HLA Typing on the MiSeq® System

Next-generation sequencing (NGS) has proven to be instrumental in advancing human disease research. NGS lends itself particularly well to HLA typing, enabling sequencing of multiple HLA genes from many samples in a single run. The data generated is higher in resolution compared to other current methods, yielding accurate results across the entire HLA genomic region and genotypes. The ability to interrogate more of the HLA genomic region can provide data critical to discovering HLA disease associations. The comprehensiveness of this technique reduces the need for additional testing to resolve ambiguities, decreasing overall turnaround time. Furthermore, NGS has the power to provide information about lesser known HLA regions, which may lead to discoveries that improve transplant outcomes.

The Illumina MiSeq NGS system is the most accurate, easiest-to-use benchtop sequencer available, making it a trusted solution for HLA typing. Take a look at the publications, presentations, and posters referenced below to see how your colleagues are using the MiSeq system for HLA typing.

Publications


Cao et al. use Illumina technology for reliable, cost-effective, and high-throughput sequence-based typing of HLA loci. “Genotyping throughput was increased over ten times, and cost was reduced over five times…as compared with Sanger sequence genotyping.”


Hosomichi et al. publish results of high-resolution HLA typing using the Illumina MiSeq system and demonstrate “phased-defined sequences of entire HLA genes, resulting in high resolution HLA typing and new allele detection.”


De Santis et al. compare the performance of different NGS technologies for high-resolution HLA typing, noting “that the MiSeq sequencer had the lowest total observable error rate.”


Wang et al. demonstrate that the Illumina MiSeq and HiSeq® NGS platforms have the capacity to “deliver low-cost, high-throughput, and accurate HLA typing.”

Press Release

HistoGenetics Selects Illumina’s MiSeq System as Next-Generation Sequencing Platform of Choice (July 2013)

Illumina announced that HistoGenetics, the leader in high-resolution sequence-based human leukocyte antigen (HLA) testing services, has selected the MiSeq sequencing system for use in its CLIA laboratory. HistoGenetics chose Illumina in part based on “the MiSeq’s quality data output and simple workflow.”
27th EFI European Immunogenetics and Histocompatibility Conference

High Throughput High Fidelity HLA Typing with Deep Sequencing

Researchers at the Stanford Genome Technology Center, Howard Hughes Medical Institute, and Stanford School of Medicine present a novel method for high-resolution, high-throughput, cost-effective HLA typing using NGS technology. They chose to use an Illumina NGS platform “based on the low error rate of the sequencing traces and the ability to generate enormous amount of sequencing reads in a cost-effective manner.”

High-Resolution HLA Typing of 1000 Genomes NGS Samples Using Paired-End Illumina Reads
Major E, Berces A, Gourraud P-A, Juhos S

Researchers at Omixon Biocomputing and UCSF School of Medicine developed an algorithm to directly genotype NGS reads from whole-genome and whole-exome sequencing data to determine HLA type. The methods showed high-accuracy HLA typing from whole-genome sequences generated using Illumina paired-end sequencing.

neXtype: Yet Another Route to the NGS Universe
Hofmann JA, Sauter J, Lange V, Bohme I, Baier DM

DKMS German Bone Marrow Donor Center and collaborators presented the neXtype software designed for HLA typing from Illumina MiSeq data.

HLA Sequence-Based Typing with Next Generation Technology

Collaborators at the Fred Hutchinson Cancer Research Center and Scisco Genetics designed an efficient and economical NGS method for HLA typing using the MiSeq system. The approach was tested on 2,500 marrow transplant donors previously typed using conventional methods.

A 3-Step Workflow for High-Throughput HLA Typing by Next Generation Sequencing

DKMS German Bone Marrow Donor Center and collaborators presented a workflow optimized for high-throughput, low-cost HLA typing using the MiSeq system. Although the primary focus was on throughput and cost-efficiency, researchers showed that they achieved “a typing resolution that exceeds the current standard of Sanger typing” using this method.

Comparing HLA Types of Targeted Amplicon Samples by Analyzing Sanger and Next Generation Sequencing Data
Tordai A, Inotai D, Major E, Berces A, Juhos S

The Hungarian National Institute of Blood Transfusion and Omixon Biocomputing presented a comparison of high-resolution HLA typing using the Illumina MiSeq system and the Ion Torrent PGM. They conclude, “we reached 100% concordance with Sanger SBT for HLA-A, B, and C, and DRB1. Results from Ion Torrent technology tend to show ambiguities due to the homopolymer errors present in their reads.”

American Society of Human Genetics

Quantitative Analysis of Mixtures By Deep Sequencing of HLA Gene Amplicons Using Next Generation Systems
Hoglund BN, Rastrou M, Goodridge M, Erlich HA, Holcomb CL

Hoglund et al. demonstrate a method for high-resolution, high-throughput genotyping of the HLA class I and class II loci from HLA allelic mixtures in plasma.
American Society for Histocompatibility and Immunogenetics

The Future Has Arrived—Routine High Throughput HLA Typing by NGS

DKMS German Bone Marrow Donor Center and collaborators describe a workflow for HLA typing using NGS on the Illumina MiSeq system that “has proven simpler, faster, better, and more cost-effective than Sanger sequencing.”

Accurate Typing of Human Leukocyte Antigen (HLA) by Next-Generation Exome Sequencing

Collaborators at Washington University School of Medicine and the Broad Institute present results of HLA typing derived from Illumina exome sequencing and describe the method as “a cost-effective alternative [to Sanger sequencing] that may avoid ambiguities and allow high-throughput HLA typing.”

neXtype: A Safe Car on the NGS Roller Coaster

DKMS German Bone Marrow Donor Center and collaborators describe the neXtype software designed for high-accuracy HLA typing from Illumina MiSeq data. The software enables a “high degree of automation [that] reduces analysis time to less than 2 hours per 2,000 loci.”

The Next Generation for Genetic Studies and Diagnostics of HLA

Collaborators at Stanford University School of Medicine and Illumina present data showing “significant progress towards understanding the evolution of HLA haplotypes, their co-evolution with infectious diseases, and their contribution to autoimmune disease and disordered pregnancy.”

Thousand Genomes and HLA Typing By NGS: Hidden Treasures in Public Short Read Data

Researchers from Omixon Biocomputing and UCSF School of Medicine demonstrate high-accuracy HLA typing from Illumina whole-genome sequences.

Next Generation HLA Sequencing on the Illumina Miseq

Researchers from the Children's Hospital of Philadelphia and the University of Pennsylvania demonstrate a streamlined NGS assay for allele-level HLA typing on the MiSeq system. The optimized assay is “a simple, robust, and scalable... [and] delivers allele level HLA typing without ambiguity.”

Deriving HLA Typing Form Whole MHC Next-Generation Sequencing Data

The Children's Hospital of Philadelphia, the University of Pennsylvania, and Omixon Biocomputing show the results of Illumina sequencing of the entire 4 Mb MHC. The method “yielded highly accurate genotypes for 33 HLA and non-HLA MHC genes.”

Complete Nucleotide Sequences for More Than One Hundred KIR Haplotypes

Researchers at Stanford University School of Medicine and Illumina present data from Illumina sequencing of 104 HLA cell lines with limited prior knowledge of KIR genotypes.

Quantitative Analysis of Mixtures by Deep Sequencing of HLA Gene Amplicons Using Next-Generation Systems

Roche Molecular, Conexio, and The Scripps Research Institute demonstrate the use of the Illumina MiSeq system for high-resolution and high-throughput genotyping of the HLA class I and class II loci derived from allelic mixtures in plasma.
A Next Generation HLA Sequencing Method Provides Robust Reliable Class II Typing of an HSCT Cohort
Smith AG, Pereira SE, Geraghty DE, Hansen JA

Collaborators at the Fred Hutchinson Cancer Research Center and Scisco Genetics demonstrate the reliability and sensitivity of Illumina MiSeq data from 2,500 marrow transplant donors previously typed using conventional methods.

NGSengine: The Ultimate Tool for NGS HLA Typing
Kooter R, Ruzius FP, Penning MT, Mulder W, Rozemuller EH

The authors present NGSengine, a software package designed for HLA typing using NGS data.

High-Resolution Typing by Next-Generation Sequencing in a Clinical HLA Laboratory

Collaborators at Massachusetts General Hospital and Omixon Biocomputing present a feasibility study measuring the performance of NGS compared to the current standard molecular HLA typing methods. Results showed concordance between HLA typing on the Illumina MiSeq system with the standard methodologies.

Primer Design for Short Amplicon-Based NGS
Lang K, Bohme I, Lange V, Schone B, Andreas JM, et al.

Researchers from DKMS Life Science Lab, DKMS German Bone Marrow Donor Center, and University Hospital Carl Gustav Carus developed a primer set for high-resolution HLA typing on the MiSeq system. The automated workflow “allows very cost-effective, high-throughput (currently about 1,500 donors per day) HLA donor registry typing.”

References