

Susan G. Komen

Research Grants – Fiscal Year 2015

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Targeting CDK8 to overcome resistance to targeted therapies in breast cancer

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Lead Organization: University of Chicago

Grant Mechanism: PDF Basic and Translational

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Public Abstract:

Metastases are the cause of most human breast cancer deaths. The overall 5-year survival rate for breast cancer has improved to 89% today, whereas the 5-year survival rate for patients with distant metastatic breast cancer is still lower than 25%. Although conventional treatments such as surgery, chemotherapy, and radiotherapy can generally control primary tumor growth, recurrent and metastatic breast tumors are often inaccessible or resistant to these treatments.

To overcome this challenge, cancer immunotherapy using the adaptive immune system has been extensively studied. With advances in cancer immunology and development of antibodies, various immunotherapeutic antibodies are currently used to systemically treat metastatic breast cancers. Although the antibody treatment can shrink tumors and slow cancer growth, tumor recurrence and metastasis persist in most patients despite the treatment. The therapeutic limitations of the antibodies for metastatic breast cancer are mainly attributed to low tumor-targeted delivery efficacy and insufficient anti-cancer immune response. Moreover, “off-target” effects of the antibody can cause severe side effects, such as autoimmune disorders. To improve current antibody immunotherapy, a clinically-viable approach for efficiently guiding the antibody to targeted tumors and inducing anti-cancer immunity is necessary.

In this proposed research, radiation will be utilized not only as a guide for delivering antibodies to the targeted tumor but also as an immune modulator for enhancing immunotherapy against breast tumor metastasis. Our research will open new opportunities for treating recurrent and metastatic breast cancer by the combination of antibody immunotherapy with radiation therapy. Our research will also provide new knowledge about the mechanism of inducing adaptive anti-tumor immunity, which will be useful for development of novel immunotherapeutic interventions. Furthermore, using FDA-approved

immunotherapeutic antibodies and current radiation therapy systems, our method will be directly applied to advanced breast cancer patients through a clinical trial program at the University of Chicago. Success in the clinical trials will reduce mortality due to breast cancer recurrence and metastasis.