Megan J. Priestley, PhD

MIT – Koch Institute for Integrative Cancer Research

Abstract:

Despite effectiveness in other tumours, immunotherapy has limited efficacy in the treatment of breast cancer. Breast tumours are one of the most common cancers in women and are a leading cause of cancer-associated mortality. Thus, there is a pressing need for the development of new treatments to expand the number of breast cancer patients who can benefit from immunotherapy.

One way in which cancer cells resist immunotherapy is by upregulating the expression of sugars known as 'glycans' on their cell surfaces. Altered glycans on cancer cells can engage inhibitory receptors on the surface of immune cells, supressing immune activation and allowing the tumour to evade the immune response. A key example are sialic acids which are universally overexpressed across diverse cancer types and are associated with enhanced tumour aggressiveness. Their receptors, 'Siglecs', are expressed by every immune cell type and when activated can suppress immune responses. Siglecs-7, -9 and -10 are heavily associated with breast cancer pathogenesis, and Siglecs-7 and -9 have been shown to restrict the response to PD-1 therapy. These 'glyco-immune checkpoints' have emerged as prominent mechanisms of immune evasion and therapeutic resistance in cancer, however there are currently no approved cancer immunotherapies that target glycans.

The aim of this project is to develop a new class of glycan-targeted cancer immunotherapies as treatments for breast cancer. Antibody-lectin (AbLec) chimeras were developed in the lab as bispecific antibody-like molecules comprising a tumour-targeting arm as well as a lectin binding domain that binds tumour glycans. We have shown that AbLecs block the ability of tumour glycans to engage lectin receptors on immune cells, therefore reducing their immunosuppressive effects. In this proposal, we will develop multiple classes of AbLecs targeted against known immune-suppressive cell subsets in breast cancer and test their efficacy as single agent and combination therapy in models of the disease. We anticipate this work will validate glyco-immune checkpoint blockade as a new modality of immunotherapy for breast cancer that promises to benefit patients ineligible for or refractory to existing treatments.

Biography:

Dr Priestley is a post-doctoral fellow at the Koch Institute for Integrative Cancer Research at MIT. She received her undergraduate and master's degrees in Biomedical Sciences at the University of Manchester (UK). During her PhD at the University Manchester, she studied the role of glycans on immune cell migration. With Prof Jessica Stark, her current work aims to establish new treatments for breast cancers by targeting glycans on the surface of cancer cells.

Her goal is to develop our understanding of the role of glycans in modulating the immune response during breast cancer, with the aim of harnessing these systems to provide novel treatments for the disease.