RESEARCH

Whole Genome Sequencing Identifies Novel Prognostic Signatures in Myelodysplastic Syndromes Treated with Allogeneic Hematopoietic Cell Transplantation- A BTM/CIBMTR Precision Medicine Initiative

WHY?

Myelodysplastic syndromes (MDS) represent a diverse group of myeloid malignancies characterized by cytopenia (low number of blood cells) and increased risk of progression to acute myeloid leukemia (AML) driven by accumulated somatic (acquired) genetic mutations in hematopoietic stem cells (HSCs) (blood-forming cells). While recurrent mutations are known to associate with poor outcomes in MDS, 10% of MDS cases have no known genetic indicators for survival prognosis. Whole genome sequencing (WGS) can detect comprehensive mutations in coding and non-coding regions that empowers discovery of novel genetic biomarkers. These biomarkers could then be used to improve outcomes for patients by allowing for more specific and personalized treatment decisions.

WHAT?

NMDP/BTM launched a precision/personalized medicine initiative to evaluate novel methods to characterize disease risk and post-transplant prognosis in MDS through the CIBMTR with funding support from the Office of Naval Research.

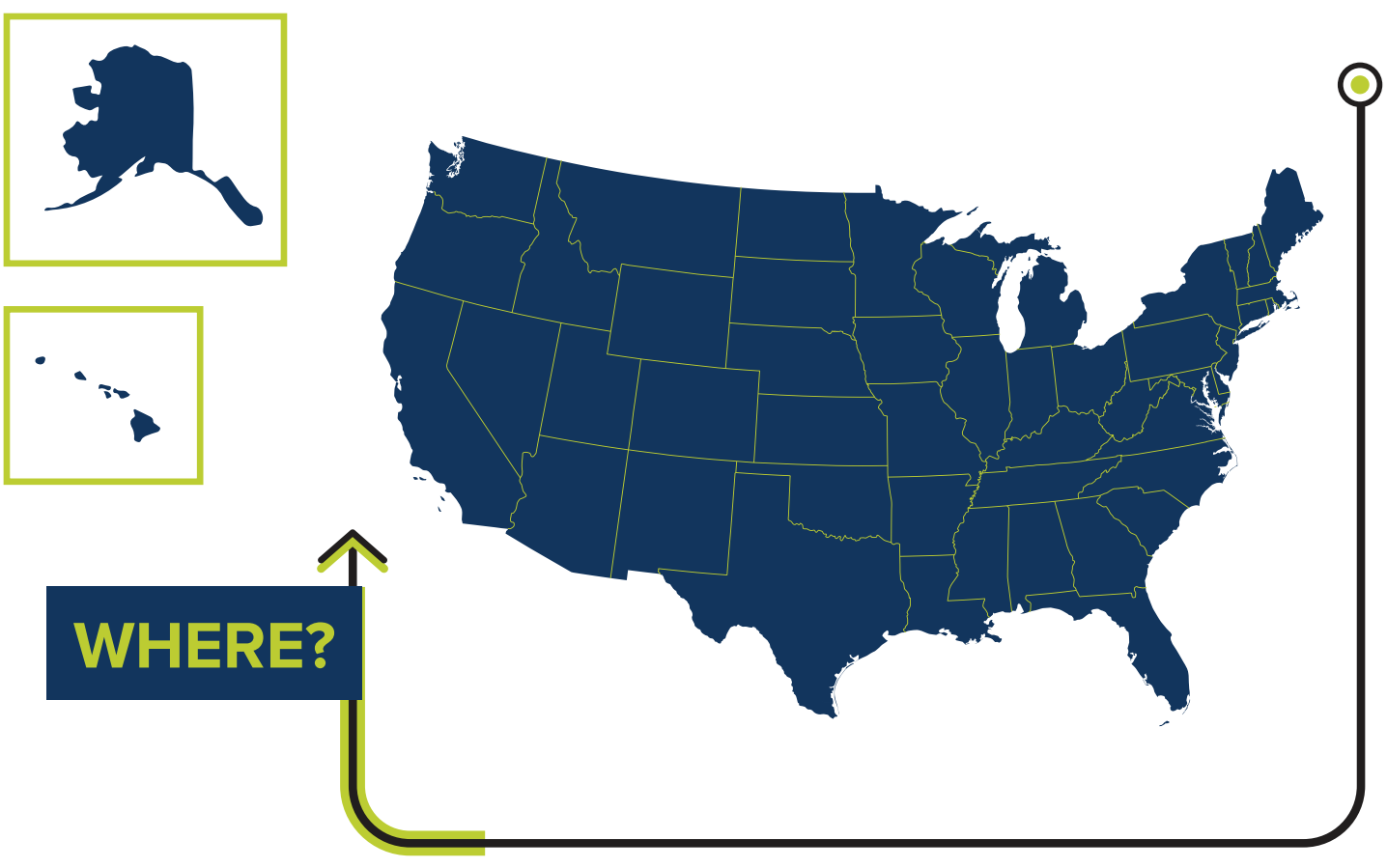
The goal of these studies are to ensure that the right patient receives the right therapy at the right time while limiting unnecessary toxicity.

WGS has been performed on about 600 allogeneic donor-recipient pairs with pre-transplant research samples available through the CIBMTR Research Repository. These genomic data, in combination with the longitudinal clinical outcome data collected through the CIBMTR Research Database, are being studied to gain insights into the MDS disease process and contributions of both donor and recipient genetic diversity to transplant outcomes.

WHO?

Patients with MDS and their allogeneic donors (both related and unrelated) with research samples available in the CIBMTR Research Repository for testing.

WHERE?



IMPACT/FINDINGS:

This initiative has reported several novel findings regarding the contribution of somatic mutations in MDS that are prognostic (predictive) for outcomes post-transplant. Additional studies could provide insights into which patients are likely to respond to certain transplant therapy and help identify new targets for potential therapeutic or curative interventions.

Although the findings of these studies need to be validated in additional populations before they are ready for clinical use, this research provides new insights into the contribution of genomic variation on outcomes in transplant for MDS.

The more detailed information scientists and doctors know and understand about the the genes and variants in the cancer, the patient, and their potential donor, the more they're able to make personalized and informed treatment decisions. We are committed to moving the field forward and utilizing genomic data to improve patient outcomes.

FROM THE EXPERTS

While the field is advancing, there is still so much we do not know – genomics is a goldmine with data that can help us to understand and act on key decisions that can save and improve patient lives, in this case for patients with myelodysplastic syndromes."

Yung-Tsi Bolon
Director, Bioinformatics and Immunobiology Research
CIBMTR

The use of precision medicine tools, like whole genome sequencing, holds the promise to unlock new insights into the treatment of complex cancers like myelodysplastic syndromes. Further understanding of the mutational landscape of the underlying malignant clones can lead to improvements in post-treatment disease monitoring and personalized treatment plans."

Stephen Spellman
Vice President, Research
Senior Scientific Director
National Marrow Donor Program, CIBMTR

This is the largest study to-date that demonstrates that whole genome sequencing as a technology can provide critical insights into predicting transplant outcomes among patients with a hematologic malignancy."

Wael Saber, MD, MS
Scientific Director, CIBMTR and Professor of Medicine,
Division of Hematology/Oncology, Department of Medicine
Medical College of Wisconsin

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