Background The unique ability of DCs to capture, process, and present antigens to the T-cells makes them attractive candidates for developing vaccines. Multiple strategies have been used to design an effective therapeutic DC-based vaccine such as

- Ex-vivo loading of DCs with immunogenic tumor antigens.
- Genetic modification of DCs for enhanced antigen presentation.
- Delivery in combination with immune checkpoint inhibitors.

Although promising, none of the strategies have shown substantial benefits. One major obstacle to overcome is immune suppression by tumor-derived factors. Studies show that the cellular lipid pool gets altered during cancer progression and cancer cells tend to make saturated and monounsaturated lipids. Intracellular accumulation of these lipids has been reported to interfere with DC function. Therefore, cancer-specific changes in the cellular lipid pool can affect the outcome of DC cancer vaccine therapy.

Methods Mouse model: We utilized C57Bl/6 mice expressing the C. elegans FAT-1 gene encoding a desaturase enzyme that converts omega 6(n6) to omega 3(n3) fatty acids. Hence, they have high n-3 fatty acids.

DC generation: Bone marrow cells derived either from WT or FAT-1 mice were cultured in cRPMI media in the presence of GM-CSF for 7 days. DCs were matured with LPS and pulsed with tumor-specific antigen overnight followed by their intradermal injection in tumor-bearing WT mice.

Tumor models: We utilized the B16F10 and TC-1 models to assess the effect of the DC vaccines derived from FAT-1 and WT animals on reducing tumor growth in WT animals.

Antigen presentation assay: We utilized CD8 T cells from PMEL-1 mice, in a co-culture assay with hgp100 pulsed DCs derived from either FAT-1 or WT animals to test the cross-presentation ability of DCs.

Results Animals vaccinated with DCs derived from FAT-1 mice showed a significant decrease in tumor growth, improved survival, and decreased cachexia compared to the animals vaccinated with WT DCs. In addition, we observed increased vaccine-specific responses in both tumor-bearing and naïve WT animals when they received the FAT-1 DC vaccine. Additionally, the antigen presentation assay showed an increased IFNγ production by the T cells when co-cultured with FAT-1 DCs.

Conclusions Our data suggests that FAT-1 DCs are significantly better than the WT DCs at cross-presentation. This can be attributed to the increased omega-3 levels and has translational potential in immune modulation and in enhancing cancer vaccine therapy.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1147-I