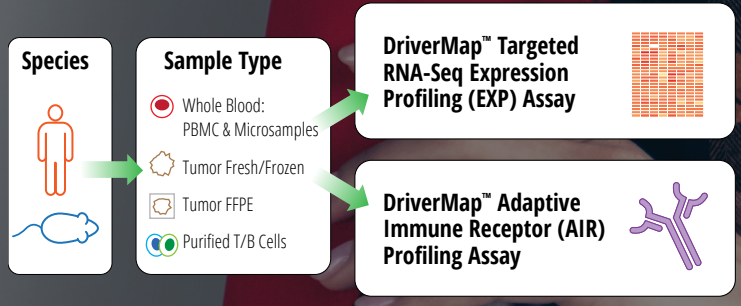
CELLECTA

DriverMap™ Technology Solution

Combine the sensitivity and specificity of RT-PCR with the multiplex analysis power of next-generation sequencing (NGS) technology for expression and immune receptor profiling applications.



DriverMap™ Targeted RNA-Seq Expression Profiling (EXP) Assay

High-performance, targeted single-tube expression profiling of 19,000 human protein-coding genes.

Start with total RNA from any source. No mRNA enrichment, rRNA or globin RNA depletion is required. Run genome-wide, multiplex RT-PCR with target-specific primers for 19,000 protein-coding genes in a single tube. (Fig 1) Expression levels for each gene of interest correlate directly to the number of reads for each amplified protein-coding transcript. Data analysis can be done on a spreadsheet.

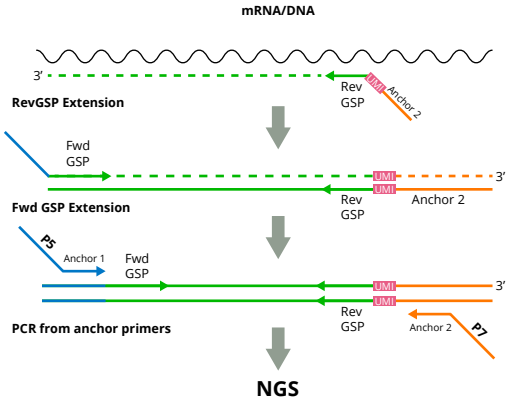


Figure 1 Outline of DriverMap Multiplex RT-PCR Technology.

The DriverMap workflow leverages the power of RT-PCR (upstream) to extend with reverse gene-specific primers (Rev-GSP), and forward gene-specific primers (Fwd-GSP) with unique molecular identifiers (UMI). A second amplification with anchor primers containing P5 and P7 Illumina indexes is used to prepare the next-generation sequencing (NGS) library.

DriverMap EXP vs. RNA-Seq

Compared to RNA-Seq, the DriverMap EXP Solution offers:

- Simple, one-tube protocol that enables processing of 96+ samples a day.
- Ability to directly use total RNA or cell lysate for small and single-cell samples.
- Improved detection of medium- and low-abundance transcripts with 5-fold less NGS sequencing depth. (Figs 2, 4)
- Broad dynamic range that enables quantitative measurement of 2-3 times more transcripts than RNA-Seq. (Fig 3)
- Straightforward data analysis that can be conveniently done on any laptop using standard spreadsheet software.

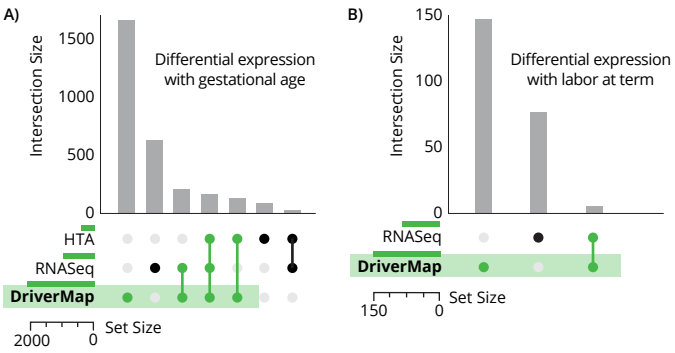


Figure 4 Comparison of three expression profiling methods for biomarker discovery.

- *3x more protein-coding aligned reads with DriverMap than RNA-Seq*
- *More sample-to-sample consistency than with RNA-Seq*
- *DriverMap expression results correlated better with qRT-PCR results*

Tarca, et al., Scientific Reports 9:848 (2019)

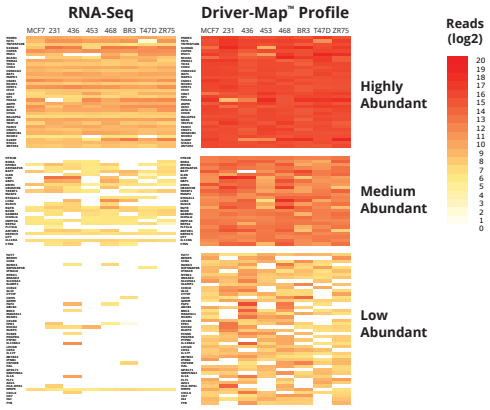


Figure 2 Comparison of the sensitivity of targeted RNA-Seq (~25 million reads/sample) vs. DriverMap EXP assay (~5 million reads/sample).

NGS read levels for selected high-abundant (10K-100K copies per sample), medium-abundant (1K to 10K copies per sample), and low-abundant transcripts (100-1K copies per sample) in 50ng of total RNA from seven common cancer cell lines.

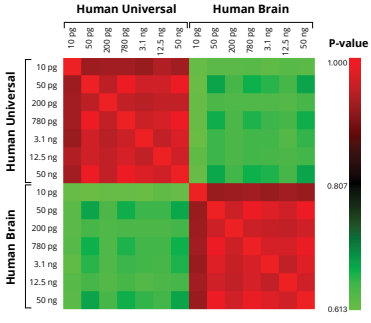


Figure 3 Sensitive and Reproducible.

The correlation (R-squared values) of detected genes between human universal RNA and total brain RNA using the DriverMap EXP assay remains highly consistent regardless of sample, across amounts ranging from 10 pg to 50 ng of starting total RNA.

DriverMap™ Adaptive Immune Receptor Repertoire Profiling (AIR)

Comprehensive adaptive immune receptor repertoire profiling for all TCR/BCR genes

Cellecta offers DriverMap™ Adaptive Immune Receptor (AIR) repertoire profiling assays for clonotype detection. Assays use targeted multiplex PCR amplification and NGS analysis to profile regions of all hyper-variable T-cell receptor (TCR) and B-cell receptor (BCR) sequences starting from RNA and/or DNA.

- **The DriverMap AIR-RNA assay** provides the most specific and quantitative detection of medium to high-abundant TCR (CDR3 or full-length) and BCR receptor regions. The highly sensitive AIR-RNA assay provides comprehensive profiling even from a limited number of cells.
- **The DriverMap AIR DNA assay** quantitatively measures the number of cells with each CDR3-specific clonotype. This, in combination with AIR-RNA data, enables the **measurement of clonal activation in T- and B-cells.**

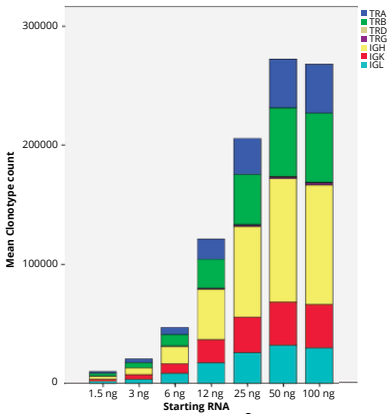


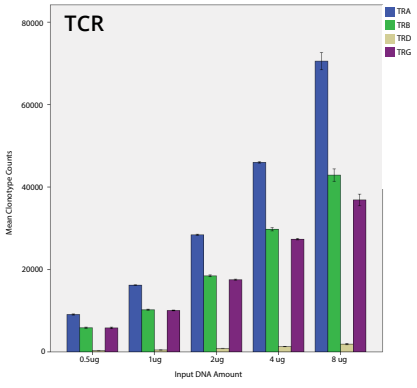
Figure 5 Clonotype distribution vs. amount of starting RNA.

Reproducible clonotype distribution of TCR and BCR chains across different input amounts starting from total RNA ranging from 1.5 ng to 100 ng of of all seven chains in a single reaction. (5 million reads/sample). Maximal sensitivity is obtained with at least 50 ng of total RNA.

DriverMap AIR performance

Validated primers with universal molecular indexes (UMI) and Calibration Standards enable quantitative profiles of all seven TCR and BCR chains from DNA or RNA from PBMC, whole blood, or tumor samples without enrichment of immune cells.

- **Profiles > 50-100K of TCR or BCR sequences** from a single sample in a single assay (Figs. 5, 6)
- **Sequence full-length or CDR3** variable region from RNA.
- **Profile both RNA and DNA** from the same sample to identify antigen-activated clonotypes



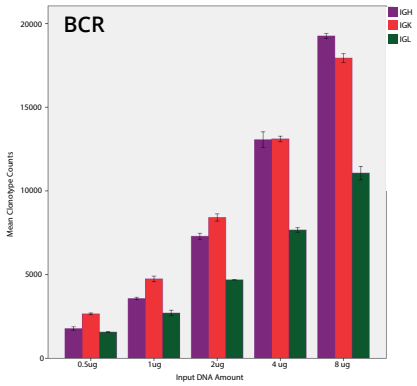


Figure 6 Clonotype distribution vs. amount of starting DNA.

Reproducible clonotype distribution of TCR and BCR chains across different input amounts ranging from 0.5 µg to 8 µg of starting DNA in separate reactions. (5 million reads/sample). The recommended optimal starting amount is 8-10 µg of DNA.

Some Applications for DriverMap™ AIR & EXP Assays

Biomarker discovery in whole blood or PBMC

- Identify specific antigen-reactive T- and B-cell clones and expression biomarkers associated with disease, patient stratification and drug treatment.
- Both AIR and EXP assays could be run in bulk RNA or directly in blood microsamples.

Ultra-sensitive detection and profiling of rare cells and activated clonotypes

- Reliable, reproducible measurements with ultra-small samples such as FFPE allow profiling from archived specimens or sorted immune cells and cell fractions.
- Detect neo-antigen activated clonotypes by comparing AIR-RNA and AIR-DNA data.

High content signaling pathway profiling in drug development

- Identify pathway activation occurring in response to drug treatment.
- Track T-cell clonality and B-cell antibody patterns for insights into mechanisms of action of immune checkpoint inhibitors for immunotherapy

Epitope discovery

- Analyze TCR sequence and structure to predict antigenic specificity.
- Validate predicted neo-antigens by measuring binding efficiency to TCR/BCR-specific clonotypes by single-cell analysis.

Antibody and Vaccine Development

- Identify neo-antigen-induced antibodies and map Ig-seq datasets to known antibody structures for antibody and vaccine development.

DriverMap Products and Services

Pre-made, ready-to-use DriverMap kits

The DriverMap EXP and AIR Assays are available as ready-to-use kits which result in sequence-ready libraries to be run on widely available Illumina NGS instrumentation. DriverMap Kits are available in two configurations for both human and mouse:

- **24-samples**
- **96-samples**

Custom DriverMap EXP and AIR profiling kits

Choose your target genes of interest and we deliver a custom primer mix and all reagents needed to profile both AIR repertoire and targeted immunophenotyping of immune cells.

Custom DriverMap expression profiling service

Cellecta offers a comprehensive end-to-end service workflow, including RNA/DNA purification, QC, library prep, NGS, and data analysis service. Bioinformatics packages include the identification of differentially expressed genes and a clonotype alignment summary table.

For more information on DriverMap kits, assay customization, or services and ordering, please **visit our website and see the DriverMap page (cellecta.com/drivermap) or email your Cellecta customer service representative at orders@cellecta.com.**

CELLECTA

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