Intratumoral plasmid IL-12 expands CD8+ T cells and induces a clinically validated CXCR3 signature in triple-negative breast cancer

Erika J. Crosby1, Hiroshi Nagata1, Melinda L. Tell1, Chaitanya R. Acharya1, Irene Wapnir1, Kaitlin Zablotsky1, Bernard A. Fox1, Carlo B. Bilulco1, Shawn M. Jensen1, Carmen Ballesteros-Merino1, Erica Browning1, Reneta Hermiz2, Lauren Svenson2, Donna Bannavvan1, Kellie Malloy Foerster1, David A. Canton1, Chris G. Twitty1, Takuya Osada3, H. Kim Lyerly4,5

1-Duke University Medical Center, Department of Surgery, Durham, NC; 2-Stanford University School of Medicine, Departments of Medicine & Surgery; 3-Stanford, CA; 4-Earls A. Chiles Research Institute, Providence Portland Medical Center, Portland, OR; 5-Oncotec Medical Incorporated, San Diego, CA; 6-Duke University Medical Center, Departments of Pathology & Immunology

Background

- Sustained disease control and prolonged survival in patients with triple-negative breast cancer (TNBC) is uncommon, highlighting the need for improved immune-based strategies particularly in poorly immunogenic tumors
- Interleukin-12 (IL-12) is involved in the generation of adaptive immune responses, an inflammatory tumor microenvironment and is critical in eliciting a productive anti-tumor immune response1
- Intratumoral injection of plasmid IL-12 (bavencogene telseplasmid; TAVO) followed by electroporation (EP) (TAVO-EP) is a gene therapy approach that drives local and immunologically relevant exposure of IL-12 with minimal systemic immune-related toxicity1,2
- CXCL9/10/11/CXCR3 axis regulates the migration, differentiation, and activation of both innate and adaptive immune cells3,4

Methods

- Murine TNBC (ATC) cells were orthotopically implanted into mice and allowed to establish prior to treatment with TAVO or control plasmid
- On Days 0, 4, and 7, the mice underwent IT administration of plasmid followed by in vivo electroporation
- Tumors were digested and CD45+ cells sorted from tumors and classified into cell types for all samples or divided by treatment groups
- Each cell type was classified in a UMAP plot of CD45+ E.
- (on day 0 Upper graph: treated tumors. Bottom graph: untreated tumors.
- Error bars represent mean ± SEM **p<0.01.
- Intratumoral TAVO administration. Tumor volumes were normalized to size at treatment initiation.
- Survival of mice in (B) (top) and comparison of activity scores (activity signature) (bottom) across untreated and treated tumors.
- Significance values are indicated by *p<0.05; **p<0.01; ***p<0.001.
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Results

Figure 1. TAVO treatment inhibits tumor growth and enhances immune cell infiltration

A. Tumor volumes. When the tumor size reached 6.7 mm in diameter, mice were randomized into two groups (A) and received intratumoral injections of plasmid following by in vivo electroporation as indicated. B. Kaplan-Meier survival curve depicting survival in TAVO treated tumors. (n=13) and control tumors (n=14).

Figure 2. Expansion and activation of T cell in TAVO treated tumors

A. T cell expansion. (top) Bar graph depicting expansion of T cells treated with TAVO compared to untreated controls.