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Application Note

Visualize the Future of Precision Medicine with Bio-Techne's Multiomics Platform: CRC Case Study

Key Takeaways:

- Bio-Techne is developing a liquid biopsy platform that analyzes gene expression, splice variants, gene fusions, mutations, DNA methylation, and proteins. This platform integrates bioinformatics and machine learning for discovery of multi-analyte biomarker signatures, allowing a multifaceted view of a patient's disease.
- ExosomeDx, a Bio-Techne brand's, proprietary exosome technologies are designed to enable the detection of early disease indicators with improved sensitivity, aiming to provide early diagnosis. We have developed the first exosome-based liquid biopsy clinical test on the market (LDT), the ExoDx Prostate Test.
- A pilot study in colorectal cancer (CRC) screening using the Bio-Techne platform shows the value of integrating multiomic readouts for enhanced CRC classification. The underlying platform can be applied to biomarker signature development and is designed for extension to downstream assay development for clinical trial applications.
- Bio-Techne is a one-stop-shop for biomarker discovery, fit-for-purpose assay development and validation, with commercialization of CDx products, enabling pharma partners to accelerate their pharmaceutical clinical trials.

Bio-Techne's Multiomics Platform: A Comprehensive Picture of Disease

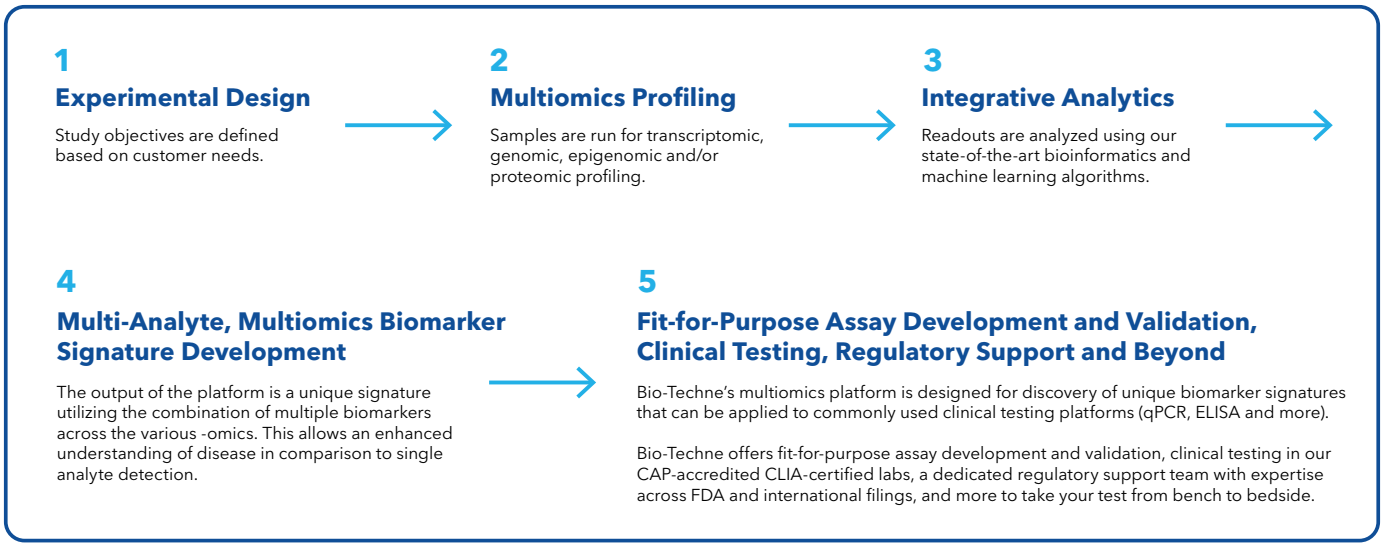
Bio-Techne's multiomics platform provides a comprehensive view of disease by combining genomic data with data from other modalities, including transcriptomics, epigenomics, and proteomics. This approach enables a multifaceted understanding of the molecular changes contributing to disease, allowing researchers to connect genotypes to phenotypes and discover novel drug targets and biomarkers.

Complex diseases, such as cancer, auto-immune disorders, and neurodegenerative diseases, create characteristic signatures in DNA, RNA, proteins, and metabolites. Multiomics technologies aim to systematically identify these signatures at different biological levels. Advances in multiomics technologies and the convenience of obtaining multiomics data are accelerating predictive, preventive, and personalized medicine practices, allowing for improved patient stratification and personalization of medicine.[1]

Table 1. Bio-Techne's Liquid Biopsy Multiomics Platform Combines the Following Elements:

Supported Sample Types	Integrated Multiomics	Bioinformatics and Machine Learning
• Plasma • Urine • Saliva • CSF	**Comprehensive analysis combining:** • Genomics • Transcriptomics • Epigenomics • Proteomics The platform harnesses the unique power of exosomal RNA and protein analysis combined with genomics and epigenomics of cell-free DNA for improved sensitivity and earlier diagnosis of disease.	Our integrative analytics aim to provide a multifaceted view of human health and disease.

Figure 1. Bio-Techne's Multiomics Platform Workflow



Case Study: Multiomics Analysis Using Bio-Techne's Platform for Enhanced CRC Classification

Pilot Study Overview

Colorectal cancer is the third most common and second deadliest cancer globally, with an estimated 153,020 new cases and 52,550 deaths in the US alone in 2023.[2] The majority of CRC screenings worldwide use fecal immunochemical tests; however, colonoscopy is also common in some regions, including the US.[3] Research is ongoing on alternative blood-based tests, however, there remains a need for improved sensitivity, especially for early-stage disease. In a pilot study, the Bio-Techne multiomics platform analyzed plasma from 48 participants, including both CRC-positive and healthy individuals, classifying with high accuracy (AUC ~0.99) using complementary omics data channels.

Methods

We analyzed samples from 24 CRC patients and 24 healthy controls using our proprietary multiomics platform to profile cfDNA, exosomal nucleic acids, and proteins. We conducted ultra-deep sequencing on long exosomal RNA, proteomic analysis of exosomal proteins, and methylome profiling of cell-free DNA. Biomarker discovery using machine learning algorithms was performed separately for each analyte, followed by integrative analysis.

Results

Each of the information channels in the multiomics platform contains tantalizing clues about the signatures that distinguish CRC samples from healthy samples. The combination of these modalities allows us to attain a truly robust distinction.

Using splice variant analysis as a representative example in the section below, we showcase the application of our feature selection process for exosomal RNA splice variants to generate a unique diagnostic signature distinguishing CRC from healthy samples. This process, and the analogous processes we have developed for the various -omics modalities described herein, can be applied to a wide range of biomarker discovery applications to support pharmaceutical drug development.

Exosomal RNA Splice Variants

We applied a splice variant detection pipeline to our RNA-seq data for the purpose of identifying differential splicing between healthy and CRC-positive samples. The top 10 most informative splice variants separate healthy samples from CRC-positive samples well, with an AUC of ~0.964 using LOOCV.

Principal component analysis shows that they can largely be distinguished along PC1 (Figure 2 (a)). Random forest analysis with the R package Boruta identified splice variants with a strong ability to distinguish between healthy and CRC (Figure 2 (b) and (c)).

For this CRC pilot study, an analogous approach was applied to DNA methylation, gene expression, splice variants, gene fusions, and proteins.

Integrated Analysis: Individual Analyte Classifiers Hold Complementary Information

Multiomics analysis was shown to provide higher performance for distinguishing CRC from healthy than any individual omics channel. As Figure 3 shows, at least one of the omics information channels correctly classifies all of the samples, but none of them is perfect.

Figure 2: Splice Variant Analysis to Distinguish Healthy Samples from CRC-Positive

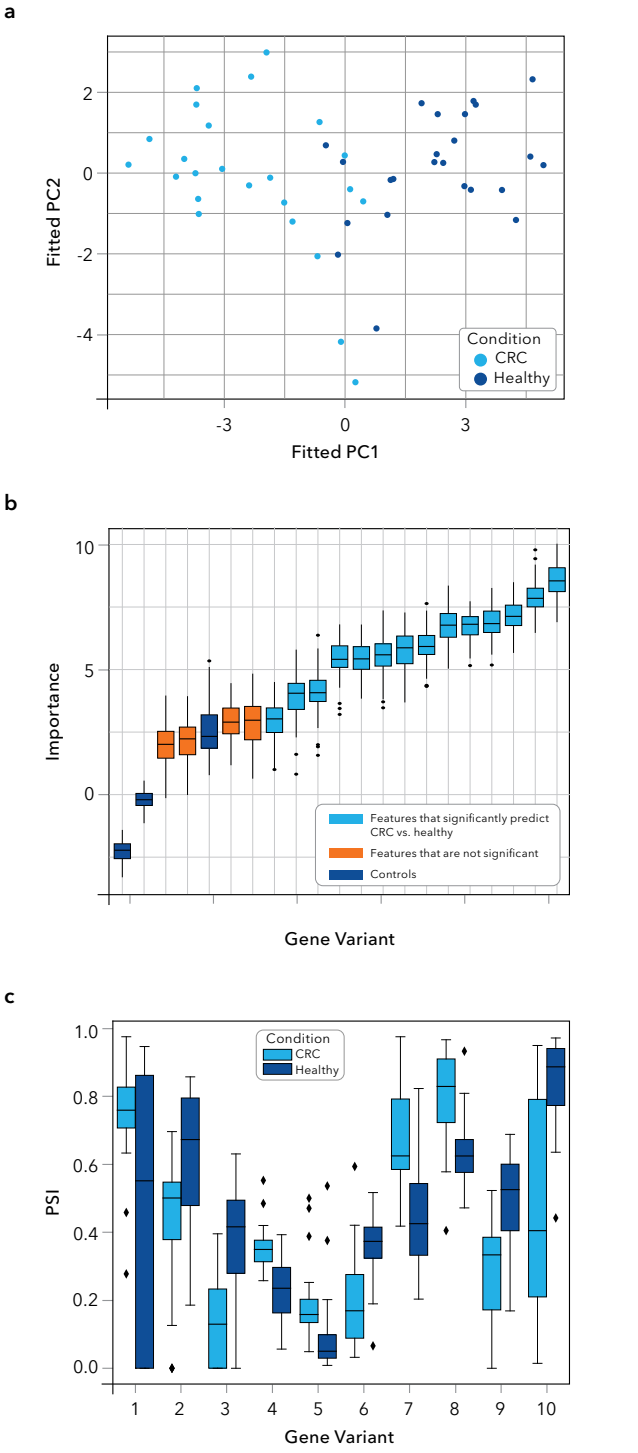
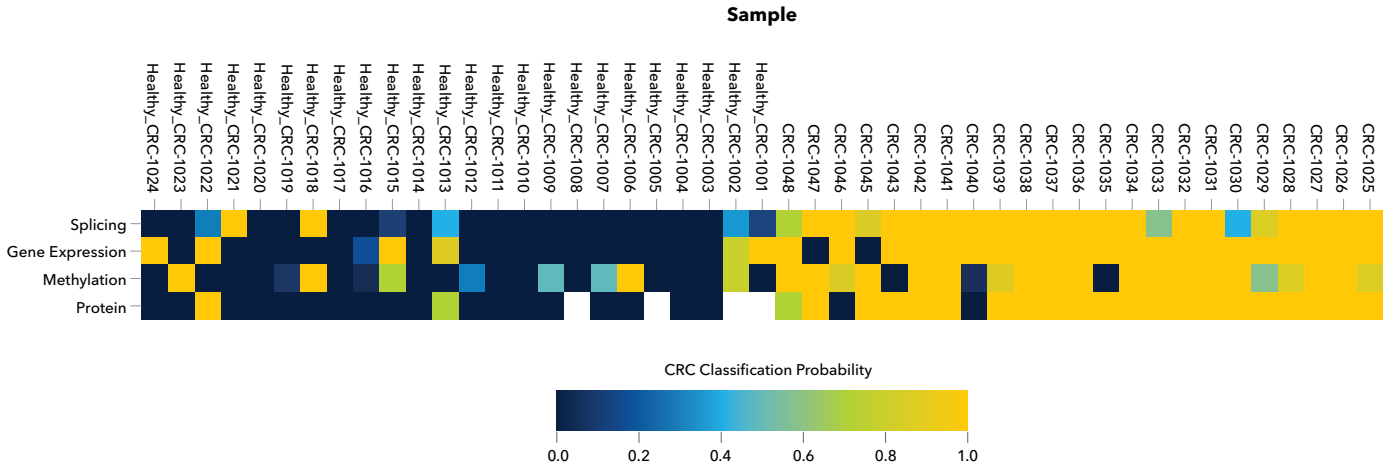


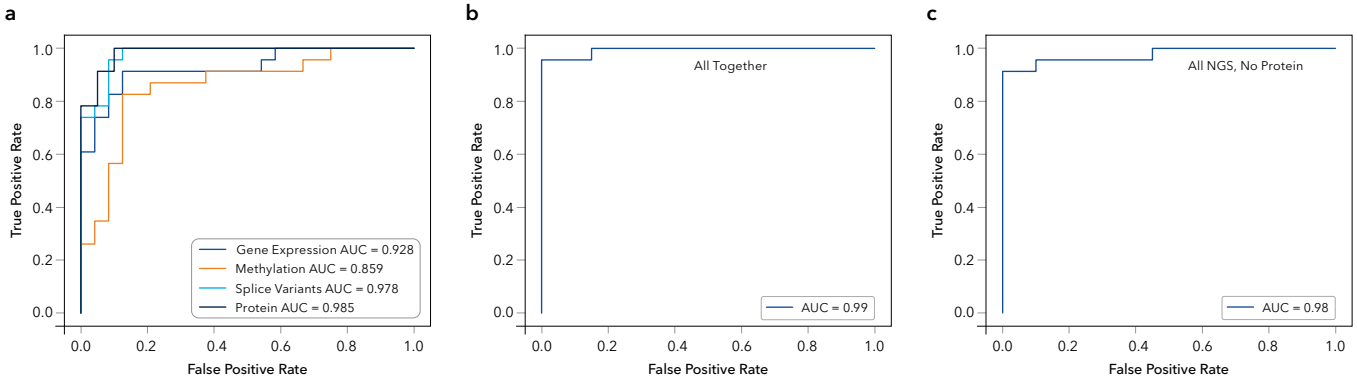
Figure 2. Splice variant analysis to distinguish healthy samples from CRC-positive. Principal component analysis shows that they can largely be distinguished along PC1. Using random forest analysis with the Boruta package for R identified splice variants with a strong ability to distinguish between healthy and CRC.

Figure 3. Probability that each sample is CRC-positive according to individual classifiers for splicing, gene expression, methylation, and protein using the top 10 markers in each.



Each processed omic channel was down-selected to the top ten explanatory targets between CRC and healthy. These markers were used to predict the probability of CRC using a leave-one-out classifier in each channel, alone and in combination (Figure 4). Notably, all ten exosomal RNA splice variant biomarkers involved genes known to be implicated in CRC from literature.

Figure 4. AUC from LOOCV analysis for each analyte alone (a), all analytes pooled (b), and all NGS analytes excluding protein (c).



Bio-Techne: Fit-for-Purpose Assay Development Solutions, and More

Bio-Techne provides precision medicine services to pharmaceutical partners, offering support for translational biomarkers, customizable assay development, and regulatory filing. With more than 20 years of experience and a range of unique technologies, we provide a comprehensive one-stop-shop approach for biomarker development, from initial discovery to downstream assay development for clinical trials.

Partner with Bio-Techne To Accelerate Your Drug Development Journey

Our multiomics platform is one component of the broad range of expertise and capabilities offered by Bio-Techne to support our pharma partners' drug development journey.

We offer:

- Biomarker discovery, with specialized expertise in liquid biopsy
- Fit-for-purpose assay development and validation solutions
- A robust portfolio of protein analysis tools
- Regulatory support for a broad range of FDA and international filings
- Kitting, manufacturing, and commercialization of IVD products

References:

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