

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



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UNIVERSIDAD
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DE COLOMBIA
SEDE BOGOTÁ

1

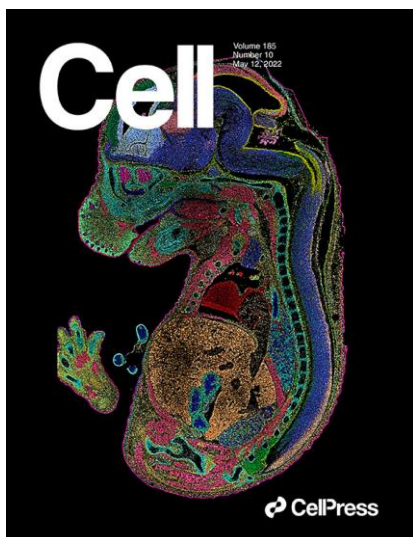
Conflictos de Interés



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



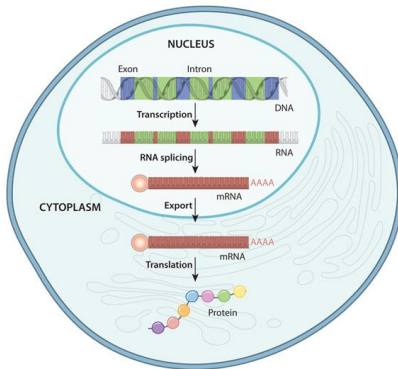
Chen et al, Cell, 2022

Contenido

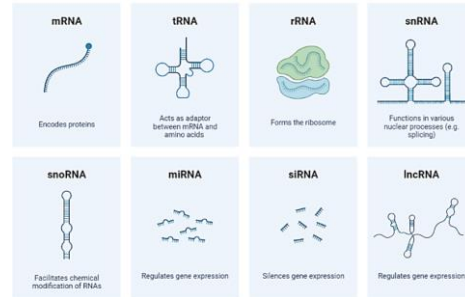
- Introducción
- Flujos de análisis de RNA-seq
- Ejemplos de aplicaciones actuales
- Perspectivas

Introducción

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



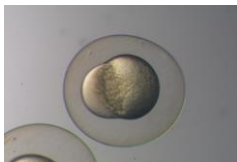
Types of RNA Produced in Cells



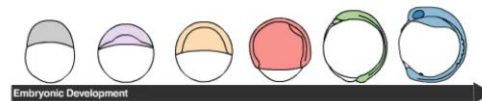
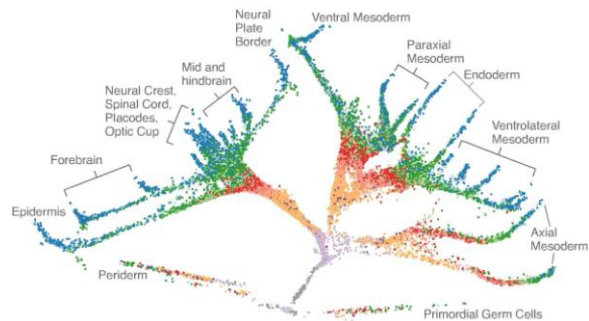
An overview of the flow of information from DNA to protein in a eukaryote, Nature; Jabbar et al, Molecular Biology Reports 2024

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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

6

Introducción

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

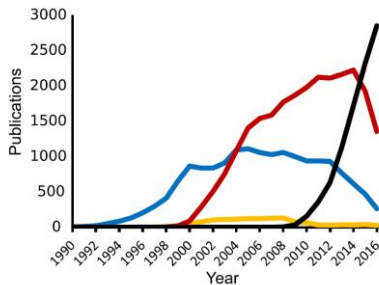


Fig 1. Transcriptomics method use over time. Published papers since 1990, referring to RNA sequencing (black), RNA microarray (red), expressed sequence tag (blue), and serial/cap analysis of gene expression (yellow) [13].

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

Table 1. Comparison of contemporary methods [23] [24] [19].

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^{-8} (limited by fluorescence detection) [27]
Dynamic range	$>10^6$ (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

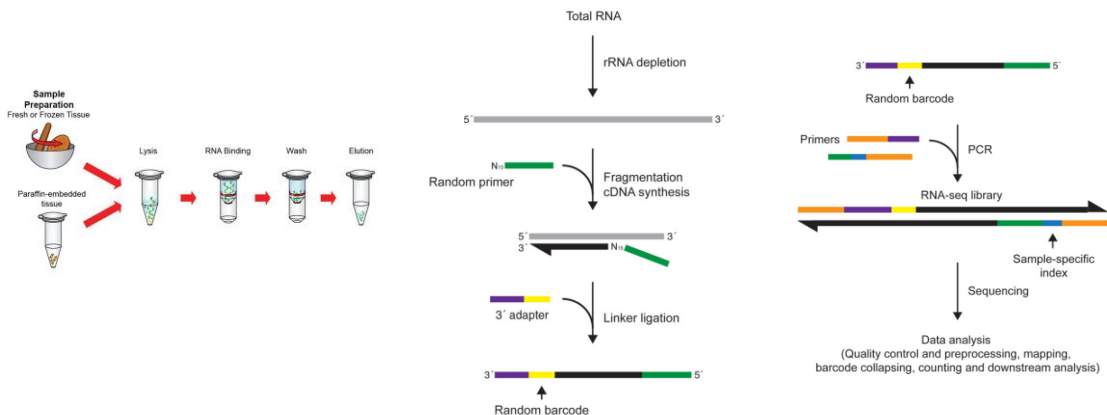
- EST
- RNA microarrays
- SAGE/CAGE
- RNA-seq

Lowe et al, PLOS Comp Biol, 2016

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Introducción

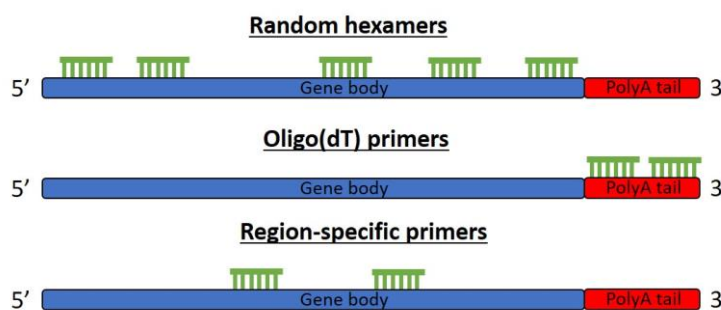
Preparación de librerías para RNA-seq



Poulsen et al, Curr Protoc Nucleic Acid Chem, 2018

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Preparación de librerías para RNA-seq



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



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**Simposio
Internacional de
Genética Humana**
Simposio de Genómica y Medicina de Precisión en la
Región Andina: "Laboratorio-Investigación-Clinica"

Secuenciación de siguiente generación y llamado de bases

[illegible]

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.



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Conesa et al, Genome Biology, 2016

Flujos de análisis de RNA-seq

RNA-seq: Basic Bioinformatics Analysis

Fei Ji^{1,2} and Ruslan I. Sadreyev^{1,3,4}¹Department of Molecular Biology, Massachusetts General Hospital, Boston, Massachusetts²Department of Genetics, Harvard Medical School, Boston, Massachusetts³Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts⁴Corresponding author: sadreyev@molbio.mgh.harvard.edu

Current Protocols in Molecular Biology e68
Published in Wiley Online Library (wileyonlinelibrary.com).
doi: 10.1002/cpmol.68
© 2018 John Wiley & Sons, Inc.

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

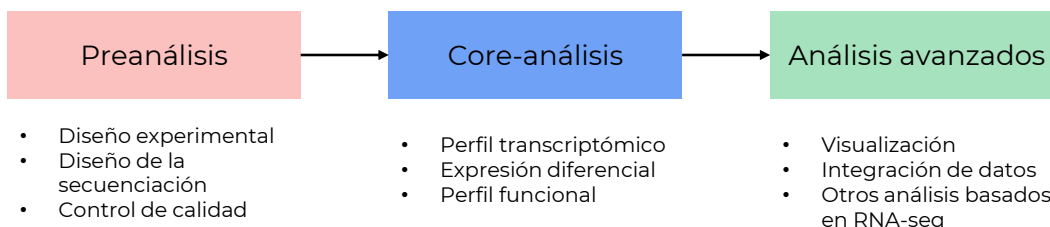


Ana Conesa^{1,2*}, Pedro Madrigal^{3,4*}, Sonia Tarazona^{2,5}, David Gomez-Cabrero^{6,7,8,9}, Alejandra Cervera¹⁰, Andrew McPherson¹¹, Michal Wojciech Saczeński¹², Daniel J. Gaffney³, Laura L. Elo¹³, Xuegong Zhang^{14,15} and Ali Mortazavi^{16,17*}



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Flujos de análisis de RNA-seq



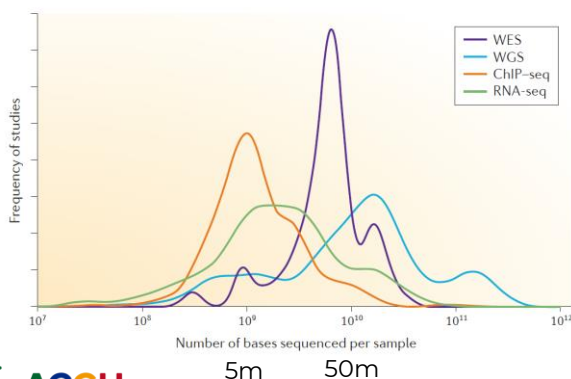
Flujos de análisis de RNA-seq

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

Flujos de análisis de RNA-seq

Número de lecturas



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.

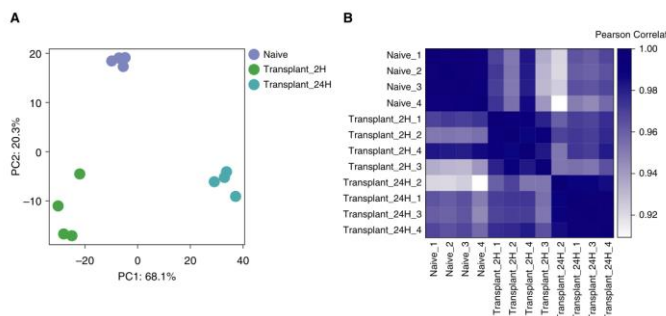
> 200m = Detección del rango completo de transcritos

Flujos de análisis de RNA-seq

Control de calidad

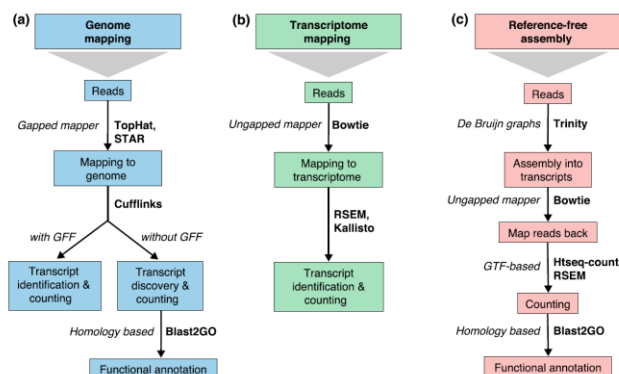
Se recomienda realizarse en los **diferentes niveles de procesamiento**

- Lecturas crudas
- Alineamiento de lecturas
- Cuantificación
- Reproducibilidad (e.g. $R^2 > 0.9$)



Flujos de análisis de RNA-seq

Estrategias de mapeo e identificación de transcritos



Conesa et al, Genome Biology, 2016??

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>

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



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



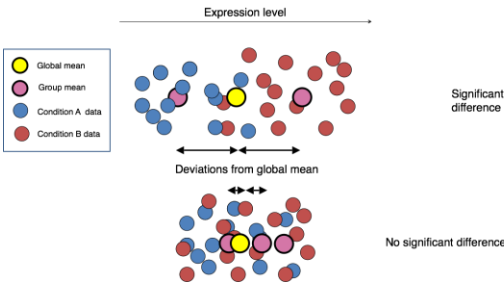
METHOD Open Access

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

Michael I Love^{1,2,3}, Wolfgang Huber² and Simon Anders^{2*}

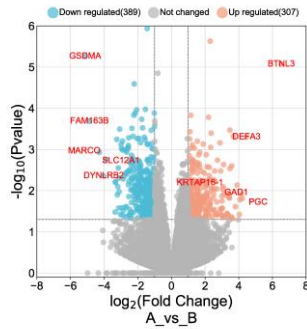
Abstract

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>.

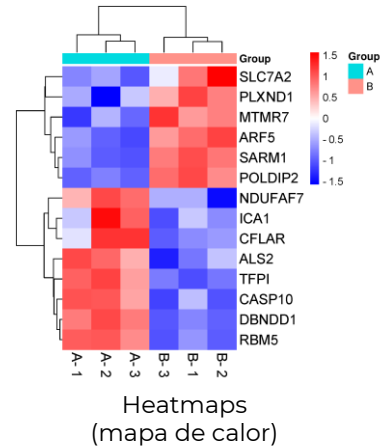


Flujos de análisis de RNA-seq

Visualización de expresión diferencial



Volcano plots



Heatmaps
(mapa de calor)

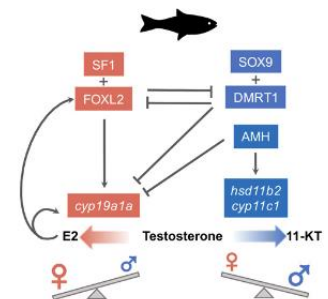
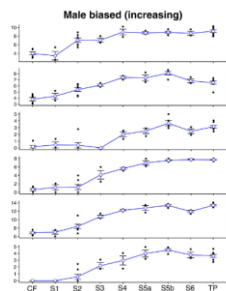
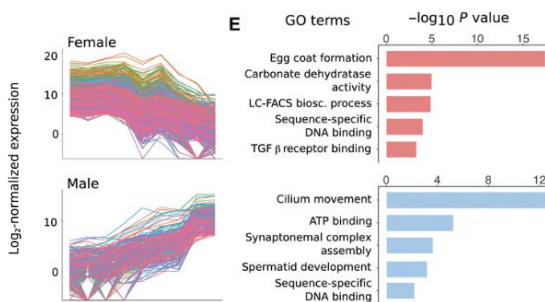


https://www.bioinformatics.com.cn/plot_basic_3_color_volcano_plot_086_en

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Flujos de análisis de RNA-seq

Perfiles funcionales



Co-expresión y
Enriquecimiento funcional

Análisis de vías
moleculares

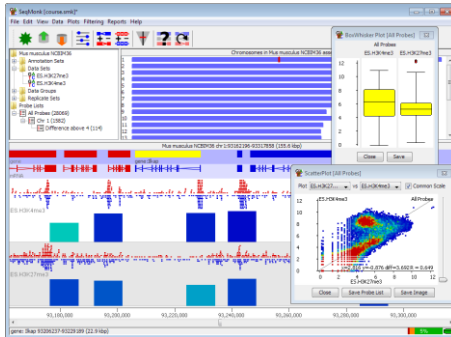


Todd et al, Science Advances, 2019

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Flujos de análisis de RNA-seq

Visualización y análisis



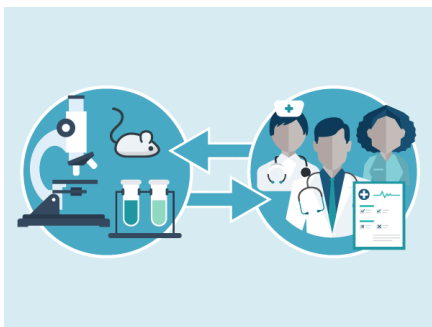
SeqMonk



IGV



23



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



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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



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} |
Ricardo Berutti^{1,2} | Holger Prokisch^{1,2}

ANNUAL
REVIEWS

Annual Review of Genomics and Human Genetics
RNA Sequencing in
Disease Diagnosis

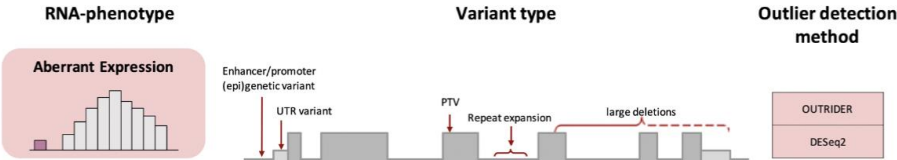
Craig Smail¹ and Stephen B. Montgomery²

¹Genomic Medicine Center, Children's Mercy Research Institute, Children's Mercy Kansas City, Kansas City, Missouri, USA; email: csmail@cmh.edu
²Department of Biomedical Data Science, Department of Genetics, and Department of Pathology, Stanford University School of Medicine, Stanford, California, USA; email: smontgomery@stanford.edu



Detección de expresión aberrante

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

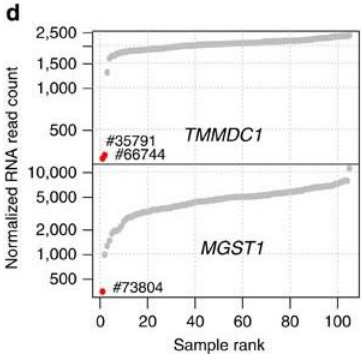
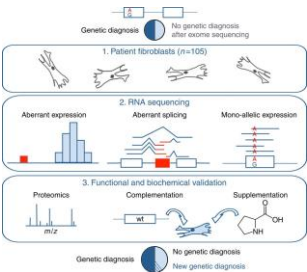


Peymani *et al*, *Pediatr Investig*, 2022; Smirnov *et al*, *Human Mutation*, 2022

Detección de expresión aberrante



ARTICLE
Received 29 Dec 2016 | Accepted 28 Apr 2017 | Published 12 Jun 2017
DOI: 10.1038/ncomms15024 OPEN
Genetic diagnosis of Mendelian disorders via RNA sequencing
Laura S. Kremer^{1,2,*}, Daniel M. Bader^{3,4,*}, Christian Mertes⁵, Robert Kopajtich^{1,2}, Garwin Pichler⁵,
Arcangela Iuso^{1,2}, Tobias B. Haack^{1,2,7}, Elisabeth Graf^{1,2}, Thomas Schwarzmayr^{1,2}, Caterina Terzile¹,
Eliška Kofářiková^{1,2}, Birgit Repp^{1,2}, Gabi Kastenmüller⁵, Jerzy Adamski⁷, Peter Lichtner¹, Christoph Leonhardt⁸,
Benoit Funalot⁹, Alice Donati¹⁰, Valeria Tiranti¹¹, Anne Lombes^{12,13,14}, Claude Jardel^{12,15}, Dieter Gläser¹⁶,
Robert W. Taylor¹⁷, Daniele Ghezzi¹¹, Johannes A. Mayr¹⁸, Agnes Rötig⁹, Peter Freisinger¹⁹, Felix Distelmaier²⁰,
Tim M. Strom^{1,2}, Thomas Metzinger^{1,2}, Julien Gagneur^{3,4} & Holger Prokisch^{1,2}



DESeq2

48 pacientes con enfermedades
mitocondriales sin etiología molecular



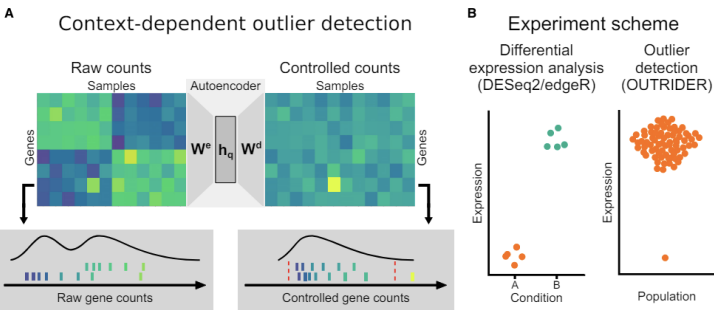
Detección de expresión aberrante

ARTICLE

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

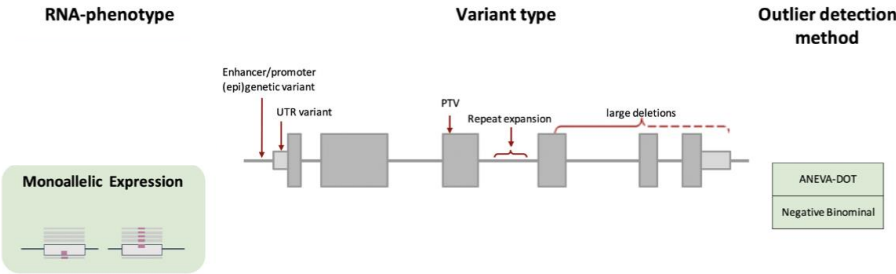
Felix Brechtmann,^{1,2} Christian Meres,^{1,2} Agnė Matuseviciūtė,^{1,2} Vicente A. Yépez,^{1,2} Žiga Avsec,^{1,2}
Maximilian Herzog,¹ Daniel M. Bader,^{1,2} Holger Prokisch,^{1,2} and Julien Gagneur^{1,2,*}

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



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.



Expresión monoalélica

nature communications



Article

<https://doi.org/10.1038/s41467-023-47764-8>

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

Received: 12 December 2022

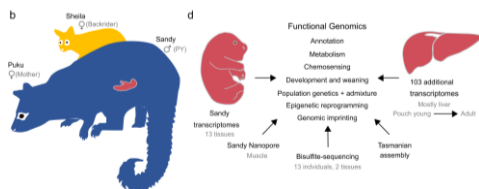
Accepted: 13 September 2023

Published online: 17 October 2023

Check for updates

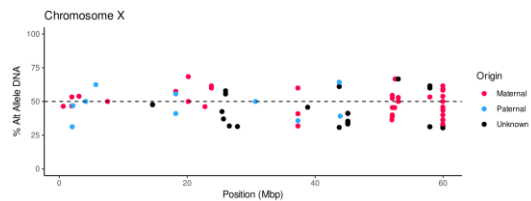
Donna M. Bond^{1,2}, Oscar Ortega-Recaide^{1,2}, Melanie K. Laird^{1,2}, Takashi Hayakawa³, Kyle S. Richardson^{1,2}, Finlay C. B. Reese^{1,2}, Bruce Kyle¹, Brooke E. McKeown-Williams¹, Bruce C. Robertson¹, Yolanda van Heest¹, Amy L. Adams⁴, Wei-Shan Chang^{4,5,6}, Bettina Haase⁴, Jacquelyn Mountcastle⁴, Maximilian Driller⁴, Joanna Collins⁴, Kerstin Howe⁴, Yasuhiko Oo^{4,6,7,8}, Françoise Thibaud-Nissen⁴, Nicholas C. Lister⁴, Paul D. Waters⁴, Olivier Fedrigo⁹, Sarah D. Jarvis^{10,11}, Neil J. Gemmell¹, Alana Alexander¹ & Timothy A. Hore^{1,2}

Nature Communications | (2023)14:6364

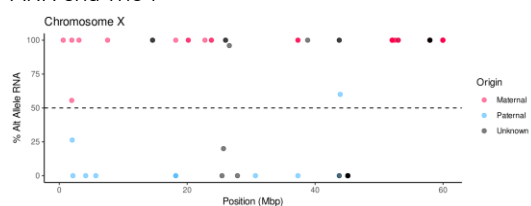


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ADN cría Trio 1



ARN cría Trio 1



Expresión monoalélica



ARTICLE

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

DOI: 10.1038/ncomms16044 OPEN

Genetic diagnosis of Mendelian disorders via RNA sequencing

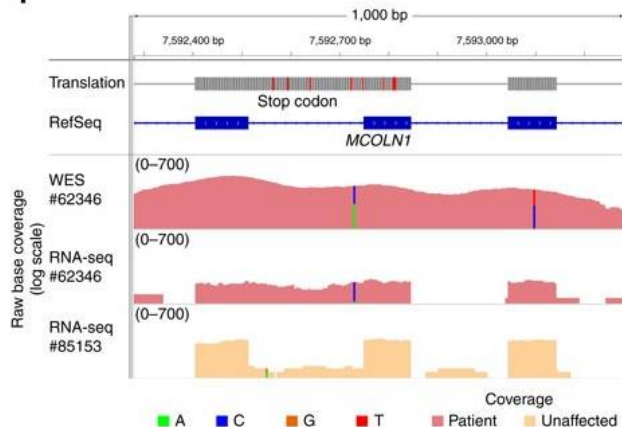
Laura S. Kemezis^{1,2,3}, Daniel M. Bader^{3,4,5}, Christian Mertes³, Robert Kopajtich^{1,2}, Garwin Pickler¹, Arcangelo Iuso^{1,2}, Tobias B. Haack^{1,2,3}, Elisabeth Graf^{1,2}, Thomas Schwarzmayr^{1,2}, Caterina Terrie¹, Eliska Kohalova^{1,2}, Brigit Repp^{1,2}, Gabi Kastnermüller⁶, Jerry Adamski¹, Peter Lichtner¹, Christoph Leonhardt⁶, Benoit Fumey¹, Alice Donati¹, Valeria Tranchesi¹, Anne Lombès^{1,3,4}, Claude Jorde^{1,2,3}, Dieter Glaser⁶, Robert W. Taylor^{1,2}, Daniele Ghezzi¹, Johannes A. May^{1,2}, Agnes Rötig⁶, Peter Freisinger^{1,2}, Felix Distelmaier^{1,2}, Tim M. Strom^{1,2}, Thomas Metzinger^{1,2}, Julien Gagneur^{3,4} & Holger Prokisch^{1,2}

Test de distribución
binomial negativa



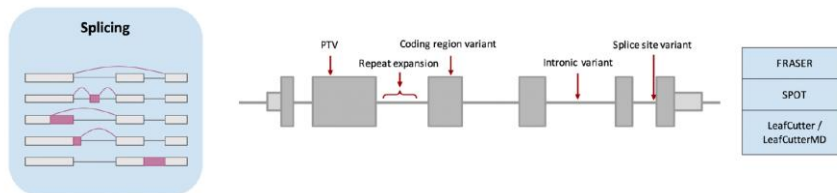
32

f

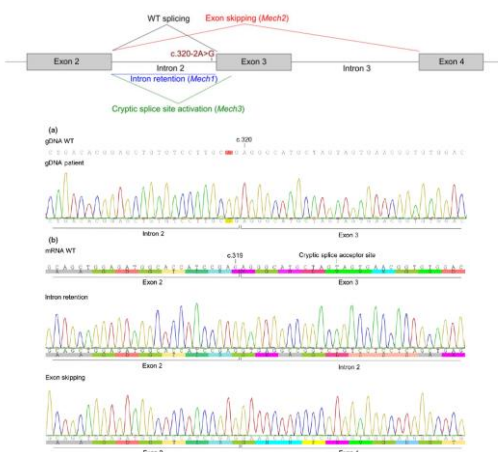


Detección de splicing aberrante

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.



Detección de splicing aberrante



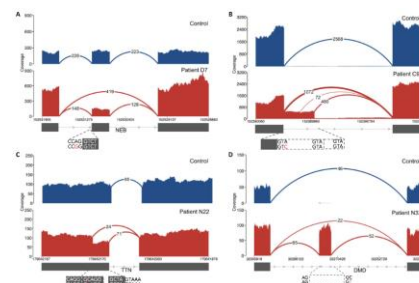
SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

GENETIC DIAGNOSIS

Improving genetic diagnosis in Mendelian disease with transcriptome sequencing

Beryl B. Cummings,^{1,2,3} Jamie L. Marshall,^{1,2} Taru Tukialainen,^{1,2} Monkol Lek,^{1,2,4,5} Sandra Donkersvoort,⁶ A. Reghan Foley,⁶ Veronique Bolduc,⁷ Leigh B. Waddell,^{4,5} Sarah A. Sanderadur,^{4,5} Gina L. O'Grady,^{4,5} Elicia Estrella,⁸ Hemakumar M. Reddy,⁹ Fengmei Zhao,^{1,2} Ben Weissburg,^{1,2} Konrad J. Karczewski,^{1,2} Anne H. O'Donnell-Luria,^{1,2} Daniel Birnbaum,^{1,2} Anna Sarkozy,¹⁰ Ying He,⁶ Hernan Gonzalez,¹⁰ Kristi Clows,¹¹ Himanshu Jais,⁶ Adam Boumazou,^{4,5} Emily C. Oates,^{4,5} Roula Ghaoui,^{4,5} Mark R. Davis,^{1,2} Nigel G. Laing,^{1,2,13} Ana Topf,¹⁴ Genotype-Tissue Expression Consortium, Peter B. Kang,¹⁵ Alan H. Beggs,¹⁶ Kathryn N. North,¹⁷ Volker Straub,¹⁸ James J. Dowling,¹⁹ Francesco Montoni,²⁰ Nigel F. Clarke,¹⁰ Sandra T. Cooper,²¹ Carsten G. Bönnemann,⁶ Daniel G. MacArthur

Cummings *et al*, *Sci. Transl. Med.* 9, eaas5209 (2017) 19 April 2017



Detección de splicing aberrante

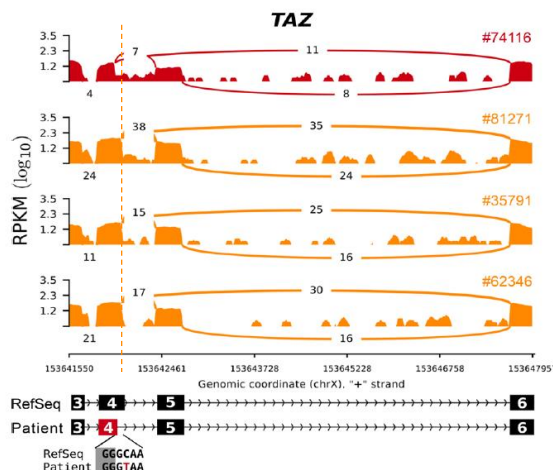
ARTICLE

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

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

Christian Merles¹, Ines F. Scheller^{1,2}, Vicente A. Yáñez^{1,3}, Muhammed H. Çalik¹, Yingqiong Liang¹, Laura S. Kremer^{4,5}, Mirjana Gusic^{4,5}, Holger Prokisch^{4,5} & Julien Gagneur^{1,3,5}

NATURE COMMUNICATIONS | (2021)12:5291 | <https://doi.org/10.1038/s41467-020-20573-7> | www.nature.com/naturecommunications



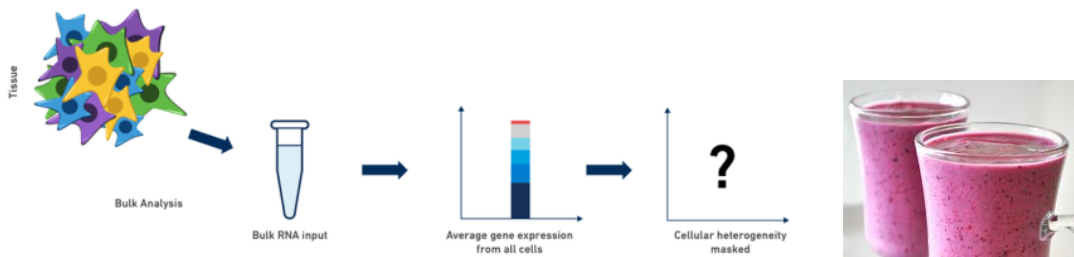
Perspectivas

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

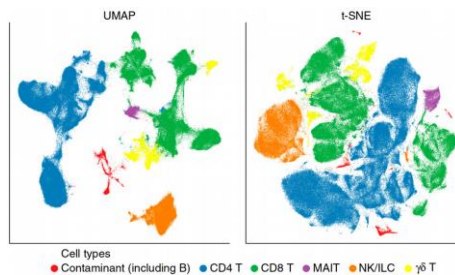
Single-cell RNA-seq

¿Por qué es útil la secuenciación de células únicas?

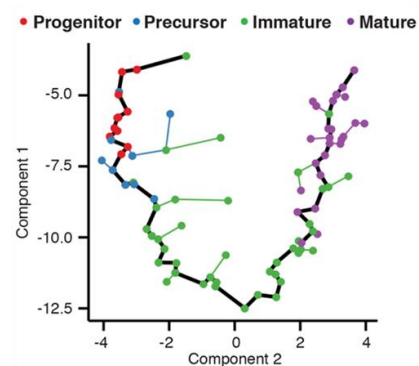


Single-cell RNA-seq

Análisis de datos



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



Pseudotiempo
(análisis de trayectorias celulares)

Single-cell RNA-seq

nature reviews genetics <https://doi.org/10.1038/s41576-023-00633-w>

Perspective [Check for updates](#)

Transitioning single-cell genomics into the clinic

Jennifer Lim^{1,2,3,4,10}, Venessa Chin^{1,2,4,10}, Kirsten Fairfax¹, Catia Moutinho¹, Dan Suan¹⁰, Hanlee Ji^{1,2} & Joseph E. Powell^{1,4,9}

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



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nature medicine

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

Impact of the Human Cell Atlas on medicine

Received: 24 August 2022 Jennifer E. Rood^{1,4}, Aidan Maartens^{2,4}, Anna Hupalowska¹, Sarah A. Teichmann^{1,2,3} & Aviv Regev^{1,5}

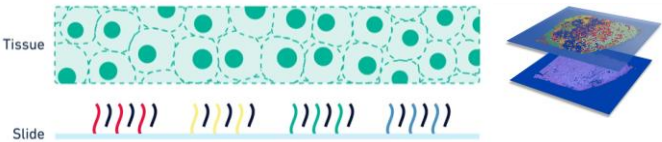
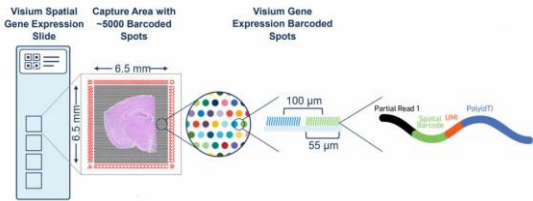
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Single-cell atlases promise to provide a ‘missing link’ between genes, diseases and therapies. By identifying the specific cell types, states, programs and contexts where disease-implicated genes act, we will understand the mechanisms of disease at 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

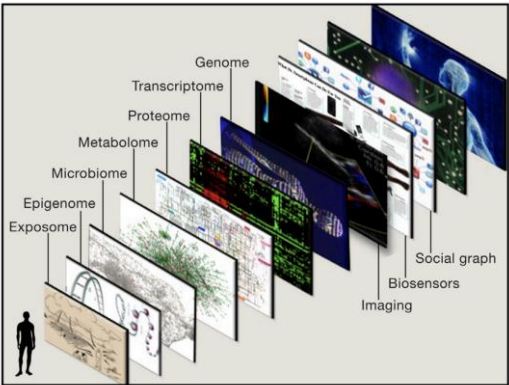
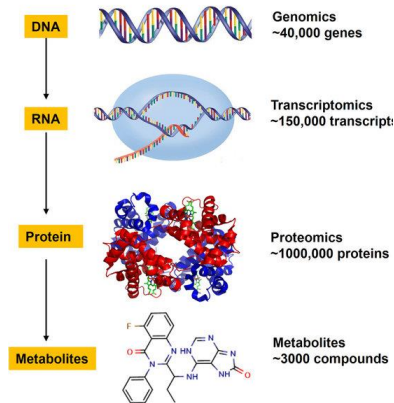
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Christoph Kuppe^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000,1001,1002,1003,1004,1005,1006,1007,1008,1009,1010,1011,1012,1013,1014,1015,1016,1017,1018,1019,1020,1021,1022,1023,1024,1025,1026,1027,1028,1029,1030,1031,1032,1033,1034,1035,1036,1037,1038,1039,1040,1041,1042,1043,1044,1045,1046,1047,1048,1049,1050,1051,1052,1053,1054,1055,1056,1057,1058,1059,1060,1061,1062,1063,1064,1065,1066,1067,1068,1069,1070,1071,1072,1073,1074,1075,1076,1077,1078,1079,1080,1081,1082,1083,1084,1085,1086,1087,1088,1089,1090,1091,1092,1093,1094,1095,1096,1097,1098,1099,1100,1101,1102,1103,1104,1105,1106,1107,1108,1109,1110,1111,1112,1113,1114,1115,1116,1117,1118,1119,1120,1121,1122,1123,1124,1125,1126,1127,1128,1129,1130,1131,1132,1133,1134,1135,1136,1137,1138,1139,1140,1141,1142,1143,1144,1145,1146,1147,1148,1149,1150,1151,1152,1153,1154,1155,1156,1157,1158,1159,1160,1161,1162,1163,1164,1165,1166,1167,1168,1169,1170,1171,1172,1173,1174,1175,1176,1177,1178,1179,1180,1181,1182,1183,1184,1185,1186,1187,1188,1189,1190,1191,1192,1193,1194,1195,1196,1197,1198,1199,1200,1201,1202,1203,1204,1205,1206,1207,1208,1209,1210,1211,1212,1213,1214,1215,1216,1217,1218,1219,1220,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Integración a ciencias multiómicas



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

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Integración a ciencias multiómicas

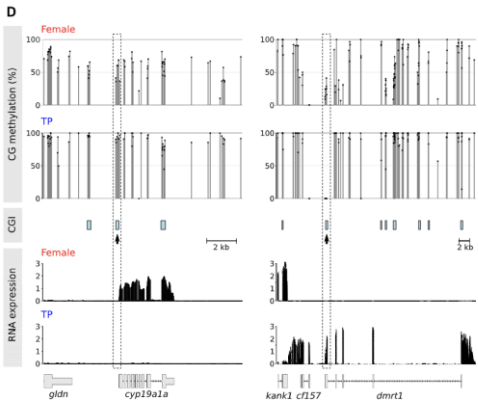
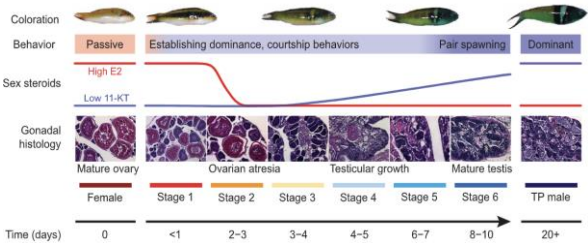
SCIENCE ADVANCES | RESEARCH ARTICLE

ORGANISMAL BIOLOGY

Stress, novel sex genes, and epigenetic reprogramming orchestrate socially controlled sex change

Erica V. Todd^{1,2}, Oscar Ortega-Recalde^{1,2}, Hui Liu^{1,2}, Melissa S. Lamm², Kim M. Rutherford¹, Hugh Cross¹, Michael A. Black¹, Olga Kardalisky¹, Jennifer A. Marshall Graves¹, Timothy A. Hore^{1,2}, John R. Godwin^{1,2}, Neil J. Gemmell^{1,2}

Todd et al., Sci. Adv. 2019; 5: eaaw7006 10 July 2019



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Integración a ciencias multiómicas

nature medicine



Article

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

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

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Multiomic neuropathology improves diagnostic accuracy in pediatric neuro-oncology

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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

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

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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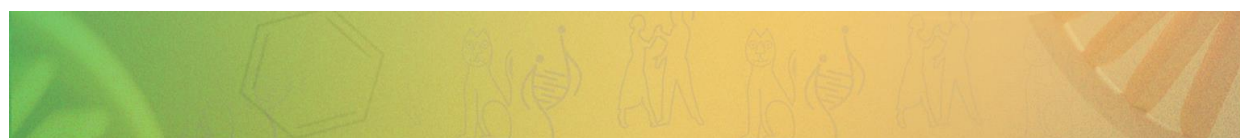
Vertebrate Genome Project



New Zealand eScience Infrastructure



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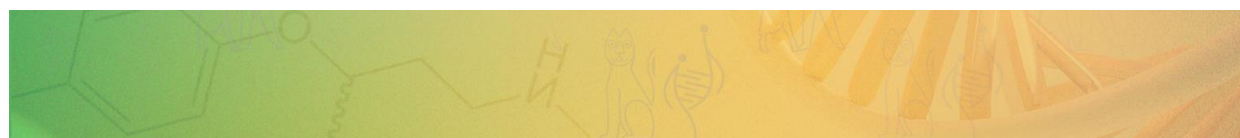
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