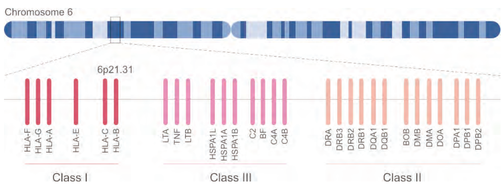
CD Genomics
The Genomics Services Company

Historically, HLA typing was governed by the phenotypic approach, and it has now evolved into molecular methods, such as real-time PCR, sequence-specific oligonucleotides, and sequencing-based techniques. The major shift in HLA typing by adapting NGS and long-read sequencing may be the transition to high-resolution HLA typing. The future role of HLA typing is believed to be driven by HLA expression, encryption of HLA haplotypes, and high-resolution HLA typing.

HLA Typing

What is HLA?

Human leukocyte antigens (HLA) are one of the most polymorphic genes encoded by genes within the major histocompatibility complex (MHC). HLA consists of two non-covalently linked polypeptide chains: a glycosylated alpha-heavy chain and a beta-light chain. The human MHC system contains the most polymorphic gene cluster of the entire human genome and comprises at least 224 genes at chromosome 6p21.3 coding for the HLA complexes. In addition, the HLA system contains three regions designated as HLA class I, class II, and class III based on the structure and function of gene products.



Polymorphisms of HLA genes

(i) Multiple motifs: related to the different HLA gene compositions and expression products, resulting in various functionally distinct motifs.
(ii) Multiple alleles: HLA gene clusters exhibit differences and polymorphism in the population with different alleles.
(iii) Co-dominant expression: all alleles express separately to yield the co-dominant phenomenon, which enhances HLA polymorphism in the population.
(iv) Gene transcription and regulation: cis-acting elements can differ depending on the allele, thus regulating gene transcription.

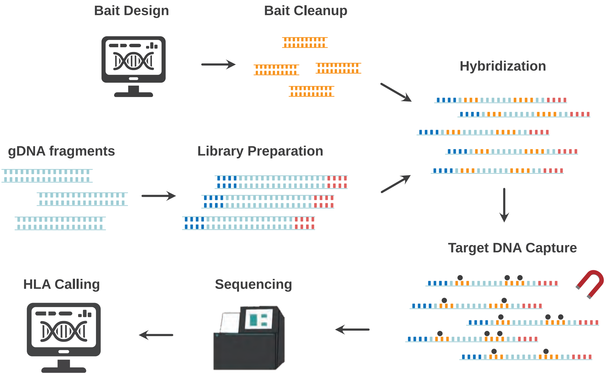
How Sequencing Fuels High-Resolutions HLA Typing

HLA Sequencing by NGS

High-quality NGS-based methods also rely on the targeted enrichment of the relevant HLA loci, either by PCR- or bait-based capturing. First, the enrichment of the target DNA, which is then followed by the sequencing of randomly fragmented DNA and finally the data analysis. The enrichment of the target can be performed by bait-based capturing, long-range PCR, or even shorter PCR amplicons that span the region of interest.

Pros and Cons

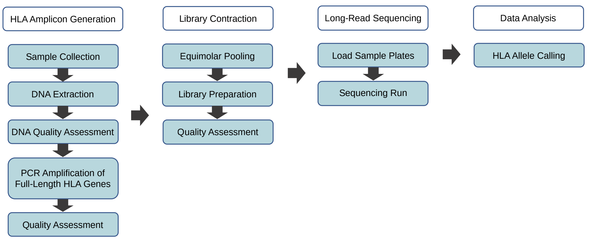
Both approaches, PCR- or bait-based, have their advantages and disadvantages. The PCR is very specific with regards to the targeted enrichment, i.e., little off-target sequence is produced through NGS and a high coverage of the target is warranted. However, PCR is liable to allelic dropouts, for example, caused by SNPs at primer locations, poorly performing primer sets, or other amplification biases. The bait-based method overcomes limitations of allelic dropouts because a few mismatches between bait and target DNA will still allow hybridization with the target.



Workflow of hybridization-based HLA Sequencing

Full-length HLA Sequencing by Long-read Seq

Meanwhile, NGS alone may not be sufficient to understand the complete haplotypes of HLA genes. To overcome these limitations, we provide an end-to-end workflow for sequencing HLA class I and II genes using long-read sequencing, SMRT technology, and Nanopore sequencing. This approach supports high-resolution HLA typing and allele-specific HLA expression.



CD Genomics High Accuray HLA Typing Solution

HLA sequencing can provide important insights into autoimmune diseases. CD Genomics offers the high-accuracy HLA typing service utilizing NGS and long-read sequencing, helping researchers study the potential mechanisms of autoimmune diseases, immune reservoirs, tumor immunogenicity, and the functional consequences of immune-related genetic variants, advancing progress in drug and vaccine development.

Our genotyping workflow covers HLA-loci, as well as the complete KIR gene family and MICA/B. NK cell reactivity against target cells is partially based on the presence of KIRs and their cognate ligands, the HLA class I molecules. MHC class I chain-related genes, MICA and MICB, have been demonstrated to ligate the natural killer (NK) cell receptor, NKG2D. Using the structures of over 40 KIR gene content haplotypes, our KIR haplotyping assay can report unambiguous combinations of KIR haplotypes. In addition, high-resolution typing of the MICA and MICB genes and the Fc-gamma receptor gene family testing are available. Our full suite of tissue-typing services can meet your various research needs.

Contact CD Genomics for more inspiration and service content.

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