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# Targeting energy metabolism in breast cancer: Implications for cancer immunotherapy

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The ability to evade immune surveillance is one of the hallmarks of cancer. Cleavage or shedding of the surface antigen, MHC class I chain-related (MIC) protein (A/ B) has been known as one of mechanisms by which cancer cells escape immune-detection. Thus any strategy to augment the surface expression of MICA/B could facilitate anticancer immune response. Here, we demonstrate that perturbation of energy metabolism by the glycolytic inhibitor, 3-bromopyruvate (3-BrPA) augments the surface expression of MICA/B in human breast cancer cell lines, MDA-MB-231 and T47D. Data from in vitro studies showed that a non-toxic, low-dose of 3-BrPA is sufficient to perturb energy metabolism as evident by the activation of p-AMPK, p-AKT and p-PI3K. Further, 3-BrPA-treatment also elevated the levels of MICA/B in human breast cancer cell lines. Significantly, 3-BrPA-dependent increase in MICA/B levels also enhanced cancer cell's sensitivity to NK-92MI-mediated cytotoxicity. In vivo, 3-BrPA-pretreated cells demonstrated greater sensitivity to NK-92MI therapy than their respective controls. The antitumor effect was confirmed by a reduction in tumor size and decreased tumor viability as evident by bioluminescence imaging. Hematoxylin & eosin, and TUNEL staining demonstrated that NK-92MI administration promoted apoptosis in 3-BrPA-pretreated cells. Taken together, our data show that targeting energy metabolism could be a novel strategy to enhance the effectiveness of anticancer immunotherapeutics.

## Biography

Shanmugasundaram Ganapathy-Kanniappan obtained his PhD degree from the University of Madras and underwent Postdoctoral training at premier institutes such as National Institute of Immunology (NII), New Delhi, University of California at Los Angeles (UCLA) and Johns Hopkins University. Currently, he is an Assistant Professor at the Johns Hopkins University School of Medicine. He has several publications in reputed journals and has written many reviews and a book chapter on cancer metabolism and therapeutic opportunities.

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