One test. Endless insights.

Whole-genome sequencing puts thousands of rare diseases in plain sight

Sabrina Malone Jenkins, MD Neonatologist University of Utah Health

illumina®

Shorten the diagnostic

CICTACTTAGCTACTIGETAGCTACTIAGCTACTIGETCTTACTGATCTTACTAGCTACTTGTCGCTGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	TAGCTACT						TGT	CTAGCT	TAAC	TGAT			
ABGUTHACUATETTACTTABGUTACTTGETABCUTHARCTGAUTTACTACTIGUTCAACTIGUTCACATAGUTCATAGUTACT<	CTCTACTTAGCT		ACTTGTCTAGCTAGCT		CTTAGCT ACTTGTC1		TTAACTGATCTTA		CTTAGCTACTTGT		CGCTTGATCTGGGAGAGCAGCT	ACTTAGCT	ACTTGTCT
TGTCTAGCTTACTTAGCTACTTGTCTAGCTAACTGATCTTAACTGATCTTCTTAGCTAGCTACTGTCTAGCTACTGCTAGCTACTGTGCTAGCTACTGTGCTAGCTACTGCTAGCTACTGATGCTGATGCTGATCTGGGGGGCATGGTGCTGATCTGGGAGGAGGCTACTTGGCTACTGGGATCTGTGCTAGCTACTGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	AGCTTAACTATCTTACTT		AGCTACTTGT	CTAGCTTAAC	TGATCTCT	ACTTAGCT	ACTTGTCTAGCTAGCTAC		TTAGCTACTTGTCTAGCT		TAACTGATCTTAACTGATCTTCT	TAGCTACT	TAGCTACT
TRATERES GAGAGEAG CTACTTAG CTACTTECTA GETTAACT GATETTAC TTAGETAC TTGTETAG CTTACTG ATCETAGA TGTTGTETGGGAGAGECAGET ACTTAGET ACTTAGET AGETTAAC TGATETTA CTTAGETA CTTGTAG CTTACTG ATGETAG TGTGTAG TTGTETAG CATGATEG AGETAGA AGETAGTG AGETAGT AGETAGET AGETAGET TTAACTGA TCTTACTT AGETAC TTGTGTAG CTTACTG ATGETAC TTGTACT TGTGTAG CATGATEG AGETAGA AGETAGTG AGETAGET AGETAGET GATACTTA GETAGET TTGTGTAG CTTGTGTAG CTTGTGAG CTACTTG ATGETAG CTAGETTA ACTGAT CTCTAGET TGTTAGETAC TTAGETAC TTGGCTAC TTGGCTAG CTTGTGAG CTACTTG TGTGTAG CTAGETTA GCTACTTA GCTACTG TCTGGCT ACTGGC TACTTAG CTACTGAT CTCTAGET ACTGGAG TGTAGETA CTTAGET CTTAGETA CTGTGTA ACTGGAT CTCTGTAG TTGTTAGC TACTGAT CTGTGTA AGETAGT CTGTGTA ACTGGAT CTCTAGET TGTTAGCA CTAGETTA CTGGCT ACTGGC TACTTA GCTAGETTA CTTAGETA CTGGCTA CTGGCT ACTGGC ACCTGA TGGCTAGETA CTGGCTA CTGGCTA CTGGCT ACTGGC ACCTGA TGGCTAGETA CTGGCTA CTGGCTA CTGGCT AGETAGT ACTGGCT ACTGGCA GCTAGETA CTAGETA CTGGCTA CTGGCTA ACCTGGC ACCTGA CTGGCGAGAGGAGG AGECAT GGTGGCTA CTGGCTA CTGGCTA CTGGCTA CTGGCTA ACT GGCTGCTAGCTGA GCTGGCTAG CTAGETTA CTGGCTA CTGGCTA ACT GGCTGCTAGCTGA GGTGCTAGET TTGGCTA CTGGCTA CTGGCTAACT GGTGGCTA CTTGGCTA CTGGCTAACT GGTCAGCT CTGGCTA CTGGCGAGGAGGCA CTGGCTACTGGCA GGTGCTGCAGCTACTGGCT CTAGETACC TGGCTGCAGCTACTGGCT CTGGCGAGGGAG CTGGCTGTACTGGCTACCTGGCGAGGGAGGCA CTGGCGCACCTGACCTG	TGTCTAGCTTCTAGCTACTTA		GCTACTTGTCTAGCTTAACTGA		TCTTAACT	СТТААСТ САТСТТСТ /		TAGCTACTTAGCTACTTGTCT		TACTTGTCTA	GCTAGCTACTCATGATGCTTGA	TCTGGGAG	CATGATGC
AGCTTAACTEATCTTACTTAGCTACTTAGCTACTTACTGATGCTACTGATGCTACTIGTCTAGCTIGTCTAGCTIGTCTAGCAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTGTCTAGCTICTAGCTICTTAGCTICTTAGCTICTTAGCTICTTAGCTICTTAGCTCTAGCTACTIGTCTAGCTICTTAGCTCTAGCTACTIGTCTAGCTICTTAGCTACTGATCTAGCTACTTAG	TTGATCTGG	GAGAGCAG	CTACTTAG	CTACTTGTCTA	GCTTAACT	GATCTTAC	TTAGCTAC	TTGTCTAG	CTTAACTG	ATCCATGA	TGCTTGATCTGGGAGAGCAGCT	ACTTAGCT	ACTTGTCT
TTAACTEA TCTTACTI AGCTACTI GCTAGCT TAACTEAT CTCTACT TAGCTACT TGTCTAGC TAGCTACT TGTCTAGC TAGCTACT TAGCT	AGCTTAAC	TGATCTTA	CTTAGCTA	CTTGTCTAG	CTTAACTG	A T G C T A C	TTGTCTAG	CATGATGC	TTGATCTG	G G A G A G C	AGCTACTT	AGCTACTT	GTCTAGC
TGATCTICTTAGETACTTAGETACTTGTETAGCTTGTETAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGCTACTTAGGCTACTTAGCTACTTGTCAGGCTACTAGCTACCTTAGCTACCTTAGCTACCTACTTAGCTTATAGCTACTGACTTAACTGATCACTGATCACTGATCACTGATCACTGATCACTGATCACTGATCACTGATCTGACTTAACTGATCTGACTTAACTGATCTGACTTAACTGATCTGACTTAACTGATCTGACTTAACTGATCTGACTTAACTGATCTGACTTAACTGATCTGACCTGACTGACTGACTGACCTTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACCTGACTGACC	TTAACTGA	TCTTACTT	AGCTACTT	GTCTAGCT	TAACTGAT	CTCTACT	TAGCTACT	TGTCTAGC	TAGCTACT	TAGCTACT	TGTCTAGC	TTAACTGA	TCTTAAC
6CTACITA6CTACITACITAGCITACITAGCIACITAGC	TGATCTTC	TTAGCTAC	TTAGCTAC	TTGTCTAG	CTTCTAGC	TACTTAG	CTACTTGT		CTAGCTTA		ACTGATCT	TAACTGAT	CTTCTTA
TICITAGE TACTTAGE TACTTGTE TACTGTE TAGETTE TAGETTE TACTGA GATGETG ATCTGGGAG ACCAGCCAT GACGCCAT GACCGCAT GATCTGG GAGAGCAG CTACTTAG CTACTGTE CTAGETTA CTGACETTA ACTGATE TACTTA GETACTGAT ACCGATE TACTGA CTACTGATE TAGETAC GCTAGETA CTTAGETA CTGTACT GACCTAA CTGATET TAACTGA CTGATETACTGA CTACTGACTACTGA TECTACTGAC TAGETACTGGGAGAGGE TGTGTAGE TTTAGETA CTTAGETA CTGATETT AGETACTT GTCTAGETTAACTG GATCTTAGETAC TGTGTAGE TTTAGETA CTTAGETA CTGATETT GTCTAGETTAACT GATCTGAC TAGETACTGGCA GCTAGETT CTTAGETA CTGAGETA CTGGTAGET GETCAGETAACT GATCTGAGEGA GCTGATETT CTTAGETA CTGAGETA CTGGTAGET GETCAGEGAG GCTGATETT CTGAGETA CTGGTAGETA CTGGCTAGETA CTGGTAGEGA GCTGGTTET TAGETACT GCTGACTT GETCAGETAGEC TTGGTGGGGGAGG GCTGGTTET TAGETACT GCTGACTT GETCAGETAGEC TTGGTGGGGGGG CTGGTGGT TAGETACTT GCTGGTAGET CTGGCTAGEC TAGETACTGGGGGGGG CTGGTGGT ACCTGGTTG GCTGGTGG CTGGTGGT CTGGTGGG CTGGTGGT ACCTGGTGG CTGGGGG AGCGGCGT CTGGCGGGGGGG CTGGTGGT GTGGTGG CTGACTG CTGGGGGG AGCGGCTA CTGGGGG CTGGGGGGGG CTGGTGGCT GGGTGG AGCGGGGG AGCGGCTA CTGGGGG CTGGCTGG TGGCTGG TGGGGGGG AGCGGCTA CTGGGGG CTGGCTGG TGGGTGG AGCTGGGG AGCGGCTA CTGGGGGG CTGGCGGGGGG AGCGGCGA CTGGGGG CTGGGGGGGGGG	GCTACTTA	GCTACTTG	TCTAGCTT	CTTAGCTA	CTTGTCTA	GCTAGCT	ACTTAGCT		ACTTGTCT		AGCTTAAC	TGATCTTA	ACTGATC
GAGAGCAGCTACITAGCTACITAGCTAGETAACTGATCTAACITAAGCTACITGTCAGCTAACTGATCTCACTTAGETACTAGETACTAGETACGCTAGCTACTTAGCTACTGATCTGACCTTAACTGATCTTAACTGATCTCTTAGCTATAGETACTAGETACTGGAGGCACTACTTAGETACTAGETACTAGETACTGGAGGCTAGETACTAGETACTAGETACTGGAGGCTAGETACTAGETACTAGETACTGGAGGCTAGETACTAGETACTAGETACTGGAGGCTAGETACTAGETACTAGETACTGGAGGCTAGETACTAGETACTGGAGGCTAGETACTAGETACTGGAGGCTAGETACTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGCTTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGCCTAGETACTGGAGGCTAGETACTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGCTAGETACTGGAGGGAGGGAGGGGGGGGGGGGGGGGGGGGG	TTCTTAGC	TACTTAGC	TACTTGTC	TAGCTTTC	TACTCATG	ATGCTTG	ATCTGGGAG		AGCAGCCAT		GATGCCAT	GATGCTT	GATCTGG
GCTAGCTACTTAGCTACTGATCTCTGATCTTAACTGATCTTCTAGCTATTAGCTACTTTAGCTACTTAGCTACTGCTAGCTACTTGGGGGGGGGCAGCTACTTAGCTACTTGTCTAGCTTAACTGATCTTAGCTATTAGCTACTTGCTACTTAGCTAGCTACTTAGCTAGCTACTTAGCTACTTGCTAGCCTTAGCTGGGAGAGCAGCTACTTAGCTACTTGCTAGCCTGTCTAGCTCTTAGCTACTTAGCTACTTGTCTAGCTAGCTACTTAGCTAGCTACTTAGCTACTTAGCTACTTGCTACTTAGCTACTTAGCTACTTGCTAGCTTAACTGATCTTAGCTACTTGTCTAGCTAGCTCTAGCTAGCTCTAGCTAGCTGTAGCTACTTGTCTAGCTTAACTGATGCTACTTGCTACTGGCTGCTACTGGCAGCCTAGCTAGCTAGCTGTGGCAGCTAGCTACTGGCAGCTATGTGCTAGCTTAGCTACTTAGCTAGTGTGGCAGCAGCTGTGGCAGCAGCTACTGGCAGCTAGCTACTGGCAGCAGCTACTGGCAGCAGCTACTGGCTGGCTGGACTGGGGGGGAAGCGGCTACTTAGCTACTTAGCTACGCTGCAGCAGCATTAGCTACTTAGCTACGCTACTGGTGGCAGCTCTAGCTGACTTAGCTACTTGGCAGCACTGGCTGGAGCAGCTACTGGCAGCAGCTACTGGCAGCAGCTACTGGCAGCAGCTACTGGTGGCAGCTCTTAGCTGACTTAGCTGCACTGGCTGGAGCAGCTACTGGCAGCAGCTACTGGCAGCAGCTACTGGCAGCAGCTACTGGCAGCAGCTACTGGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCA	GAGAGCAG	CTACTTAG	CTACTTGT	CTAGCTTA	ACTGATC	TTACTTA	GCTACTTGTC	Т	AGCTTAACTGA		TCTCTACT	TAGCTAC	TTGTCTA
TGTETAGE TTAACTGA TETTACTT AGCTACTT GTETAGETT AACT GATETETAGE TACTTGETAGETA CAGETAGETA CAGETAGETA CAGETAGETA TTAACTGATETTAACT CTGATCTT CTTAGETA CTTAGETA CTTGTCTA GETTEGTAGE GTETAGET TAACTGAT CTCTGTCT AGETACTT GETTAGETAGEC TTGATCTGGGGGGGG TTGTCTAGE CTTTACTGACTT GETAGETAGEC TACTGGCAGEC TACTGGGGGGGGGCAGET TGTCTAGE CTTTACTTACTGACTGATETT GETAGECT TACTGGCAGEC TACTGGGGGGGGGCAGET TGTCTAGE CTTTACTTACTGACTGATETT GETAGECT TACTGGCAGEC TACTGGGGGGGGCAGET GETCAGETAGETAGETAGETGCAGETAGETG CTAGETTA ACTGGATCT GETAGECT TAGETAGECT TAGETAGEC TACTGGCAGECAGETAGETA CTAGETTA ACTGGATCT CTCACTT GETAGECT TAGETAGECT TAGETAGECT TACTGGCAGECA CTAGETTA ACTGGTCT CTCACTTAGECT CTAGECTACT CTAGETAGE CTGGCTGGA CTGCGGGG AGCAGECTA CTTAGETAGE CTGGCTTGG TCGCTTGGA TCTGGGGGG AGCAGECTA CTTAGETAG CTGGCTAGE TGGCTGGA TCTGGGGGG AGCAGECTA CTTGGCTAGE CTGGCTAGE TGGCTGGA TCTGGGGGG AGCAGECTA CTTGGCAGE TTGTCTAGE CTTAACTG ATCTCTAC TTAGETAC TTGTCTAG CTGGCTAGE TGGCTGC TTAGETAC TTGGCTAC TTGGCTAGE CTGGTGCT TAGETAGECTGTT TGCTAGE TGGTTGGT TAGETAC TTGGCTAC TTGGCTAGE TGCTGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	GCTAGCTA	CTTAGCTA	CTTGTCTA	GACCTTA	CTGATCT	TAACTGA	TCTTCTTAG	CTAC	TTAGCTACTT	GTC	TAGCTTTTGATCTGGGAGAGC	AGCTACT	TAGCTAC
CTGATCIT CTTAGCTA CTTAGCTA CTTGACTA GCTGATGATGC TTGATGATGC CTGATGGGAGAG CAGCTACTTAGCTA CTTAGCTGATCTT ACTTAGCTACT GTCTAGCT TAACTGAT CTCACTT AGCTACTT GTCTAGCTAGC TACTGGGAGGGAGG CAGCTACTTAGCTAACT GATCTTAACTGATCTT AGCTACTT TGTCTAGC TAACTGAT GTCAGCT GACTAGCT TAACTGATC TACTGGATC CTAGCTA ACTGATCT CTACTTAG CTACTT GTCTAGCT TAACTGATC TTACTTAGCTA CTAGCTA ACTGGATC CTACTTAG CTACTTGT CTAGCTAG CTACTTAGCTA CTAGCTAG CTGGGAG AGCAGCTA CTAGCTAG CTGTGTCA GTCTTACCT GATCTTACC TGTGTAGG CTTAACTG ATCTGTCA CTTAGCTAC TTGGCTAG CTGGTGC TAGCTAC TTAGCTAC TTGGCTAG TTGTCTAG CTGACTGA TCTGGGAG AGCAGCTA CTGTGTGG CTGCTAGC GATCTGC TTAGCTAC TTGGCTAC TTGGCTAG CTGGCTAC TTAGCTAC TTGGCTAG CTGATGG TGTCTAGC TGGTTGC TGGCTGC TTAGCTAC TTGGCTAG CTGCTGGATG CTGGATG CTGGATG GCTGGATG GATCTTG TGTCTAGC TACTTAGC TAGCTGC TAGCTGC TGGCTGG TGTCTAGC TACTTAGC TAGCTGC TAGCTGC TGGC TAGCTAC TCGATGG CTGGATG GCTGGATG GGGGAT GATGGTTG	TGTCTAGC	TTAACTGA	TCTTACTT	AGCTACT	I GTCTAGC	TTAACT	GATCTCT	ACTTAGC	TACTTGTC	TAGCTA	GCTACTTAGCTACTTGTCTAGC	TTAACTG	ATCTTAA
GTCTAGCT TAACTGAT CTCTACTT AGCTACTT GTCTAGCTAGCC TACTTAGCTACTT GTCTAGCTAACTGGATCTTCTTAGC TACTTAGCTAC TTGTCTAGC CTTACTT AGCTACTT GTCACGTT TACTGAGCAC TTGTCTCT ATGCTAACTGATCTTCTTAGC TACTTAGCTACTT GTCAGCTT ATGCTAACTG GTCACTTAGCT ATGCTAACTG GTCACTTAGCT ATGCTAACTG GTCACTTAGCT ATGCTAACTG GTCACTTAGCT ATGCTAACT GTCACTTAGCT ATGCTAACT GTCACTTAGCT ATGCTAACT GTCACTTAGCT ATGCTAACT GTCACTTAGCT GTCACTTAGCT CTACTTAGCT ATGCTAACT GTCACTTAGCT GTCACTTAGCT TTAGCTAC TTAGCTACT CTTAGCTAC TTAGCTACC TTAGCTACC TTAGCTAC TTAGCTACC TTAGCTACC TTAGCTAC TTAGCTAC TTAGCTACC TTAGCTACCT TTAGCTACCTACCTACCTACCTACCTACCTACCTACTACCTAC	CTGATCTT	CTTAGCTA	CTTAGCTA	CTTGTCT	GCTTCA	TGATGC	TTGA	T C T G G G A G A G	CAGCTA	CTTAGCTA	CTTGTCTAGCTTAACTGATCTT	ACTTAG	CTACTT
TTGTCTAG CTTTACTT AGCTACTT GTCTAGCT TAACTGATC TTACTTAGCTA CTTGTCCTCT ATACTTA GCTACTTGT CTAGCTTA ACTGATCT CTACTTAG CTACTTGT CTAGCTAG CTACTGAGC TACTGGTCT TAACTGAT CTACTGT GCTACTTG TCGTGA TCGGGAG AGCAGCTA CTTAGCTAC CTGTGTA GCTTAACT GATCTTAC TTAGCTAC TTAGCTAC TTGTCTAG CTTAACTG ATCTCTAC TTAGCTAC TTGTCTAG CTGCTAG CTAGCTAC TTAGCTAC TGGTGAG CTGGTATC TGGCTAG CTACTGGT ATCTTAACT GATCTTC TTAGCTAC TTGGCTAC TTGTCTAG CTCCTAGC TACTGGTG CTGGTTGT GGAGGAT GATCGTAG TTGTTAGC TACTTGTC TAGCTACT TGGCTACT TGTCTAGC TAGCTAC TCGATG CTGGATG CTGGATG CTGGAGCAT GATGCTTG	GTCTAGCT	TAACTGAT	CTCTACTT	AGCTACTI	GTCTAG	CTAGC	T.	ACTTAGCTACTT	GTO	CTAGCTTAACT	GATCTTAACTGATCTTCTTAGC	TACTT	GCTAC
CTAGCITA ACTGATCT CTACTTAG CTACTTGT CTAGCTAG CTACTTAGC TACTTGTCTT TAACTGAT CTTACTTA GCTACTTG TCGGCTGA TCTGGGAG AGCAGCTA CTTAGCTA CTGTCTA GCTTAACT GATCTTAC TTAGCTAC TTGTCTAG CTTAACTG ATCTCAC TTAGCTAC TGGCTAG CTGAGCAC TTAGCTAC TGGCTGG ATCTTAAC TGATCTC TTAGCTAC TTGGCTAC TGGTCAG CTCTGGC TACTTGTC TAGCTAC GGAGGAT GATCGTTG TTGTCTAGC TACTTGTC TAGCTGTC TAGCTACT TGTCTAGC TGGTCAG CTGGATG CTGGATCT GGAGGAT GATGCTTG TTGTCTAGC TACTTGTC TAGCTGC TAGCTGC TAGCTAC TGGATG CTGGATG CTGGATG CTGGATG CTGGATG	TTGTCTAG	CTTTACTT	AGCTACTT	GTCTAGCT	TAAC1	GATC		TTACTTAGCTA		CTTGTCCTCT	ATTACTTA	GCTA	CTTGT
GETACTEG TEGETIGA TETAGGAG AGCAGETA ETTAGETA CTEGETA CTEGETA GATETTAC TEAGETAC TEGETAC TEGETAG ETAACEG ATECTEAC TEAGETAC TEGETAG CTAGETAC TAGETAC TEGETAG CTEACEG ATECTEAC TEAGETAC TEAGETAC TEGETAG CTECEAG CALENCE TAGETAC TAGETAA CEGATGT AACEGATG TECTEAGE TACTEGEE TAGETECT TAGETACE TAGETACE TAGETAG CTEGATG CTEGATG CEGAGGAT GATGETEG ATECTEAGE TACTEGEE TAGETECT TAGETACE TAGETACE TAGETACE CTEGATG CTEGATG CEGAGGAT GATGETEG	CTAGCTTA	ACTGATCT	CTACTTAG	CTACTTGT	CTAG	CTAG		CTACTTAGC		TACTTGTCTT	TAACTGAT	CTTA	CTTA
TTGTCTAG CTTAACTG ATCTCTAC TTAGCTAC TTGTCTAG CTAGCTAC TTAGCTAC TTAGCTAC TTGTCTAG CTTAACTG ATCTTAAC TGAACTTC TTAGCTAC TTAGCTAC TGTCTAG CTTCTAGC TACTTAGC TACTGATG CTGATCT GGGAGGAT GATGGTTG TTCTTAGC TACTTAGC TACTGTC TAGCTTCT TGCTAGC TGTCTGGC TAGCTAC TCATGATG CTTGATCT GGGAGGAT GATGGTTG	GCTACTTG	TCGCTTGA	T C T G G G A G	AGCAGCTA	CTTA	GCTA		CTTGTCTA		GCTTAACT	GATCTTAC	TTAG	CTAC
ATCITAAC TGATCITC ITAGCTAC ITAGCTAC ITGTCTAG CITCTAGC TACTTAGC TACTTGTC TAGCTTAA CTGATCIT AACTGATC Ticttagc tacttgtc tagctict tagctact tgtctagc tagctac catgatg citgatct ggaggat Angela catgatg citgatct tgtctagt catgatg citgatca tgtctagt	TTGTCTAG	CTTAACTG	ATCTCTAC	TTAGCTAC	TTGT	CTAG		CTAGCTAC		T T A G C T A C	TTGTCTAG	CTTA	ACTG
TICTIAGE TACTIGET TAGETECT TAGETACT TETETAGE TAGETAC CATGATE CETEGATET GERAGEAT GATGETTE	ATCTTAAC	TGATCTTC	TTAGCTAC	TTAGCTAC	TTGT	CTAG	CTTCTAGC	TACTTAGC	TACTTGTC	TAGCTTAA	CTGATCTT	AACT	GATC
	TTCTTAGC	TACTTAGC	TACTTGTC	TAGCTTCT	TAGC	TACT	TGTCTAGC	TAGCTAC	TC A T G A T G	CTTGATCT	G G G A G C A T	GATG	CTTG
AILIGGGA GAGLAGLI ALITAGLI ALITAGLIA GLITAALI GATLIAL ITAGLIAL ITAGLIAG LITAALIG AILLAIGA IGLITGAT IGLITGAT	A T C T G G G A	GAGCAGCT	ACTTAGCT	ACTTGTCTA	GCTT	AACT	GATCTTAC	TTAGCTAC	TTGTCTAG	CTTAACTG	ATCCATGA	TGCT	TGAT
CTGGGAGAG CAGCTACTT AGCTACTT GTCTAGCTTAA CTGATCTT ACTTAGCTA CTTGTCTA GCTTAACTG ATGCTACT TGTCTAGCATGATGCTTGATCTG GGAGAGCA	CTGGGAGAG	CAGCTACTT	AGCTACTT	GTCTAGCTTAA	C T G A	TCTT	ACTTAGCTA	CTTGTCTA	GCTTAACTG	A T G C T A C T	TGTCTAGCATGATGCTTGATCTG	G G A G	AGCA
GCTACTTAGCTACTTGTCTA GCTTAACTGATCTTAGCT ACTTGTCT AGCTTAACTGATCTGTCTAGCTAGCTAGCTAGCTAGCTACTTGTCTAGCTTAACTGA TAGCTACT	GCTACTTAGCTACTTGTCTA		GCTTAACTGATCTTACTTAGCT ACT		GTCT	AGCTTAACTGATCTCTACTTAG		CTACTTGTCTAGCTAGCTACTT		AGCTACTTGTCTAGCTTAACTGA	TAGCTACT		
TGTCTAGCTTAACTGAT CTCTACTTAGCTACTTGTCT AGCTAGCT ACTTAGCTATCTTGTCTTTA ACTGATCTTAGCTAC TTGTCGCTTGATCTGGGAGAGGC AGCTACTT	TGTCTAGCTTAACTGAT		CTCTACTTAGC	CTCTACTTAGCTACTTGTCT AG		AGCT	ACTTAGCT	ACTTGTCTTTA	ACTGATCTTA	CTTAGCTAC	TTGTCGCTTGATCTGGGAGAGC	AGCTACTT	
AGCTACTTAGCTA CTTAGCTA CTTGCTAGCTA CTTGCTAGCTA ACTGATCTCTACT TAGCTACTTGCTAGCTAGCTA CTTAGCTA	AGCTACTTGTCT		A G C T T A A C TA T C T T A C		CTTA	GCTA	CTA CTTGTCT		AGCTTA ACTGATCTCTACT		TAGCTACTTGTCTAGCTAGCTA	CTTAGCTA	

There are many ways to investigate the genetic cause of disease, yielding varying results. The current standard of care is far from optimal and can:

Involve multiple tests



Include average of or up to 8 physicians^{1,2}



Take 5-7 years^{1,2}

Result in 2-3 misdiagn<u>oses</u>1 During this time, patients and their families may experience a long, expensive, emotional diagnostic odyssey.

up to

80%

of rare disease are genetic or have a genetic subtype^{1,3-5}

What are you missing with current tests?

Traditional methods for genetic analysis are limited in the type of variants they detect and the amount of genome coverage they provide, reducing their potential utility.



Single-gene tests

Provide data for only one gene, which may or may not be informative for diagnosis



Multigene panels

Focus on a minimal selection of genes with known clinical relevance and do not allow for examination of new and emerging targets



Chromosomal microarrays (CMA)

Analyze < 0.01% of the genome, missing opportunities to find underlying genetic causes for disease⁶

Whole-exome sequencing (WES)

Sequences the protein coding regions of genes that account for around 2% of the genome leaving 98% unexplored

It is clear WGS is contributing significantly to end diagnostic odysseys in rare disease. With guidelines advocating use as a first-tier test,¹⁰ inclusion in national health care systems,¹¹ and increasing evidence of economic value when used as a first-tier test,¹² genome sequencing appears to be on the path toward standard of care.

Single-Nucle Insertions & Copy Numb Repeat Expa

Structural \

Mitochond

Paralogs

*Variant detection may vary depending on laboratory and test offering NGS = next-generation sequencing, PCR = polymerase chain reaction

Iterative testing places additional burdens on an already stressed health care system, requires multiple patient samples, adds complexity to test ordering, and increases the cost and time to answer.

Whole-genome sequencing (WGS) provides the most comprehensive analysis of geneomic variants among all clinical genomic testing methods⁷⁻⁹

	Sanger*	Targeted NGS*	PCR*	CMA*	WES*	WGS*
eotide Variants (SNVs)	~	~	~		~	~
Deletions (Indels)	~	~	~	~	~	~
er Variants (CNVs)		~	~	~	~	~
ansions			~			~
ariants (SVs)				~	~	~
al	~	~			~	~
	~		~			~

Limited capabilities
Capable

your diagnostic potential

"In situations where there is not the luxury of waiting, I see it as a moral imperative and an obligation for us to do everything possible in these cases to get to an answer as quickly as possible."

Luca Brunelli, MD, PhD Neonatologist University of Utah Health

WGS provides the broadest coverage of the human genome and includes regions NOT targeted by other methods.^{13,14} In a large randomized-controlled trial, WGS demonstrated the greatest success in finding a diagnosis in rare disease.¹⁵

Advantages of WGS:

Get to a diagnosis faster, with lower costs^{16,17}

Find actionable answers, even when a negative result is returned¹⁸

Enable more personalized care management than other genomic tests¹⁵

Obtain a comprehensive view across the genome, including coding and noncoding regions¹⁶

Detect a diverse range of variants in a single assay^{16,19-26}

In addition, WGS data can be stored and reanalyzed as new gene-disease associations are discovered.

Of all genomic testing methods, whole-genome sequencing has the potential to offer the highest likelihood of finding a diagnosis.27

TAGCTACTAGTAGTAGTAGCA CTAACTACTAGCA CTACTAGTAGCA CTTAC ACTGA AGCTA AGCTA AGCTA AGCTA TGTCT CATGATCTTAACT ACTAG ATCAT TAGCA TAGCA TAGCA TAGCA TAGCA TAGCA TAGCA TAGCA ATCAT TAGCA TAG GCTIAA TTAGCTA TAACTGA TTAGCTACTT CTGG TCTA CTGG TCTA AGCT TAAC TGGG AGAG GATC TTCTT CTAG CTAC CTACTGTCTAGCT AACTGATCTTCTTAGCT AACTGATCTTCTTAGCT CITIAA GCTAGCTT GCTAGCTA CTTAGCTA CTTAGCTA CTTAACTG CTTAGCTA CTTAGCTA CTTAGCTAC AGCT ACTT GCTACTGCTTGCT TAGC TGCT TAGC TGCT TAGC GAGC TAGC ACTG CTGG GAGA TAGCT ACTG ACTIG IGG IGGE IGGE IGGE AACTG ATCIT CTTAG GCATG ATCIT CTTAG TCTTA CTTAGC TACT TCTTA CTTAGC TACT TCTTA AGCTACC TACT TTCTTA AGCTACT IGTC CACT AGCTAC TGTC CACT TAG CTAC TTGT GATC TAG CTAC TTG TAGC TAG CTAC TTAG TTAGC CTA CTTAG TTAGC CTA CTTAGTCT CTGTC CTAGTCT CTGTC CTAGTCT CTGTC CTGTC CTGTC CTGTC CTGTC CTGCC CTGTC CTGCC CTGCCA CTCCTAGC CTGCCA CTCCTAGCCA GTCTAG CTTAG ACTCAT GATG GGCACGC TACT GCTACTTG TCTA ACTCTTAC TGAT TIAGCTAC TTG TIAGCTAC TTG TTAGCTAC TTG TTG TCTA GCTT AGCT ACTG TCTA TTCT AGCTACTA AGCT TAACTGAT TGAT CTTACTA GCTAC ACTAGCTA GCTAC TACTGA GCTAC TACTGA GCTAC TGACTA GCTAC TGACTA GCTAC TGACTA GCTAC TGACTA GCTAC TGACTA ACTGATC AGCTACT AGCTACT ACGCT CTACT ACTGA TAACT TAACT AGCTA CTTGT ACCTA CTTGT ACCTTA CTTGT ATCTT AGCT CTTGT ATGTC ATGCT ACCTAC TACTT ACIGAICII CITGAICTEGGA TAGCT ACTTG CTTCT ACTTG CTTCT ACTG CTTCT ACTG ACTGAICT ACTGAICT CTTACT ACTGAICT CTTAC CTTAC ACTGG CTCAC CTGAICTACA CTGAICTAGA TCTTAACTG. TTGTC T. GCTCA G. GCTAG GCTAG GCTACT AGATCAT AGATCAT TAACTG CTACTA AGCTACTA AGCTACTA AGCTACT AGCTAC CTACTA TACTTA TACTTA ATCT TAGCTACITGICTA ATGAT GCTTG GGGA GAGCA ACTTG TCTAG CTGA TCTTC TCTTA GCTTA CTGA TCTTAC GCTAC TGATCT TAAC GGATCTTAC GCTAC TGATCT TCTAG CTTAC GATCC TTACT GATCC TTACT CTTETCTAGCTTCT GATCC TAGCT TAGCT CTTA GATCT TCTTA GATCT CTTGTCTAGCTTA CTTGTCTAGCTTA GATCT GATCTGGGAGCAT TAGCT TGATCTGGGAGCAT TTGTCTAGCTTAAC TAGCT GCATG ACTIAGCIALIGIC TIAGC TACTE AGCTT AACTG AGCTA CTTAG GAGCA CCTAG GAGCA CCTGC CTGATCCTGCC CTGATCCTGGGAGA GATCT GGGAGA GGTC GGGAGA GGTC GGGAGA CCTAG CTAGC TAACTA TTAGC TAACT GGAGA GCTAA GGAGA GCTAA GCTAAT AGCTA ATCTC TACTT CTACT TGATGC

Advances in genomic testing are leading to answers faster than ever before.

- A single, comprehensive WGS test can provide more information and be completed more quickly than multiple, iterative tests²⁸
- ----- WGS can save years on the time to diagnosis compared to standard genetic testing^{29,30}

WGS can help provide answers more quickly in patients with immature phenotypes or those with heterogenous symptoms.³

WGS can provide answers faster than standard testing*

Acutely ill NICU infants:

Time to diagnosis using WGS vs standard genetic tests in the NICU

Rapid WGS²⁹ = 13 days Rapid WGS²⁹ = 13 days Standard testing = 107 days

Pediatric patients:

Average time to diagnosis using WGS vs standard genetic tests in pediatric patients



* Standard tests include: CMA, fluorescence *in situ* hybridization (FISH), karyotype, targeted gene panels, methylation studies, and gene detection or duplication assays.

Sawyer was on an 8-year diagnostic odyssey before his family found an answer with WGS.³²



Increased actionability

WGS has been shown to impact clinical management

Study	Impact of clinical management driven by genetic diseases diagnosed by WGS	% Change in management
Dimmock (2021) ¹²	Change in surgical procedures, medication, diet, and length of hospital course	61%
Lee (2021) ³³	Immediate changes in treatment strategies after undergoing WGS	23%
Krantz (2021) ¹⁵	Clinical management modification, including change of treatment and care	75%
Wang (2021) ³⁴	Therapeutic strategy change including transplant, diet, medication change, etc	48%
Sandford (2019) ³⁵	Genome-informed changes in pharmacotherapy and transition to palliative care	76%
French (2019) ¹⁷	Modification of treatments and care pathways and/or informing palliative care decisions	70%
Scocchia (2019) ³⁶	Clinical management modification including referrals to specialists, avoidance of invasive muscle biopsies, additional clinical investigations, genetic counseling, and palliative care	49%
Mestek-Boukhibar (2018) ³⁷	Enabled counseling on prognosis, avoidance of unnecessary investigations, and informed recurrence risk	30%
Petrikin (2018) ²⁹	Enable consideration of acute precision intervention in time for critically ill patients	95%
Farnaes (2018) ¹⁹	Avoidance of invasive test and/or transplant, reducing patient costs by \$800,000-\$2,000,000	72%
Bick (2017) ³	Supported treatment decisions and/or medical surveillance	75%
van Diemen (2018) ³⁸	Withdrawal of intensive care treatment	71%
Stravopoulos (2016) ³⁹	Increased diagnostic yield of WGS can have a significant impact on clinical care and management that goes beyond genetic counseling	79%

When WGS is implemented early in the diagnostic pathway, it has the potential to offer life-changing options to patients and their families. Identifying a disease-associated variant can lead to a diagnosis that can inform care management or future family planning.

Difference in change of management rates with WGS vs CMA²⁷

Rate from patients with change of management is higher with WGS than with CMA*

WGS

CMA

A diagnosis can be life-changing



Changes to care may include:



Pharmacotherapy



Referral to specialists



Avoidance of unnecessary procedures or treatments



Access to precision medicinebased approaches



Informed reproductive risk counseling for parents and other family members

A promising

for all

WGS and WES are already in use and showing positive results in several neonatal intensive care units (NICU)^{15,40} and is recommended by the ACMG as a first or second-tier test. With its improved diagnostic performance and faster time to answer, WGS holds the promise of helping patients and their families end a diagnostic odyssey—or prevent one altogether—and focus on care management.

→ Click here to learn how patients have benefited from WGS

Request WGS for your patients from your preferred laboratory



Now recommended by the ACMG

In 2021, the American College of Medical Genetics and Genomics (ACMG) released guidance recommending the use of WES or WGS as first- or second-tier tests in patients with one or more congenital anomalies prior to one year of age or intellectual disabilities/ developmental delay prior to eighteen years of age.¹⁸

References

1. Shire. Rare Disease Impact Report: Insights from patients and the medical community. Global Genes website. globalgenes.org/wp-content/uploads/ 2013/04/ShireReport-1.pdf. Published 2013. Accessed March 17, 2022.

2. Global Commission on Rare Disease. Global commission to end the diagnostic odyssey for children with a rare disease. globalrarediseasecommission. com/. Accessed March 17, 2022.

3. Bick D, Jones M, Taylor SL, Taft RJ, Belmont J. Case for genome sequencing in infants and children with rare, undiagnosed or genetic diseases. J Med Genet. 2019;56(12):783-791. doi:10.1136/jmedgenet-2019-106111

4. Nguengang Wakap S, Lambert DM, Olry A, et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. Eur J Hum Genet. 2020;28:165–173. doi.org/10.1038/s41431-019-0508-0

5. Ferreira CR. The burden of rare diseases. Am J Med Genet A. 2019;179(6):885-892. doi:10.1002/ajmg.a.61124

6. Illumina. Data on file. March 2022.

7. Lionel AC, Costain G, Monfared N, et al. Improved diagnostic yield compared with targeted gene sequencing panels suggests a role for whole-genome sequencing as a first-tier genetic test. Genet Med. 2018;20(4):435-443. doi:10.1038/gim.2017.119

8. Dolzenko E, van Vugt JJFA, Shaw RJ, et al. Detection of long repeat expansions from PCR-free whole-genome sequence data. Genome Res. 2017;27(11):1895-1903. doi:10.1101/gr.225672.117

9. Chen X, Schulz-Trieglaff O, Shaw R, et al. Manta: rapid detection of structural variants and indels for germline and cancer sequencing applications. Bioinformatics. 2016;32(8):1220-1222. doi:10.1093/bioinformatics/btv710

10. Malinowski J, Miller DT, Demmer L, et al. Systematic evidence-based review: outcomes from exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability. Genet Med. 2020;22(6):986-1004. doi:10.1038/s41436-020-0771-z

11. 100,000 Genomes Project Pilot Investigators, Smedley D, Smith KR, et al. 100,000 Genomes Pilot on Rare-Disease Diagnosis in Health Care - Preliminary Report. N Engl J Med. 2021;385(20):1868-1880. doi:10.1056/NEJMoa2035790

12. Dimmock D, Caylor S, Waldman B, et al. Project Baby Bear: Rapid precision care incorporating rWGS in 5 California children's hospitals demonstrates improved clinical outcomes and reduced costs of care. Am J Hum Genet, 2021 May 29S0002-9297(21)00192-0. doi: 10.1016/j.ajhg.2021.05.008

13. Meienberg J, Bruggmann R, Oexle K, Matyas G. Clinical seguencing: is WGS the better WES?. Hum Genet. 2016;135(3):359-362. doi:10.1007/s00439-015-1631-9

14. Belkadi A, Bolze A, Itan Y, et al. Whole-genome sequencing is more powerful than whole-exome sequencing for detecting exome variants. Proc Natl Acad Sci U S A. 2015;112(17):5473-5478. doi:10.1073/pnas.1418631112

15. NICUSeg Study Group, Krantz ID, Medne L, et al. Effect of Whole-Genome Sequencing on the Clinical Management of Acutely III Infants With Suspected Genetic Disease: A Randomized Clinical Trial. AMA Pediatr. 2021;e213496. doi:10.1001/jamapediatrics.2021.3496

16. Lionel AC, Costain G, Monfared N, et al. Improved diagnostic yield compared with targeted gene sequencing panels suggests a role for whole-genome sequencing as a first-tier genetic test. Genet Med. 2018;20(4):435-443. doi:10.1038/gim.2017.119

17. French CE, Delon I, Dolling H, et al. Whole genome sequencing reveals that genetic conditions are frequent in intensively ill children. Intensive Care Med. 2019;45(5):627-636. doi:10.1007/s00134-019-05552-x

18. Manickam K, McClain MR, Demmer LA, et al. Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021;10.1038/s41436-021-01242-6. doi:10.1038/s41436-021-01242-6

19. Farnaes L, Hildreth A, Sweeney NM, et al. Rapid whole-genome sequencing decreases infant morbidity and cost of hospitalization. NPJ Genom Med. 2018:3:10. doi:10.1038/s41525-018-0049-4

20. Lindstrand A, Eisfeldt J, Pettersson M, et al. From cytogenetics to cytogenomics: whole-genome sequencing as a first-line test comprehensively captures the diverse spectrum of disease-causing genetic variation underlying intellectual disability. Genome Med. 2019;11(1):68. doi:10.1186/s13073-019-0675-1

21. Sanghvi RV, Buhay CJ, Powell BC, et al. Characterizing reduced coverage regions through comparison of exome and genome sequencing data across 10 centers. Genet Med. 2018;20(8):855-866. doi:10.1038/gim.2017.192

22. Dolzhenko E, van Vugt JJFA, Shaw RJ, et al. Detection of long repeat expansions from PCR-free whole-genome sequence data. Genome Res. 2017;27(11):1895-1903. doi:10.1101/gr.225672.117

23. Gross AM, Aiay SS, Rajan V, et al. Copy-number variants in clinical genome sequencing: deployment and interpretation for rare and undiagnosed disease. Genet Med. 2019;21(5):1121-1130. doi:10.1038/s41436-018-0295-y

24. Chen X, Sanchis-Juan A, French CE, et al. Spinal muscular atrophy diagnosis and carrier screening from genome sequencing data. Genet Med. 2020:22(5):945-953. doi:10.1038/s41436-020-0754-0

25. Alfares A, Aloraini T, Subaie LA, et al. Whole-genome sequencing offers additional but limited clinical utility compared with reanalysis of whole-exome sequencing. Genet Med. 2018;20(11):1328-1333. doi:10.1038/gim.2018.41

26. Chen X, Schulz-Trieglaff O, Shaw R, et al. Manta: rapid detection of structural variants and indels for germline and cancer sequencing applications. Bioinformatics. 2016;32(8):1220-1222. doi:10.1093/bioinformatics/btv710

28. Sun F, Oristaglio J, Levy SE, et al. *Genetic Testing for Developmental* Disabilities, Intellectual Disability, and Autism Spectrum Disorder [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Jun. (Technical Briefs, No. 23.) Available from: ncbi.nlm.nih.gov/books/NBK304462/

0045-8

30. Soden SE, Saunders CJ, Willig LK, et al. Effectiveness of exome and genome sequencing guided by acuity of illness for diagnosis of neurodevelopmental disorders. Sci Transl Med. 2014;6(265):265ra168. doi:10.1126/scitranslmed.3010076

31. Orphanet. Prevalence of rare diseases: Bibliographic data, Orphanet Report Series, Rare Diseases collection, January 2022, Number 1: Diseases listed in alphabetical order. orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_ diseases_by_alphabetical_list.pdf. Accessed March 17, 2022.

32. Sawyer's Journey. facebook.com/sawyersjourneyTRIP12/. Created March 13, 2014. Accessed December 15, 2021.

33. Lee HF, Chi CS, Tsai CR. Diagnostic yield and treatment impact of whole-genome sequencing in paediatric neurological disorders. Dev Med Child Neurol. 2021 Aug;63(8):934-938. doi: 10.1111/dmcn.14722

27. Clark MM, Stark Z, Farnaes L, et al. Meta-analysis of the diagnostic and clinical utility of genome and exome sequencing and chromosomal microarray in children with suspected genetic diseases. NPJ Genomic Med. 2018;3:16. doi. org/10.1038/s41525-018-0053-8

29. Petrikin JE, Cakici JA, Clark MM, et al. The NSIGHT1- randomized controlled trial: rapid whole-genome sequencing for accelerated etiologic diagnosis in critically ill infants. NPJ Genom Med. 2018;3:6. doi:10.1038/s41525-01834. Wang H, Lu Y, Dong X, et al. Optimized trio genome sequencing (OTGS) as a first-tier genetic test in critically ill infants: practice in China. Hum Genet. 2020:139(4):473-482. doi:10.1007/s00439-019-02103-8

35. Sanford EF, Clark MM, Farnaes L, et al. Rapid Whole Genome Seguencing Has Clinical Utility in Children in the PICU. Pediatr Crit Care Med. 2019;20(11):1007-1020. doi:10.1097/PCC.000000000002056

36. Scocchia A, Wigby KM, Masser-Frye D, et al. Clinical whole genome seguencing as a first-tier test at a resource-limited dysmorphology clinic in Mexico. NPJ Genom Med. 2019;4:5. doi:10.1038/s41525-018-0076-1

37. Mestek-Boukhibar L, Clement E, Jones WD, et al. Rapid Paediatric Sequencing (RaPS): comprehensive real-life workflow for rapid diagnosis of critically ill children. J Med Genet. 2018;55(11):721-728. doi:10.1136/jmedgenet-2018-105396

38. van Diemen CC, Kerstjens-Frederikse WS, Bergman KA, et al. Rapid Targeted Genomics in Critically III Newborns. Pediatrics. 2017;140(4):e20162854. doi:10.1542/peds.2016-2854

39. Stavropoulos DJ, Merico D, Jobling R, et al. Whole Genome Sequencing Expands Diagnostic Utility and Improves Clinical Management in Pediatric Medicine. NPJ Genom Med. 2016;1:15012-. doi:10.1038/npjgenmed.2015.12

40. Global Disease Commission. Ending the diagnostic odyssey for children with a rare disease. globalrarediseasecommission.com/Report. Published 2019. Accessed March 17, 2022.

illumina[®] No rare disease will go unseen.

Learn more at www.illumina.com

© 2022 Illumina, Inc. All rights reserved M-GL-00728