MyAML™ Technical Information

LabPMM
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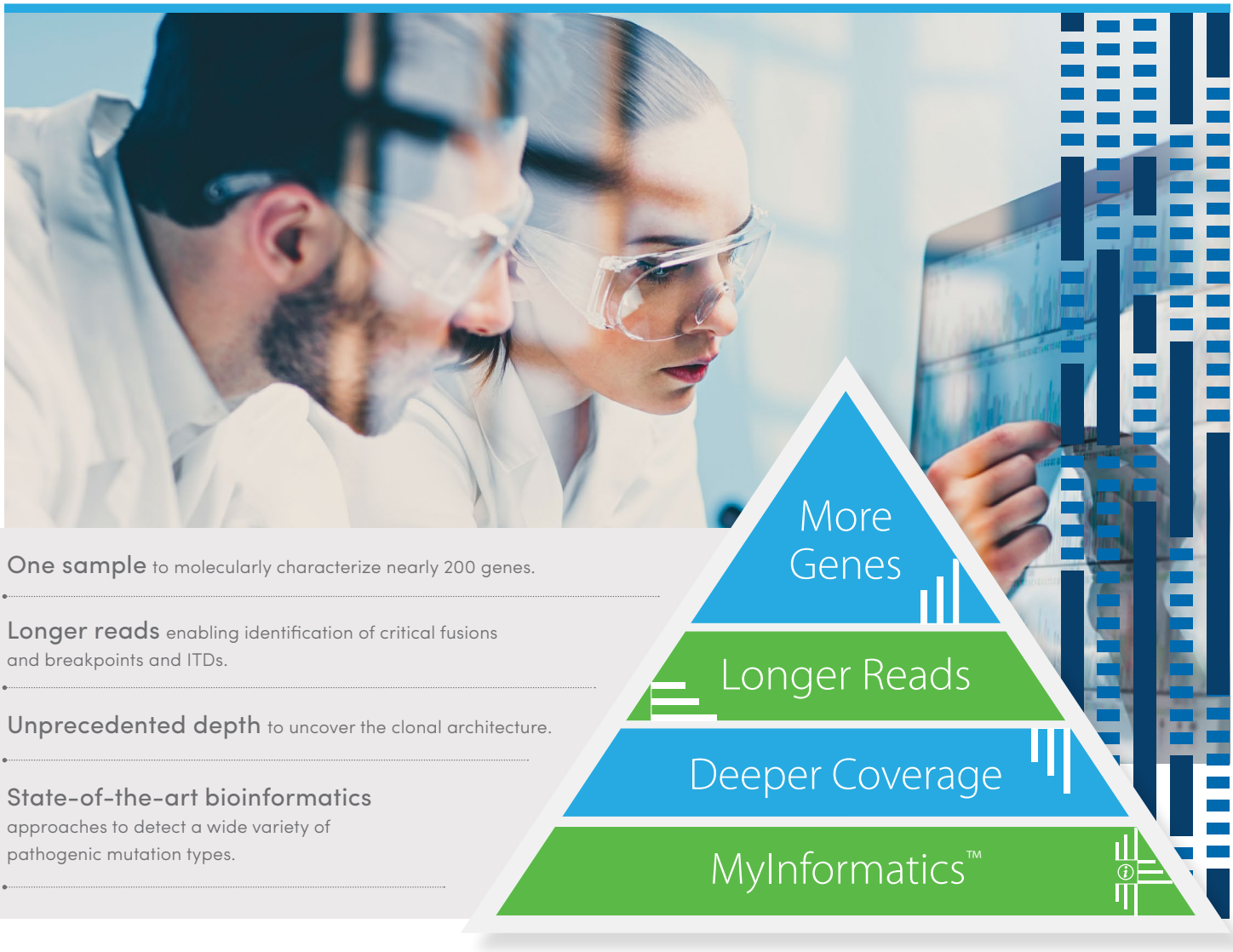


One sample to molecularly characterize nearly 200 genes.

Longer reads enabling identification of critical fusions and breakpoints and ITDs.

Unprecedented depth to uncover the clonal architecture.

State-of-the-art bioinformatics approaches to detect a wide variety of pathogenic mutation types.

Assay Uses

This assay has been optimized for the investigation and characterization of the genomic landscape of AML. MyAML is a targeted panel that covers the coding and non-coding exons of nearly 200 genes along with breakpoint hotspots within 36 of these genes identified in somatic gene fusions. MyAML combines long read chemistry and deep sequencing with an optimized and validated custom bioinformatics pipeline, MyInformatics™, to specifically examine genomic variants in AML patients.

Method

MyAML is a next generation targeted sequencing product.
Using customized design, the coding regions and potential genomic breakpoints within known somatic gene fusions are sequenced with 300bp paired end reads on an Illumina platform to an average depth of coverage >1,000x. Using MyInformatics, we identify single nucleotide variants (SNVs), indels, inversions and translocations and copy number variants (CNVs). In addition, allelic frequencies can be calculated to investigate potential aneuploidy and clonality.

Specimen Requirement

Peripheral blood in EDTA or HEP
Bone Marrow in EDTA or HEP
3-5 µg of high quality genomic DNA

Background

MyAML represents a significant improvement over current next generation sequencing (NGS) cancer panels and AML targeted assays for the interrogation of genes associated with the prognosis and stratification of AML patients. By focusing on a single cancer, MyAML has been optimized for the investigation and characterization of the genomic landscape of AML.

NCCN and ELN guidelines recommend that newly diagnosed AML patients have genomic testing for a subset of genes. It is widely recognized that each patient holds a unique profile of somatic mutations leading up to AML. Additionally, clonal architecture within each patient is widely varied.

MyAML can not only identify mutations in those genes recommended by NCCN, but several other candidate genes that may show prognostic significance. By deep sequencing all genes known or predicted to be involved in AML pathogenesis, physicians can improve their understanding of the of the clonal architecture of their patient and follow these clones throughout treatment.

MyAML™ Gene List

Structural rearrangements under NCCN/ELN guidelines

Inv(16) t(16;16) t(8;21) t(15;17) +8 t(9;11) -5 5q- -7 7q- 11q23 inv(3) t(3;3) t(6;9) t(9;22)

These regions also include genes from the "fusions and gene rearrangements" below.

Fusions and gene rearrangements (36 genes)

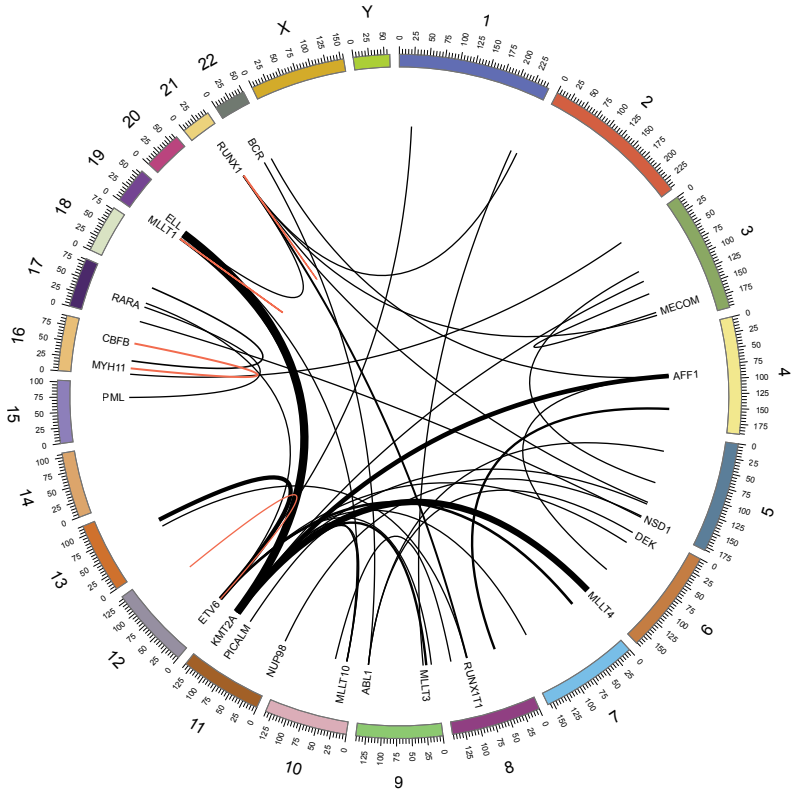
Including 5'UTRs, exons, recombination intron breakpoint hotspots, non-coding exons, and 3'UTRs.

ABL1 ADGRG7 AFF1 BCR CBFB CREBBP DEK EIF4E2 ELL ETV6 GAS6 GAS7 KAT6A KAT6B KMT2A MECOM MKL1 MLLT10 MLLT1 MLLT3 MLLT4 MYH11 NSD1 NUP214 NUP98 PICALM PML RARA RBM15 RPN1 RUNX1 RUNX1T1 SEPT5 SET TFG TMEM255B

Genes (158 genes)

Including 5'UTRs, exons, non-coding exons, and 3'UTRs.

ABCC1 ACVR2B ADRBK1 AKAP13 ANKRD24 ARID2 ARID4B ASXL1 ASXL2 ASXL3 BCOR BCORL1 BRINP3 BRPF1 BUB1 CACNA1E CBL CBX5 CBX7 CDC73 CEBPA CEP164 CPNE3 CSF1R CSTF2T CTCF CYLD DCLK1 DDX1 DDX23 DHX32 DIS3 DNAH9 DNMT1 DNMT3A DNMT3B DYRK4 EED EGFR EP300 EPHA2 EPHA3 ETV3 EZH2 FANCC FLT3 GATA1 GATA2 GFI1 GLI1 HDAC2 HDAC3 HNRNPK HRAS IDH1 IDH2 IKZF1 JAK1 JAK2 JAK3 JMJD1C KDM2B KDM3B KDM6A KDM6B KIT KMT2B KMT2C KRAS MAPK1 METTL3 MST1R MTA2 MTOR MXRA5 MYB MYC MYLK2 MYO3A NF1 NOTCH1 NOTCH2 NPM1 NRAS NRK OBSCN PAPD5 PAX5 PDGFRA PDGFRB PDS5B PDSS2 PHF6 PKD1L2 PLRG1 POLR2A PRDM16 PRDM9 PRKCG PRPF3 PRPF40B PRPF8 PTEN PTPN11 PTPN14 PTPRT RAD21 RBBP4 RBMX RPS6KA6 SAP130 SCML2 SETBP1 SETD2 SF1 SF3A1 SF3B1 SMC1A SMC3 SMC5 SMG1 SNRNP200 SOS1 SPEN SRRM2 SRSF2 SRSF6 STAG2 STK32A STK33 STK36 SUDS3 SUMO2 SUPT5H SUZ12 TCF4 TET1 TET2 THRB TP53 TRA2B TRIO TTBK1 TYK2 TYW1 U2AF1 U2AF1L4 U2AF2 UBA3 WAC WAPAL WEE1 WNK3 WNK4 WT1 ZBTB33 ZBTB7B ZRSR2



Above: Circos plot depicting a subset of translocations and inversions identified using MyAML translocations (black) and inversions (red) are depicted by curved lines (with width proportionate to the number of times the variant was observed) connecting two chromosomal regions together.

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