Proyecto Baby Lince

II JORNADA ENFERMEDADES MINORITARIAS
23-24 de mayo de 2024

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Unidad de Diagnóstico Molecular y Genética Clínica
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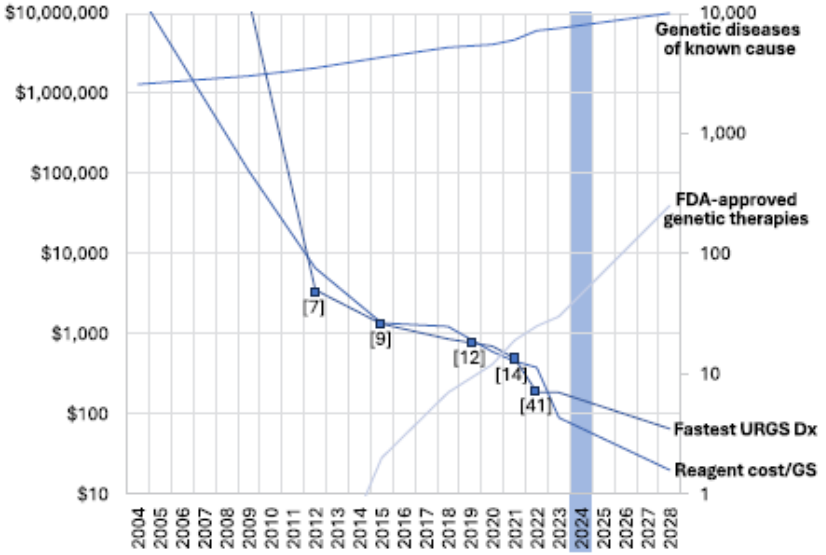
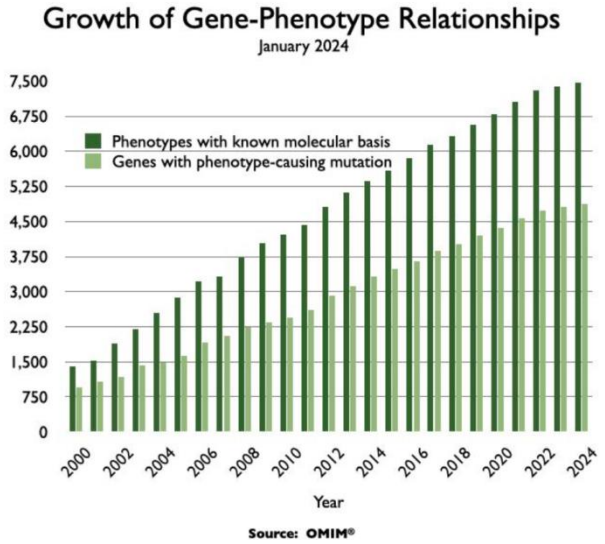
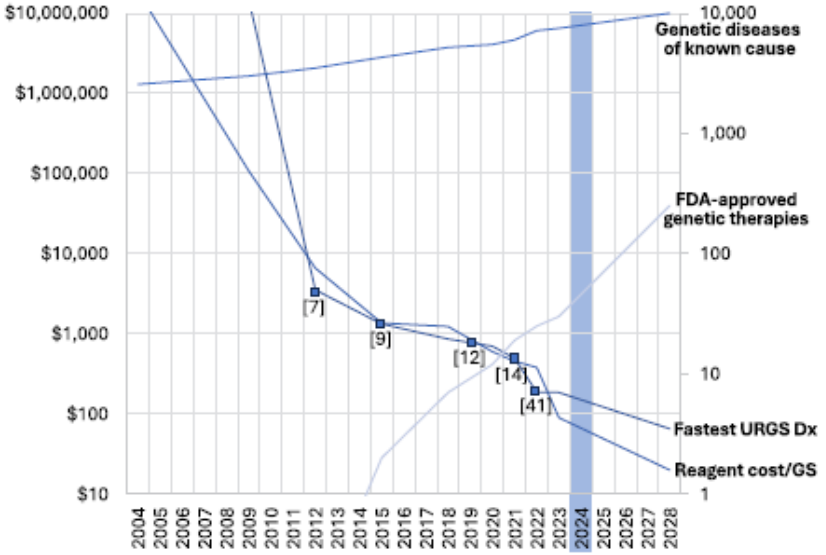
HOSPITAL UNIVERSITARIO SON ESPASES

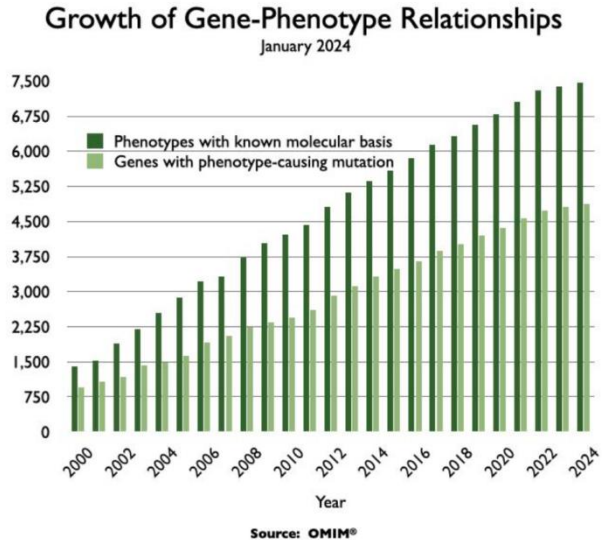
Introducción





Introducción





- 75% de las enfermedades genéticas debutan en la edad pediátrica.

- 15% de los ingresados en Cuidados Intensivos neonatales
- 40% de la mortalidad

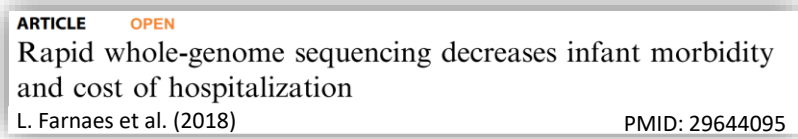
Introducción

- Los trastornos genéticos contribuyen de manera significativa a la **mortalidad y morbilidad** de los pacientes pediátricos afectados, requiriendo ingresos prolongados en UCIN, UCIP
- La **identificación temprana** de la causa genética subyacente favorece un **manejo personalizado (medicina personalizada)**
- Estudios previos sugieren que la secuenciación rápida del exoma o genoma completo (**rWES/rWGS**) es la **prueba genética de primera línea** más adecuada en niños críticos con sospecha de un trastorno genético


Genetics inMedicine ORIGINAL RESEARCH ARTICLE © American College of Medical Genetics and Genomics

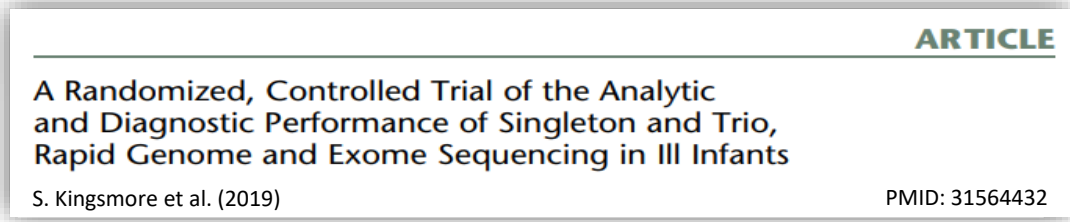
A prospective evaluation of whole-exome sequencing as a first-tier molecular test in infants with suspected monogenic disorders

Z. Stark et al. (2016) PMID: 26938784


ARTICLE OPEN

Rapid whole-genome sequencing decreases infant morbidity and cost of hospitalization

L. Farnaes et al. (2018) PMID: 29644095


ARTICLE

A Randomized, Controlled Trial of the Analytic and Diagnostic Performance of Singleton and Trio, Rapid Genome and Exome Sequencing in Ill Infants

S. Kingsmore et al. (2019) PMID: 31564432

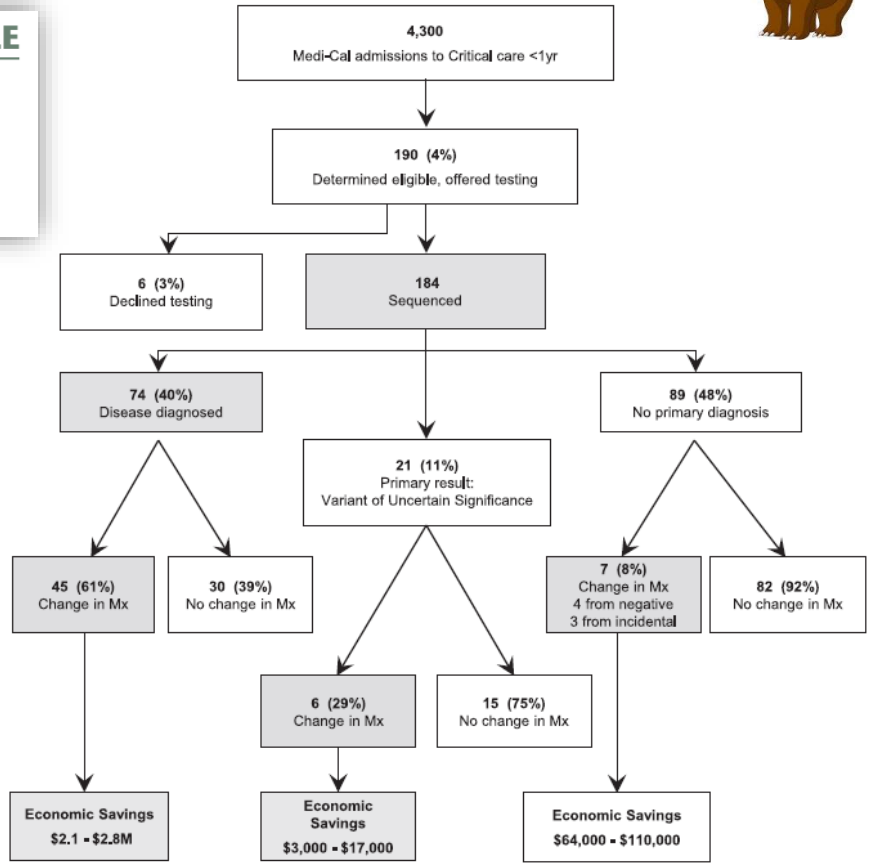
Proyectos Baby (EEUU)

ARTICLE

Project Baby Bear: Rapid precision care incorporating rWGS in 5 California children's hospitals demonstrates improved clinical outcomes and reduced costs of care

David Dimmock,[1,*] Sara Caylor,[1] Bryce Waldman,[1] Wendy Benson,[1] Christina Ashburner,[2]

- Tiempo respuesta 3 días
- Rendimiento Dx= 40% (74/184)
- Cambio en el manejo clínico 32%

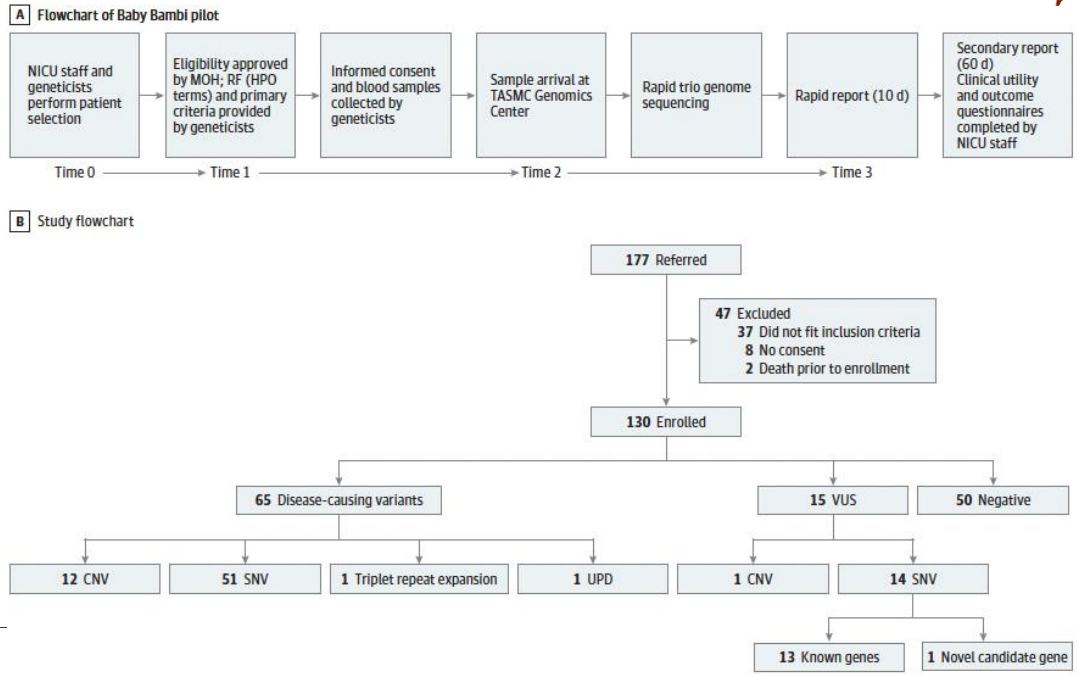


Proyectos Baby (Israel)

Press Releases

The Ministry of Health's Baby Bambi Program for Whole-Genome Sequencing (WGS) in the Various Neonatal Intensive Care Units in Israel

- TAT 7 days was feasible in a national public health care setting
- 50% to 62% diagnostic rate



JAMA Network Open

Original Investigation | Pediatrics

National Rapid Genome Sequencing in Neonatal Intensive Care

Daphna Marom, MD; Adi Mory, PhD; Sivan Reytan-Miron, MSc; Yam Amir, MSc; Alina Kurolap, PhD; Julia Grinshpun Cohen, PhD; Yocheved Morhi; Tatiana Smolkin, MD; Lior Cohen, MD; Shmuel Zangen, MD, MHA; Adel Shalata, MD, PhD; Arieh Riskin, MD, MHA, PhD; Amir Peleg, MD; Karen Lavie-Nevo, MD; Dror Mandel, MD; Elana Chervinsky, MD; Clari Felszer Fisch, MD; Vered Fleisher Sheffer, MD; Tzipora C. Falik-Zaccai, MD; Jonathan Rips, MD; Noa Ofek Shlomai, MD; Smadar Eventov Friedman, MD, PhD; Calanit Hershkovich Shporen, MD; Sagie Josefsberg Ben-Yehoshua, MD; Aryeh Simmonds, MD; Racheli Goldfarb Yaacobi, MD; Sofia Bauer-Rusek, MD; Hussam Omari, MD; Karin Weiss, MD; Ori Hochwald, MD; Arie Kolfman, MD; Omer Globus, MD; Nurit Assia Batzir, MD; Naveh Yaron, MD; Reeval Segel, MD; Iris Morag, MD; Orit Reish, MD; Aviva Eliyahu, MD; Leah Leibovitch, MD; Marina Eskin Schwartz, MD, PhD; Ramy Abramsky, MD; Amit Hochberg, MD; Anat Oron, MD; Ehud Banne, MD; Igor Portnov, MD; Nadra Nasser Samra, MD; Amihood Singer, MD; Hagit Baris Feldman, MD

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Gene	Transcript	Variant	Phase	Inheritance	Syndrome	MIM No.	Precision management
Tailored precision drugs							
ODC1	NM_002539.3	c.1307_1311 delinsT, p.Thr436IlefsX11	Heterozygote	De novo	Bachmann-Bupp syndrome	619075	Eflornithine (research drug)
PNPO	NM_018129.3	c.284G>A p.Arg95His	Homozygote	AR	Pyridoxamine 5-prime-phosphate oxidase deficiency	610090	Pyridoxal phosphate supplement
COL1A1	NM_000088.4	c.1066G>T, p.Gly356Cys	Heterozygote	De novo	Osteogenesis imperfecta 3	166200	Bisphosphonates
KCNQ1	NM_000218.3	c.421G>A, p.Val141Met	Heterozygote	De novo	Short QT syndrome, 2	192500	Channel-specific blockade of IK1
COL1A1	NM_000088.4	c.3488G>A, p.Gly1163Glu	Heterozygote	De novo	Osteogenesis imperfecta 2-3	166200	Bisphosphonates
MVK	NM_000431.4	c.1129G>A, p.Val377Ile (maternal); c.1039G>A, p.Gly347Arg (paternal)	Compound heterozygote	AR	Mevalonate kinase deficiency	260920	Interleukin 1 receptor antagonist (anakinra), bone marrow transplant
Palliative care							
SETBP1	NM_015559.3	c.2608G>A, p.Gly870Ser	Heterozygote	De novo	Schinzel-Giedion midface retraction syndrome	269150	Transferred to nursing home
STXBP1	NM_003165.3	c.1095_1096del, p.Cys366ProfsTer13	Heterozygote	De novo	Developmental and epileptic encephalopathy 4	612164	Transferred to nursing home
CHD2	NM_001271.4	c.295-125A>G	Heterozygote	De novo	Developmental and epileptic encephalopathy 94	615369	Supportive care
CACNA1A	NM_001127222.2	c.294-16973C>T	Heterozygote	De novo	Developmental and epileptic encephalopathy 42	617106	
Trisomy 18	NA	NA	NA	NA	NA	NA	Supportive care

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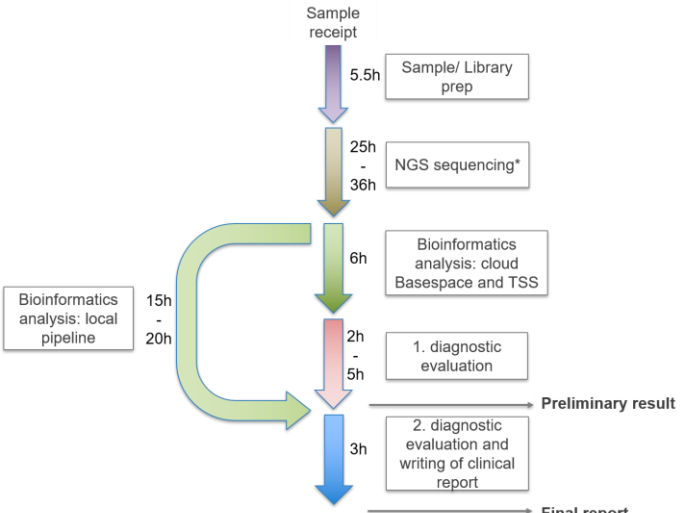
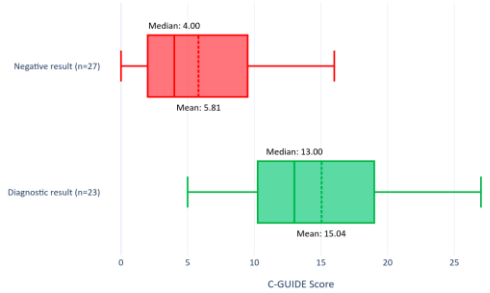
Proyectos Baby (Alemania)

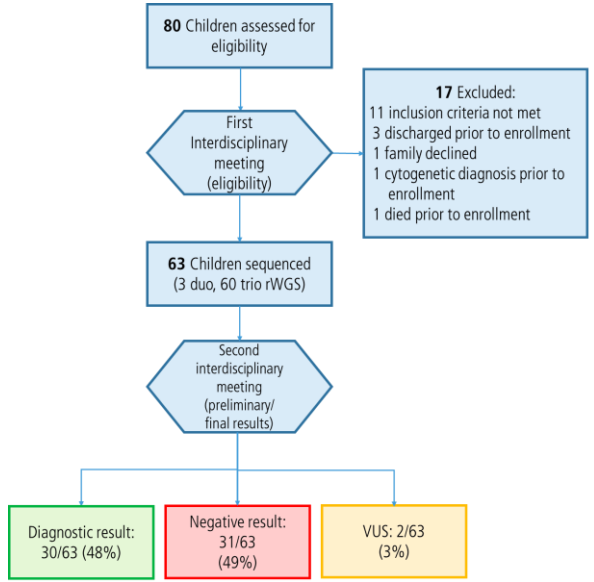


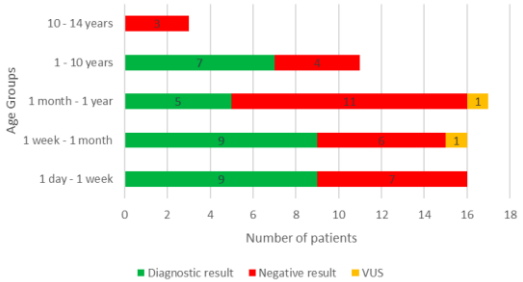


Rapid trio whole genome sequencing in critically ill children – preliminary results of the first German multicenter study ("Baby Lion")

Bernd Auber*[1], Gunnar Schmidt[1], Chen Du[1], Alexander von Gise[2], Bettina Bohnhorst[3], Michael Sasse[2], Harald Köditz[2], Michaela Losch[1], Bernd Haermeyer[1], Benedikt Schnur[1], Florian Kaisen[1], Sandra von Hardenberg[1]

[1]Department of Human Genetics, Hannover Medical School, Hanover, Germany, [2]Department of Pediatric Cardiology and Intensive Care Medicine, Hannover Medical School, Hanover, Germany, [3]Department of Pediatric Pulmonology and Neonatology, Hannover Medical School, Hanover, Germany





- Tiempo respuesta 3 días
- Rendimiento Dx= 48% (30/63)

Proyectos Baby (España; Baby Lince)

- Proyecto multicéntrico
  - PI22/01823; 22/01743 (ISCIII)
  - Illumina
- 150 casos (450 genomas)

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Proyectos Baby (España; Baby Lince)

TAT: 10-14 días

H12O

H Arrixaca

HVdH

Datos clínicos

REDCap
Research Electronic Data Capture

HUSE

H La Paz

Evaluación de la utilidad clínica

Genet Med. 2022 Feb;24(2):430-438. doi: 10.1016/j.gim.2021.10.005. Epub 2021 Nov 30.

The Clinician-reported Genetic testing Utility InDEx (C-GUIDE): Preliminary evidence of validity and reliability

Robin Z Hayeems [1], Stephanie Luca [2], Wendy J Ungar [3], Viji Venkataramanan [2], Kate Tsiplova [2], Naazish S Bashir [2], Gregory Costain [4], Cara Inglese [5], Vanda McNiven [6], Nada Quercia [7], Andrea Shugar [7], Grace Yoon [4], Cheryl Cytrynbaum [7], Lucie Dupuis [7], Zhuo Shao [6], Stacy Hewson [7], Cheryl Shuman [8], Ritu Aul [6], Eriskay Liston [7], Riyana Babul-Hirji [7], Alexandra Bushby [9], Eleanor Pullenayegum [9], Lauren Chad [10], M Stephen Meyn [11]

Baby Lince Objetivos

Evaluar en una red de 5 hospitales terciarios del Sistema Nacional de Salud español:

- La eficacia diagnóstica del rWGS.
- Tiempo de respuesta.
- Utilidad clínica.
- Percepción padres.
- Describir las características clínicas y moleculares de la cohorte.
- Identificar nuevas enfermedades genéticas.
- ¿Evaluación costes?

Muchas gracias

Contacto: fernando.santos@ssib.es