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Multiplexed HLA mRNA Preparation for Downstream Sequencing

Human Leukocyte Antigens (HLA) are protein complexes residing on cell surfaces responsible for regulating immune responses. HLA haplotype sequencing is integral to the development of personalized therapies and diagnostics. It is also paramount to the understanding of T cell mediated immunity. There are over six classical major HLA loci with over 32,000 alleles. Current typing modalities include probe-based hybridization, nested PCR and RNA-seq. Unfortunately, these protocols require outsourcing, which costs about \$400 per sample (for low resolution mapping) and has a turn around time of 2-4 weeks. This is prohibitively expensive for large numbers of samples.

Researchers at the Biodesign Institute of Arizona State University have developed a novel method for amplifying and barcoding HLA mRNA for downstream long read nanopore sequencing. The sequencing results can then be used for genotyping the Human Leukocyte Antigen of individuals. Six of the HLA genes' mRNA can be simultaneously amplified in a single reverse transcription polymerase chain reaction with barcodes also being attached to identify which individual the sequence came from. An average per loci depth of coverage of 1000x can be observed.

This novel method streamlines the preparation and sequencing of cDNA libraries of major HLA loci, reducing both cost and turnover time, and making HLA haplotype sequencing more realizable and available.

Potential Applications

- HLA haplotype sequencing
 - Personalized therapies
 - Diagnostics
 - Understanding T cell mediated immunity
 - Other immunologic studies

Benefits and Advantages

- Low-cost, rapid turnaround time and portability
 - Can receive results in the same day, anywhere (existing methods cost over \$400 and take upwards of 4 weeks).
- Cost-effective compared to existing methods
- Easy workflow for upstream processing and multiplexing nucleic acid for downstream sequencing
- Applicable for any long-read sequencing (B cell receptors, viral sequencing, etc.)
- Can theoretically multiplex 1000 people with a cost of only \$2 in reagents/person
- This is a targeted approach for HLA with designed and tested primers
- The third thing is a set of bioinformatics tools for analyzing the data in real time

For more information about this opportunity, please see

[Kask et al – J Immunol - 2023](#)

For more information about the inventor(s) and their research, please see

[Dr. Anderson's departmental webpage](#)