

## Patient Impact Story

# The Gift of Birthdays

A child's first birthday is a big milestone for every family. But for Tammie, it was bittersweet. At almost 12 months of age her daughter Gracie, who was born with Down syndrome, was diagnosed with acute myelogenous leukemia (AML).



It was a Wednesday when Tammie got the devastating news. She was planning little Gracie's birthday party for Saturday when the pediatrician called saying Gracie had an acute form of leukemia and required immediate treatment. "She had her first round of chemo on her birthday," says Tammie who, along with her husband, made a paper hat and a Happy 1st Birthday banner using supplies from the hospital playroom. "Even though it all happened so fast, I made sure Gracie celebrated her first birthday."

AML is an aggressive cancer. Current treatment approaches involve intensive, high dose chemotherapy where patients, like Gracie, must stay in the hospital for numerous months. "Unfortunately, this intensive chemotherapy has long-term side effects like heart damage," says Dr. Berman, one of Canada's top pediatric haematologist/oncologists and researcher with the Centre for Genomics Enhanced Medicine (CGEM).

Currently, Dr. Berman is co-chair of an international clinical trial focused on decreasing the intensity of chemotherapy treatment for children with Down Syndrome AML. He explains, "For the first time, on this protocol, we are adjusting the treatment for each child, reducing the toxicity of the chemotherapy for those who are responding well and giving more aggressive therapy to those who are not responding well." The trial encompasses more than 200 hospitals worldwide, as part of the Children's Oncology Group, and will enroll 256 patients.

Dr. Berman and his team were also the first in Canada to transplant human leukemia cells into zebrafish embryos to test safer, less toxic treatments for AML. "Zebrafish are an excellent model because they are genetically similar to humans," says Dr. Berman. "We can fluorescently label the

transplanted cancer cells, administer chemotherapy drugs just by adding them to the fish water, and use a microscope to literally watch how the cells respond because the zebrafish embryos are transparent."

Compared to mice, zebrafish are considerably less expensive and each female can produce 200 embryos a week, offering researchers significant capacity to screen multiple drugs very quickly. In fact the research team was able to use the zebrafish to pre-clinically demonstrate how certain drugs could limit the long term side-effects of chemotherapy and protect the heart, without impacting the effect of chemotherapy drugs to kill the leukemia cells.

In addition to using the zebrafish model to rapidly screen drugs, Dr. Berman is motivated by its vast potential to identify which genes are important in causing leukemia and which genes are important drug targets for beating leukemia. Understanding which leukemias respond well to which drugs due to the activation of particular genetic pathways and whether a child has a genetic mutation in that pathway will be critical in helping clinicians determine which treatment works best.

*"In the future, we will be able to tailor the therapy to the child based on the responses of their leukemia in the zebrafish to a particular drug," says Dr. Berman.*

After eight months of chemotherapy, Gracie won her battle against cancer. "She's our little warrior princess," says Tammie. At home Gracie is all smiles. She's having fun with her family, making new friends, and determined to make her fourth birthday the best one yet.