Multiple myeloma is the second most common blood cancer in the United States, with more than 96,000 people living with the disease or in remission. It is largely incurable by current standard treatments, and treatment for relapsed patients remains a challenge. Thus new therapeutic interventions are needed to further improve long-term outcomes of multiple myeloma patients.

The Solution

University of Michigan team led by Zaneta Nikolovska-Coleska, M.S., Ph.D., developed a class of potent and selective inhibitors of a protein called Mcl-1 (myeloid cell leukemia 1) which regulates the cell death pathway. These novel inhibitors block the interactions between Mcl-1 and pro-death proteins, and specifically kill multiple myeloma (MM) cell lines. In collaboration with Moshe Talpaz, M.D.; and Luke F. Peterson, M.S., Ph.D., the novel Mcl-1 inhibitors are tested for their in vivo efficacy in multiple myeloma murine models.

Inhibition of Mcl-1 makes cancer cells more susceptible to chemotherapy, and offers significant benefits for patients including eliminating or reducing the frequency of relapse, and improving the quality of life. MM accounts for 10 percent of all blood cancers in the United States.
**Novel Mcl-1 targeted therapy** for multiple myeloma improves the treatment efficacy, prolonged disease control, and patient quality of life.

**Significant Need**
MM remains largely incurable by current standard treatments, particularly in patients with refractory/relapsed disease, and new therapeutic interventions are needed. Recent advances in gene and protein expression studies of MM have shown that one of the factors for developing resistance to chemotherapy by myeloma cells is due to defects in the pathway responsible for “cleaning” old or damaged cells. Mcl-1 protein is one of the proteins that regulate this pathway.

**Compelling Science**
The Mcl-1 protein plays a major role in cell survival and is associated with chemo-resistance in many human cancers including MM. This novel therapeutic approach inhibits the Mcl-1 function and overcomes the cell death resistance. It improves the efficacy, impacts the quality and duration of patient responses to standard therapy while minimizing the toxicity.

**Competitive Advantage**
In addition to treating MM, Mcl-1 has been validated as a potential therapeutic target for other cancers, including acute myeloid leukemia (AML), pancreatic, breast, colon and melanoma.

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**MTRAC Project Key Milestones**

- **Evaluation of Mcl-1 inhibitors in a panel of MM-established cell lines as single agents and their combination with standard treatment of MM**
  - Assess the activity of Mcl-1 inhibitors in MM primary samples, determine the Mcl-1 survival dependency of patient samples and integrate the obtained results

- **Determine the pharmacokinetic profile of the Mcl-1 inhibitors**
  - Evaluate the in vivo efficacy, safety and pharmacodynamics activity profile of Mcl-1 inhibitors in animal models of MM as single agents and in combination

- **Initiate negotiations for licensing the technology from the University of Michigan and prepare applications for extramural-funding opportunities**

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**Overall Commercialization**

- **Commercialization Strategy**
  - Potential U-M spin-out company. Option to license with existing biopharmaceutical company.

- **Regulatory Pathway**
  - Completing critical preclinical data to support licensing with biotech and pharmaceutical companies.

- **Product Launch Strategy**
  - To be determined by licensee.

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**Intellectual Property**

- Patents submitted, including one issued and two provisional, for three classes of Mcl-1 inhibitors.

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**Zaneta Nikolovska-Coleska, M.S., Ph.D.**