

## Lay Abstract

### *Mesenchymal stem cells as platinum nanoparticle delivery system for metastatic breast cancer treatment*

Breast cancer is the second most common cause of cancer deaths among women. The initial tumor is not the main cause of mortality, but rather it is when breast cancer has metastasized to other organs, particularly the brain, that breast cancer becomes deadly. Metastatic breast cancer in the brain is difficult to treat as common chemotherapy drugs are not able to efficiently pass the blood-brain barrier to treat the tumor. Treatments for metastatic breast cancer are often aggressive and can lead to decreased quality of life for the patient, with many patients needing to abort chemotherapy due to complications arising from its side effects, thus contributing to mortality. Human mesenchymal stem cells (hMSCs), multipotent cells that can be obtained from various human tissues, have the ability to pass the blood brain barrier and are also capable of homing to areas of inflammation, such as brain metastasis. They also can both uptake and release nanoparticles. Platinum (Pt) nanoparticles (NPs) are a novel potential treatment option due to their demonstrated efficacy as a cancer treatment along with selectivity towards cancer cells, resulting in less toxicity to the patient. Using hMSCs as a delivery vehicle to transport Pt NPs to the brain will provide a low toxicity treatment that holds promise to not only improve the survival rate for metastatic breast cancer patients, but also improve the quality of life of patients undergoing treatment.

This proposal will focus on an aggressive triple negative breast cancer that is likely to metastasize and for which there currently are no targeted treatments. Preliminary studies with Pt NPs and triple negative breast cancer cells show a remarkable anti-cancer effect while remaining nontoxic to healthy cells at the same doses. Additionally, preliminary studies demonstrated the hMSCs are able to uptake and release Pt NPs, killing breast cancer cells while remaining non-toxic to the hMSCs. This proposal will build on this preliminary work, optimizing the delivery of Pt NPs by hMSCs by adjusting the initial uptake of Pt NPs and timing of release for optimal triple negative breast cancer cell death while remaining nontoxic to healthy cells. Finally, the Pt NP loaded hMSC's will be administered to a mouse model with triple negative breast cancer metastasized to the brain to determine the efficacy and toxicity of the hMSC delivered Pt NPs.

This research addresses the overarching challenge of revolutionizing treatment regimens by replacing them with ones that are more effective, less toxic, and impact survival. Through the combination of the cancer homing and brain penetrating properties of the hMSCs and the selectivity of the Pt NPs for the cancer cells with limited toxicity to healthy cells, this treatment for metastatic breast cancer will revolutionize treatments for metastatic breast cancer in the brain, directly impacting survival. This research also addresses the overarching challenge of eliminating the mortality associated with metastatic breast cancer because the proposed hMSC delivered Pt NPs will have less side effects than the traditional chemotherapy drugs currently used to treat metastatic breast cancer. The side of effects of traditional chemotherapy can force patients to stop treatment, directly increasing mortality. By offering a treatment with less toxicity to healthy cells, these patients can continue treatment.

Successful completion of the proposed work will lead to clinical trials of this novel treatment. Pt NPs delivered in hMSCs can directly improve the lives of patients living with metastatic breast cancer, enabling a less toxic treatment option for those that are unable to continue current treatments due to the debilitating side effects of the common chemotherapeutics.