NEWS RELEASE

City of Hope and TGen Research Reveals What Potentially Causes a Leukemia to Become More Aggressive

10/11/2023

- Research focuses on chronic myeloid leukemia with the goal of creating a new therapy for patients
- Study funded by Robert & Lynda Carter Altman Family Foundation Research Fund

LOS ANGELES--(BUSINESS WIRE)-- Scientists with City of Hope®, one of the largest cancer research and treatment organizations in the United States, and the Translational Genomics Research Institute (TGen), part of City of Hope, may have discovered one of the causes for a type of leukemia to develop into a more aggressive form, according to **recent research** published in Nature Communications.

City of Hope's Guido Marcucci, M.D., and team conducted the research. (Photo: Business Wire)

Led by **Guido Marcucci**, M.D., City of Hope professor and chair, Department of Hematologic Malignancies Translational Science, director, Gehr Family Center for Leukemia Research, and chief, Division of Leukemia, and **Bin Zhang**, Ph.D., associate professor, City of Hope's Department of Hematologic Malignancies Translational Science, the research team analyzed the RNA of chronic myeloid leukemia cells (CML) and found that miR-142, an RNA molecule that regulates cell metabolism, was missing.

Researchers hypothesized that the lack of this small RNA molecule has important implications, as its absence allows CML cells to expand and eventually develop into a more aggressive form of the disease called blastic phase (BP), which is the equivalent of secondary acute myeloid leukemia (sAML). SAML is deadly and has limited treatment options.

The team developed a synthetic version of miR-142 and tested it in mouse models of BP CML. They found that

adding miR-142 prevented CML transformation and some mice with BP CML were even cured of their disease.

Researchers also found that adding tyrosine kinase inhibitors, which is a Food and Drug Administration-approved therapy for CML, increased the anti-leukemic activity of the synthetic miR-142.

“What’s exciting is that we have potentially discovered how we can knock down the leukemia stem cells, which are the equivalent ‘queen bees’ of the disease, and how we can keep them from producing more cancer cells,” Zhang said.

The only current curative option for CML that has developed into BP is a blood marrow or stem cell transplant. A transplant may not work in some patients or can create serious side effects.

“More options are urgently needed for these patients. Our team will now work on developing synthetic miR-142 therapy for use in patients in clinical trials, hopefully as soon as next year,” Marcucci said.

Leveraging TGen’s unique molecular profiling platforms, this study also uncovered that the loss of miR-142 in CML causes major changes in the tumor metabolism.

“These key metabolic changes are at the heart of the transformation of CML into blast crisis, which, unfortunately, is associated with poor treatment options,” said **Patrick Pirrotte**, Ph.D., associate professor at TGen and director of City of Hope’s Integrated Mass Spectrometry Shared Resource. “These new molecular findings provide interesting new avenues for therapies.”

The CML research can be applied to finding better treatments for myeloproliferative neoplasms since both are diseases of the bone marrow.

The research was funded by the Robert & Lynda Carter Altman Family Foundation Research Fund in honor of actress, singer-songwriter and advocate Lynda Carter Altman’s husband, Robert, who developed myelofibrosis, a myeloproliferative neoplasm of the bone marrow, which eventually transformed into sAML.

The Carter Altman fund supports City of Hope and TGen’s two-track approach to developing leading-edge diagnostic and treatment technologies for myeloproliferative neoplasms and their transition into sAML. One track funds research such as that led by Marcucci and his team and focuses on accelerated development of new medicines at City of Hope with the goal of enabling a first in-human clinical trial of an investigational new therapy to mitigate disease progression.

Another track funds a diagnostic project at TGen using genomic sequencing to uncover strategies to pinpoint and

prevent disease progression.

“Current gene-based information of patients with myeloproliferative neoplasms and AML rely on a ‘Cliffs Notes’ version (several hundred of our 22,000 genes) that require two weeks or more to obtain. Thanks to the Carter Altman Foundation, the TGen team is viewing all 3 billion letters of a patient’s genome in two days or less. In today’s era of mining massive data, we believe this new tool can uncover more information more quickly, offering greater benefit to patients," said **Jeffrey Trent**, Ph.D., TGen president and research director, and the project leader at TGen.

About City of Hope

City of Hope's mission is to deliver the cures of tomorrow to the people who need them today. Founded in 1913, **City of Hope** has grown into one of the largest cancer research and treatment organizations in the U.S. and one of the leading research centers for diabetes and other life-threatening illnesses. City of Hope research has been the basis for **numerous breakthrough cancer medicines**, as well as human synthetic insulin and monoclonal antibodies. With an independent, National Cancer Institute-designated comprehensive cancer center at its core, City of Hope brings a uniquely integrated model to patients spanning cancer care, research and development, academics and training, and innovation initiatives. City of Hope’s growing national system includes its Los Angeles campus, a network of clinical care locations across Southern California, a new cancer center in Orange County, California, and treatment facilities in Atlanta, Chicago and Phoenix. City of Hope’s affiliated group of organizations includes **Translational Genomics Research Institute** and **AccessHope™**. For more information about City of Hope, follow us on **Facebook**, **Twitter**, **YouTube**, **Instagram** and **LinkedIn**.

About TGen, part of City of Hope

Translational Genomics Research Institute (TGen) is a Phoenix, Arizona-based nonprofit organization dedicated to conducting groundbreaking research with life-changing results. TGen is part of City of Hope, a world-renowned independent research and treatment center for cancer, diabetes and other life-threatening diseases. This precision medicine affiliation enables both institutes to complement each other in research and patient care, with City of Hope providing a significant clinical setting to advance scientific discoveries made by TGen. TGen is focused on helping patients with neurological disorders, cancer, diabetes and infectious diseases through cutting-edge translational research (the process of rapidly moving research toward patient benefit). TGen physicians and scientists work to unravel the genetic components of both common and complex rare diseases in adults and children. Working with collaborators in the scientific and medical communities worldwide, TGen makes a substantial contribution to help patients through efficiency and effectiveness of the translational process. Follow TGen on **Facebook**, **LinkedIn** and Twitter **@TGen**.

Letisia Marquez

626-476-7593

lemarquez@coh.org

Source: City of Hope