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Advances in **Whole Exome Sequencing**

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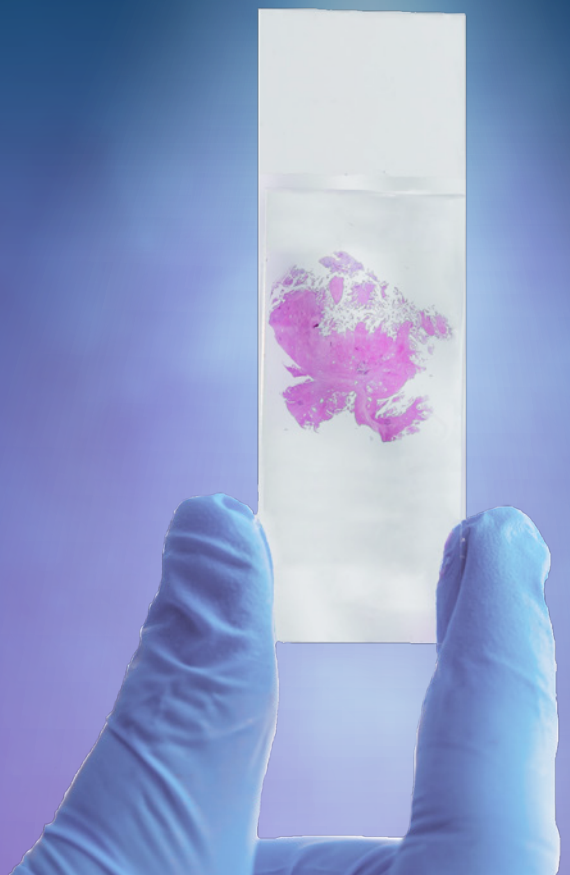

Unlocking the Genome: The Impact of Whole Exome Sequencing on Disease Research

Targeted approach offers improved efficiency and cost savings compared to broader methods.

Whole exome sequencing (WES) is a vital technique that allows scientists to target and sequence the protein-coding regions of the genome. Focusing on these critical areas is an important strategy, as a majority of all known disease-related genomic variations stem from inherited or newly acquired changes in protein-coding genes.[1] The targeted approach of WES offers improved efficiency and cost savings compared to broader methods like whole genome sequencing (WGS), allowing researchers to more effectively identify key genetic variants. Countries like Germany have also demonstrated the advantages of WES through recent initiatives, leading to a shift away from targeted panels toward this more comprehensive approach for identifying rare diseases.[2] This introductory overview covers the transformative impact of WES and its recent advances, widespread adoption, and role in understanding complex diseases like cancer.

Broad profiling with WES

WES offers scientists an unbiased analysis of an organism's entire coding sequence and is routinely used in genetic profiling. This powerful tool facilitates the precise detection of copy number alterations (CNAs) through the analysis of variations in the copy count of specific genomic regions.[3] Furthermore, it provides an accurate determination of complex biomarkers critical to understanding various diseases, such as cancer. Among these complex biomarkers are the homologous recombination repair deficiency (HRD), tumor mutational burden (TMB), and microsatellite instability (MSI). HRD determined through WES indicates a tumor's inability to repair DNA double-strand. Additionally, TMB and MSI are key for identifying responsiveness to certain molecular agents, with TMB indicating mutation frequency and MSI signifying mismatch repair deficiency.[4]

Advancements enhancing WES capabilities

Historically, constraints in next-generation sequencing (NGS) technologies and challenges in the computational analysis of WES data restricted

its wider implementation. These challenges included the high costs and scalability of sequencing, managing the extensive data produced, and the requirement for sophisticated bioinformatics and statistical analysis tools.[5] Moreover, processes like variant calling require complex analysis pipelines while sequencing errors complicate the ability to accurately identify variants, necessitating advanced algorithms for consistent genotype calling and variant filtering.

Several developments have led to overcoming these hurdles. Primarily, the evolution of NGS technologies has been a major factor in the advancement of WES. These technological enhancements have notably lowered sequencing costs and minimized the likelihood of sequencing errors that could be mistaken for genetic variants. In addition, the increase in sequencing speed and data generation has made it possible to produce large-scale datasets and undertake more experimental work. The creation of extensive public databases has provided standards for data comparison and annotation, which has greatly enhanced our understanding of variants and their consequences.[6] Furthermore, the improvements in computational capabilities have increased the flexibility and accessibility of bioinformatics analysis by enabling the handling of these large-scale datasets.

Current trends in WES

More recently, scientists are utilizing WES in various research settings as an alternative to extensive gene panels. One study comparing WES with targeted gene panels for cancer research (summarized in **Chapter 6** highlights how WES assays, like the xGen™ Exome Research Panel v2, demonstrate superior coverage and performance over traditional approaches. After assessing the ability of WES and nine cancer-specific targeted sequencing panels to identify known cancer pharmacogenetic variant-drug interactions and driver mutations, the xGen Exome Panel outperformed the targeted panels. These findings underscore how WES can be employed as a comprehensive tool for understanding the genomic tumor profile of pan-cancer types.

Shift toward larger panels

Another emerging trend is the development of guidelines and government lead initiatives in different nations that have gradually favored the use of larger genomic panels, such as WES and WGS. For instance, the UK has made progress with its Genomics England project that incorporates WGS into its scientific framework, and Canada is advancing its infrastructure to better accommodate WES.[7] Similarly, in the United States, there is an increasing trend toward broader use for both WES and WGS. In Germany, a three-year prospective study highlighted the effectiveness of WES for identifying rare diseases, resulting in its adoption as a standard service.[2] Each of these changes significantly impacts the adoption of WES for clinical research, enabling a wider implementation of this technology.

Future proofing research with WES

A key feature of WES is its thorough coverage of protein-coding regions, which supports both immediate analysis and any future re-evaluations as our knowledge of the genetic drivers of various diseases advances. Re-analyzing WES data is

crucial as it utilizes updates in genetic databases, variant classification tools, and the interpretation of phenotypes to uncover new variants. This "future-proofing" ability allows for targeted investigations through virtual gene panels and ensures the data remains relevant for emerging needs, maximizing the long-term utility of the genetic information collected.

Closing thoughts

WES continues to offer scientists a targeted, cost-effective method for exploring the protein-coding regions of the genome. Its capabilities for comprehensive profiling along with its detection of crucial biomarkers make WES an invaluable tool for understanding the genetic profile of diseases. Advancements in computational analysis and NGS technologies have significantly enhanced the efficiency and accessibility of WES. These advancements have also accelerated the shift toward larger genomic panels and the acceptance of WES in translational research settings. The re-analysis of data highlights the future-proofing of WES and ensures its relevance and utility in the constantly evolving field of genomic medicine research. The remainder of this eBook will serve as a valuable guide for new and experienced researchers either starting their journey in WES or optimizing their current work.

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Whole Exome Sequencing for Cancer Research

WES can fast-track research in areas such as cancer genomics.

Overview

Genetic mutations are more likely to impact health outcomes when they occur in protein-coding genes. Exons that make up the protein-coding genes comprise 1% of the human genome, so focusing sequencing on this portion of the genome is more cost-effective than whole genome sequencing and will provide more comprehensive data than other sequencing methods. This approach can fast-track research in areas such as cancer genomics, which will benefit from the identification of novel biomarkers.

What is Whole Exome Sequencing?

Identifying the DNA sequence of all the protein-coding genes in a genome is called whole exome sequencing (WES). This is a targeted next generation sequencing method using hybridization capture. This next generation sequencing approach uses parallel sequencing, providing a faster turnaround time than Sanger sequencing or shotgun sequencing. Exome sequencing panels can be expanded to include noncoding genes and other genetic elements that are relevant to cancer.

What Can Whole Exome Sequencing Do?

WES reveals mutations in disease-associated genes. Therefore, it could:

- Identify patient groups at higher risk for certain cancers
- Provide a clearer picture of genetic abnormalities that effect tumor progression, such as microsatellite instability
- Identify heritable mutations

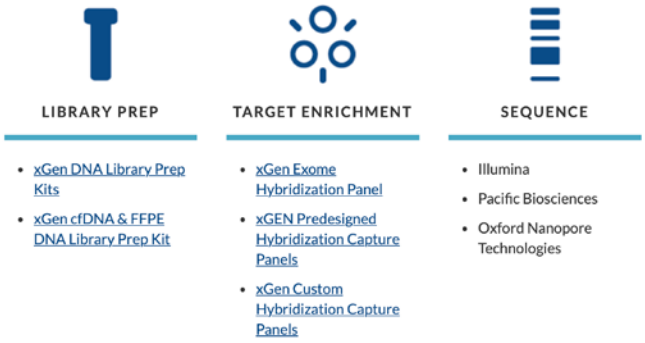
Benefits of Whole Exome Sequencing for Cancer Research

Using NGS technology gives researchers more comprehensive data and more discovery power than can be achieved through PCR. In cancer research, comprehensive data is used for tumor profiling. Deeper sequencing enables more accurate somatic mutation identification WES also provides the opportunity for greater discovery power for revealing heritable mutations compared to PCR. WES is provided at a lower cost with a faster analysis time than whole genome sequencing (WGS). WES using NGS also has a faster turnaround time than other types of sequencing like Sanger or shotgun sequencing.

Cancer Whole Exome Sequencing Workflow

Exome sequencing is a type of targeted next generation sequencing. After genomic material is ex-

tracted from the sample, sequencing libraries must be prepared. Library prep includes hybridization capture with core reagents and the addition of adapters to identify the samples or molecules in the sample and to allow the DNA to interact with the sequencing system. Exome sequencing specifically enriches or captures the exome before the sequencing step.



The IDT Advantage

IDT offers library preparation, adapters, hybridization capture and enrichment panels for cancer exome sequencing. Streamlined library prep workflows and flexible kit configurations accommodate multiple study designs. The enrichment panels are comprised of individually synthesized and quality controlled xGen biotinylated hybridization probes, so custom content can be added to the exome panel to fit specific research needs, such as detecting important events like gene fusions. Discovery research and prototyping can be performed using xGen™ Custom Hyb Panels-Accel, which are fast and cost-effective. Once you finalize your design, you can use xGen Custom Hyb Panels-Production to create a custom panel for long-term studies using a single manufacturing lot for superior consistency. These kits are compatible with Illumina sequencing systems.

Get Started with Whole Exome Sequencing

Working in an area that would benefit from exome sequencing? Just starting? See how you can easily improve your workflows and results.

xGen Exome Hyb Panel

The xGen Exome Research Panel v2 consists of 415,115 individually synthesized and quality controlled oligonucleotide probes. The xGen Exome Research Panel v2 spans a 34 Mb target region (19,433 genes) of the human genome and covers 39 Mb of end-to-end tiled probe space.

LEARN MORE

xGen Custom Hyb Panels

xGen Custom Hyb Panels include your choice of high-fidelity, individually synthesized, 5'-biotinylated oligos for targeted NGS research. IDT proprietary DNA synthesis produces rapid, high-quality panels that can be optimized, expanded, and combined with other panels in research studies.

LEARN MORE

xGen NGS DNA Library Preparation

Whether your research focuses on decoding the genomic sequences of complex microbial communities or identifying inherited germline single nucleotide polymorphism (SNPs) from degraded samples, xGen DNA Library Preparation Kits have simple workflows that provide confident results.

LEARN MORE

Minimal residual disease (MRD) research

Tomorrow's cancer research breakthroughs are on the horizon. The xGen MRD solution offers a complete sample preparation workflow including custom MRD hybridization capture panels delivered quickly and affordably.

LEARN MORE

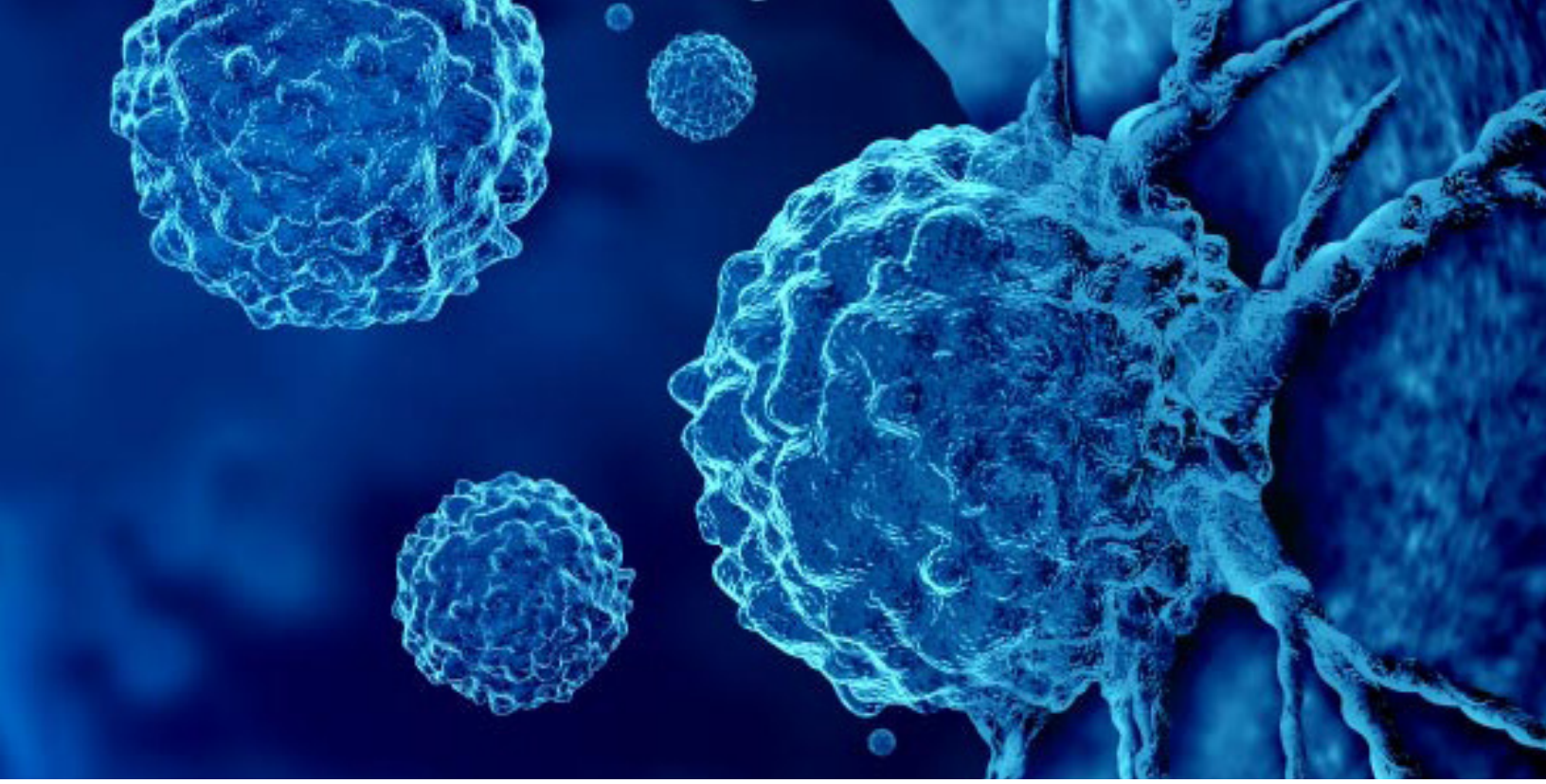
5 Ways Whole Exome Sequencing Is Changing the Way We Investigate Cancer

WES price drop has revolutionized cancer research.

In just the last few years, panel sequencing for cancer research has fallen out of favor as the prices for whole exome sequencing (WES) have dropped dramatically. This trend has huge implications for cancer researchers, who can now gather and bank the entire exome for future reference—with the banking of whole genomes possibly just around the corner.

5 ways whole exome sequencing (WES) is revolutionizing cancer research

1. 85% of disease-causing variants[1] are found within the exome; therefore, WES may provide researchers with the best cost vs. benefit in terms of the amount of biological insight attributed from a single sample, given WES can be run on mid-throughput sequencers.
2. Current options for tumor profiling include immunohistochemistry (IHC), fluorescence in situ hybridization (ISH) and, more recently, small panel next generation sequencing (NGS). Yet, each of these tests have their limits, including subjectivity and a tendency to miss key variants. WES, meanwhile, can identify single-nucleotide variants, insertions, deletions, copy number changes, and fusions, all of which may drive cancer growth. Among the many things WES can do is capture documented, relevant alterations while at the same time allowing researchers to make new discoveries.
3. Some common concerns around WES are gaps in coverage and the depth of coverage. However, it has been demonstrated that when supplemented with additional hybrid capture probes, it is possible to improve



exome panel coverage to catch almost 99% of exons.[2]

4. New disease gene discovery is much easier with WES. Every year, an average of 270 new disease[3] genes are discovered, and updating and revalidating panel tests to look for these diseases is expensive and time-consuming. An alternative approach is to have targeted gene sets built out on an exome backbone. This method leverages the advancements that have been made in bioinformatics analysis and allows labs to achieve a more efficient sequencing workflow; this method returns only the relevant genes of the condition the researcher is investigating.

5. Researchers can take advantage of emerging trends in WES by understanding the technical aspects of sequencing. It is much less expensive and more efficient to offer many tests to be performed on the same technical platform. Patient choice and cost will be the driving factors boosting WES past panel testing.

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Timing and Origins of Local and Distant Metastases in Lung Cancer via WES

Using WES data, team provides report of genomic drivers of metastasis as well as metastatic timing and evolution.

Background

Metastasis is the leading cause of death in cancer patients.[33] Although the molecular mechanisms and evolutionary trajectory of metastases are well described for cancers such as breast and colorectal, they remain a black box for the most prevalent cancer globally: lung cancer.

Leveraging paired primary tumor and metastasis samples with whole exome sequencing (WES) data could help unravel the genetic mechanics of lung cancer metastases.[34] Knowledge resulting from such studies could help inform early cancer detection and treatment strategies to decrease lung cancer deaths.

In this study, Zhong and colleagues perform WES and phylogenetic analyses of 174 primary tumor (PT) and metastatic tumor (MT) samples, with 40 paired PT-MT sets to produce the most detailed analysis of lung cancer metastasis to date. They describe the genomic alterations that drive metastasis in lung cancer, and, using the PT-MT paired samples, they model metastatic timing. Finally, using a small subset of PT samples with multiple MTs, the evolutionary origins of metastases are described.

Datasets

To elucidate genomic drivers of metastasis in lung cancer, this study leveraged two datasets:

Study cohort: A total of 174 samples from primary and metastatic tumors, including 40 PT-MT pairs, underwent whole exome sequencing and analysis. All PT samples were treatment naive, and no PT samples received systemic treatment.

MSK LUAD: The Memorial Sloan-Kettering Cancer Center lung adenocarcinoma study dataset served as an independent dataset for comparing results observed in the study dataset and for identifying additional signatures. Genomic information for PT and MT samples were obtained from cBioPortal.

Genomic Drivers of Metastasis

WES data revealed a number of genomic alterations in both PT and MT samples. Generally, concordance between PT and MT samples was higher with clonal alterations, while non-clonal alterations had highly variable PT-MT concordance. The site of metastasis also influenced PT-MT concordance.

Further analyses revealed specific gene alterations associated with the transition from PT to MT. The most significant alterations were amplification of RICTOR, KDM2A, and NKX2-1, mutations in NPIPA2, WDR87, NPIPA1, C16orf3, and DDX1, chromosomal arm 20p gain, and chromosomal arm 11p loss. After comparison with the MSK LUAD cohort, MYC, NKX2-1, and RICTOR amplification as well as arm 20p gain and 11p loss remained robust signatures of metastasis, and the study authors suggest these specific changes may act as drivers of metastasis in lung cancer.

Each genetic alteration was also associated with specific metastases, suggesting that distinct events could drive different metastases. For example, RICTOR amplification and arm 11p loss were enriched in brain metastasis samples while NPIPA1 mutation was enriched in lymph node metastasis. The dataset analysis found that MYC amplification was another mutation associated with deadly lung cancer, suggesting that this genetic alteration could drive metastases. While these data imply that distinct molecular features might drive metastasis, further research is needed to confirm these observations.

Modeling Metastatic Timing

Early cancer screening and treatment success could be improved by research studies that try to understand metastatic timing. Using the published tool SCIMET,[31] Zhong and colleagues predicted the dissemination time for all PT samples in the study dataset. The simulation revealed that over half of PT samples were from late dissemination. Most early dissemination samples were lymph node metastases.

Comparing these results to diagnosis timing of metastasis revealed that lymph node metastases took longer to diagnose than the late dissemination, non-lymph metastasis events. These results emphasize the importance for improved early cancer detection and reveal an opportunity area for research into an improved lung cancer detection and treatment plan.

Evolution of Metastases

Given the observations around metastasis timing, a natural follow up question was whether late dissemination metastases were seeded by the primary tumor or by the early lymph node metastases. To answer this question, Zhong and colleagues reconstructed tumor phylogenies from 8 PT samples with multiple MTs. The majority of MT samples were determined to be derived from the PT and not the lymph node MT. The research data suggest that a wider time window for successful resection following detection of lymph node metastasis exists and could prove to be relevant for treatment plans upon further investigation.

Conclusion

Leveraging WES data from two lung cancer datasets with PT and MT samples, Zhong and colleagues provide the most detailed report to date of genomic drivers of metastasis as well as metastatic timing and evolution. Their results show that most metastases are late-dissemination, and that these later MTs come from the PT and not from lymph node MTs. This apparent opportunity window for earlier detection suggests that further research on these results could pave the way for improved lung cancer detection and treatment strategies.

This chapter is excerpted from IDT's Whole Exome Sequencing Handbook. References are available in the handbook.

Achieving a Deeper Exploration and Understanding of Underlying Biology with WES

Data revealed hundreds of rare variant-trait associations, including novel LOF variants and protective variants.

Introduction to the UK Biobank (UKB)

Understanding the consequences of altering every single protein coding gene in the human genome can facilitate a more thorough understanding of the molecular mechanisms behind disease, drive further studies for enhancing treatment strategies, and even enable precision medicine-based approaches.[37]

Capturing rare variants, pathogenic variants, and loss of function mutations (LOFs) through whole exome sequencing (WES) is a critical component of this research program. The largest open access effort to date toward achieving this is the UK Biobank (UKB) (data available to approved researchers at: http://ukbiobank.ac.uk/). This dataset is collected from prospective, population-based study of over 500,000 individuals (including mother-father-child units) with extensive phenotypic and genetic data. Importantly, these datasets are readily available to the scientific research community.

Exploration of the first ~50,000 participants highlighted the value of genome sequencing in large population-based studies. Sequencing results of the entire 500,000 sample cohort only strengthened and expanded upon the findings from the initial subset. This effort illustrates the utility of WES for researching gene function(s), for identifying novel gene-trait associations (including rare variants), and for identifying effector genes underlying genome-wide association study (GWAS) signals.

What the First 50,000 Samples Revealed

The first detailed analysis of the first 50,000 sequenced samples yielded several important discoveries:

- Most of the 4 million variants (98.6%) were rare, with a frequency of less than 1%
- LOF analysis not only replicated existing studies, but also identified novel variants. Some of these were also identified in another dataset, the DiscovEHR study (http://www.discovehrshare.com/).

- A total of 2% of the 50,000 samples had variants of significance
- Correlations between BRCA1 and BRCA2 mutation and incidence of 5 cancers (breast, ovarian, prostate, melanoma, and pancreatic) well-reported in the literature were replicated in this study

Of the novel variants detected in this study, five were found to be of particular interest due to the large effects they had on traits: PIEZO1 on varicose veins, COL6A1 on corneal resistance, MEPE on bone density, and IQGAP2 and GMPR on blood cell traits. Based on these results, the study authors expected further significant biological insights from sequencing the remainder of the UKB samples.

Confirming Initial Observations

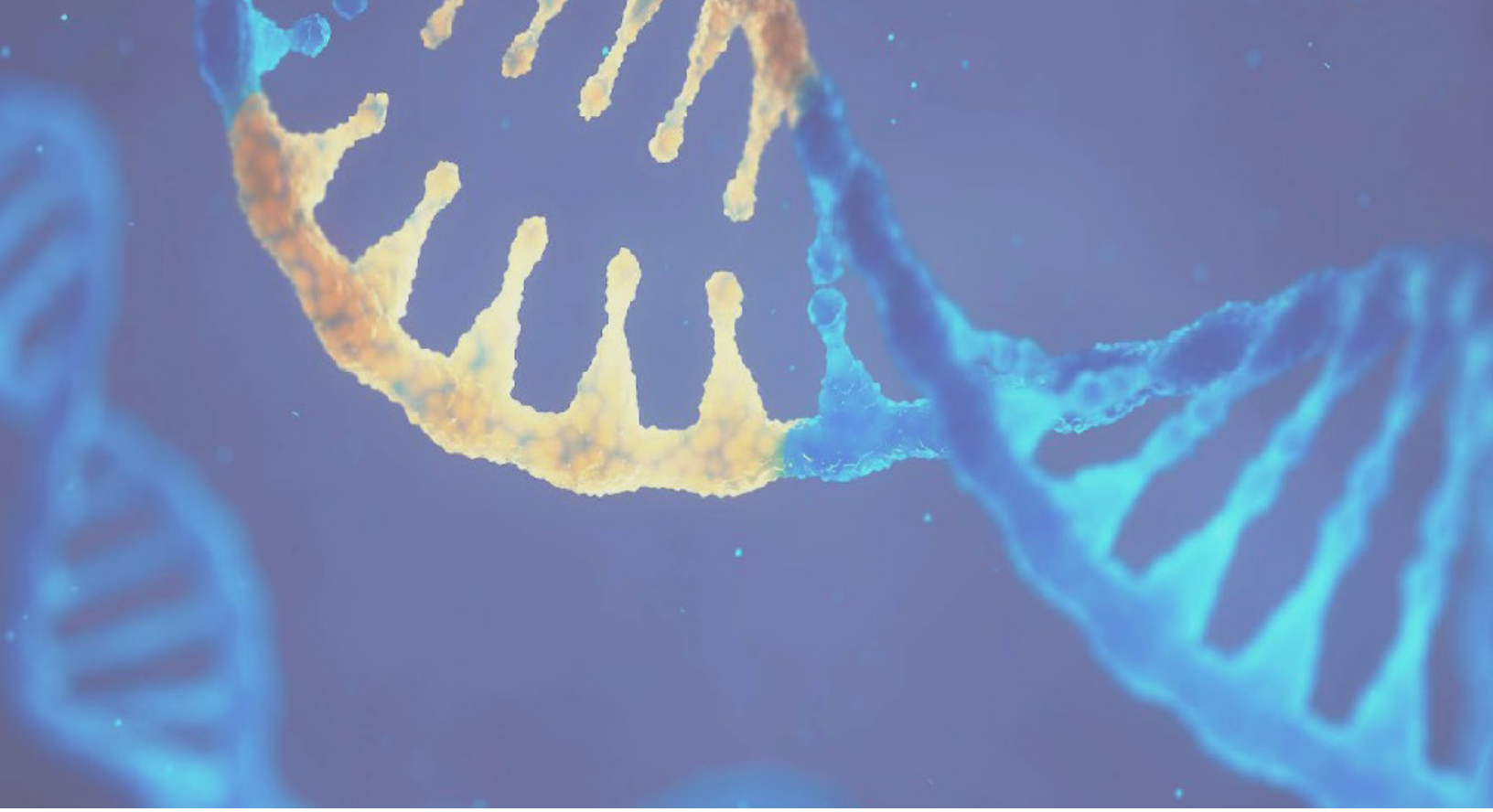
Sequencing the remaining ~450,000 samples confirmed that most (99.6% in the full set vs. 98.6% in the first 50,000 samples) variants are rare, highlighting the importance of access to such large-scale WES datasets for discovery. The association between PIEZO1 and varicose veins was even more pronounced in the 500,000 samples, further emphasizing the utility of large-scale datasets. This observation is of particular interest, given that there is currently no treatment for varicose veins in the lower extremities. It is just one example, however, and other research groups performing their own analyses with the UKB could identify numerous additional and significant associations.

A Deeper Exploration

Understanding quantitative traits such as body mass index (BMI) can benefit from large genetic studies. In the 500,000 genomes of the UKB, several variant-quantitative trait associations were identified. Of these, 13 associations proved to be protective against certain diseases. The associations between MAP3K15 variants with hemoglobin A1c, lower serum glucose, and protection from type 2 diabetes were corroborated with the DiscovEHR cohort. Considering all rare gene-trait associations (not just the protective ones), 69% of those observed in the UKB were replicated in the DiscovEHR cohort; including only those associations with at least 80% power for replication led to a replication rate of 81%.

Importantly, some of the variant-quantitative trait associations had existing literature support. For example, the association between ASGR1 variants and low apolipoprotein B levels corroborated existing research on ASGR1 haploinsufficiency and cardiovascular disease risk, which supported the development of anti-ASGR1 antibodies as a potential therapeutic. Identifying (and confirming) such associations using large-scale genome sequencing studies like the UKB emphasizes the utility and importance of such datasets for future genetics research and potential translation to the clinic.

To explore the utility for using rare variant associations identified through WES data to pinpoint effector genes, investigators in this study combined the WES data with GWAS generated for each of the traits they identified in association with a rare variant. Their results showed strong agreement between GWAS and WES results, suggesting that WES data could be used to identify effector genes for thousands of GWAS loci. The specific association between the HAL variant and the GWAS peak for serum vitamin D levels illustrates how WES and GWAS can be analyzed together to find new associations, in this case, between HAL and both vitamin D levels and skin cancer.



Tying WES analysis more directly with specific phenotypes, this study also identified gene variant associations with MRI images that accompanied over 36,000 genomes. As with the other variants and diseases, rare variant-trait associations were observed, some of which were protective, and many of which have existing literature support.

While the majority of genomes in the UKB belong to Caucasian individuals, there is representation of East Asian, South Asian, and African ancestry as well. Many of the observations made with the Caucasian subset were preserved when considering only the non-Caucasian genomes. However, sample sizes were considerably lower comparatively, and novel, ancestry-specific associations are likely. The observations reported here suggest that such large-scale WES efforts capturing non-European ancestry will be critical for human genetics research in the future.

Conclusion

The UKB is the largest known open access compilation of WES and phenotypic data in a prospective, population- based study, containing data on over 500,000 samples. Exploring the data revealed hundreds of rare variant-trait associations, including novel LOF variants and protective variants. Several of these had existing literature support, and could be confirmed using an independent dataset. Importantly, WES data were used to identify effector genes for GWAS loci, expanding the utility of such large-scale genome sequencing efforts. This study as well as others focusing on non-European ancestry are likely to yield important genetic discoveries for years.

This chapter is excerpted from IDT's Whole Exome Sequencing Handbook. References are available in the handbook.

Putting Theory into Practice—Whole Exome Sequencing (WES) vs Targeted Gene Panels

A performance and value analysis

Background

As with many cancers, early detection and diagnosis are key to treating patients to improve their outcome. Next generation sequencing (NGS) aids the discovery and characterization of gene-specific mutations that have the potential to be tumorigenic. Along the path to that discovery, liquid biopsy has been leading the way. Liquid biopsies can help detect the emergence of early cancer cells as well as any reoccurrence and residual disease as the disease progresses.[2] Present day, researchers are using NGS panels for targeted sequencing of liquid biopsy and tissue samples to glean the most insight possible from the genomic tumor profile of pan-cancer tumor types in hopes of more success in its treatment and survival rate.

Asking the question: How to choose the right panel for cancer research?

Of the commercially available research panels that focus on cancer variants or pharmacogenetic variant-drug interactions (specifically for targeted sequencing of tumor tissue), the authors questioned whether the best approach was to use several targeted sequencing panels to sequence the cancer samples, or use the exome sequencing pipeline which many labs commonly use today?

Creating a custom knowledgebase

Tilleman and colleagues created a custom meta-knowledgebase from five already existing knowledgebases as a truth-o-meter to catalog, cross-reference, and understand to what extent the currently known cancer pharmacogenetic variant-drug interactions are identified by either the latest pan-cancer targeted sequencing panels or the whole exome panel (WES). Both these panel types were also compared with driver mutations and fusion genes in The Cancer Genome Atlas (TCGA).

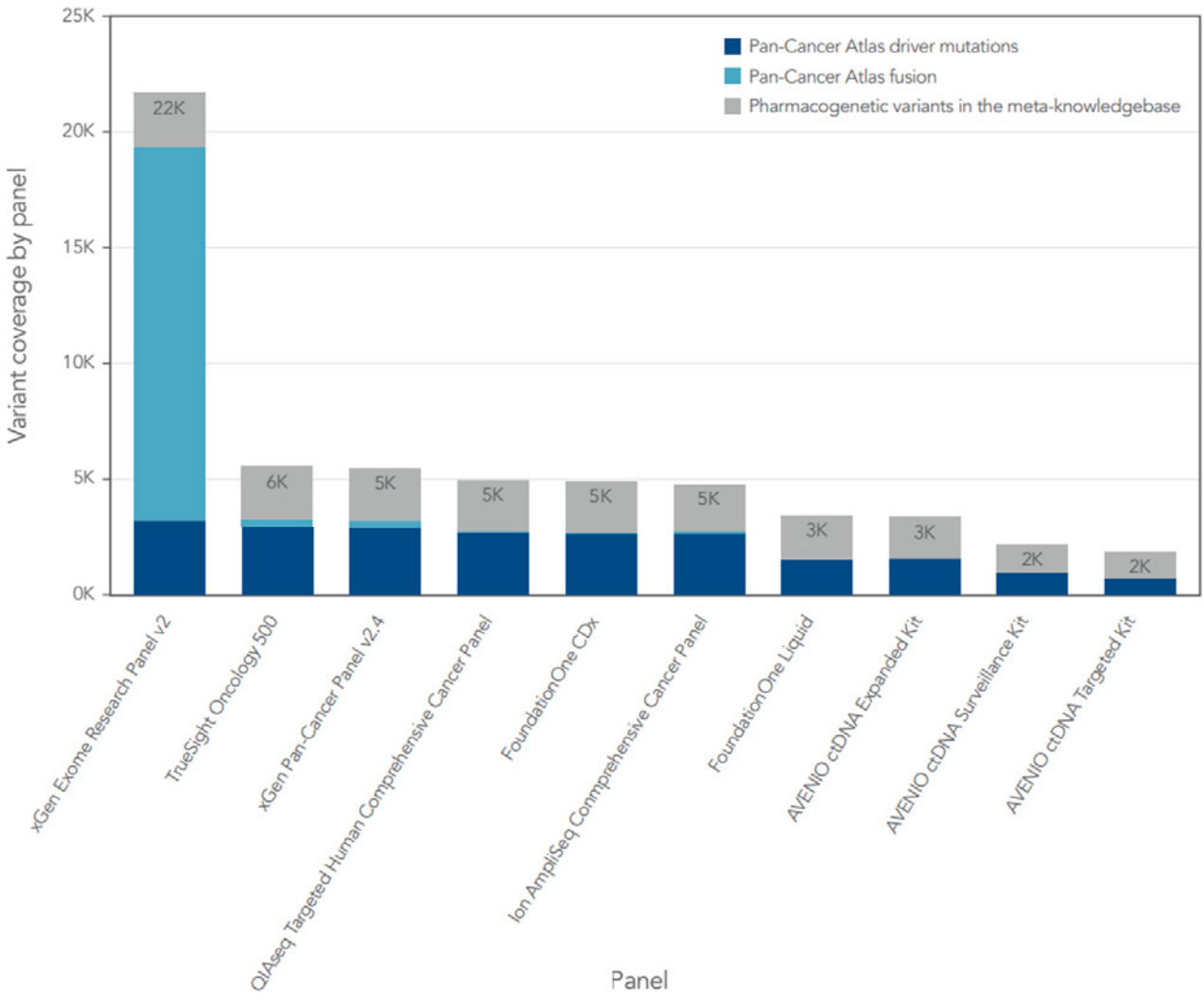
Comparing panels—a bioanalytical study

This study filtered the knowledgebases mentioned above to narrow its comparative spotlight to nine recently developed (or updated) cancer-specific

targeted sequencing panels from market leaders, and a highly representative WES panel, expressly the [xGen™ Exome Research Panel v2 from IDT.]

Details for each considered panel:

- Ion AmpliSeq® Comprehensive Cancer Panel (Thermo Fisher Scientific): PCR-based targeted sequencing panel containing 409 genes
- xGen Pan-Cancer Panel v2.4 (IDT): Hybridization-based targeted sequencing panel that includes 532 genes
- TrueSight® Oncology 500 Panel (Illumina): Targets 523 genes, covering most variants in the National Comprehensive Cancer Network (NCCN)



- QIAseq® Targeted Human Comprehensive Cancer Pane (QIAGEN): Targets 275 genes covering the most commonly occurring mutations in cancers
- AVENIO® ctDNA Targeted Kit (Roche): Targets 17 genes optimized for lung cancer and colorectal cancer targeted treatments
- AVENIO ctDNA Expanded Kit: Targets an extended number of 77 genes to include a broader spectrum of therapies
- AVENIO ctDNA Surveillance Kit: Targets 197 genes optimized for longitudinal tumor burden monitoring in lung cancer and colorectal cancer
- FoundationOne® CDx Panel (Foundation Medicine): Targeting 324 genes for all solid tumors with multiple companion diagnostics
- FoundationOne Liquid Panel: Targeting 70 genes
- xGen Exome Research Panel v2 (WES): Spans a 34 Mb target region of the human genome, including 19,433 genes

Conclusion

The superior coverage of a whole exome panel outperformed the cancer-specific targeted sequencing panels that were investigated throughout this in-depth study using knowledgebase comparisons and complex bioinformatics. The xGen Exome Research Panel v2 targets a slew of driver mutations and fusion genes called out in the Pan-Cancer Atlas as well as the most pharmacogenetic variants in the custom meta-knowledgebase Tilleman and associates built for their study. At 71% coverage, this exome panel also tackled the most pharmacogenetic variant-drug interactions known to the meta-knowledgebase in comparison to the other cancer-specific panels.

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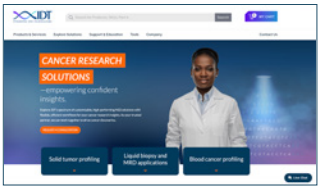
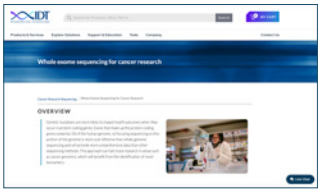
Resources



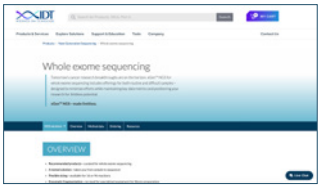
Cancer Research Solutions



Whole Exome Sequencing for Cancer Research

Cancer Identification Research

Tumor Mutational Burden (TMB) & Microsatellite Instability (MSI)



Whole Exome Sequencing


REVOLUTIONIZING PRECISION MEDICINE

ADVANCEMENTS IN ONCOLOGY RESEARCH

Revolutionizing Precision Medicine: Advancements in Oncology Research