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LEADING THE FIGHT AGAINST TRIPLE-NEGATIVE BREAST CANCER

Working to achieve cutting-edge therapies to activate the body's immune response

At the University of Michigan Health Rogel Cancer Center, we are committed to giving people hope for a healthier tomorrow, even when they face a difficult diagnosis. Our doctors and scientists are focused on helping people to survive and experience the best quality of life possible through the most advanced treatments, innovative research, and world-class care. **We are grateful for the support of Think Pink Rocks in our fight against triple-negative breast cancer.**

FACING CHALLENGES

Triple-negative breast cancer (TNBC) is relatively rare and very aggressive, and there are few treatments available. It is referred to as a "cold" tumor because it often goes unnoticed by the body's immune system. This means that people who have TNBC often face a poor prognosis and are unlikely to benefit from immunotherapy, a type of treatment that helps the body's own immune system fight tumors and is often very effective against many other types of cancer.

With the support of Think Pink Rocks, James Moon, Ph.D., the John G. Searle Associate Professor of Pharmaceutical Sciences, is **advancing a new frontier in immunotherapy** that is centered around STING activation, a type of immunotherapy that holds great promise for people who have TNBC. STING (STimulator of INterferon Genes) is a protein in cells that activates the immune system. STING plays an important role in immunity by causing cells to produce type-1 interferon, which protects cells and helps the body fight viruses, certain types of bacteria, and other pathogens. It also helps the immune system to recognize tumor cells.

There are existing therapies called STING agonists that help to activate STING. Though they are an incredible step forward in cancer treatment, conventional STING agonists have several major limitations Dr. Moon is working to address. Conventional STING agonists are usually injected directly into tumors, so they cannot reach cancer that has spread. Administering them by IV infusion does not solve this problem because they degrade so quickly in the body that they do not have time to accumulate in tumors. Conventional STING agonists do not cross the cell membrane, limiting their ability to activate STING. They may also be less effective in some people because of natural variations in STING across the population.

We believe that STING agonists have great potential in the fight against TNBC if we can find ways to overcome these limitations.

CUTTING-EDGE RESEARCH

Funding from Think Pink Rocks is supporting the pioneering work of Dr. Moon to develop the next generation of STING agonists. Dr. Moon's lab focuses on the use of nanotechnology to deliver drugs, and in this case, the goal is for a nanoparticle to deliver STING agonists to cells. With the use of nanoparticles, Dr. Moon is working to achieve a therapy that is potent enough to maximize STING activation and can be administered by IV infusion so it can work throughout the body, rather than just at the injection site.

Dr. Moon is studying the use of nutritional metal ions in STING agonist therapy and discovered that manganese(2+),



James Moon, Ph.D.

“Our nanoparticle system is very effective... we see very strong immune activation in tumor tissues. We think this therapy is killing and eliminating tumor cells.” — James Moon, Ph.D.

an ionized form of manganese, increases the activity of four different conventional STING agonists **up to 77 times**.

Dr. Moon and his team mix Manganese(2+) with various STING agonists to create nanocrystals. They then stabilize the nanocrystals by coating them with a type of lipid. “Nanoparticles are now widely used in medicine,” says Dr. Moon. “One example is the COVID vaccine. They are very safe because the lipids that are used to coat them are very similar to those that are in our cell membranes.” The coated nanocrystals created by Dr. Moon’s team are called CDN-Manganese Particles (CMP). The CMP are stable enough to be administered by IV and their lipid coating enables them to cross the cell membrane, **an incredible achievement in TNBC research**.

ADVANCING NEW TREATMENTS

CMP has outperformed other STING agonists in living models and may prove to be a breakthrough in TNBC therapy and research. “Our nanoparticle system is very effective in living models with triple-negative breast cancer. They are living longer, and we see very strong immune activation in tumor tissues. We think this therapy is killing and eliminating tumor cells,” says Dr. Moon. “Once we understand how the drug is working in living models, we can make further improvements to the efficacy of the nanoparticles and then move the therapy to the clinical setting.”

Dr. Moon’s groundbreaking work with CMP could be a game changer for people with TNBC by opening the door to an entirely new world of safe, effective, and widely-applicable

treatment options. The generosity of Think Pink Rocks “is allowing us to further develop our nascent technology to improve immunotherapy and benefit patient outcomes in the future,” says Dr. Moon. We look forward to seeing how this work progresses over the project period and updating you on our milestones and achievements.



WITH GRATITUDE

Thank you for your generosity, steadfast support, and leadership in the fight against TNBC. You are helping us to pursue the development of incredible and promising new treatments that may revolutionize the future of TNBC treatment and save lives. We could not do our work without you.

For more information, please contact the Michigan Medicine Office of Development:
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