Children's Mercy Kansas City

SHARE @ Children's Mercy

Research at Children's Mercy Month 2023

Research at Children's Mercy Month

5-2023

Macrophage Mediated Cancer Cell Targeting

Molly Leyda Children's Mercy Kansas City

Jacqelyn Nemechek Children's Mercy Hospital

John Szarejko Children's Mercy Kansas City

John M. Perry Children's Mercy Hospital

Douglas Myers Children's Mercy Hospital

Let us know how access to this publication benefits you

Follow this and additional works at: https://scholarlyexchange.childrensmercy.org/research_month2023

Recommended Citation

Leyda, Molly; Nemechek, Jacqelyn; Szarejko, John; Perry, John M.; and Myers, Douglas, "Macrophage Mediated Cancer Cell Targeting" (2023). *Research at Children's Mercy Month 2023*. 2. https://scholarlyexchange.childrensmercy.org/research_month2023/2

This Poster is brought to you for free and open access by the Research at Children's Mercy Month at SHARE @ Children's Mercy. It has been accepted for inclusion in Research at Children's Mercy Month 2023 by an authorized administrator of SHARE @ Children's Mercy. For more information, please contact hlsteel@cmh.edu.

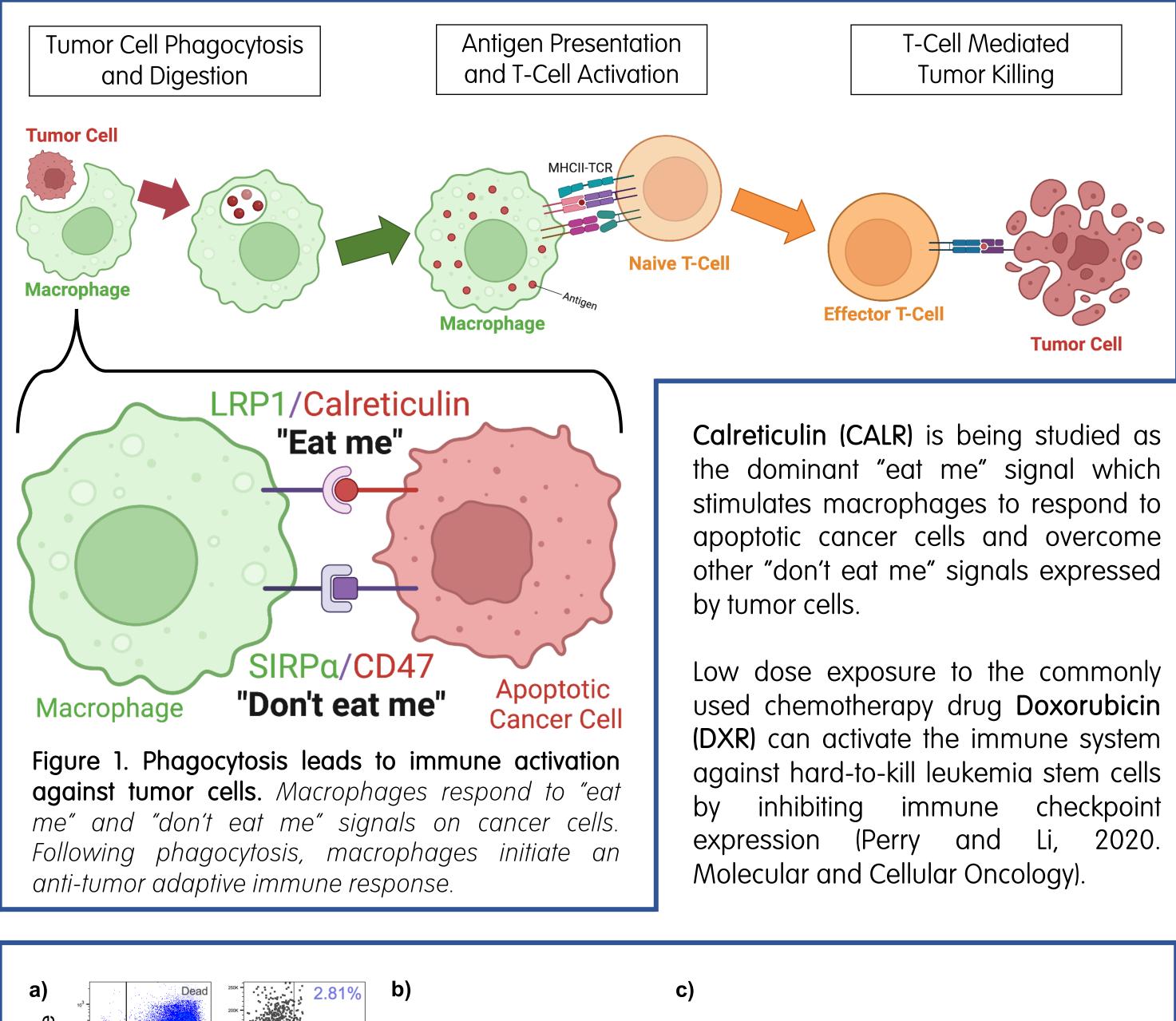
Macrophage Mediated Cancer Cell Targeting

Molly C. Leyda, Jacqelyn Nemechek, John Szarejko, Fang Tao, Tykeem Manor, John Perry, Doug Myers

Children's Mercy Kansas City – Department of Hematology, Oncology, and Blood and Marrow Transplant

BACKGROUND

Macrophages are a diverse and widespread type of innate immune cell which play an important role in homeostasis and defense. In a process called phagocytosis, macrophages engulf dying cells, foreign substances, and pathogens. As professional antigen presenting cells (APCs), macrophages can present antigens from phagocytosed cells and initiate an adaptive immune response against remaining cells of the same type. Despite the immunosuppressive nature of the tumor microenvironment, macrophages have tumor infiltrating abilities where they either promote or inhibit cancer development. Questions remain about how macrophages recognize, or fail to recognize, cancerous cells for clearance, and how they promote vs. inhibit tumor progression.



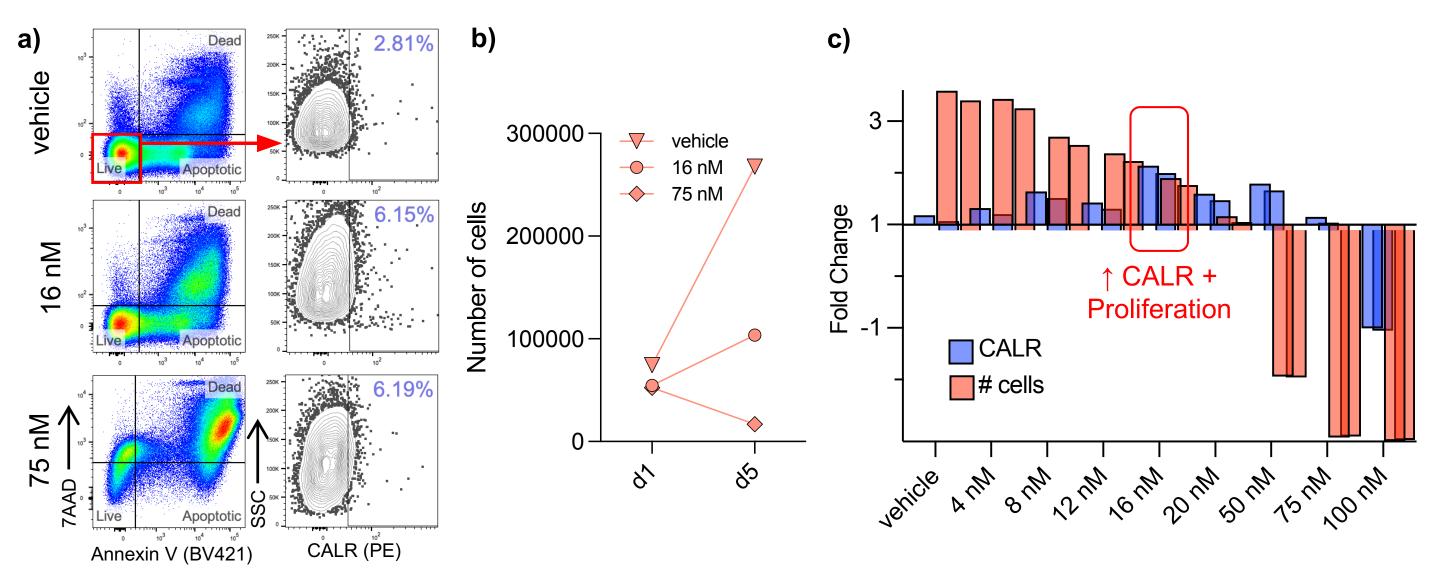


Figure 2. Low dose DXR induces pre-mortem calreticulin expression on Kasumi-1 pediatric leukemia cells. Data from Jackie Nemechek. a) Flow cytometry analysis of calreticulin expression in live cells at representative low and high DXR doses. b) Live cell numbers. c) Fold change of calreticulin expression and cell numbers show that 16 nM induces peak calreticulin expression while still supporting cell growth.



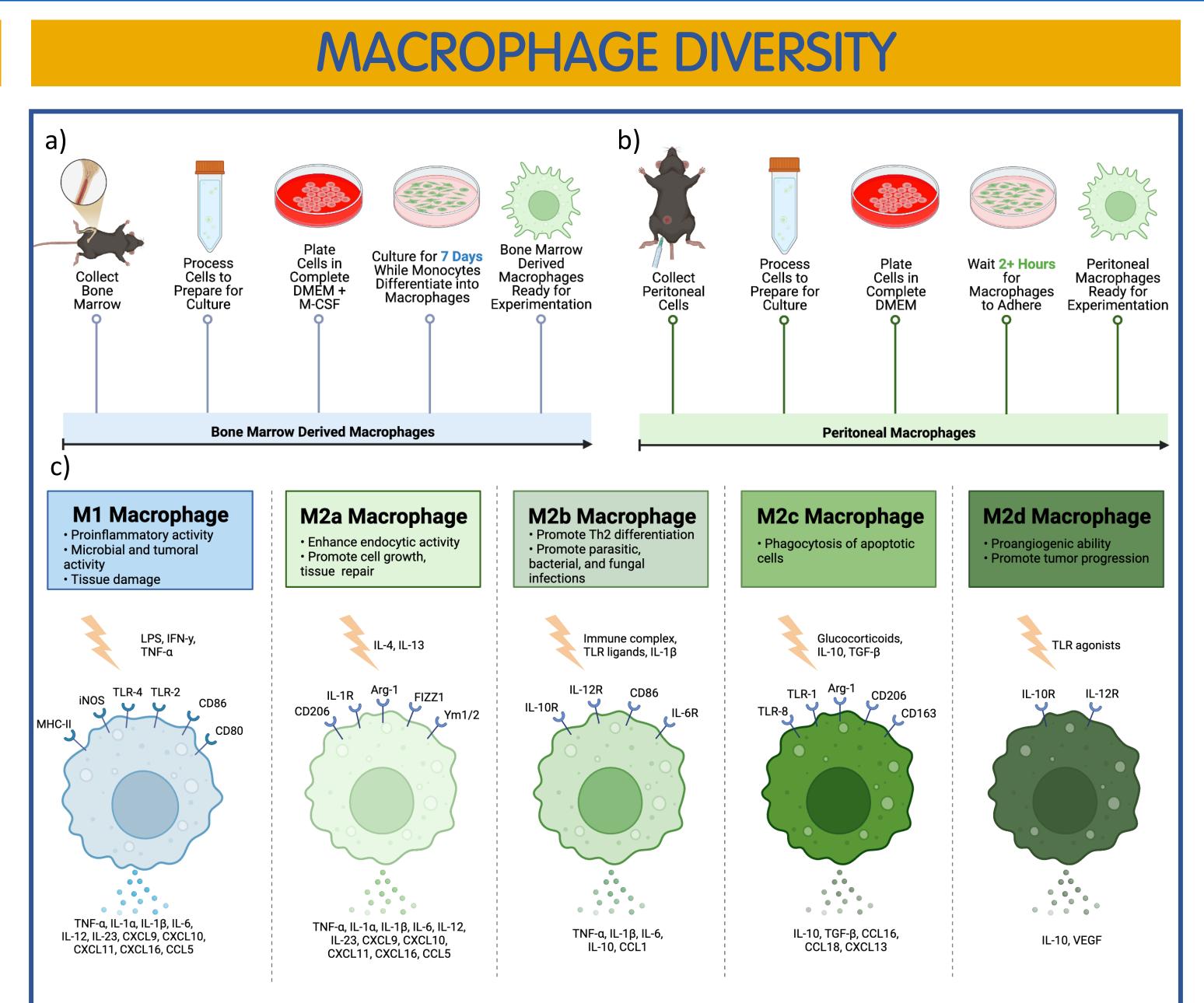
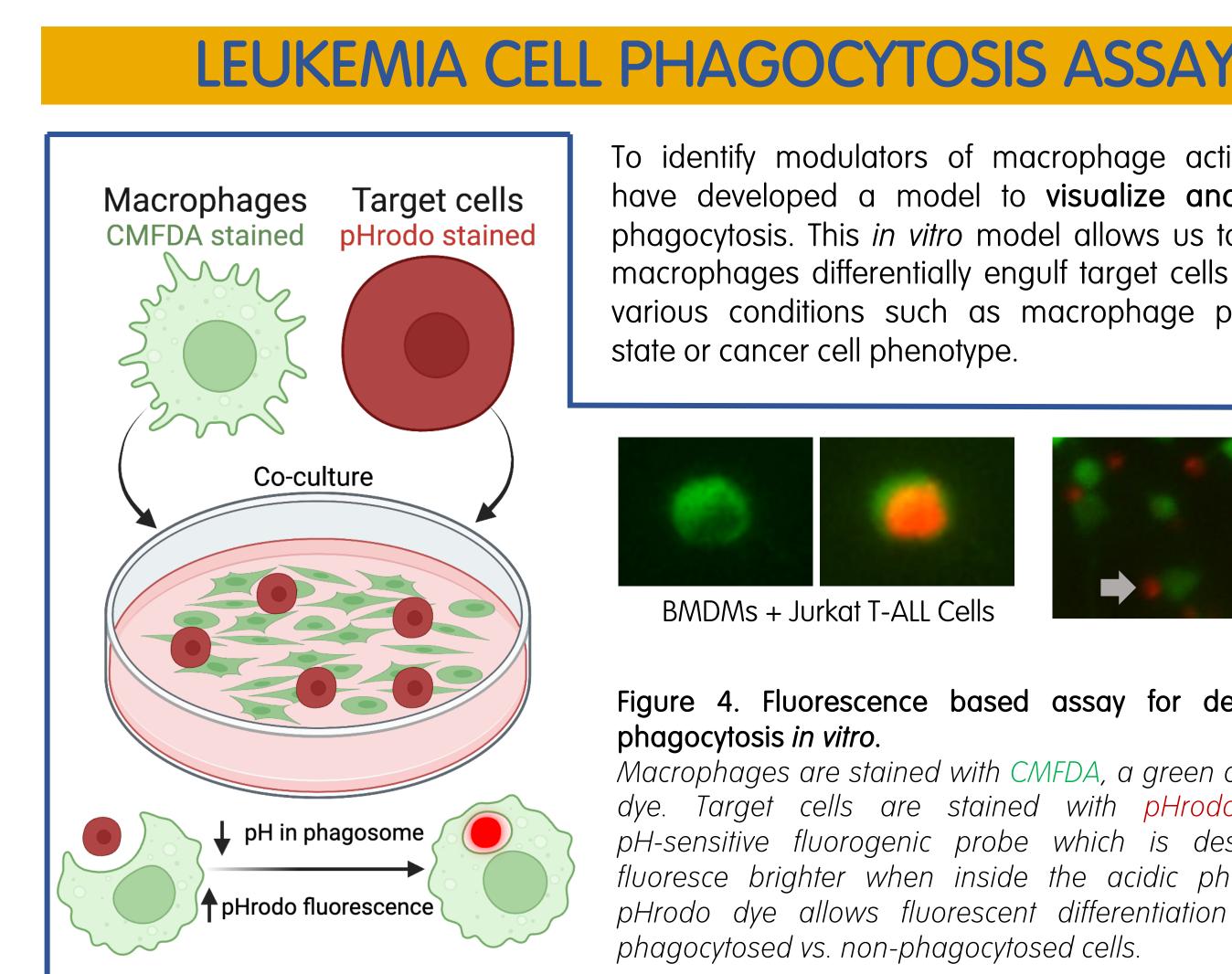
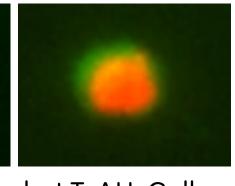


Figure 3. Primary murine macrophages can be differentiated and polarized *in vitro*. a) Bone marrow cells are cultured with macrophage colony stimulating factor (M-CSF) for 7 days while monocytes differentiate into mature bone marrow derived macrophages (BMDMs) which adhere to the plate. b) 2 hours of culturing peritoneal cells allows already mature macrophages to adhere to the plate. c) Macrophages exhibit extreme plasticity in their structure and function based on signals received from their microenvironment. They can be grouped into "polarization states" based on cytokines released and markers expressed. It is important to remember that macrophages are constantly flowing between these states.



To identify modulators of macrophage activation we have developed a model to visualize and quantify phagocytosis. This *in vitro* model allows us to test how macrophages differentially engulf target cells based on various conditions such as macrophage polarization state or cancer cell phenotype.



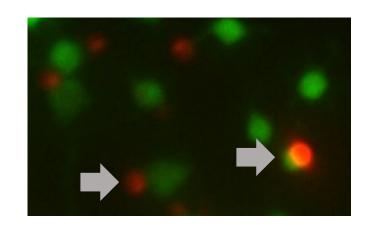
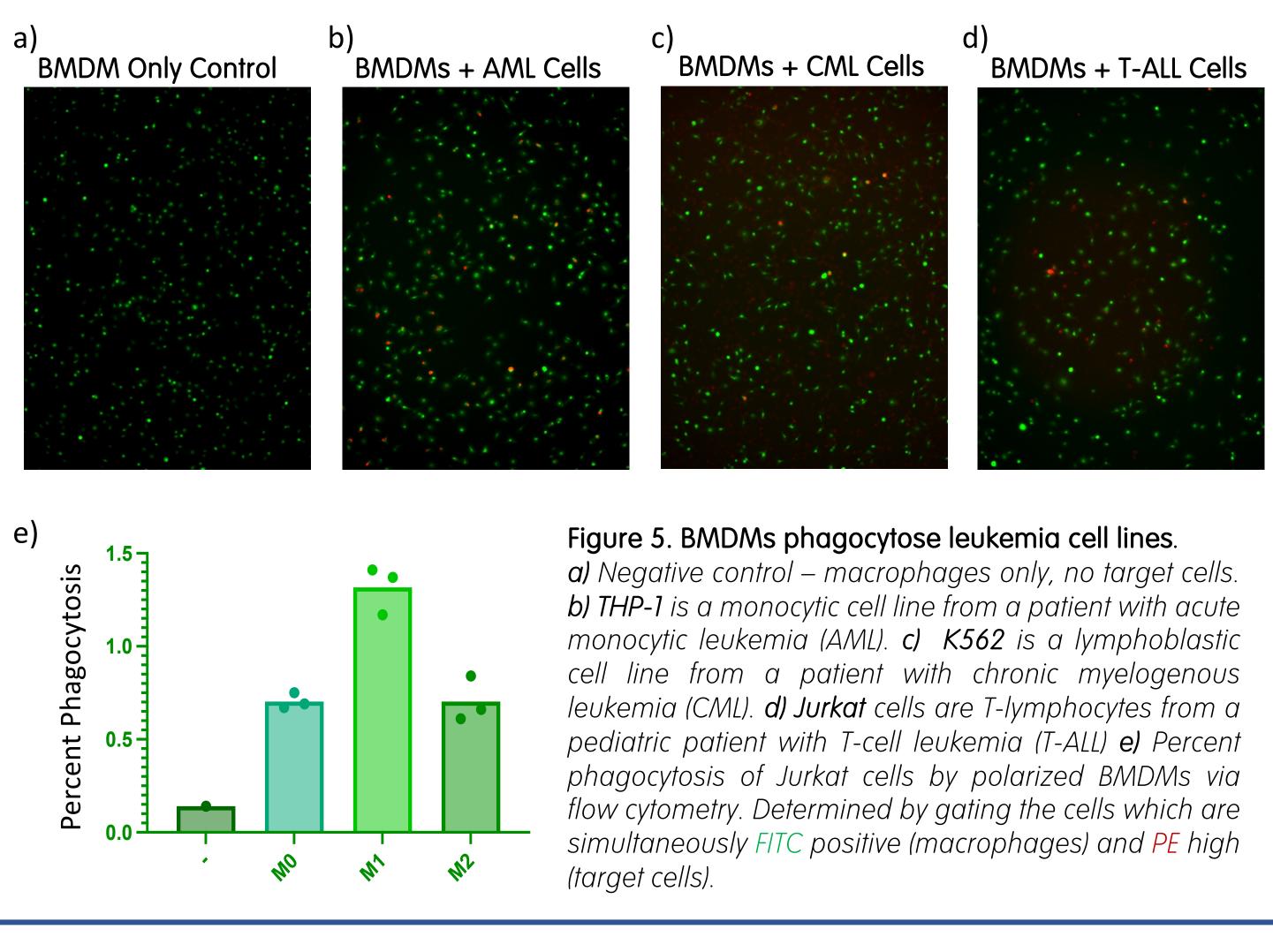
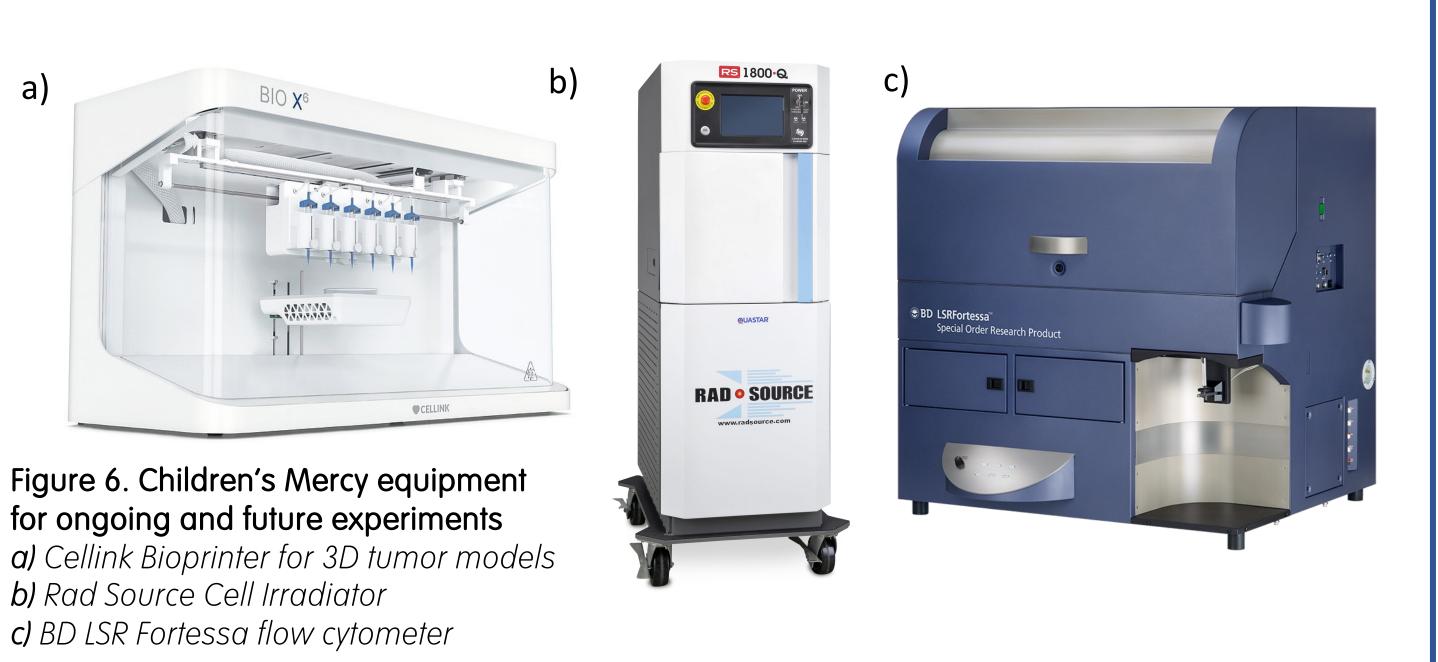


Figure 4. Fluorescence based assay for determining

Macrophages are stained with CMFDA, a green cell tracker dye. Target cells are stained with pHrodo red, a pH-sensitive fluorogenic probe which is designed to fluoresce brighter when inside the acidic phagosome. pHrodo dye allows fluorescent differentiation between phagocytosed vs. non-phagocytosed cells.





b) Rad Source Cell Irradiator *c)* BD LSR Fortessa flow cytometer



ONGOING & FUTURE

Treat target cells with radiation and low dose DXR to examine apoptosis and phagocytosis Induce macrophage polarization and assess effect on phagocytosis capability Assess CALR expression on target cells and the effect on macrophage response Test a CALR-targeting chimeric antigen receptor on macrophages Bioprint 3-dimensional tumor models to test macrophage homing and phagocytosis