

***Engineered human pluripotent stem cells to generate enhanced natural killer cells for cancer therapy***

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Induced pluripotent stem cells (iPSC) are being used to engineer enhanced immune cells for cancer immunotherapies. Natural killer (NK) cells play a key role in tumor immunosurveillance, and unlike T and B cells, these cells kill tumor cells without being restricted to specific antigens.

However, upon the activation of NK cells during their expansion in the clinic for adoptive transfer or in the tumor environment, these cells can downregulate key receptors that diminish their function. The objective of this project is to engineer NK cells so they can be grown to significant numbers in culture for improved function in cancer patients.

We have made considerable progress in the first year of our RMM grant. iPSC have been engineered to generate NK cells that over express the key cell activating receptor CD16a, by preventing its downregulation through a normal proteolytic process mediated by ADAM17. This was accomplished by expressing a mutated version of CD16a as well as gene-targeting ADAM17 in iPSC. In the next phase of our project, we will examine the anticancer activity of our engineered NK cells. Our long-term goal is to generate a renewable source of “super” NK cells to enhance current therapies and the patient’s immune system in killing cancer cells.