

CANCER RESEARCH

LaFramboise analyzes inherited genetic mutations linked to leukemia

In the Department of Genetics at Case Western Reserve University, Thomas LaFramboise, Ph.D., and his research team are discovering which genetic mutations determine a person's susceptibility to developing leukemia.

Whether or not someone develops cancer depends on where certain mutations are located within your genetic material. LaFramboise, an associate professor, and his team leverage the processing power of the Ohio Supercomputer Center's Owens Cluster to find exactly where these potentially cancerous mutations occur.

"There are certain inherited mutations that probably give people a slightly elevated risk of acquiring a specific disease. In our case, we're looking at things that are related to leukemia," LaFramboise said.

In most cases, no one knows exactly in which genes the mutations reside. To find them, LaFramboise and his team use software packages, such as Bowtie, SAMtools and GATK, which are available via OSC. These tools allow the team to view and compare healthy individuals' genes to genes in patients with leukemia. The team can then identify the location where the mutations occur.

While there is already extensive research on non-inherited (sporadically occurring) mutations, there is

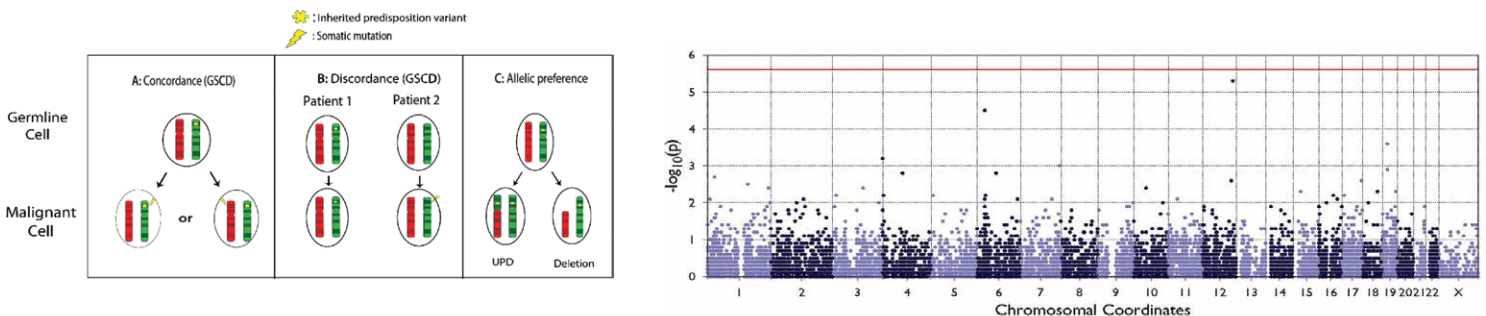
less information about inherited mutations in leukemia.

"The project I'm using OSC for is about mutations that are inherited from the patient's father or mother," LaFramboise said.

LaFramboise's research involves studying thousands of people with leukemia and thousands without, giving the team a large amount of raw DNA sequences—composed of four nucleotide bases of a DNA strand, represented as various combinations of As, Cs, Gs and Ts—to comb through.

"We have six-and-a-half billion of these letters in each of our cells, so there is a lot of data analysis that goes on, which is why OSC is such a valuable resource," LaFramboise said. "Because we have to store all that data and analyze all that data, we lean heavily on the Cluster."

There are several outcomes possible from LaFramboise's research. The first is a genetic test that could tell people their risk level of developing leukemia. Another is advancements in genetic counseling, so parents can learn the likelihood of their child developing leukemia. A third possibility is that if researchers, LaFramboise and his team, can identify why a certain mutation plays a role in the onset of cancer, drugs might be developed to prevent or treat it. ◀



{LEFT} Thomas LaFramboise, Ph.D., associate professor at Case Western Reserve University, is working toward a way to discover which genetic mutations determine a person's susceptibility to developing leukemia. This image shows the biological rationale for statistical tests. In each case, an inherited susceptibility allele is present in the gene. {RIGHT} Here each point represents a gene, and is plotted according to its chromosomal location (horizontal axis) and statistical significance for carrying inherited mutations that contribute to leukemia susceptibility (vertical axis).

PROJECT LEAD // THOMAS LAFRAMBOISE, PH.D., CASE WESTERN RESERVE UNIVERSITY RESEARCH TITLE // GERMLINE CONTRIBUTORS TO MDS SUCCEPTIBILITY: INTEGRATING CLUES FROM THE MALIGNANT GENOME FUNDING SOURCE // CASE WESTERN RESERVE UNIVERSITY WEBSITE // MENDEL.GENE.CWRU.EDU/LAFRAMBOISELAB