DHM | RI

Immuno-oncology Services Guide

Progressing frontiers in immune therapy: Applying a successful multiomics approach to development, production, and QC

DHMRI is a specialized CRO, offering extensive outsourced multiomic capabilities in immuno-oncology research. Our well-equipped Genomics, Metabolomics and NMR laboratories can support the development/research of different immuno-oncology products by:

- **Identifying specific tumor "neoantigens"**
- **Measuring the mutational load of the tumor**
- **Phenotypically characterizing the metabolomic status of a cell therapy product, tumor and/or the patient**
- **Performing metagenomic analyses on patient cohort populations**
- **Developing biomarkers for specific tumors**
- **Microbiome studies to aid in understanding variations in treatment response**

Immunotherapies, which aim to exploit the host immune system to produce a systemic response against tumors, are currently among the most clinically-promising cancer treatments. By recognizing "neoantigens", or by detecting certain tumor signals such as abnormal metabolism, DNA damage or unfolded proteins, they pivot the role of the host immune system to one of cancer treatment. One of the most promising immunotherapeutic approaches is immune checkpoint blockade (ICB) therapy, which has shown efficacy in the treatment of many solid tumors [1, 2].

However, cancer cells can develop different mechanisms to escape and inhibit host immune responses, including the reduction of antigen presentation, secretion of immunosuppressive mediators, limitation of glucose, and upregulation of tryptophan degradation enzymes and immune checkpoint molecules [1].

It is now apparent that a combination of different therapeutic strategies - such as ICB together with the promotion of tryptophan production, or the combination of ICB and a vaccine against the tumor antigens - might lead to the most effective therapy.

In addition, recent studies have shown how individual responses to the same cancer treatment can vary as they are influenced by tumor, host, and environmental factors. Interestingly, differences in gut microbiome composition have also been associated with variations in response to treatment, opening a new area of research [1, 2].

Given this highly complex biology, researchers need to undertake a multiomic approach to the development, production, and QC of immune therapy products. See over for our specilalist multiomic capabilities in immuno-oncology research.

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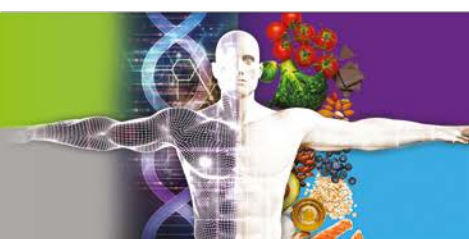

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Genomics Services

DNA sequencing

- Germline mutations (e.g. BRCA2)
- Exome sequencing in PBMCs (30X; blood)
- Whole Genome Sequencing (30X; blood)
- Somatic mutations (e.g. de novo driver mutations, rare pathogenic mutations in the context of germline DNA)
- Targeted panel (primary tumor or metastatic mutational burden)
- Exome (primary tumor or metastatic mutational burden; neoantigen discovery)
- Pre- vs post-treatment studies
- Mutational frequency

Transcriptomics

- NanoString target panels in PBMCs or tumor (custom or predesigned - both mRNA or miRNA)
- RNA-seq discovery (neoantigen detection; biomarker discovery; tumor microenvironment)

Epigenetics (altered methylation patterns and other epigenetic changes)

- miR-Seq
- DNA methylation
  - Epic Array Illumina (850K)
  - Agilent SureSelect targeted approach (epigenome 80 Mb)
  - Whole Genome Bisulfite Sequencing

Histone modifications

- ChIP-Seq (H3K27/H3K4/H3K9 etc.)

10 X Chromium

- Single Cell RNA expression in tumor
  - Cells or nuclei (legacy samples)
  - Pre- and post-treatment / progression
- Phased genomic CNV profiling
- Single Cell Multione ATAC + Gene Expression, simultaneously profile gene expression with chromatin landscaping

Microbiome analysis

- Microbiome diversity studies using 16S ribosome profiling
- Microbiome functional characterization (Metagenomics)

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Metabolomics Services

Therapeutic response/prognosis

- Uncover changes in metabolic pathways due to treatment or between cancer/cell types
- Targeted treatment based on metabolic state of cancer

Metabolic assessment of the tumor microenvironment

- Measurement of metabolites involved in glycolysis, the TCA cycle, and glutaminolysis (Warburg effect)
- Glutamine and aspartate measurement for anaplerotic state determination

Metabolic assessment of the patient

- Cancer cachexia assessment
- Microbiome metabolites panel
- Metabolomics Discovery Panel

Custom targeted analyses for specific metabolic pathways

Certain cancer types will be known, or hypothesized, to have alterations in specific metabolic pathways. Additionally, certain therapies will be known, or hypothesized, to alter specific metabolic pathways. Targeted analyses can be created to examine these pathways

Oxidative stress and inflammation response (9-hode, 13-hode, glutathione, cysteine, glutamate and glycine)

References

1. Henry T. Marshall and Mustafa B.A. Djamgoz (2018). Immuno-Oncology: Emerging Targets and Combination Therapies. Front. in Oncology 8: Article 315.
2. Le Bourgeois, T., et al. (2018). Targeting T Cell Metabolism for Improvement of Cancer Immunotherapy. Front. in Oncology 8: Article 237.

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