Diana Gonzalez
December 20, 2018

Novel Use of CRISPR for Cancer Research at Sylvester

In Dr. Jonathan Schatz's laboratory at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine, researchers have pioneered a new use for CRISPR, the genomic editing tool at the center of much media attention.

Soumya Sundara Rajan, Ph.D., MSc, in the laboratory.

"We are the first to use CRISPR in this way," said Dr. Schatz, an associate professor of medicine. "The novelty of our work is that we are the first to develop a mouse model of a hematologic malignancy by using CRISPR to create a specific chromosomal translocation in transplantable blood stem cells."

Translocations occur when parts from two chromosomes break off and switch places. These rearrangements, which interfere with cell functions, are associated with many blood cancers

including lymphomas.

A researcher working with Dr. Schatz, Soumya Sundara Rajan, Ph.D., MSc, made that happen in the lab by using two snippets of guide RNA, each encoded with a sequence that makes it bind to a specific spot in the genome. Blood stem cells in a plate are bathed with a solution that causes them to take up a DNA "vector." The vector is engineered to cause expression in the cells of the RNA snippets and the CRISPR associated protein Cas9, which does the editing.

"When the guide RNA finds the specific sequence, Cas9 will recognize this and make a cut in the DNA," Dr. Schatz said. "We had CRISPR make a break in the middle of those genes to cause a translocation. When we transplant the cells to recipient mice, they lead to formation of lymphoma tumors because of the translocation we engineered."

It took 300 days from the time of transplantation for them to exhibit signs of anaplastic large cell lymphoma, which usually affects adolescents and young adults.

Now that there is evidence the technique works, researchers in the Schatz lab are applying this novel use of CRISPR to create other fusion oncogenes to model additional lymphomas and leukemias.

"The reason this is so exciting is such models of disease that mimic the human disease closely make preclinical testing of new therapeutic strategies for these diseases more clinically relevant" explained Dr. Rajan.

At the American Society of Hematology annual meeting in

December, Dr. Rajan presented the abstract for this work – "CRISPR/Cas9 Generation of *Npm1-Alk* in Transplantable Murine Hematopoietic Stem Cells Accurately Models ALK-Positive Lymphoma in Recipients."

Dr. Rajan begins a post-doctoral fellowship at the National Cancer Institute in January.