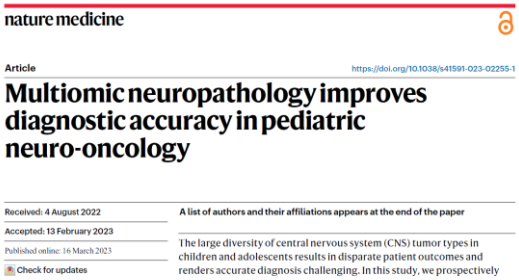
Accepted: 12 May 2023

Published online: 8 June 2023

Check for updates

Sebastian Lunke[1,2,3], Sophie E. Bouffler[3], Chirag V. Patel[4], Sarah A. Sandaradura[5,6], Meredith Wilson[5,6], Jason Pinner[7,8], Matthew F. Hunter[9,10], Christopher P. Barnett[11,12,13], Mathew Wallis[14,15], Benjamin Kamien[16], Tiong Y. Tan[1,17], Mary-Louise Freckmann[17], Belinda Chong[1], Dean Phelan[1], David Francis[1], Karin S. Kassahn[18,19], Thuong Ha[12,18,19], Song Gao[12], Peer Arts[12,13,18,19], Matilda R. Jackson[3,12], Hamish S. Scott[3,12,13,18,19], Stefanie Eggers[1], Simone Rowley[1], Kirsten Boggs[3,5,7], Ana Rakonjac[3,5,7], Gemma R. Brett[1,2], Michelle G. de Silva[1,2,20], Amanda Springer[9,10], Michelle Ward[16], Kirsty Stallard[17], Cas Simons[20], Thomas Conway[20], Andreas Halman[1], Nicole J. Van Bergen[1,21], Tim Sikora[9,10], Liana N. Semcesen[3], David A. Stroud[1,2,20], Alison G. Compton[1,2,20], David R. Thorburn[1,2,20], Katrina M. Bell[1,20], Simon Sadedin[1,2,20], Kathryn N. North[2,3,20], John Christodoulou[2,3,6,20] & Zornitza Stark[1,2,3]

290 pacientes reclutados WGS
153 sin Dx -> 19 nuevos Dx (12,9%)



nature medicine

Article

https://doi.org/10.1038/s41591-023-02255-1

Multiomic neuropathology improves diagnostic accuracy in pediatric neuro-oncology

Received: 4 August 2022

Accepted: 13 February 2023

Published online: 16 March 2023

Check for updates

A list of authors and their affiliations appears at the end of the paper

The large diversity of central nervous system (CNS) tumor types in children and adolescents results in disparate patient outcomes and renders accurate diagnosis challenging. In this study, we prospectively

1204 pacientes reclutados
metilación DNA + panel DNA-seq
+ RNA-seq

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Mensajes principales

- Las técnicas de secuenciación de ARN por métodos de siguiente generación (RNA-seq) son **metodologías robustas y sensibles para evaluar el transcriptoma**.
- No existe un flujo de trabajo bioinformático único para todos los escenarios, **es necesario establecer dicho flujo y adoptar mejores prácticas** de acuerdo con los objetivos del estudio.
- RNA-seq es una tecnología madura que puede ser utilizada en diferentes **escenarios clínicos y de investigación biomédica**.
- Existen **numerosas áreas de investigación y desarrollo** dentro de este grupo de técnicas. Es de esperar que su implementación sea mayor en el futuro.

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Agradecimientos

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Mauricio Rey Buitrago
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María Paula Meléndez-Flórez
Erika Sofia Torres-Narvaez

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Nora Constanza Contreras Bravo
Adrien Morel
Carlos M. Restrepo

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Milena Rondón-Lagos

Instituto Nacional de Cancerología
Rafael Parra-Medina
Julian Riaño-Moreno
William Torres-Jara

University of Otago
Timothy A. Hore
Alana Alexander
Melanie K. Laird
Donna M. Bond

Vertebrate Genome Project

New Zealand eScience Infrastucture

45

¡GRACIAS!

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Asociación Colombiana de Genética Humana - ACGH

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