Children's Mercy KANSAS CITY

ADVANCING HEMATOLOGY AND ONCOLOGY CARE THROUGH GENOMICS

DISCOVERING LINKS BETWEEN GENETICS AND HEMATOLOGY/ONCOLOGY

Genomics is changing the way pediatric cancers are identified and treated. The Division of Hematology/Oncology/BMT at Children's Mercy Kansas City, working with the hospital's internationally known Genomic Medicine Center, is at the forefront of research to better understand the genomics of pediatric cancer and blood diseases. Several studies currently underway show the potential translational impact of genomics on diagnosis and care for pediatric patients.

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UNCOVERING THE ROLE OF GENOMICS IN INFANT ALL

When babies are diagnosed with acute lymphoblastic leukemia (ALL) before their first birthday, the disease is highly aggressive. Approximately 65 percent of these babies will relapse within about a year of starting treatment, and few of those will survive.

Erin Guest, MD, Director of the Children's Mercy Cancer Genomics Program, and her team are trying to determine why certain babies' leukemia relapses. While all babies with ALL are high-risk, it would be helpful to be able to predict which babies were more likely to have poor outcomes.

The team is sequencing the genomes of leukemia cells to learn answers to important questions:

- What is driving the growth of the cancer?
- Which mutations in cancer cells make it more sensitive or resistant to treatment?
- What genes are turned off and on?

The ultimate goal of Dr. Guest's ongoing research is to target therapies to the genetics of the leukemia cells to kill them and prevent any relapse.

HOW GENETIC VARIATIONS AFFECT OUTCOMES IN HISPANIC PEDIATRIC ALL PATIENTS

Hispanic pediatric patients have a 15 percent higher incidence of ALL than do Caucasians. Survival rates also differ. Caucasians have at least a 93 percent survival rate, while Hispanics experience a survival rate between 75-85 percent.

What factors contribute to the difference in pediatric outcomes between Hispanic and Caucasian patients? What can we do to address them?

These are questions of interest to Terrie Flatt, DO, MA, pediatric hematologist/oncologist and Director of the

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HOW GENETIC VARIATIONS AFFECT OUTCOMES IN HISPANIC PEDIATRIC ALL PATIENTS

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Children's Mercy HOPE Clinic (Hematologia Oncologia Puente de Esperanza).

In his research, funded by The Midwest Cancer Alliance, Dr. Flatt is focused on the cytogenetics of cancer cells. Hispanics tend to have a higher incidence of poor prognostic features. For example, a specific mutation turns stem cells and cancer cells on and off. Hispanics have a higher incidence of this mutation, which is important because a targeted drug action could be designed to address it.

Dr. Flatt is collaborating with centers in Mexico, where they see patients with a mix of ancestry differences (Spaniard, Aztec, Mayan, etc.). They test these individuals to learn percentages of racial background and correlate these numbers to cytogenetics. The next step is to look at genetic variations that are specific to populations to aid in the understanding of how different groups respond to cancer and to treatment.

Although the study is still in its recruitment phase, Dr. Flatt is recognized globally for his expertise in this arena. To date, he's given more than 30 international talks on this topic.

IDENTIFYING GENETIC VARIANTS IN HEMOPHILIA USING DRIED BLOOD SPOTS

When a patient has hemophilia, molecular analysis is an ideal diagnostic tool because it helps predict disease manifestations, such as inhibitor development, and it provides family planning support to female carriers. However, the test is expensive, which means many patients avoid it. Plus, it typically takes several weeks to receive results, which could prove dangerous to newborns at risk of spontaneous bleeding.

Shannon Carpenter, MD, MS, Associate Division Director, Section of Hematology at Children's Mercy, and several of her colleagues set out to address this issue. Their goal was to identify the mutation causing hemophilia in patients through genomic sequencing using dried blood spots. This method significantly lowered the turnaround time and the cost of testing.

The team conducted a single-center, prospective pilot study, where they developed a sequencing assay to identify genetic variants in the factor VIII and IX genes using dried blood spots. The study demonstrated that DNA can be extracted and analyzed for variants in factor VIII and IX genes from dried blood spots on filter paper. Potential applications of this new technology include clinical molecular analysis in patients with known hemophilia, newborn screening, carrier identification and improved diagnosis in underserved areas.

LEADING THE WAY IN RESEARCH

With support from the Genomic Medicine Center, oncology and hematology researchers at Children's Mercy are consistently focused on new discoveries. Research is focused in three areas: determinants of disease, interventions, and cancer control and supportive care. They conduct broad clinical testing and innovative research for all patients, both with new diagnoses of cancer and relapses, while closely monitoring insights learned at other research centers, to advance their care for all children with difficult-to-understand diseases.

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT CANCER 2018-19

LEARN MORE ABOUT HEMATOLOGY AND ONCOLOGY GENOMIC RESEARCH.

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