Hospital Universitario Ramón y Cajal

Enfermedades Musculares en la Infancia y Adolescencia(XIV)

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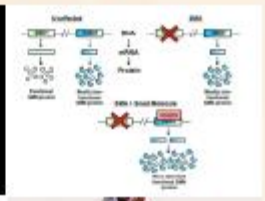
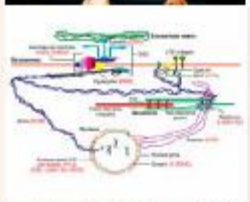

Servicio de Pediatría. B. García Cuartero. Jefe de Servicio

30 y 31 de Marzo de 2017

Salón de Actos. Planta 0 centro.
Hospital Universitario Ramón y Cajal

Inscripción: GRATUITA enviando un correo electrónico indicando nombre y filiación a glorenzosanz@yahoo.es

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Dra. S. Rekarte García	Neurología infantil S. de Pediatría.

Curso de Formación Continuada de las Profesiones Sanitarias
de la Comunidad de Madrid - 1,9 Créditos
(nº de expediente: 07-AFOC-00841.8/2017)

Enfermedades Musculares en la Infancia y Adolescencia (XIV)

JUEVES 30 de Marzo

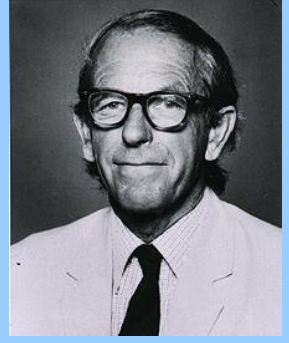
8:30	ENTREGA DE DOCUMENTACIÓN
9:25	Presentación
9:30	MESA REDONDA: Miopatías en la infancia y adolescencia (I) Moderador: Dr.A. García Ron
	Importancia de la historia clínica y la exploración en la evaluación de las enfermedades neuromusculares. Dr. E. Gutiérrez Rivas
	Genoma, exoma y paneles de genes en la investigación de las enfermedades neuromusculares. Dr.A. Jiménez Escrig
	Perspectivas terapéuticas en las miopatías congénitas. Dra. F. Munell Casadesus
11:00	COLOQUIO
11:30	DESCANSO. Café
12:00	INAUGURACIÓN OFICIAL
12:15	MESA REDONDA: Miopatías en la infancia y adolescencia (II) Moderador: Dr. G. Lorenzo Sanz
	Resultados de los ensayos clínicos con *Nusinersen* en AME tipo I. Dr. S.I. Pascual Pascual
	Exoesqueletos biónicos: una alternativa terapéutica en AME. Dra. E. García Armada
	Presente y futuro de los ensayos clínicos en AME. Dr. E. Tizzano Ferrari
13:45	COLOQUIO
14:00	COMIDA DE TRABAJO
16:30	MESA REDONDA: Miopatías en la infancia y adolescencia (III) Moderador: Dr.A. Verdú Perez
	Importancia del diagnóstico genético en la enfermedad de Duchenne. Dra. P. Gallano Petit
	¿Que aporta la biopsia muscular al diagnóstico de las distrofinopatías? Dr.A. Hernández Laín
17:30	COLOQUIO
17:45	MESA REDONDA: Miopatías en la infancia y adolescencia (IV) Moderador: Dra. B. Martínez Menéndez
	Novedades en el tratamiento de la enfermedad de Duchenne. Dr. M. Madruga Garrido
	Diagnóstico y tratamiento de las manifestaciones cardiológicas de las distrofinopatías. Dr. L. Fernández Pineda
18:45	COLOQUIO
19:15	FIN DE LA JORNADA

VIERNES 31 de Marzo

9:30	MESA REDONDA: Miopatías en la infancia y adolescencia (V) Moderador: Dra. C. Hernández Chico
	Importancia de las organizaciones de pacientes y el paciente "experto" en enfermedades neuromusculares. M. Suarez Felgueroso
	Aspectos clínicos y moleculares de la miotonía congénita. Dr. J. Molano Mateos
10:30	COLOQUIO
10:45	MESA REDONDA: Miopatías en la infancia y adolescencia (VI) Moderador: Dr. R. Simón de las Heras
	Neuropatía inflamatoria desmielizante crónica. Aspectos clínicos y terapéuticos. Dr.A. Guerrero Sola.
	Estrategias de neuroprotección en las neuropatías periféricas. Dr. G. Gutiérrez Gutiérrez
12:15	COLOQUIO
12:30	DESCANSO. Café
13:00	MESA REDONDA: Miopatías en la infancia y adolescencia (VII) Moderador: Dra. R. Buenache Espartosa
	Terapia enzimática en la enfermedad de Pompe. Casos clínicos. Dra. M. García Romero.
	Terapia enzimática en la enfermedad de Fabry. Casos clínicos. Dr. F.J. Aguirre Rodríguez
14:00	COLOQUIO
14:30	ENTREGA DE DIPLOMAS Y CLAUSURA DEL XIV CURSO

Genoma, exoma y paneles de genes en la investigación de las enfermedades neuromusculares.

Dr. A. Jiménez Escrig



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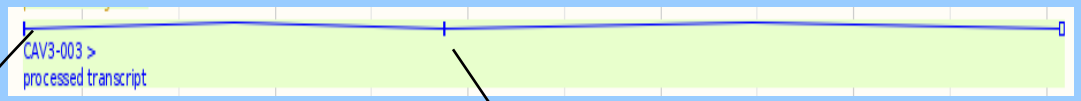

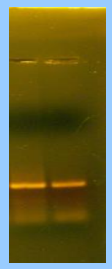

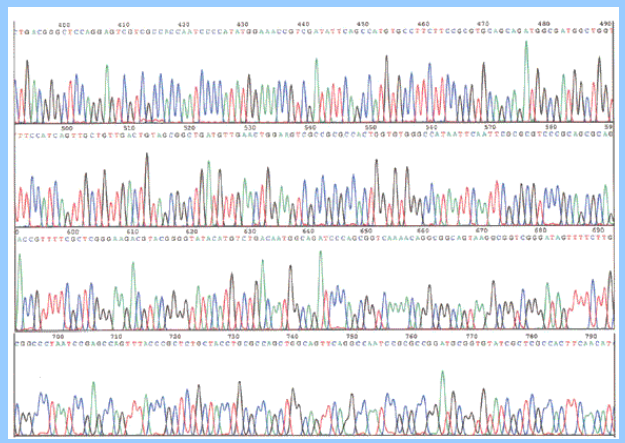

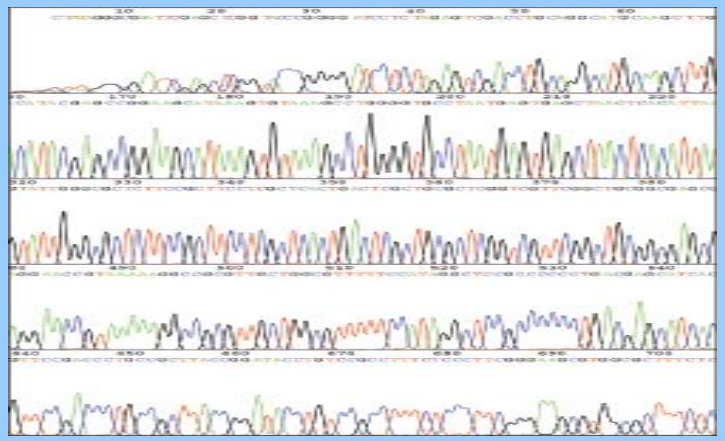

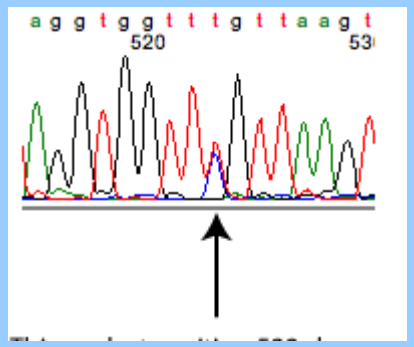

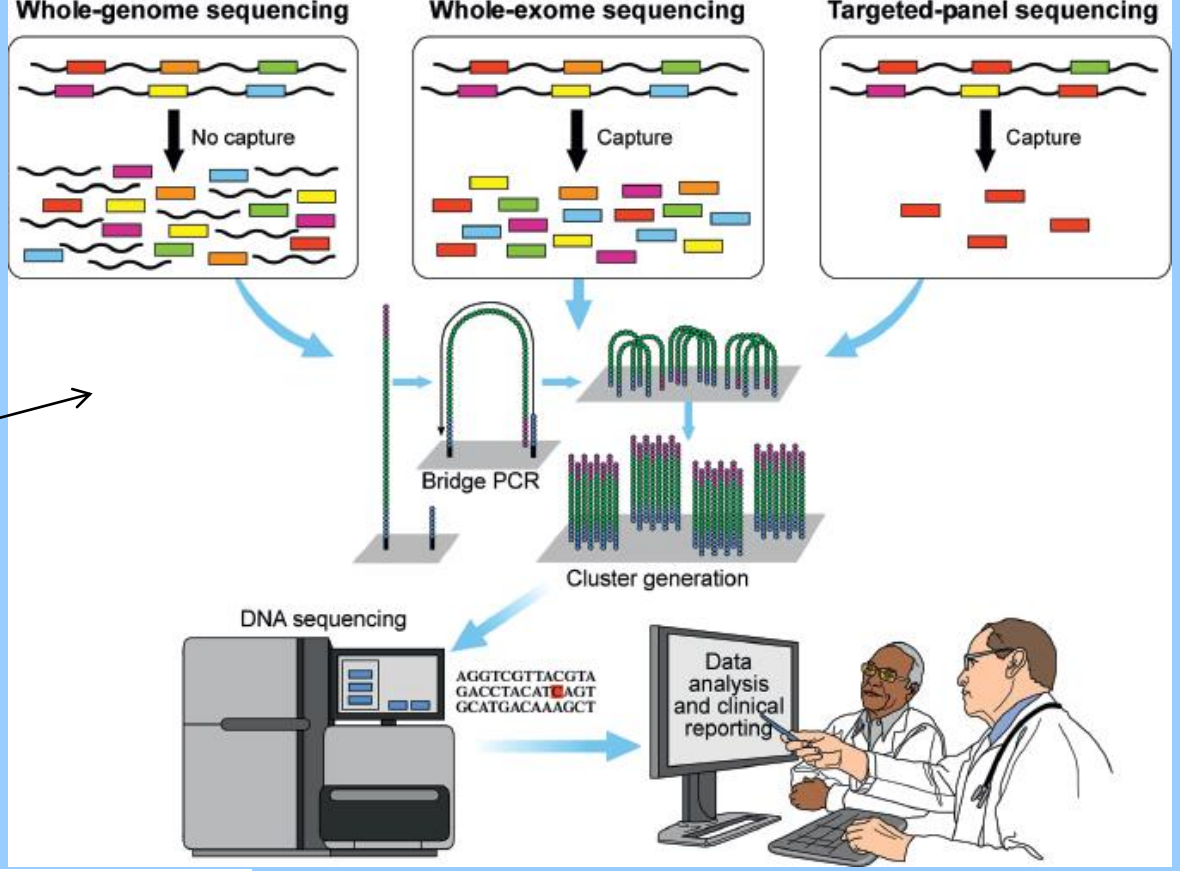


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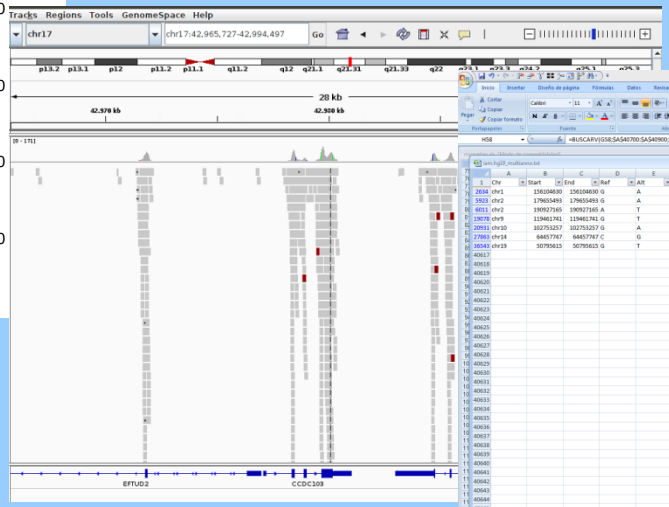

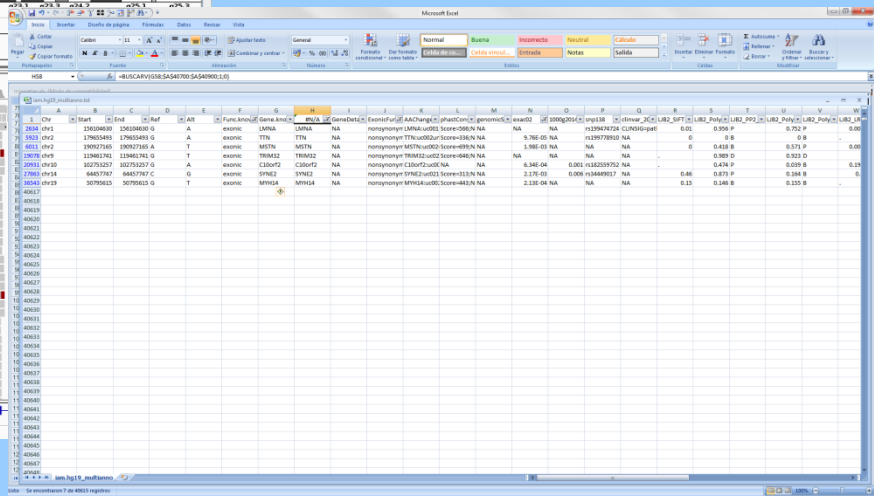

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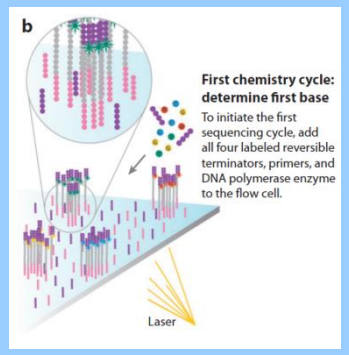

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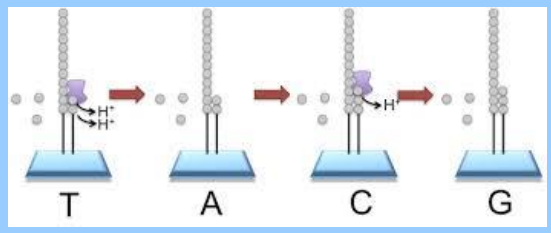
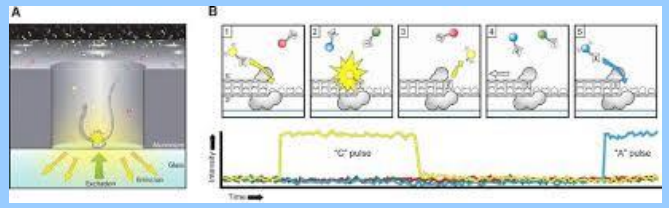


150-400 bases

PACIFIC B.



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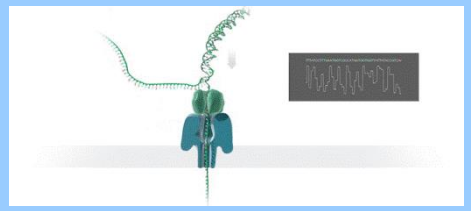

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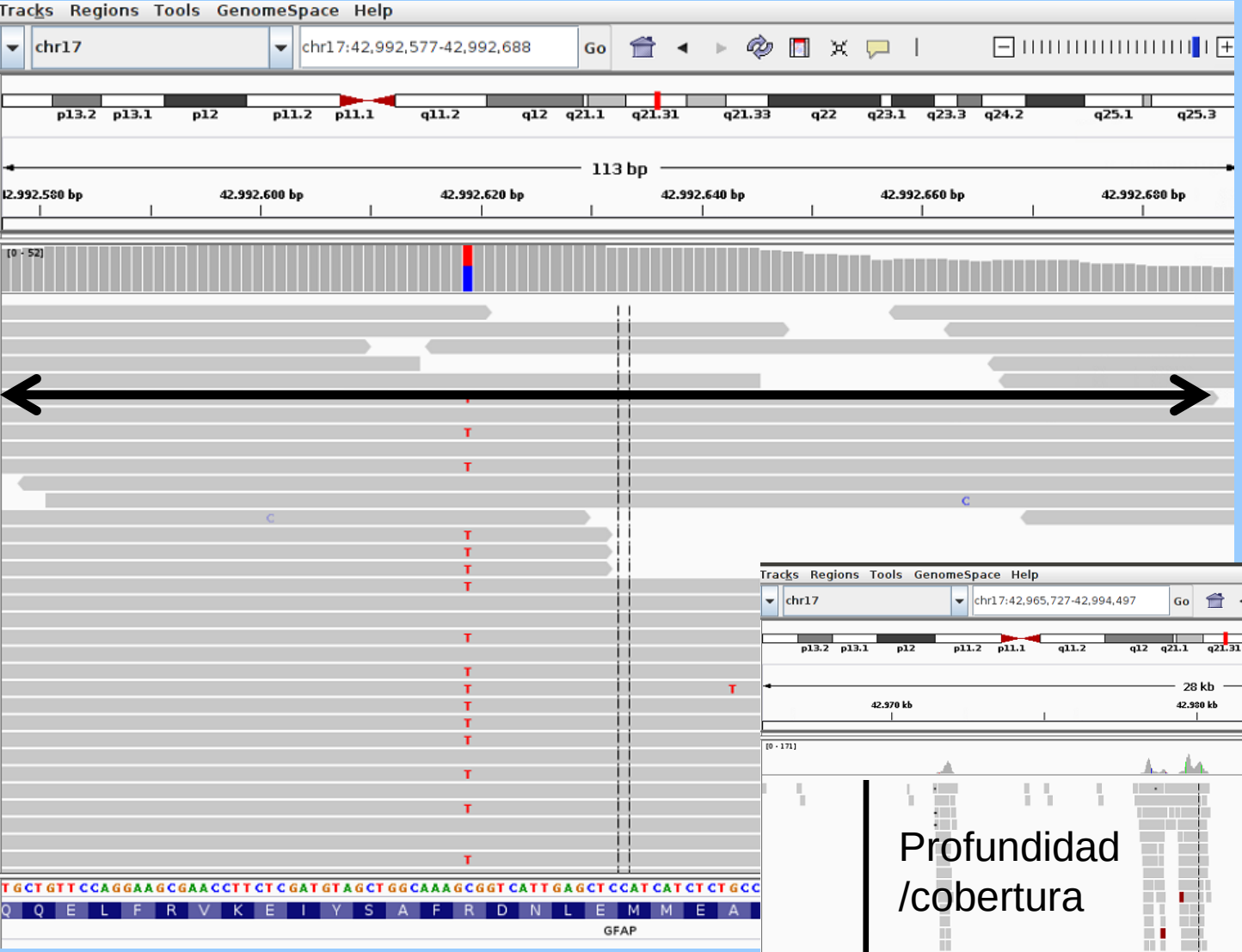
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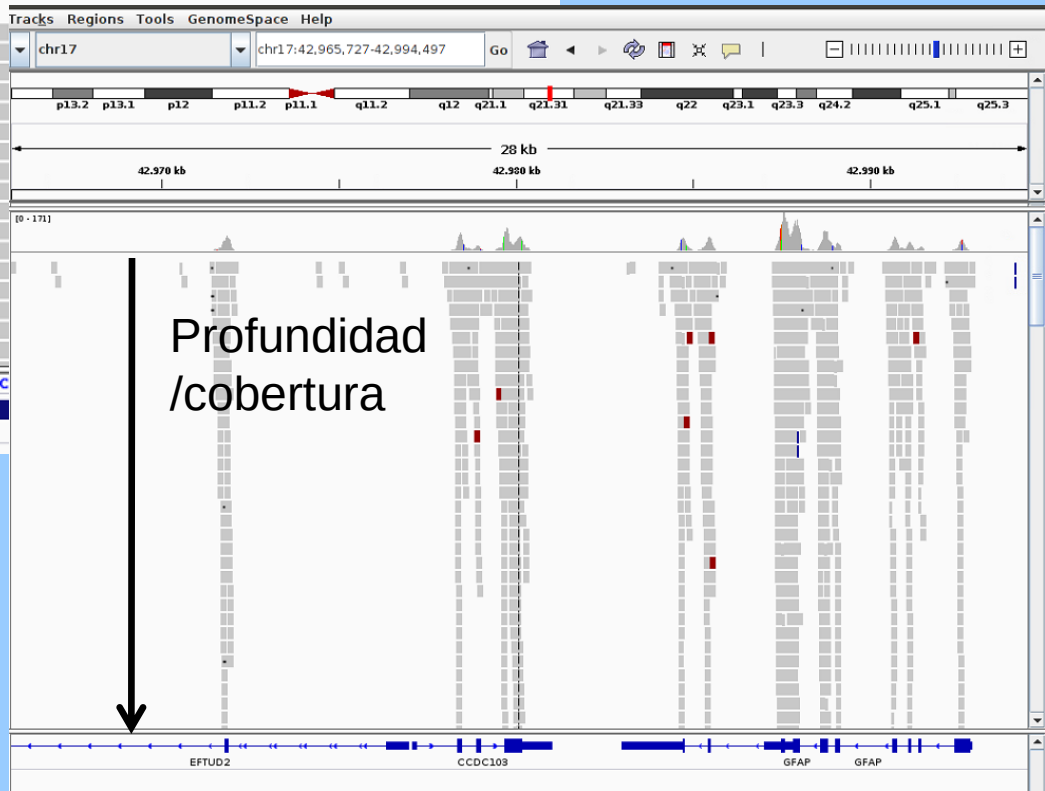
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Center for Genomics and Transcriptomics

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6 weeks of Sequencing
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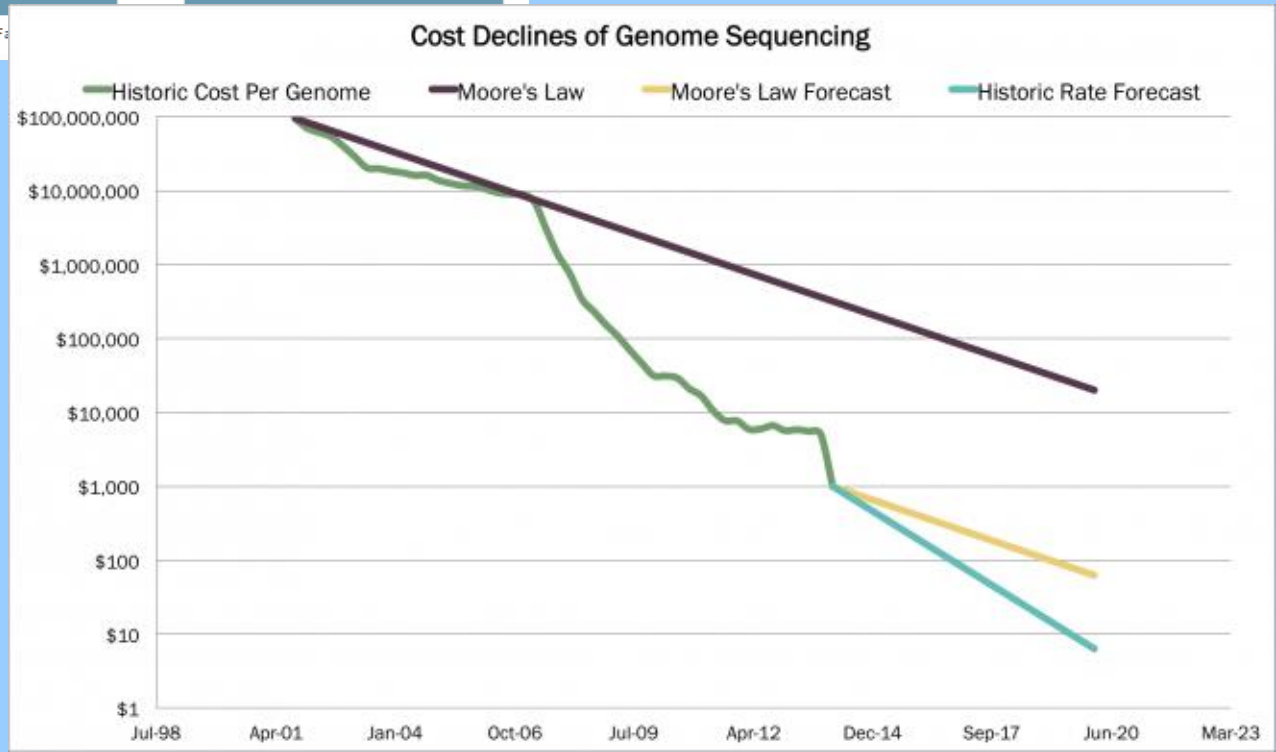
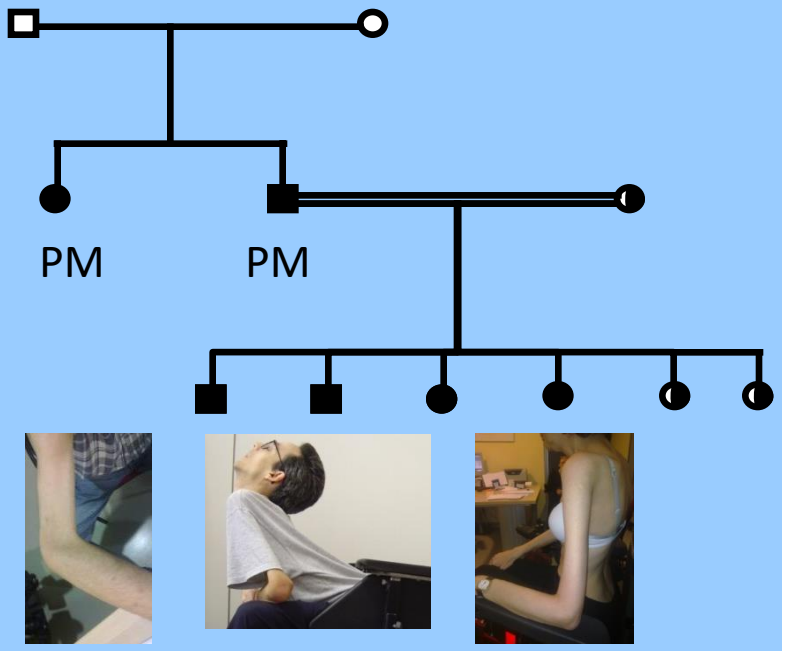
90 Gigabases raw data in FastQ format	10 Gigabases raw data in Fa	





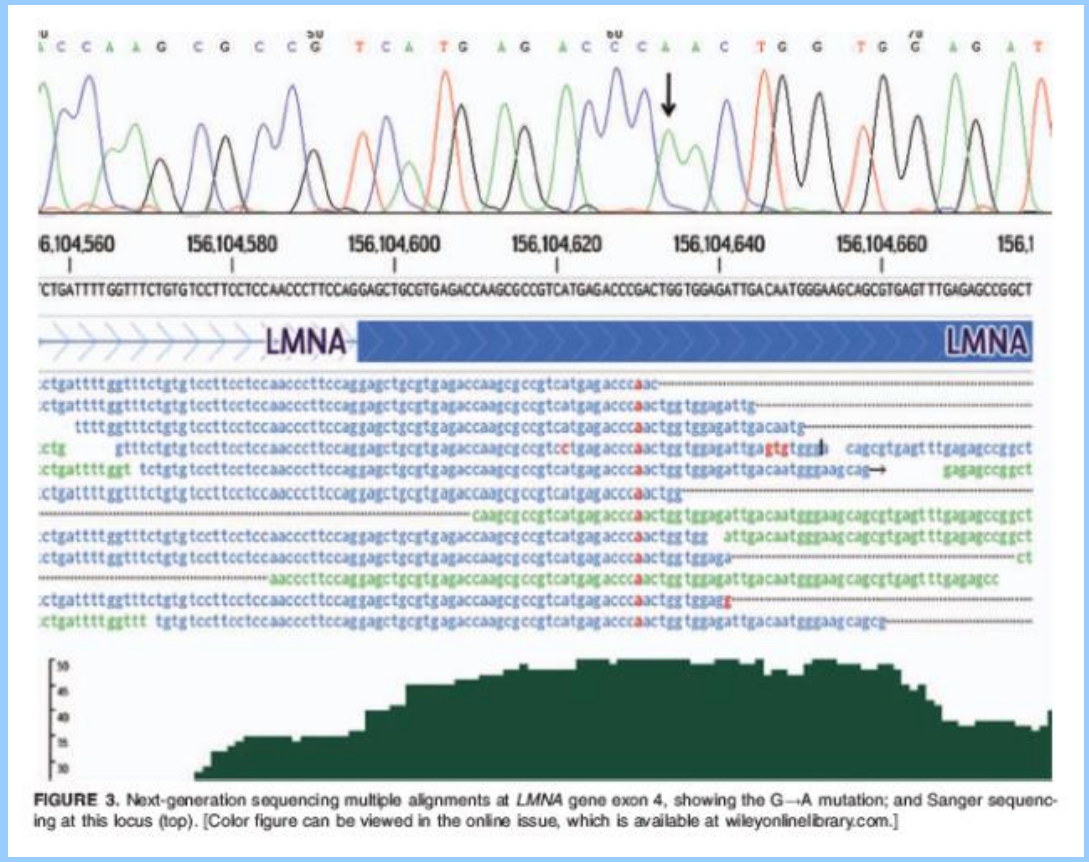


FIGURE 3. Next-generation sequencing multiple alignments at *LMNA* gene exon 4, showing the G→A mutation; and Sanger sequencing at this locus (top). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

CASE OF THE MONTH

AUTOSOMAL RECESSIVE EMERY-DREIFUSS MUSCULAR DYSTROPHY CAUSED BY A NOVEL MUTATION (R225Q) IN THE LAMIN A/C GENE IDENTIFIED BY EXOME SEQUENCING

ADRIANO JIMENEZ-ESCRIG, MD, PhD,[1,2] ISABEL GOBERNADO, MD,[2,3] MERCEDES GARCIA-VILLANUEVA, MD, PhD,[4] and ANTONIO SANCHEZ-HERRANZ, BS, PhD[2,5]

[1] Servicio de Neurologia, Hospital Ramon y Cajal and Universidad de Alcala, 28034 Madrid, Spain
[2] Unidad Central de Apoyo a Estudios Genomicos, IRYCIS, Madrid, Spain
[3] Servicio de Psiquiatria, Hospital Ramon y Cajal, Madrid, Spain
[4] Servicio de Anatomia Patologica, Hospital Ramon y Cajal, Madrid, Spain
[5] Servicio de Neurobiologia, Hospital Ramon y Cajal, Madrid, Spain

Accepted 10 October 2011

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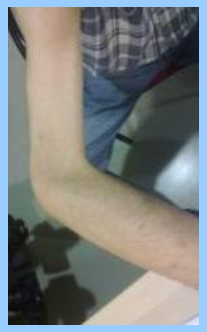

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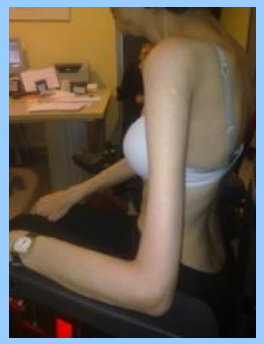

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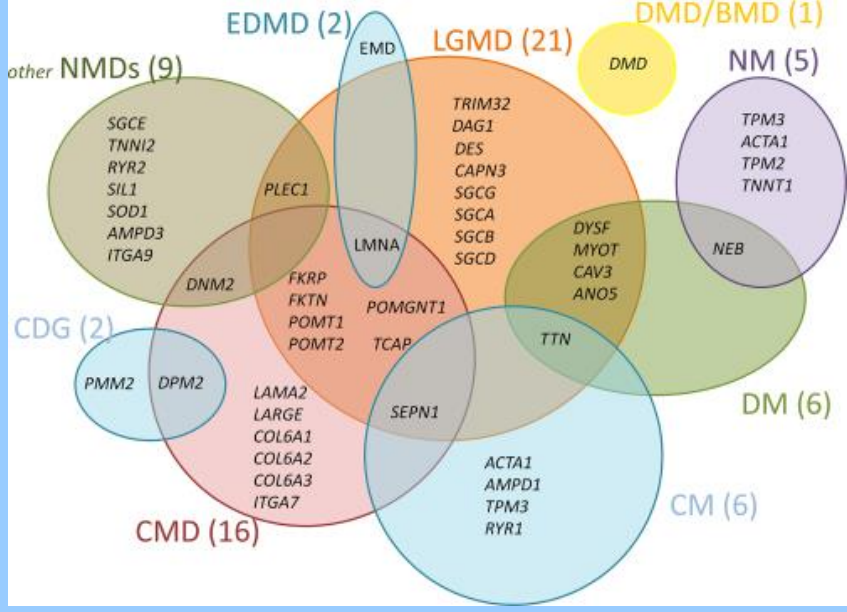

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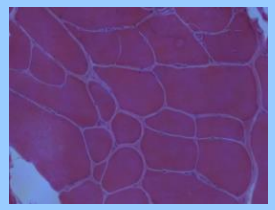

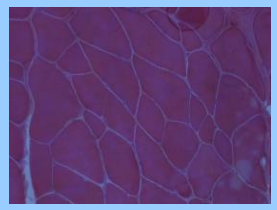

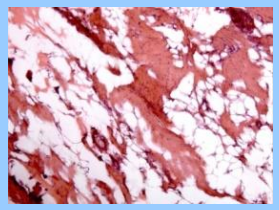

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disferlina

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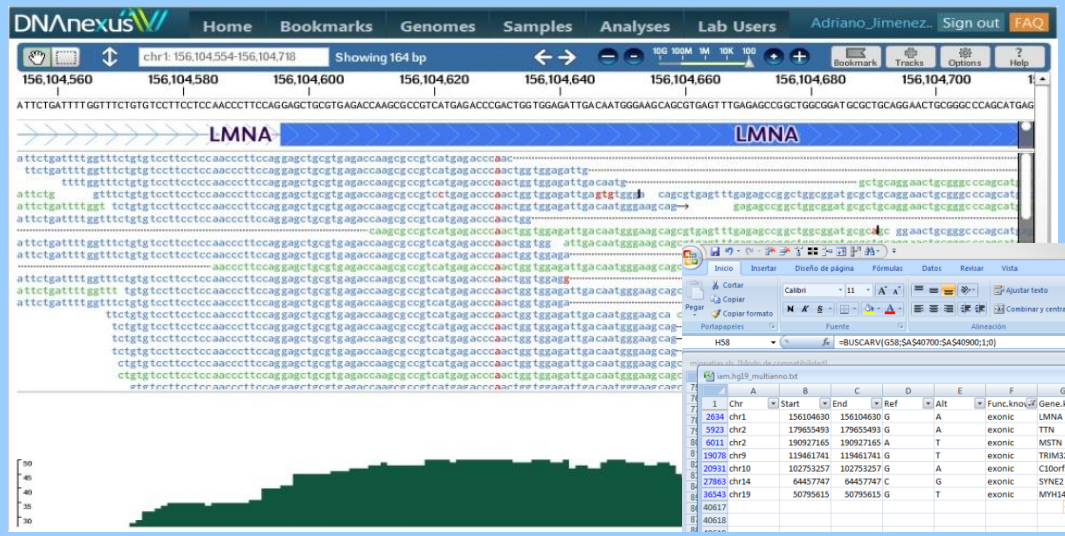

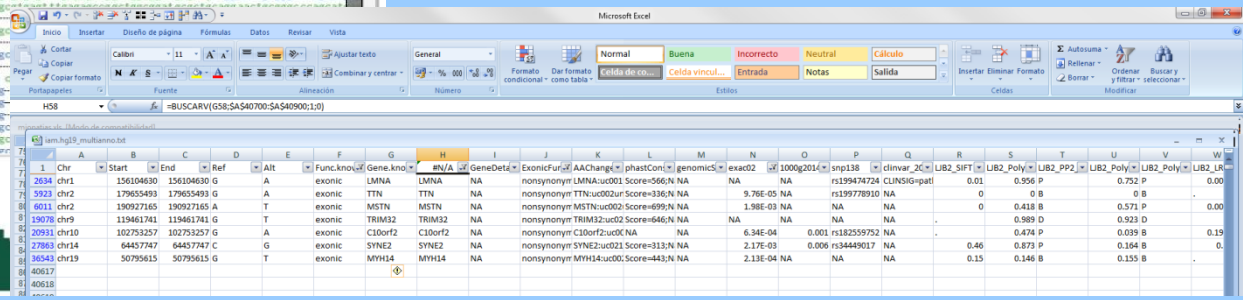

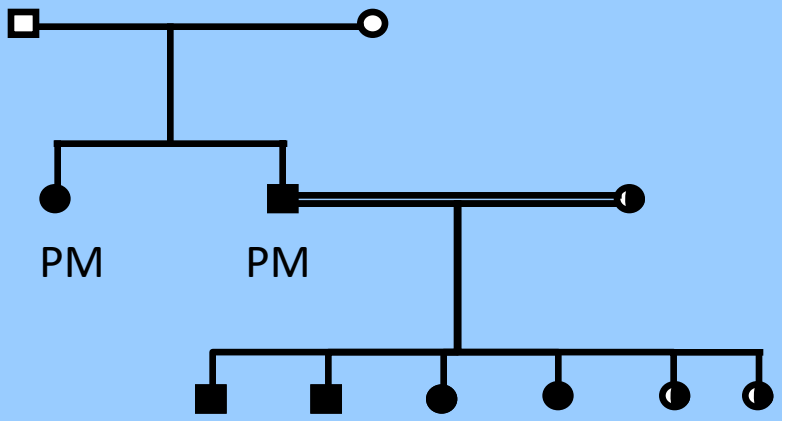

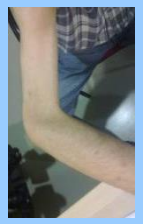

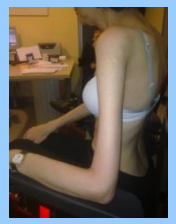

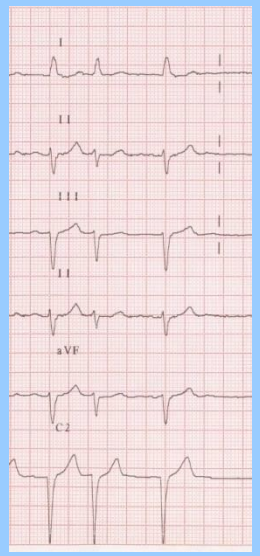

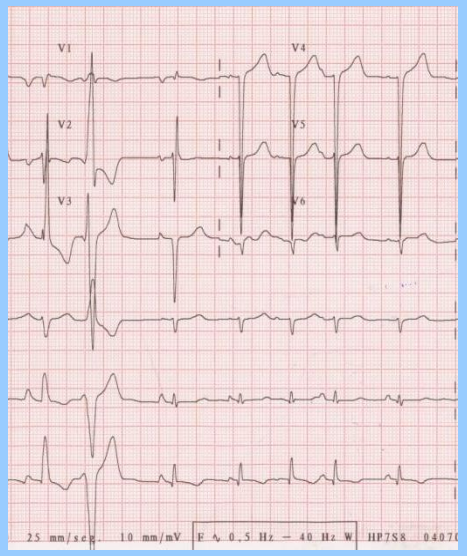

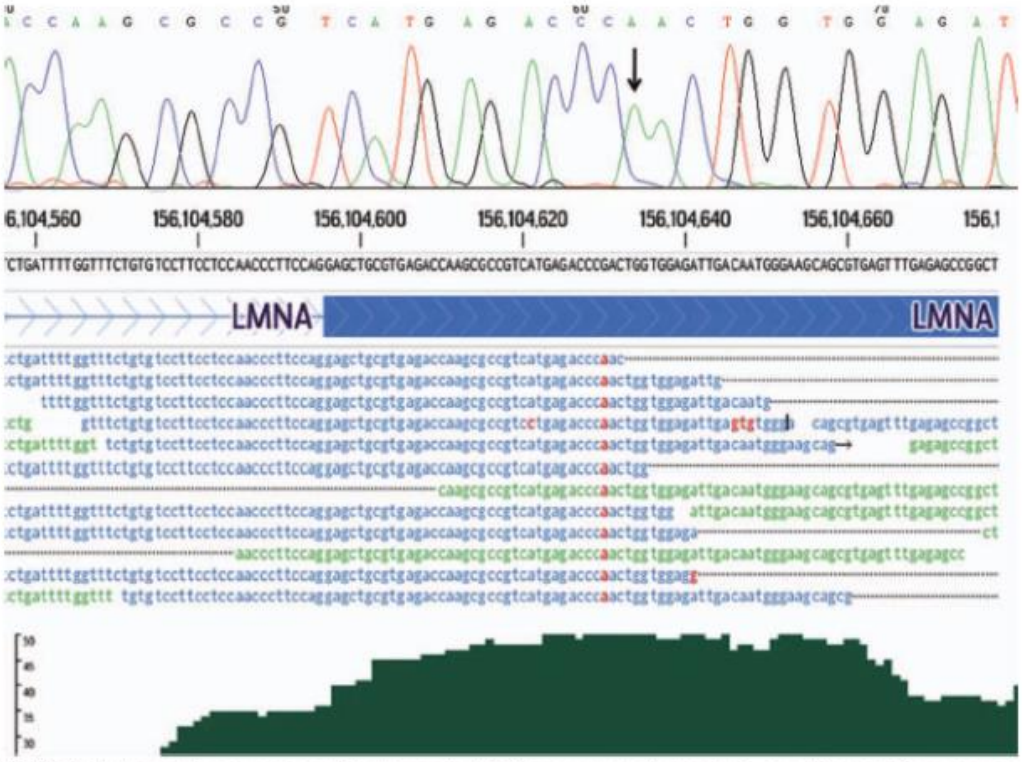

FIGURE 3. Next-generation sequencing multiple alignments at *LMNA* gene exon 4, showing the G→A mutation; and Sanger sequencing at this locus (top). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

CASE OF THE MONTH

AUTOSOMAL RECESSIVE EMERY-DREIFUSS MUSCULAR DYSTROPHY CAUSED BY A NOVEL MUTATION (R225Q) IN THE LAMIN A/C GENE IDENTIFIED BY EXOME SEQUENCING

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[4] Servicio de Anatomia Patologica, Hospital Ramon y Cajal, Madrid, Spain
[5] Servicio de Neurobiologia, Hospital Ramon y Cajal, Madrid, Spain

Accepted 10 October 2011

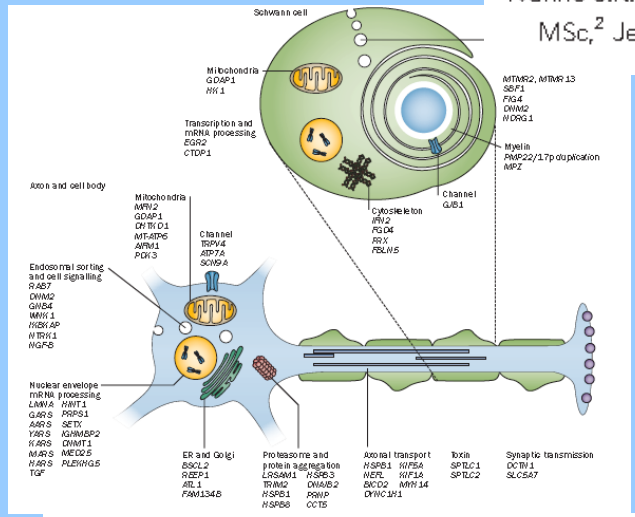
Exome Sequencing Allows for Rapid Gene Identification in a Charcot-Marie-Tooth Family

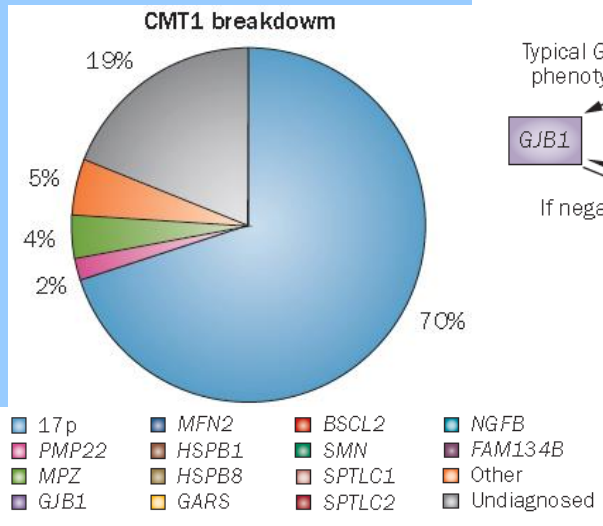
Gladys Montenegro, BSc,[1] Eric Powell, BSc,[1] Jia Huang, PhD,[1] Fiorella Speziani, MA,[1] Yvonne J.K. Edwards, PhD,[1] Gary Beecham, PhD,[1] William Hulme, BSc,[1] Carly Siskind, MSc,[2] Jeffery Vance, MD, PhD,[1] Michael Shy, MD,[2] and Stephan Züchner, MD[1]

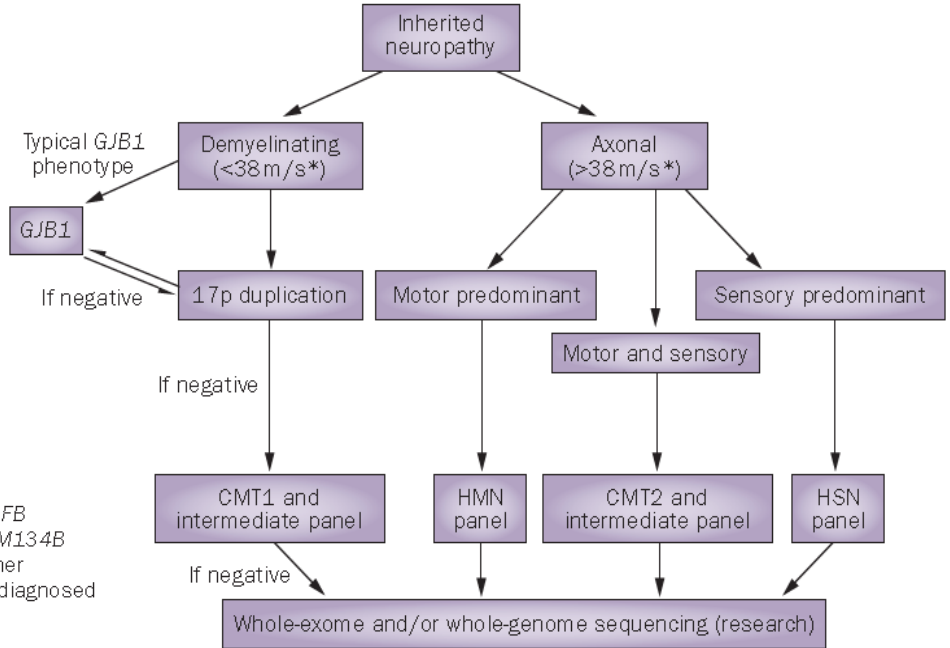
ANN NEUROL 2011;69:464–470

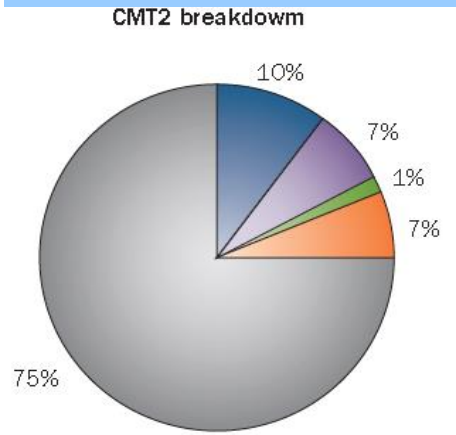
N Engl J Med 2010;362:1181-91.

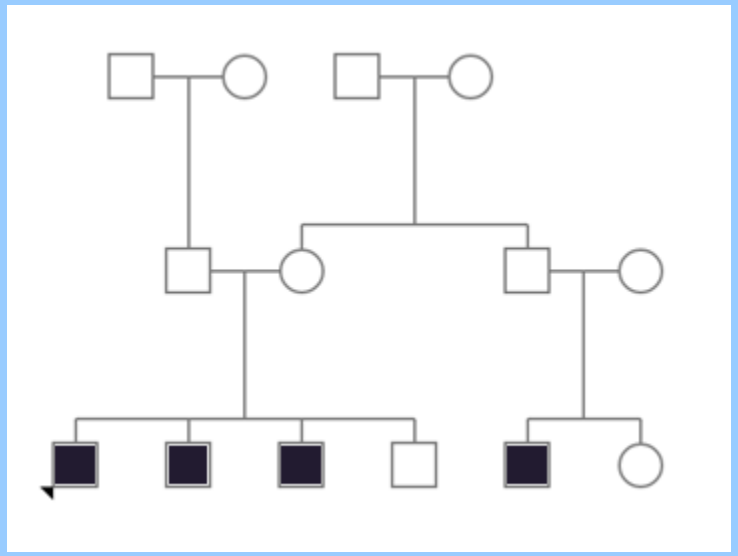
Whole-Genome Sequencing in a Patient with Charcot–Marie–Tooth Neuropathy

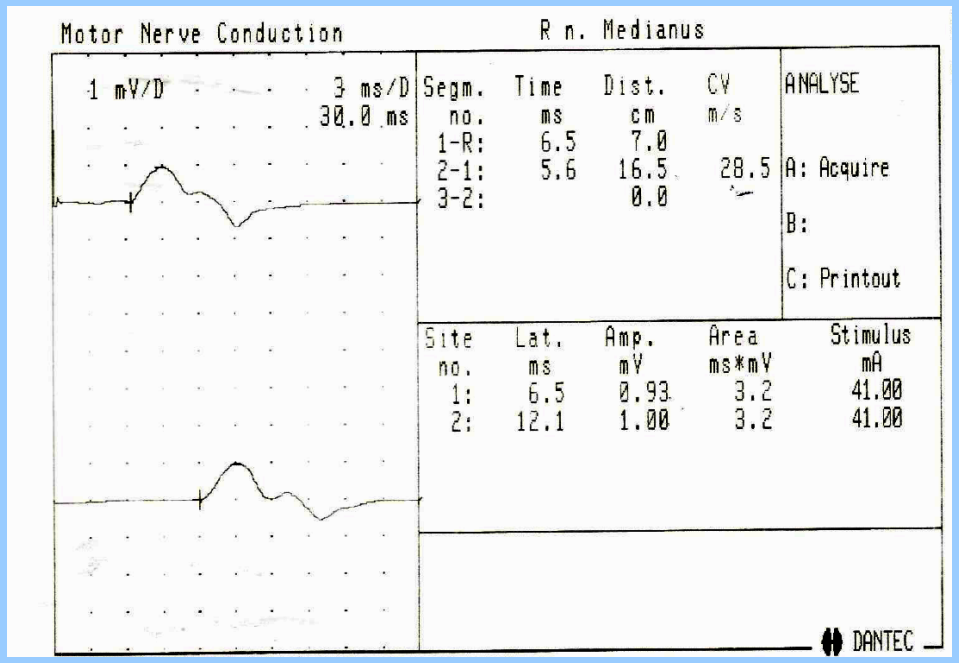












En el análisis de las regiones codificantes y regiones intrónicas adyacentes de los 87 genes del panel Charcot Marie Tooth no se han identificado variantes patogénicas ni variantes posiblemente patogénicas.

CLINICAL GENETICS An International Journal of Genetics, Molecular and Personalized Medicine

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doi: 10.1111/cge.12015

Genetics of the Charcot-Marie-Tooth disease in the Spanish Gypsy population: the hereditary motor and sensory neuropathy-Russe in depth

Sevilla T, Martínez-Rubio D, Márquez C, Paradas C, Colomer J, Jaijo T, Millán JM, Palau F, Espinós C. Genetics of the Charcot-Marie-Tooth disease in the Spanish Gypsy population: the hereditary motor and sensory neuropathy-Russe in depth.
Clin Genet 2013: 83: 565–570. © John Wiley & Sons A/S. Published by Blackwell Publishing Ltd, 2012

Four private mutations responsible for three forms demyelinating of Charcot-Marie-Tooth (CMT) or hereditary motor and sensory neuropathy (HMSN) have been associated with the Gypsy population: the *NDRG1* p.R148X in CMT type 4D (CMT4D/HMSN-Lom); p.C737_P738delinsX and p.R1109X mutations in the *SH3TC2* gene (CMT4C); and a G>C change in a novel alternative untranslated exon in the *HK1* gene causative of CMT4G (CMT4G/HMSN-Russe). Here we address the findings of a genetic study of 29 Gypsy Spanish families with autosomal recessive demyelinating CMT. The most frequent form is CMT4C (57.14%), followed by HMSN-Russe (25%) and HMSN-Lom (17.86%). The relevant frequency of HMSN-Russe has allowed us to investigate in depth the genetics and the associated clinical symptoms of this CMT form. HMSN-Russe probands share the same haplotype confirming that the *HK1* g.9712G>C is a founder mutation, which arrived in Spain around the end of the 18th century. The clinical picture of HMSN-Russe is a progressive CMT disorder leading to severe weakness of the lower limbs and prominent distal sensory loss. Motor nerve conduction velocity was in the demyelinating or intermediate range.

T Sevilla[a,b], D Martínez-Rubio[c,d], C Márquez[e], C Paradas[e], J Colomer[d,f], T Jaijo[d,g], JM Millán[d,g,h], F Palau[c,d] and C Espinós[d,i,j]

[a]Department of Neurology, Hospital Universitari i Politècnic La Fe, Valencia, Spain, [b]Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Valencia, Spain, [c]Genetics and Molecular Medicine Unit, Instituto de Biomedicina de Valencia, Consejo Superior de Investigaciones Científicas (CSIC), Valencia, Spain, [d]Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Valencia, Spain, [e]Department of Neurology, Hospital Virgen del Rocío, Seville, Spain, [f]Department of Neurology, Hospital Sant Joan de Déu, Barcelona, Spain, [g]Grupo de Investigación en Enfermedades Neurosensoriales, Instituto de Investigación Sanitaria (IIS) La Fe, Valencia, Spain, [h]Genetics Unit, Hospital

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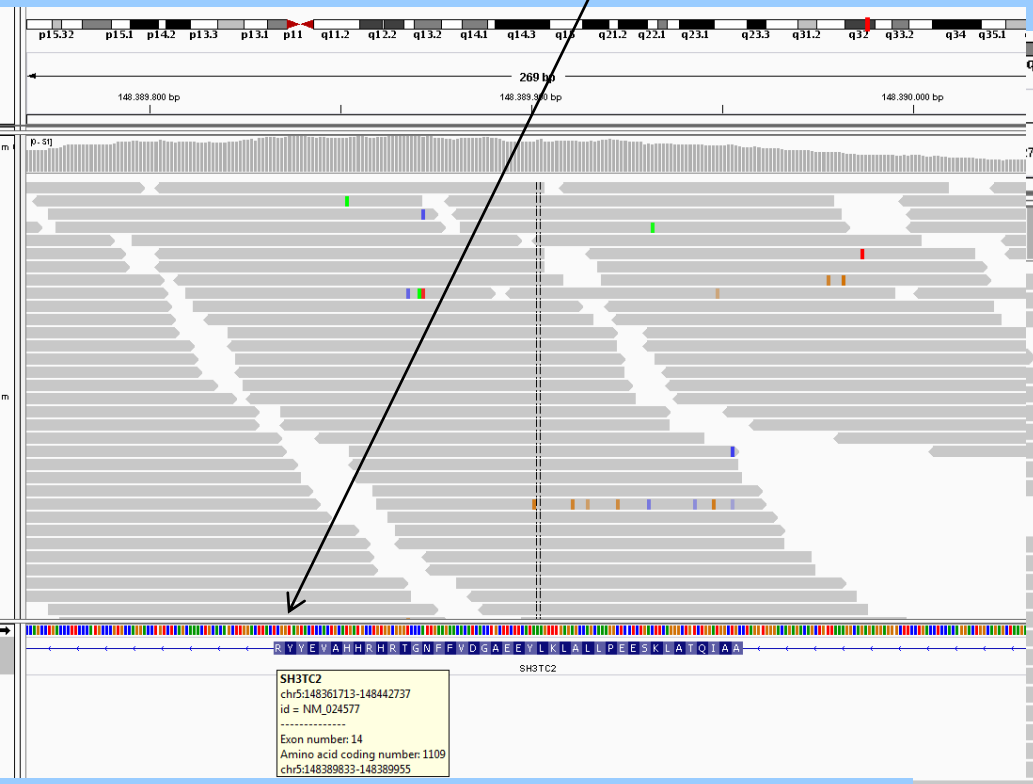
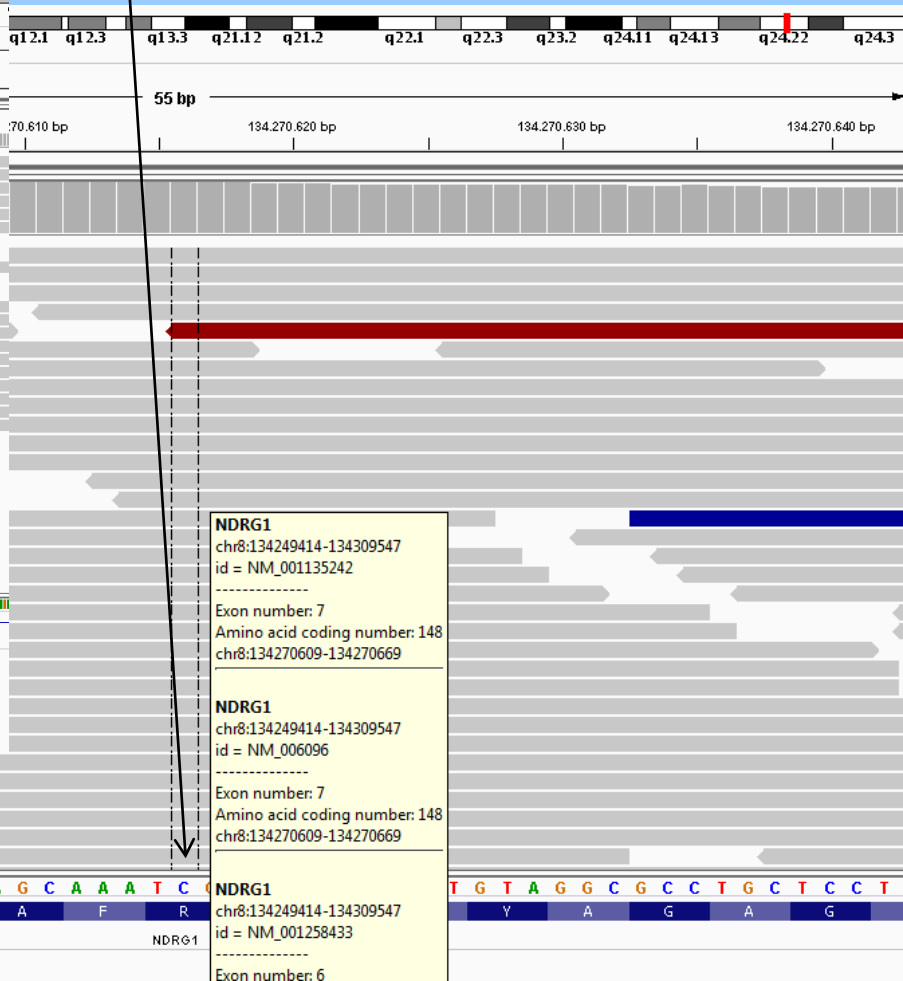
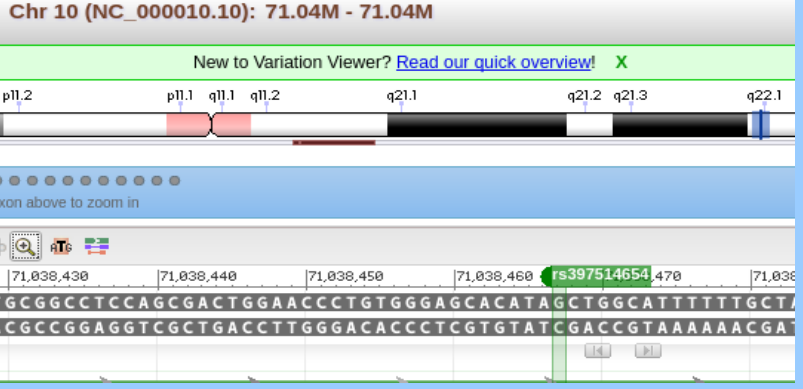
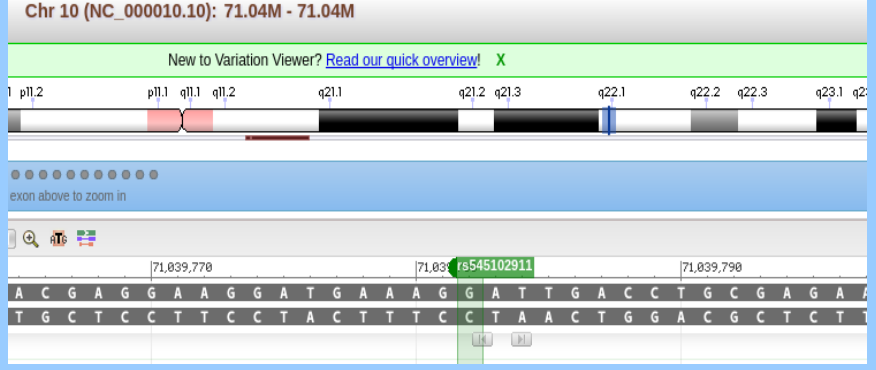





Chr 10 (NC_000010.10): 71.04M - 71.04M
New to Variation Viewer? Read our quick overview! X
rs397514654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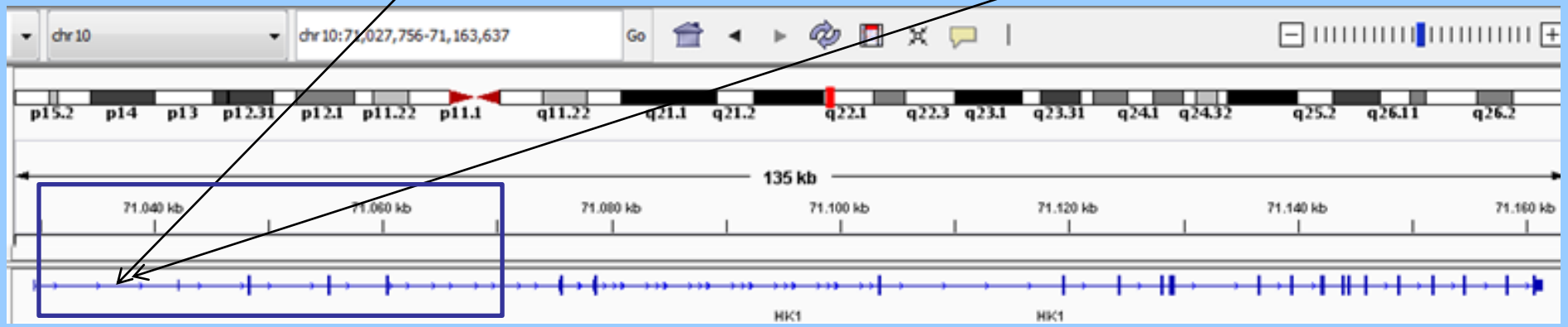
chr 10
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Go
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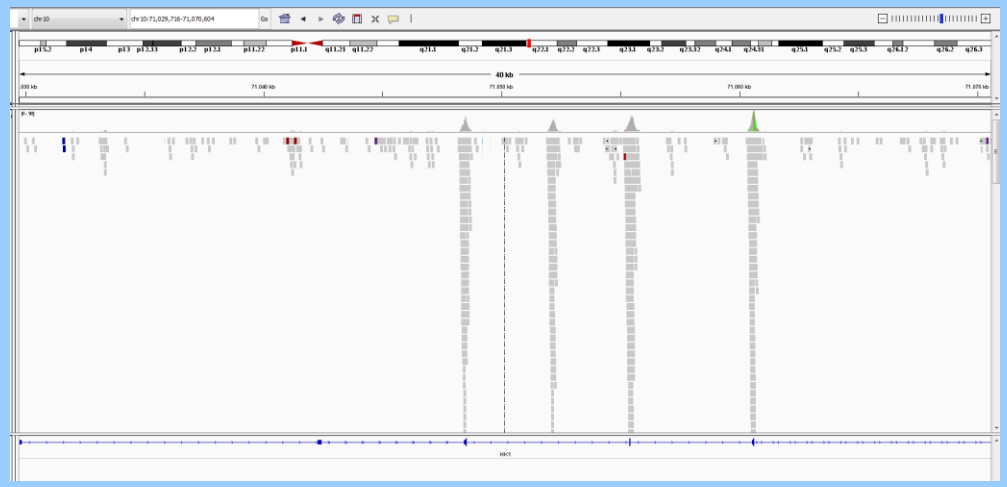
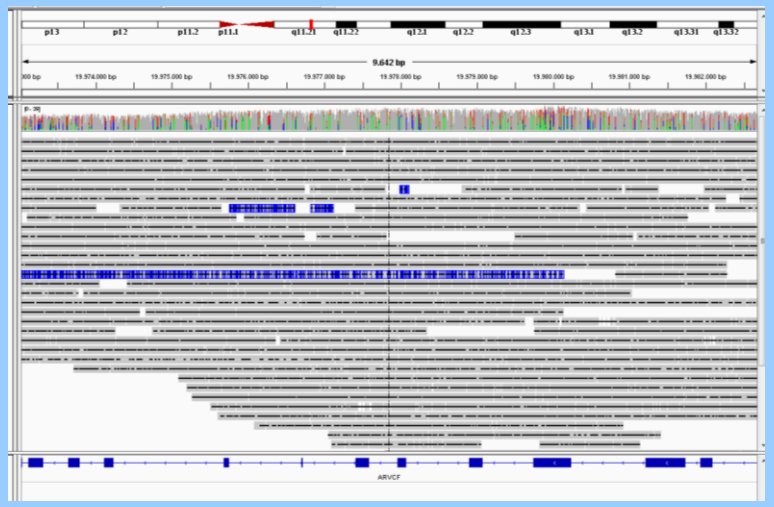
HK1
HK1





Demyelinating CMT Panel

FORMS AND DOCUMENTS

Test Requisition Test Info Sheet

TEST DETAILS

Genes:	DNM2 , EGR2, FGD4 , FIG4, GDAP1, GJB1, INF2, LITAF, MFN2, MPZ, MTMR2, NDRG1, NEFL , PMP22, PRPS1, PRX, SBF2, SH3TC2, YARS
Disorders:	» Charcot Marie Tooth (CMT)
Clinical Utility:	» Molecular confirmation of a clinical diagnosis » To assist with decisions about treatment and management of individuals with neuropathy » Testing of at-risk relatives for specific mutation(s) previously identified in an affected family member » Prenatal diagnosis for known familial mutation(s) in at-risk pregnancies

Neurología

Mostrar 100 filas por página Buscar Buscador de Servicios

Descripción	Modalidad	Plazo *	Referencia	Ficha
	Deteccion de grandes deleciones/duplicaciones en el gen FOXC1, mediante MLPA	Semanas	LV1567	+ INFO
	Secuenciación completa del gen FOXC1	5 Semanas	LV1697	+ INFO
	Secuenciación completa del gen PITX2	Consultar	LV2312	+ INFO
Bloom síndrome				
	Secuenciación masiva y Secuenciación Sanger del g en BLM	6 Semanas	LV2419	+ INFO
Cavernomatosis Múltiple				
	Detección de la mutación c.1363C>T en el gen KRIT1	4 Semanas	LV0459	+ INFO
	Secuenciación completa del gen KRIT1	Consultar	LV0759	+ INFO
	Secuenciación completa del gen CCM2	Consultar	LV1258	+ INFO
	Secuenciación Sanger del gen PDCD10	6 Semanas	LV2515	+ INFO
	Estudio de deleciones/duplicaciones en los genes KRIT1, CCM2 y PDCD10 mediante MLPA.	4 Semanas	LV2552	+ INFO
Charcot Marie Tooth, Enfermedad				
	Secuenciación masiva panel de 49 genes: AARS, AIFM1, ARHGEF10, C12orf65, DHTKD1, DNAJB2, DNM2, DYNC1H1, EGR2, FBLN5, FGD4, FIG4, GARS, GDAP1, GDAP1L1, GJB1, GNB4, HADHB, HK1, HSD17B4, HSPB1, HSPB8, IGHMBP2, INF2, KARS, KIF1B, LITAF, LMNA, LRSAM1, MARS, MED25, MFN2, MPZ, MTMR2, NDRG1, NEFL, PDK3, PLEKHG5, PMP22, PRPS1, PRX, RAB7A, SBF1, SBF2, SH3TC2, SURF1, TRIM2, TRPV4, YARS.	6 Semanas	LV3144	+ INFO
Charcot-Marie-Tooth axonal tipo 2O, enfermedad				
	Secuenciación masiva y Secuenciación Sanger del gen DYNC1H1	6 Semanas	LV1831	+ INFO

GENETAQ
CENTRO DE GENETICA MOLECULAR

Nº Informe: 91.143

Málaga, 7 de agosto de 2014

Paciente	Nombre	Prueba (código)
11-569	[redacted]	CHARCOT- MARIE TOOH (NGS-012)

FAM 192

INFORMACIÓN CLÍNICA: Paciente con Charcot-Marie-Tooth, variante axonal de la enfermedad. Estudios previos de *MFN2*, *GDAP1*, y *GARS* negativos.

RESULTADO: SE HA IDENTIFICADO UNA MUTACIÓN PATOGÉNICA.
Se ha identificado mediante NGS la presencia en hemicigosis de la mutación patogénica c.425G>A en el gen *GJB1*. Este cambio es una mutación missense que conduce a la sustitución p. Arg142Gln, según la secuencia de referencia NM_000166.5.

Dicha mutación se encuentra descrita en la base de datos Human Gene Mutation Database (HGMD) con el número de acceso CM940834 asociada a la enfermedad de Charcot-Marie-Tooth (Ionasescu (1994) Hum Mol Genet).

METODOLOGÍA EMPLEADA:
Se han secuenciado las regiones codificantes y las zonas intrónicas adyacentes de los genes: YARS, KIF1B, MFN2, LMNA, MPZ, RAB7A, SH3TC2, GARS, HSPB1, NEFL, GDAP1, NDRG1, EGR2, SBF2, MTMR2, FGD4, TRPV4, HSPB8, LITAF, AARS, PMP22, DNM2, PRX, MED25, GJB1, PRPS1, FIG4, LRSAM1, BSCL2, HK1, DYNC1H1 y INF2
Generación de librerías y enriquecimiento mediante el kit TruSight One (Illumina). Cuantificación de librerías mediante Qubit (Invitrogen) y estudio de tamaños obtenidos mediante Bioanalyzer (Agilent). Secuenciación paired-end de 150 pb mediante el secuenciador masivo MiSeq (Illumina), obteniéndose una cobertura media en las regiones analizadas del 95.5x, siendo el 96.5% de éstas > 20x. Las variantes se han generado tras un alineamiento al genoma de referencia (UCSC hg19) mediante el software MiSeq Reporter que incluye el alineador BWA y el variant caller GATK.
Anotación de las variantes de acuerdo a las secuencias de referencia citadas en la base de datos Human Gene Mutation Database (HGMD). Las variantes de interés clínico han sido comprobadas mediante secuenciación Sanger. El listado de variantes benignas puede ser solicitado bajo petición, al igual que las secuencias de referencia utilizadas. Prueba realizada con reactivos experimentales. Los resultados de la técnica han de considerarse de validez experimental.

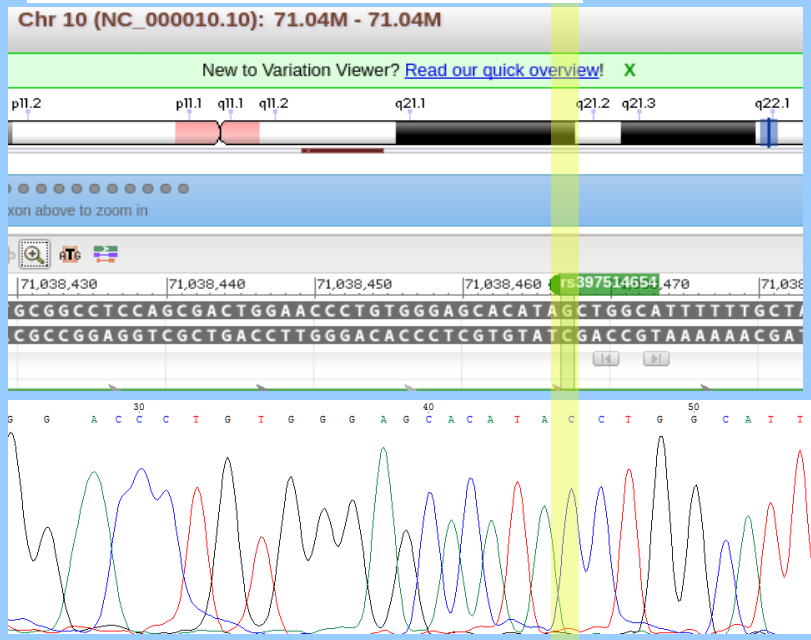
Table 1: Sequence capture performance results for the 51 neuropathy genes included in the panel.

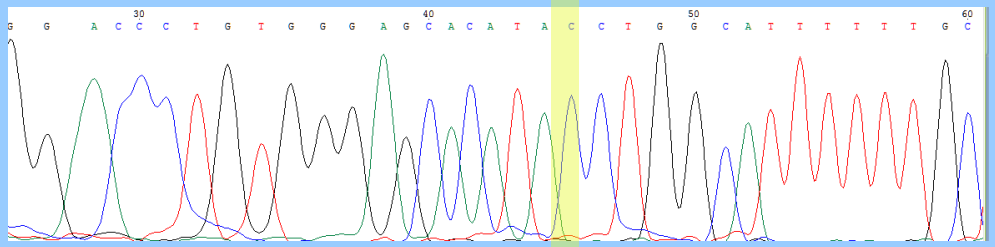
Gene	GenBank accession and version number	Neuropathy phenotype	Average coverage	% Bases ≥ 2x coverage	% Bases ≥ 30x coverage
AARS	NM_001605.2	CMT2	642	100.0	100.0
ARHGEF10	NM_014629.2	Slow NCV	620	100.0	97.7
ATP7A	NM_000052.6	dHMN	295	100.0	94.4
BSCL2	NM_001122955.3	dHMN	845	100.0	100.0
CTDP1	NM_004715.4	CCFDN	488	100.0	87.7
DCTN1	NM_001135041.2	dHMN	972	100.0	99.8
DNM2	NM_001005361.2	CMT2 and ICMT	449	100.0	96.6
DYNC1H1	NM_001376.4	CMT2	662	100.0	99.3
EGR2	NM_000399.3	CMT1, DSN, and CMT4	1328	100.0	100.0
FAM134B	NM_001034850.2	HSAN	296	100.0	88.5
FGD4	NM_139241.2	CMT4	410	100.0	100.0
FIG4	NM_014845.5	CMT4	480	100.0	100.0
GAN	NM_022041.3	GAN	472	100.0	93.1
GARS	NM_002047.2	CMT2, dHMN	427	100.0	92.9
GDAP1	NM_001040875.2	CMT2, CMT4, and ICMT	591	100.0	100.0
GJB1	NM_000166.5	CMTX	513	100.0	98.0
HK1	NM_033500.2	CMT4	654	100.0	95.9
HSPB1	NM_001540.3	CMT2 and dHMN	429	100.0	80.4

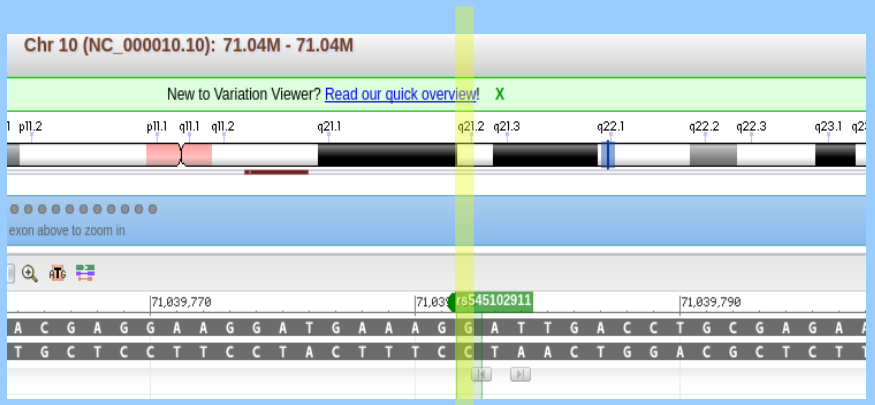
HK1	AltT2 exon	g.9712G>C
HK1	downstream of AltT2 exon	g.11027G>A

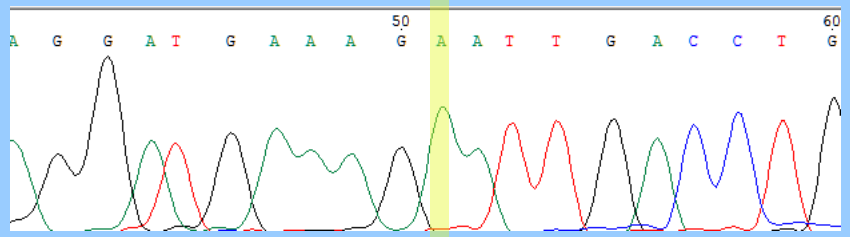
c.-249-3818G>C / g.9712G>C

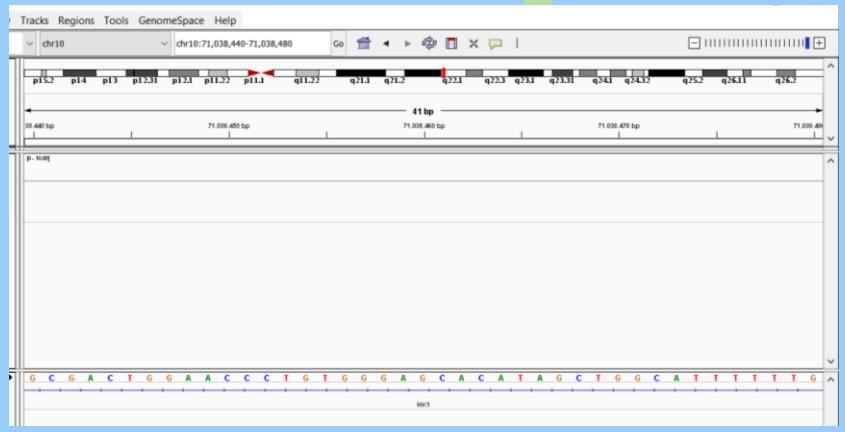
c.-249-2503G>A / g.11027G>A

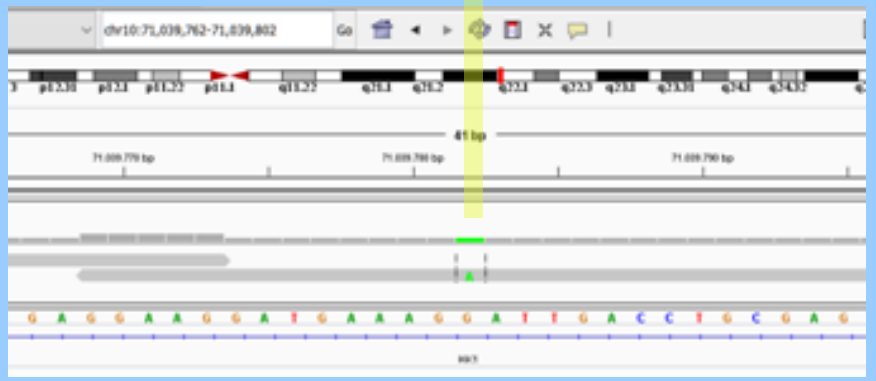




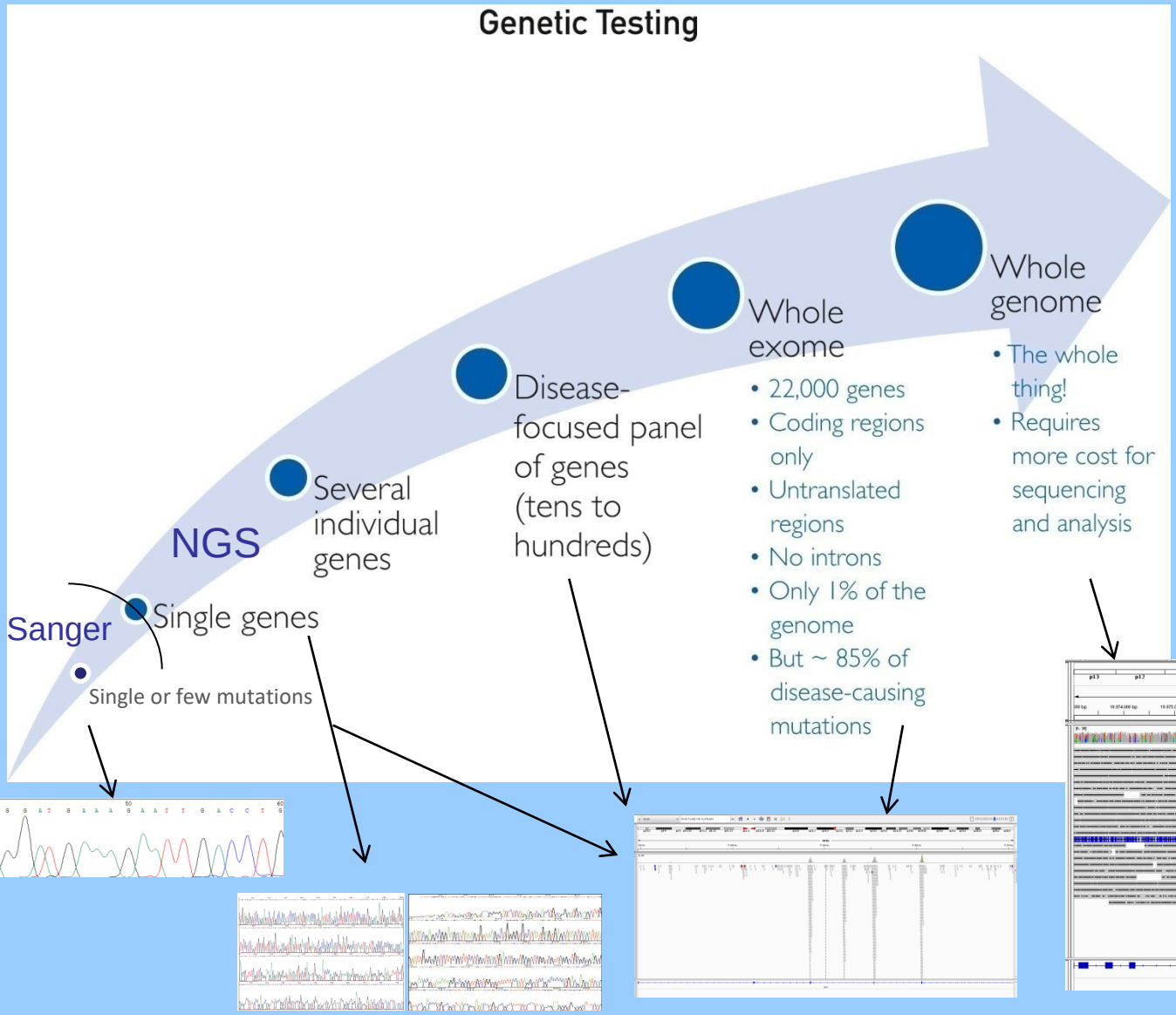




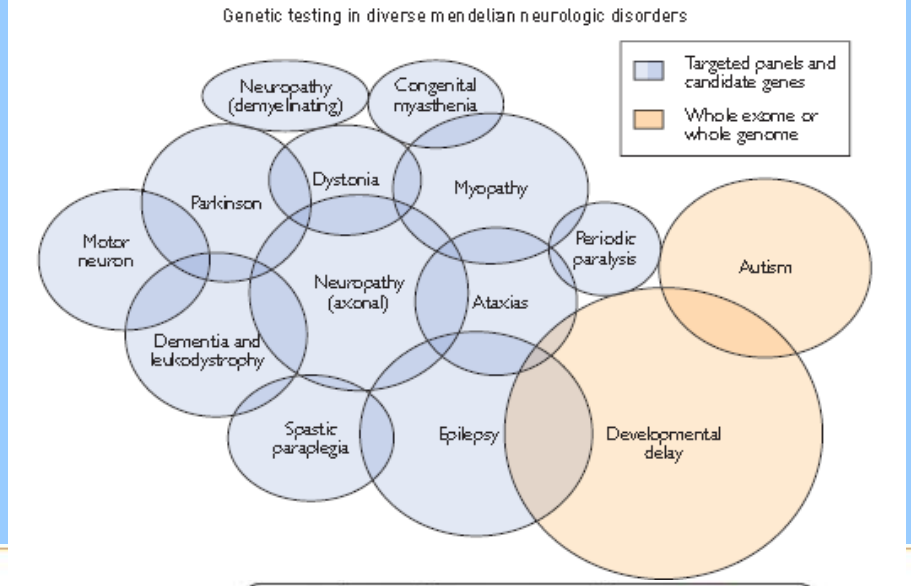


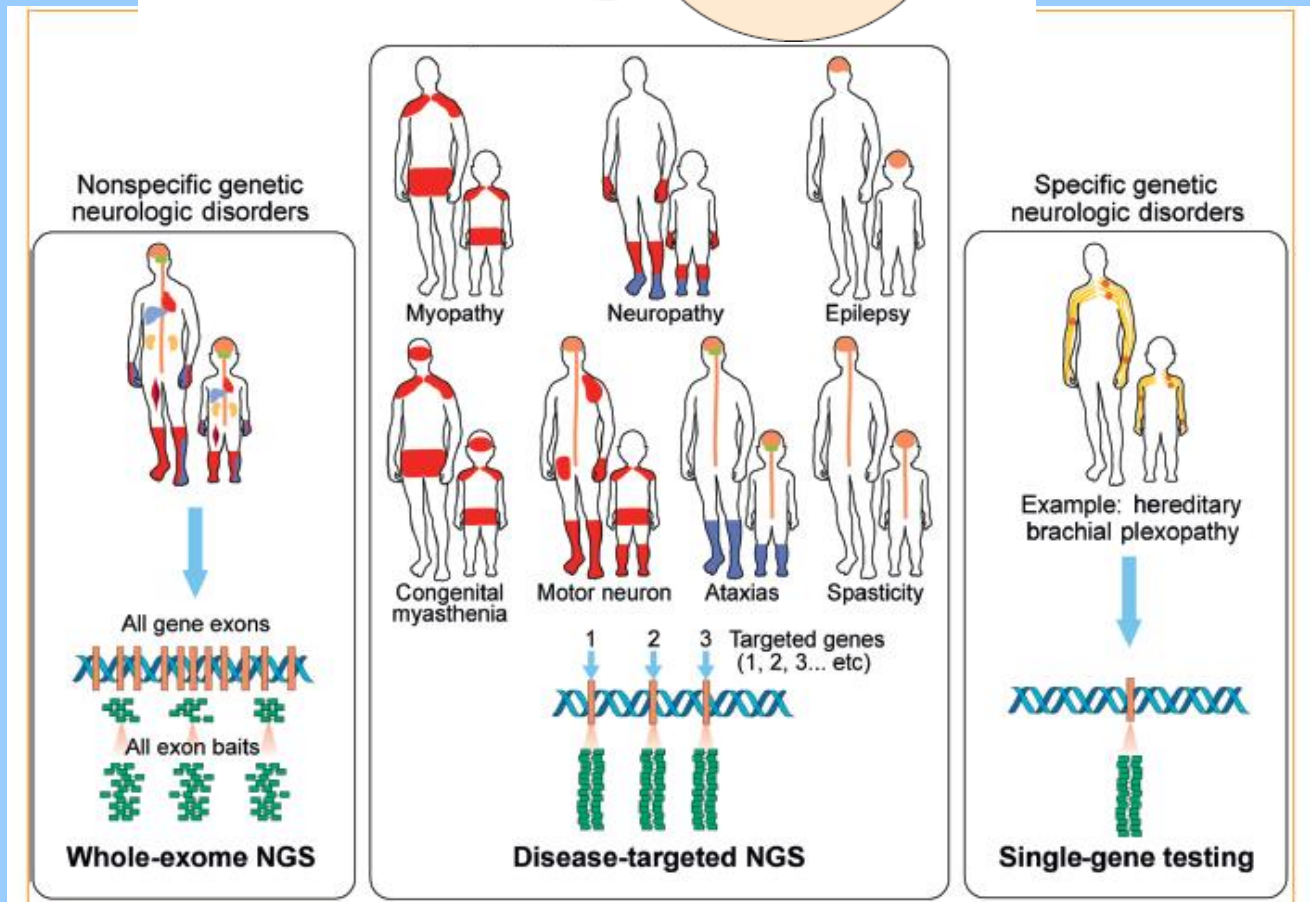


RESUMEN Y CONCLUSIONES



V: más información
D:coste/incertidumbre


Genetic testing in diverse mendelian neurologic disorders
Targeted panels and candidate genes
Whole exome or whole genome
Neuropathy (demyelinating)
Congenital myasthenia
Dystonia
Myopathy
Parkinson
Motor neuron
Periodic paralysis
Autism
Neuropathy (axonal)
Ataxias
Dementia and leukodystrophy
Spastic paraplegia
Epilepsy
Developmental delay


Nonspecific genetic neurologic disorders
All gene exons
All exon baits
Whole-exome NGS
Myopathy
Neuropathy
Epilepsy
Congenital myasthenia
Motor neuron
Ataxias
Spasticity
1
2
3
Targeted genes (1, 2, 3... etc)
Disease-targeted NGS
Specific genetic neurologic disorders
Example: hereditary brachial plexopathy
Single-gene testing