The Research Center of Leukemia and Childhood Malignancies

Cancer is the leading cause of death from disease in children. Leukemias and hematopoietic malignancies are the most common types of cancer in children. Although mortality rates for these malignancies have declined significantly, the cure involves intensive and toxic chemotherapy. Our ultimate goal is to cure all children with leukemia and cancer with personalized adjustment of therapy to the severity of the disease and to the molecular genetic abnormalities in the cancer cells. A prerequisite for the achievement of this goal is better understanding of how children get leukemia and what are the differences between normal and cancer cells. This can be realistically achieved by translational research utilizing modern sophisticated genetic and biochemical tools.

Specific research interests:

The role of chromosome 21 in leukemogenesis: Leukemias, like every cancer, are caused by changes in the DNA which include changes in the structure or number of the chromosomes. Extra copy of chromosome 21 is often found in leukemias. Children with Down syndrome have an extra chromosome 21 in their normal cells and have a marked increase in the risk of developing leukemia. We therefore study the leukemias of Down Syndrome with the ultimate goal of identify and characterize abnormalities associated with chromosome 21 leukemias in children. These studies have already lead to important discoveries such as the GATA1 mutations in the myeloid leukemias of Down Syndrome and the cooperation with the chromosome 21 transcription factor ERG in lymphoid leukemias of Down Syndrome and the involvement of JAK2 in the lymphoid leukemias. This discovery may lead to specific therapies of these leukemias. Furthermore, elucidation of the role of trisomy 21 in leukemia may contribute to the general understanding of the role of chromosomal aneuploidy in cancer.

Our research utilizes cutting edge genomic and post-genomics technologies working o both primary human hematopoietic stem cells, primary leukemia cells and mouse models, studying genes, proteins and micro-RNAs.

The Genetic Basis of Brain Metastasis in Leukemia and Solid Tumors: Metastasis to the brain is one of the most devastating complications of cancer and of childhood leukemia. To prevent this complication most children get either irradiation or intra-spinal chemotherapy with long lasting effects on neuropsychological functions. We want to find the factors that determine specific spread of cancer cells to the brain in order to personalize treatment to high risk patients and to provide a base for novel more specific less toxic therapies. To approach this challenging problem we use genomic, cell culture and mouse models. Initial studies identified three genes predicting brain metastasis of lung cancer and that increased expression of interleukin 15 in primary leukemia cells is associated with increased spread to the central nervous system.
SIL (STIL) – a protein regulating mitosis and survival of cancer cells. The SIL (SCL TAL1 Interrupting Locus - STIL) gene was identified because of its involvement in childhood T-ALL. Our studies have revealed a far broader role for SIL. It encodes a cytosolic protein that is important for embryonic development and Hedgehog signaling. Physiologically it regulates the entrance to mitosis. Interestingly it has been recently identified to be mutated in familial microcephaly, a condition is which all the mutated genes encode regulators of mitosis. It is overexpressed in many types of cancers and its silencing by RNA interference technologies results in cancer cell death in-vitro and in-vivo. Our current research aims are to reveal how SIL regulates mitosis and survival and how could it be targeted for cancer therapy.7-13

Clinical studies of childhood acute lymphoblastic leukemia (ALL): Prof Shai Izraeli is the co-chair of the Israel National Study of childhood ALL and the head of the Biology and Diagnosis Committee of the European "BFM" group studying childhood leukemia4,14.

Recent and highly relevant publications