TwinStrand DuplexSeq™ AML MRD Solution

TWINSTRAND BIOSCIENCES

Next Generation Sequencing is a powerful emerging method for detecting residual acute myeloid leukemia (AML) after treatment. However, current methods produce an abundance of sequencing errors which obscure low-frequency leukemia-defining mutations.

The TwinStrand Duplex Sequencing™ AML MRD assay is orders of magnitude more sensitive and specific than other NGS based MRD assays, offering unprecedented opportunities for clinical research and drug development.

Duplex Sequencing AML MRD

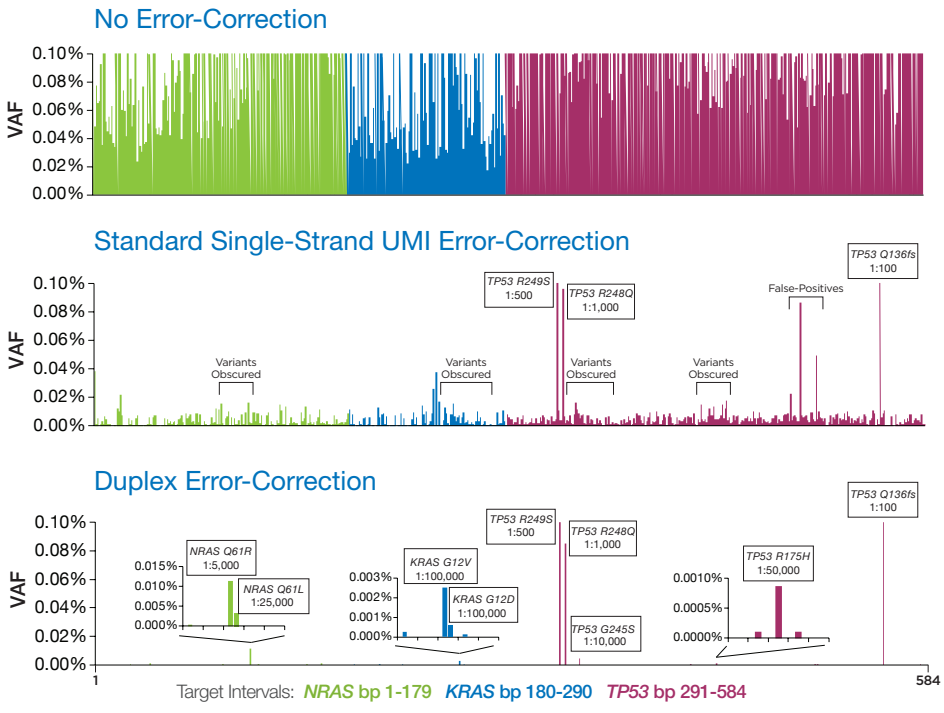
- >100-fold higher resolution than other error-corrected NGS methods
- The 29 gene, 58kb panel encompasses loci mutated in 90%-95% of adult AML patients
- Assay enables sub-1/10,000 limit of detection anywhere in target region

Duplex Sequencing MRD Technical Performance

Cell line DNA mixture models patient with MRD

Gene	Mutation	Predicted VAF
TP53	Q136fs	$1x10^{-2}$
TP53	R249S	$2x10^{-3}$
TP53	R248Q	$1x10^{-3}$
NRAS	Q61R	$2x10^{-4}$
TP53	G245S	$1x10^{-4}$
NRAS	Q61L	$4x10^{-5}$
TP53	R175H	$2x10^{-5}$
KRAS	G12D	$1x10^{-5}$
KRAS	G12V	$1x10^{-5}$

Sequence to >1M Duplex molecular depth



The TwinStrand Duplex Sequencing AML MRD assay was used to sequence a serially-diluted mixture of AML mutation-containing DNA to a Duplex depth >1,000,000x. Target clones were identified to levels <1/100,000 with 100% sensitivity and specificity.

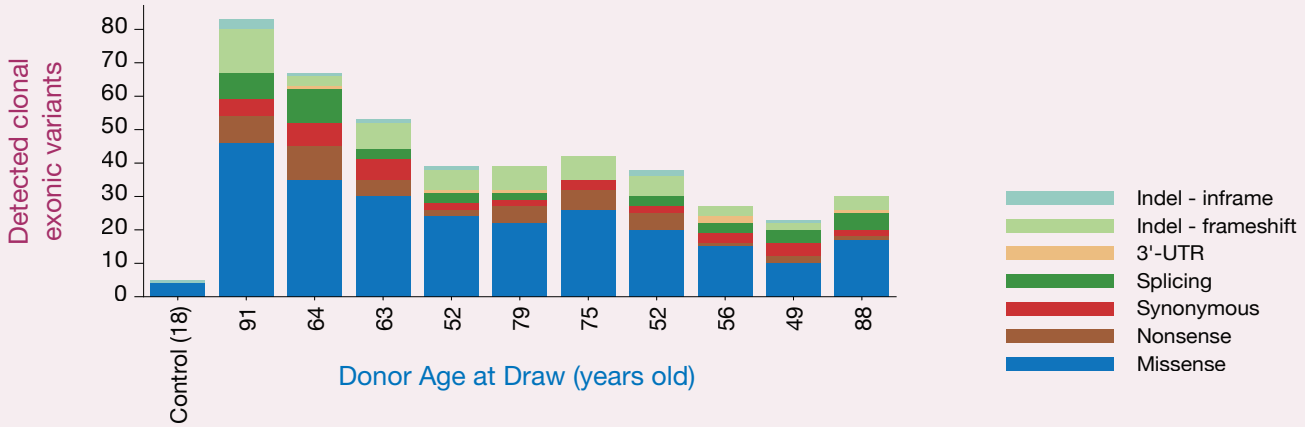
AML MRD Panel Overview

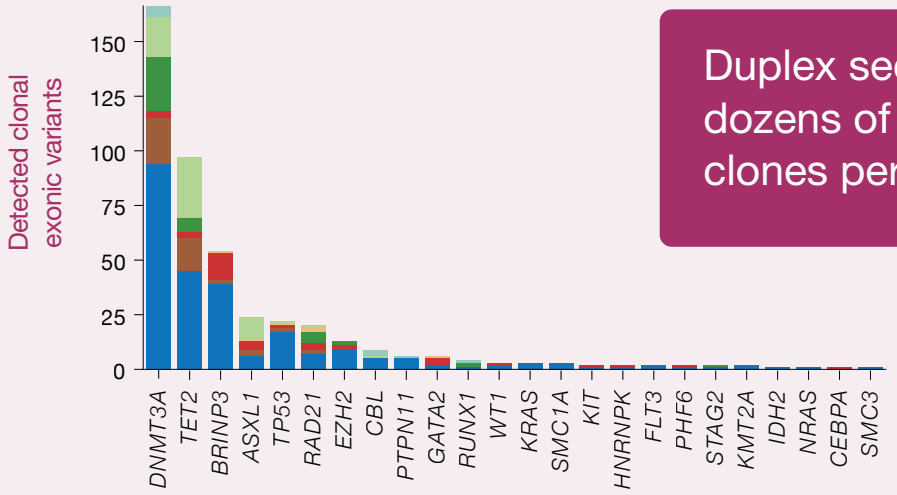
Panel Overview

The AML panel encompasses the whole coding region or hotspots in 29 genes recurrently mutated in Acute Myeloid Leukemia (AML), Myelodysplastic Syndrome (MDS), and Clonal Hematopoiesis (CHIP).

Genes in Panel					
ASXL1	*FAM5C (BRINP3)*	*IDH2*	*NPM1*	*RAD21*	*TET2*
CBL	*FLT3*	*KIT*	*NRAS*	*RUNX1*	*TP53*
CEBPA	*GATA2*	*KRAS*	*PHF6*	*SMC1A*	*U2AF1*
DNMT3A	*HNRNPK*	*MLL (KMT2A)*	*PTEN*	*SMC3*	*WT1*
EZH2	*IDH1*	*MYH11-CBFB*	*PTPN11*	*STAG2*	

Clonal Hematopoiesis





Duplex sequencing detects dozens of synchronous CHIP clones per individual with aging.