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Public/Lay Abstract

The use of immunotherapy has changed the face of patient care for many cancers. Unfortunately, robust, long-term responses to immunotherapy are not being observed in metastatic breast cancer (MBC). Recent studies from our lab and others suggest that this is because several metastatic sites of breast cancer such as the lungs lack the immune cells that are required for immunotherapy to induce a strong anti-tumor response. We have recently developed a drug that is capable of blocking the function of a critical factor require for the growth MBC cells. Through these studies we have discovered that this drug not only directly inhibits the growth of the tumor cells, but when administered to animals it also results in increased recruitment of immune cells into existing metastatic tumors. This effect is described as turning these metastases from being "immune cold" to "immune hot." Increasing immune cell presence in metastases was an important first step, but tumor cells also have several mechanisms to prevent immune cells from eliminating them. Therefore, the present study seeks to combine our growth inhibitory drug with currently approved immune therapies that are known to be highly effective in activating immune cells to eliminate tumor cells (*i.e.* alemtuzumab). We think that with the proper immune cells recruited into metastatic lesions the use of immune therapies will now be highly effective reducing established metastatic lesions. The combination of two involves several issues that must be completely understood about both drugs to when and how much of either drug should be given. Therefore, the studies proposed here seek to achieve this understanding and will include conducting preclinical drug combination experiments using several metastatic model systems.

To accomplish these goals and develop new and effective therapies for MBC patients we have assembled a team of investigators consisting of Dr. Wendt who has a long-standing expertise in metastatic breast cancer research, Dr. Lim who has recently made major contributions to our understanding of how immune therapies work and how to better target tumor cells with this approach, and Dr. Zhang who is a medicinal chemist that has developed the immune recruiting compounds under investigation. This newly formed team constitutes the initiation of the immuno-oncology program within the Purdue Institute of Drug Discovery (PIDD). The PIDD and this developing program are fully backed by Purdue University and has the necessary infrastructure, equipment, and personnel support to drive the next generation of immune related therapies. With Dr. Wendt among the leadership a major focus of this program will continue to be MBC.