TREATMENT WITH SMALL MOLECULE NSC243928 IN MOUSE MAMMARY TUMOR MODEL INDUCES CHANGE IN TUMOR MICROENVIRONMENT ASSOCIATED WITH ANTI-TUMOR IMMUNE RESPONSES

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Background: Previously, we identified that NSC243928 induces cell death in triple negative breast cancer cells in a LY6K dependent manner. NSC243928 has been reported as an anti-cancer agent in NCI small molecule library. The molecular mechanism of NSC243928 as an anti-cancer agent in the treatment on tumor growth in the syngeneic mice model is not established. With the success of immunotherapies, novel drugs which may elicit an anti-tumor immune response in addition to effecting cancer cell death are of high interest for developing novel drugs to treat solid cancer.

Methods: We focused on studying if NSC243928 may elicit an anti-tumor immune response in the in vivo mammary tumor models of 4T1 and E0771.

Results: We observed that treatment with NSC243928 induced in vivo tumor mass reductions. The bulk RNA seq analysis of tumor isograft samples showed that NSC243928 generates anti-tumor immune responses in both models. NSC243928 induced cell surface calreticulin expression, indicative of immunogenic cell death in both tumor cell lines at the micromolar concentrations. NSC243928 treatment led to reduced MDSCs in the peripheral blood and increased levels of intra-tumoral immune cells namely- patrolling monocytes and MHC II positive tumor associated macrophages in both mouse models. We observed that NSC243928 showed intra-tumoral immune response such as increased NKT cells, decreased PMN-MDSCs and increased B1 cells in the E0771 mouse model.

Conclusions: Taken together we conclude that NSC243928 induces a superior immune response in the E0771 mouse mammary tumor model. Further studies are required to understand the link of NSC243928 associated anti-tumor immune response to determine the adequate molecular signature associated NSC243928 efficacy could be identified, which will be beneficial to future drug development.

Acknowledgements: NIH, NCI, R01 CA227694.
   DOD, USUHS, VPR-NFP-74-9824.
   NIH, NCI, R21 CA256424.
   Biomedical Instrumentation Center, USUHS.
   The American Genome Center, USUHS.
   National Cancer Institute, National Institute of Health.

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