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CAPTURE-BASED SEQUENCING FOR COMPREHENSIVE, COST-EFFECTIVE MULTIPLE MYELOMA PROGNOSTICS AND MONITORING

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Technology Description

Researchers at Washington University developed a prognostic assay for multiple myeloma that detects the full range of common multiple myeloma mutations using a single capture-based sequencing platform. This technology utilizes probes designed to analyze 465 genes associated with multiple myeloma for cost-effective, fast, comprehensive coverage that could be used to personalize treatment.

Multiple myeloma (MM) is a fatal disorder marked by a variety of genetic changes: copy number alterations (CNAs), single nucleotide variants (SNVs) and translocations. Traditional assays, such as exome sequencing, either require time and computationally-intensive analysis or cannot detect all these types of mutations simultaneously. This new cost-effective, single-platform capture-based sequencing approach solves those problems with genomic analysis that detects the full range genetic variations including both primary (activating) and secondary (disease progression) mutations. This system incorporates computational methods to discover new mutations and elucidate known genetic variations at sequencing depth as low as 100x. This personalized information could then be integrated into a prognostic model to increase precision over the current International Staging System (ISS). This tool offers the potential for large-scale evaluation of patients with multiple myeloma, helping researchers and clinicians identify those at high risk to stratify them for basic research, clinical trials or individualized treatment plans.

Stage of Research

The inventors validated this platform by sequencing 95 primary tumor-normal pairs to a mean depth of 104x and demonstrated high concordance in detecting mutations previously identified by exome sequencing and FISH analysis. These studies also identified a new gene (IGLL5) that may be a target or biomarker for high risk multiple myeloma. (Publication)

Applications

- **Personalized medicine for multiple myeloma**:
  - prognostic tool with potential to improve predictive power by combining comprehensive mutation analysis with traditional International Staging System (ISS) data
  - patient stratification for clinical trials
  - treatment and disease progression monitoring
- **Research**: basic studies and target discovery for multiple myeloma

Key Advantages

- **Single platform for multiple types of mutations**:

  - simple yet comprehensive set of 465 genes includes coverage across the entire V, D and J regions
  - simultaneously analyzes CNAs, SNVs and translocations
  - detects known mutations and discovers new mutations
  - identifies both primary mutations that initiate malignant events and secondary mutations that drive disease progression
  - probes could also be used for RNA sequencing for gene expression analysis
- **Faster, deeper and more cost-effective sequencing** than exome sequencing:
  - targeted subset of disease-associated genes decreases turn-around-time by reducing total amount of sequencing and computational analysis
  - suitable for scaling up to use on a large number of patient samples

Patents: Automated exposition of known and novel multiple myeloma genomic variants using a single sequencing platform (U.S. Patent Application, Publication No. 20180126354)

Publications: White BS, Lanc I, O'Neal J, et al. A multiple myeloma-specific capture sequencing platform discovers novel translocations and frequent, risk-associated point mutations in IGLL5. *Blood Cancer J.* 2018;8(3):35. Published 2018 Mar 21.