Acute myelogenous leukemia (AML) is the second most frequent leukemia in children and is more difficult to treat than acute lymphoblastic leukemia. Using current strategies, only about half the children diagnosed with AML will be cured. Bone marrow transplantation is an important strategy that can allow cure of AML, but children need to be in near or complete remission for bone marrow transplant to be likely to be successful. Many children are referred with relapsed AML to Cincinnati Children's Hospital, and we urgently wish to have appropriate options for treatment for these children. Chemotherapy can be effective in this circumstance but many of the children who are referred have had prior exposure to a lot of chemotherapy that has been ineffective, or they have damaged a critical organ such as kidneys and heart that will not allow further chemotherapy.

In this trial we plan to use donor cells from mismatched family members, most likely parents, to try and attack the leukemia in a different way. These cells are called cytokine induced memory-like natural killer cells. The first description of the use of this approach was published in the journal Science Translational Medicine in 2016 from the group of Dr. Todd A. Feniger at Washington University School of Medicine (Romee R et al, Sci Transl Med. 2016 September 21; 8(357)). In this study, the authors described the generation of clinical volumes of cytokine induced memory-like NK cells after treatment in the laboratory with proteins including interleukin 12, interleukin 15 and interleukin 18. These cells had enhanced responses to cytokines or activating receptor re-stimulation for weeks to months after this pre-activation. In effect, they were natural killer cells that were primed to hunt down and kill leukemia cells. In studies in the laboratory, these authors found but memory-like NK cell function or responses whether effective against AML cells and did not require high levels of tissue matching. These authors performed a first in human phase I clinical trial in which adults were given memory-like NK cells which proliferated and expanded in the AML patients and demonstrated good responses in their leukemia. Clinical responses were observed in 5 of 9 evaluable patients including 4 complete remissions. This was achieved with essentially no toxicity and was feasible in patient with significant organ impairment. Further personal conversations with Dr. Fehniger have demonstrated that these in a larger group of patients than those published these clinical responses have continued. This treatment is attractive because it will allow us to induce remission in children who are otherwise would be unable to go to transplant and unable to have their leukemia cured. All the techniques necessary for generating clinical grade cell product are available and preliminary work to generate these cells from normal donors is currently ongoing. We anticipate that these cells would serve as a platform to add additional strategies such as check point inhibitors or IL-15 superagonist that would further enhance the therapy of treatment once we have established our ability to generate the cells and give them safely.