Development of a Lung Cancer Vaccine using Embryonic Stem Cells

Kavitha Yaddanapudi, PhD
Assistant Professor
Department of Medicine
University of Louisville

Presenter Disclosure Information

No Relationships to Disclose

Vaccination against Cancer with Embryonic Material

Concept of this Study

Animals or humans immunized with embryonic material may be capable of recognizing and destroying neoplastic cells.

Embryonic Stem Cells and Cancer Stem Cells

Oct-4, Nanog, Sca-1 and Bmi-1: Expressed in embryonic stem/progenitor cell and cancer-initiating stem cells (CICs).

Hypothesis

Vaccination with Embryonic Stem Cells (ESC) induces immune response that can target the cancer stem cells present in the tumor and thus can control the tumor growth.

Embryonic Stem Cells as a Vaccine against Lung Cancer

A Undifferentiated murine ESC (ES-D3 cells)

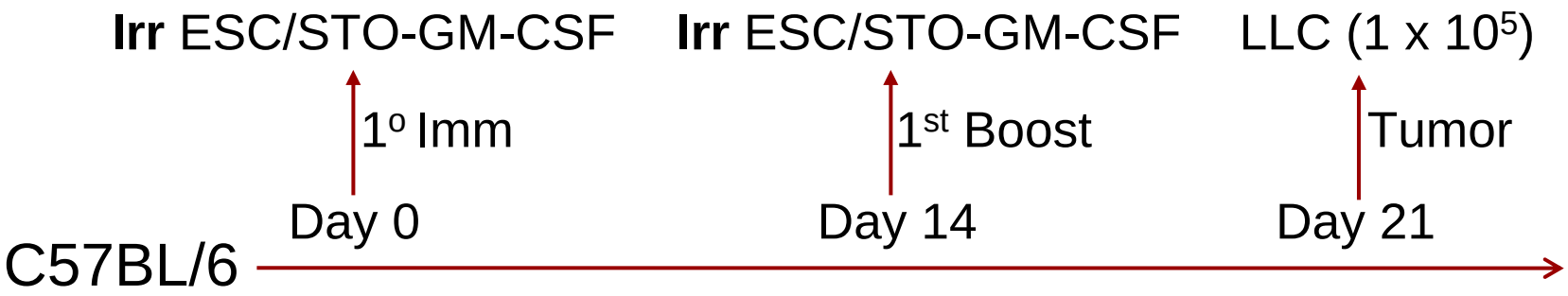
+

Fibroblasts Expressing GM-CSF (STO/GM)

I

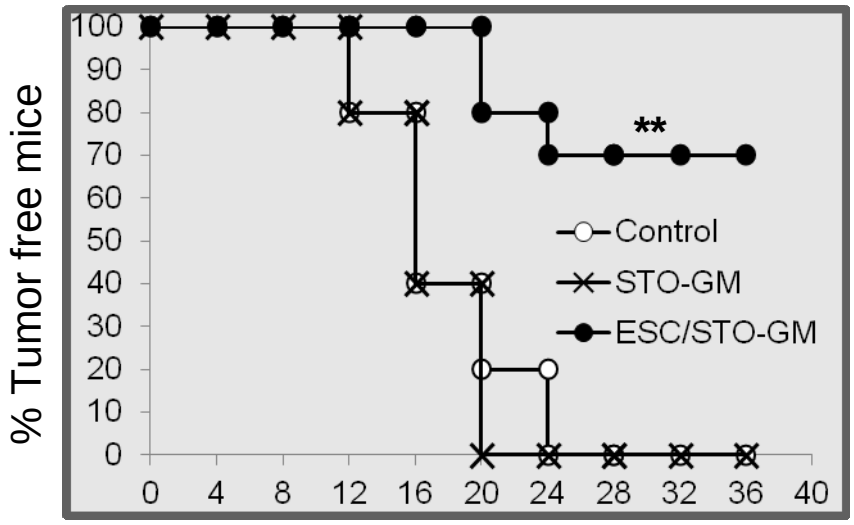
γ- Irradiation at 15 Gy

B



ESC vaccination prevents the outgrowth of an implanted lung adenocarcinoma

A



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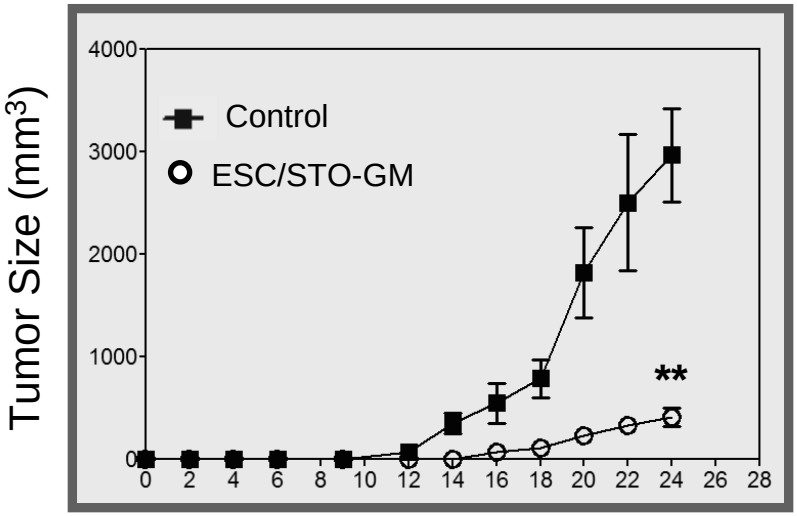
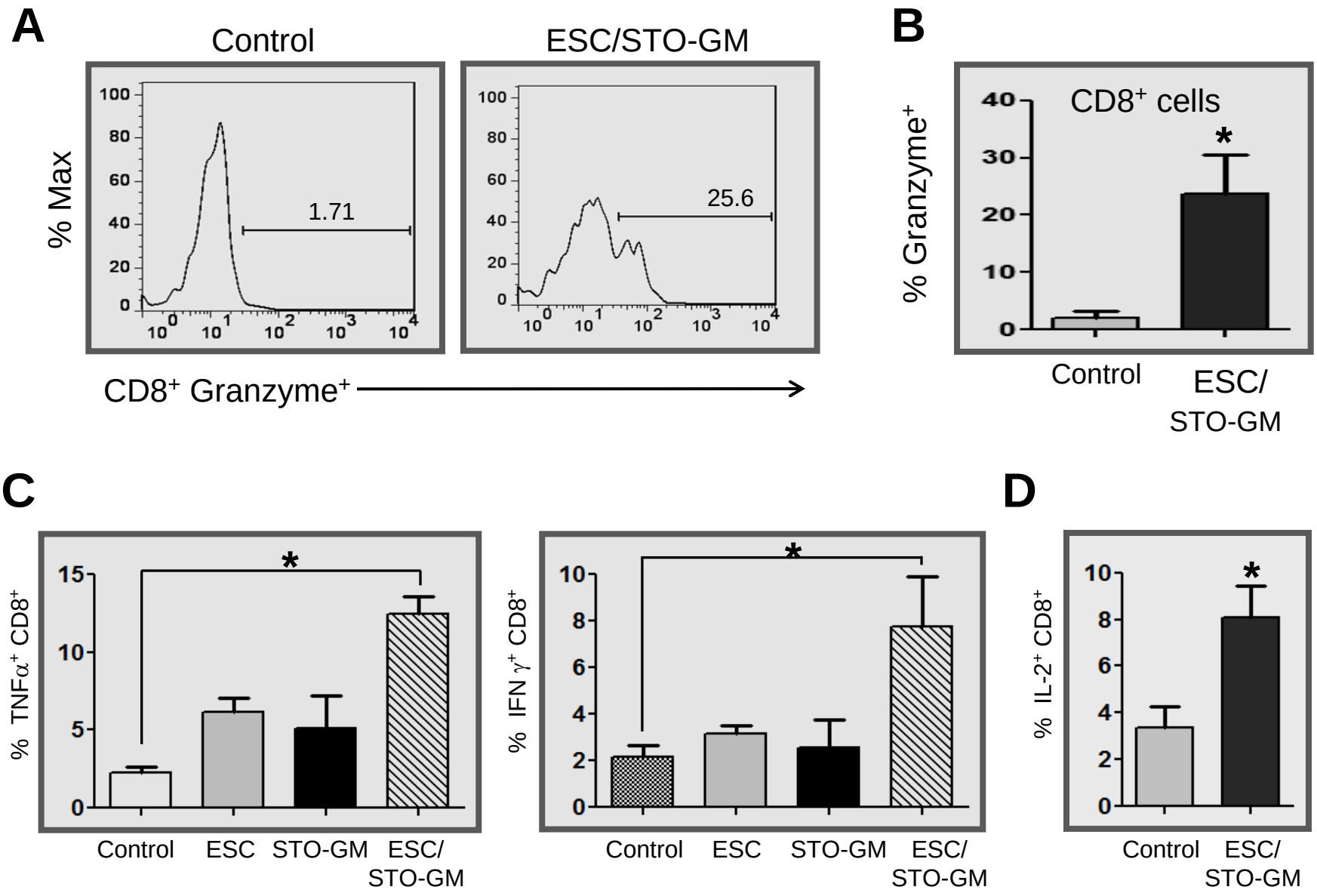
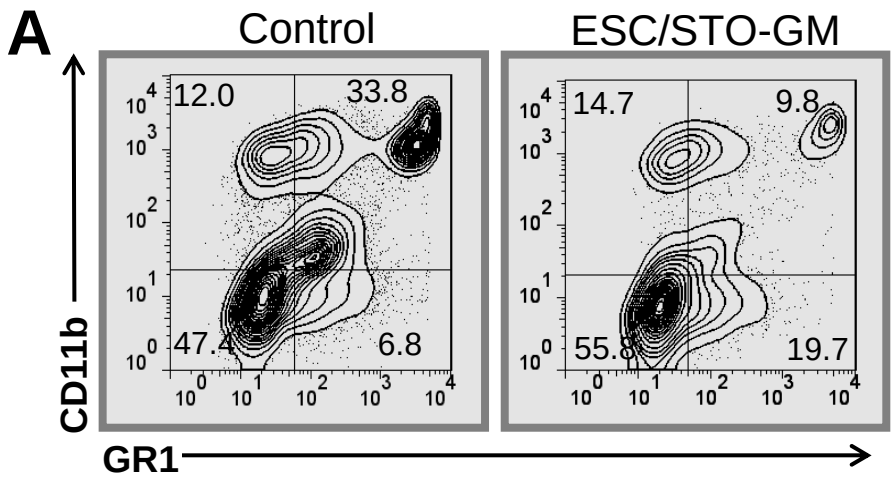
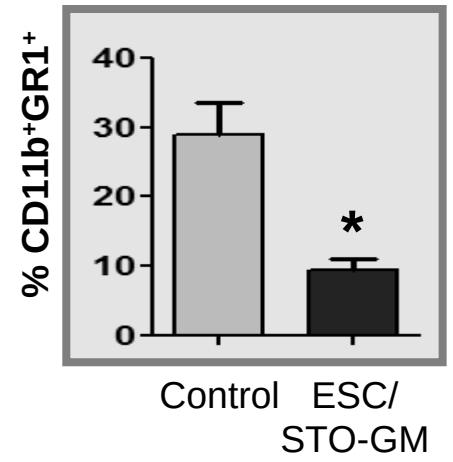


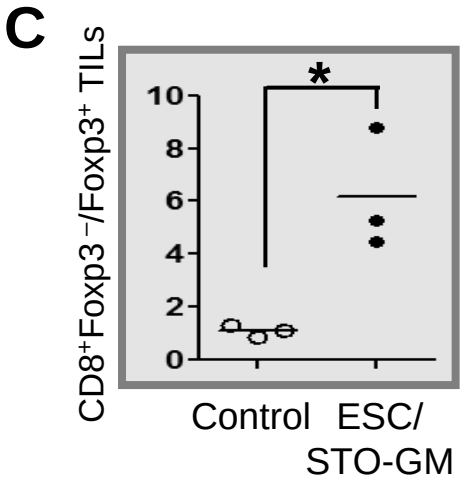
ESC vaccination induces CD8+ T cell-mediated effector responses

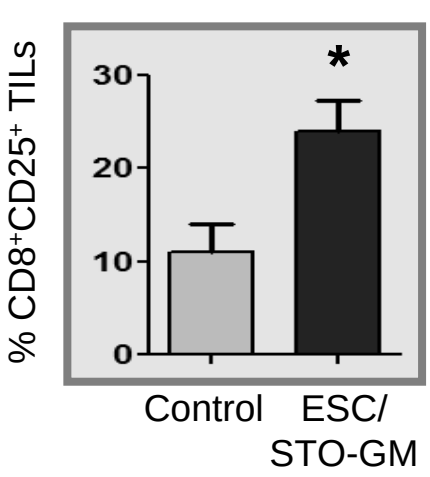


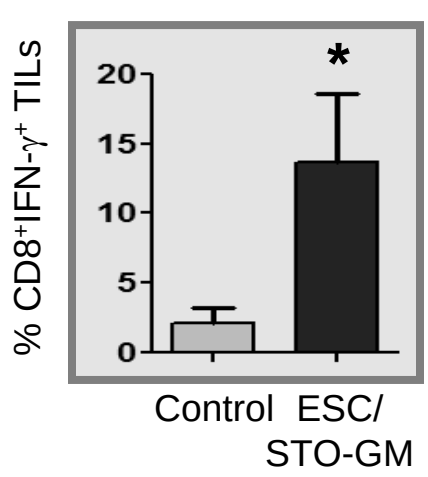
ESC vaccination reduces MDSCs and increases the ratio of CD8$^+$ T cells to T_{regs} in the tumor



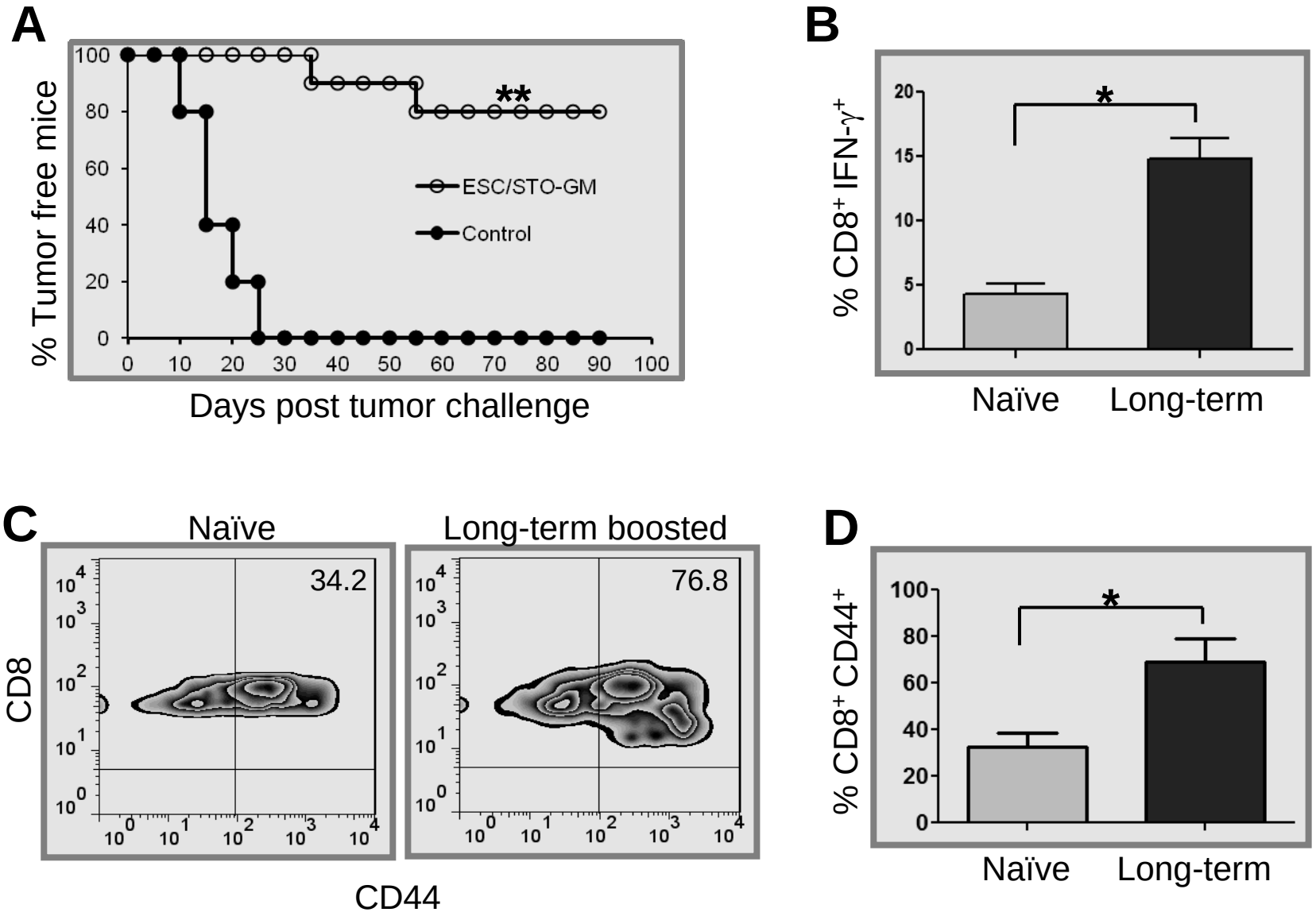




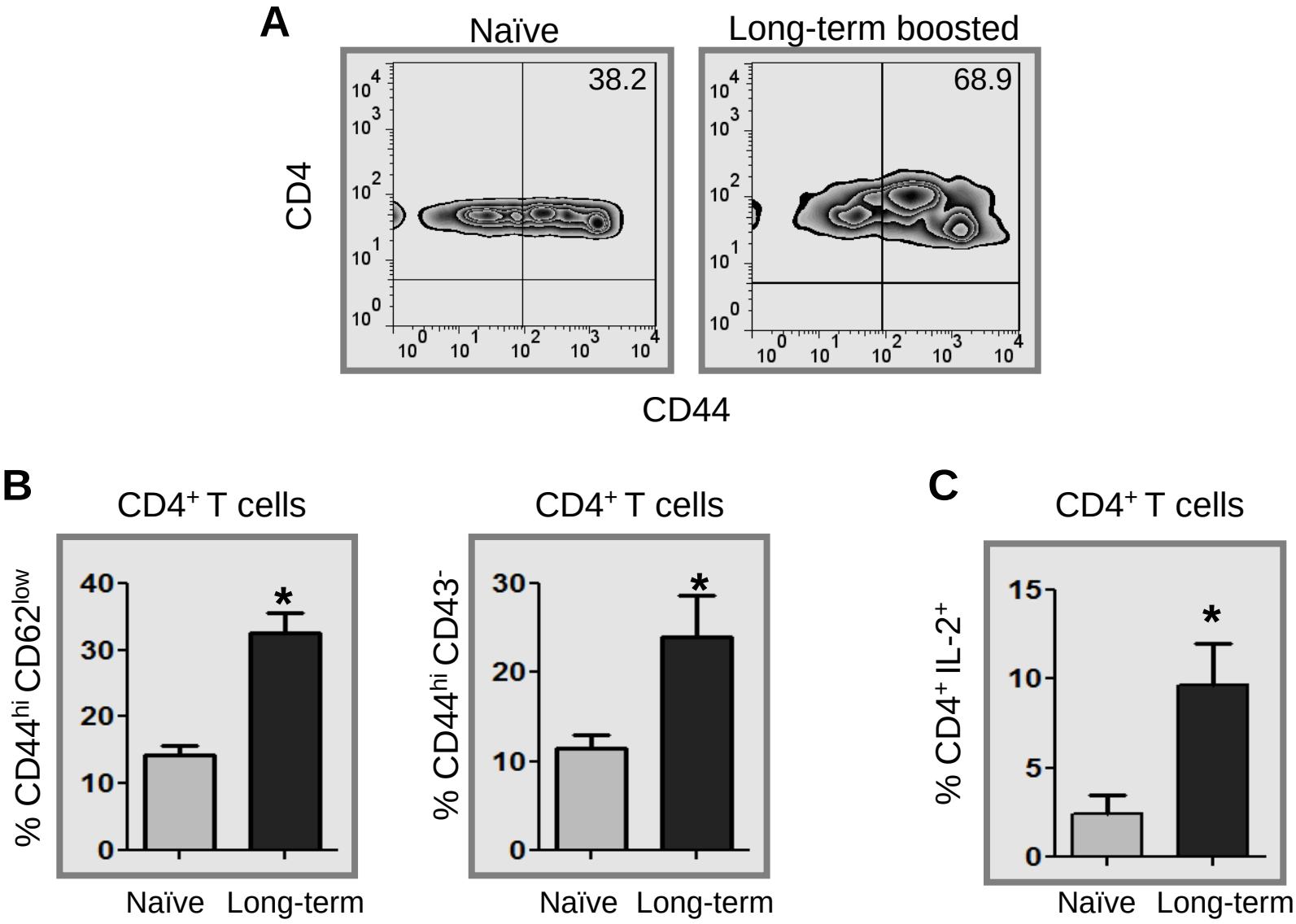




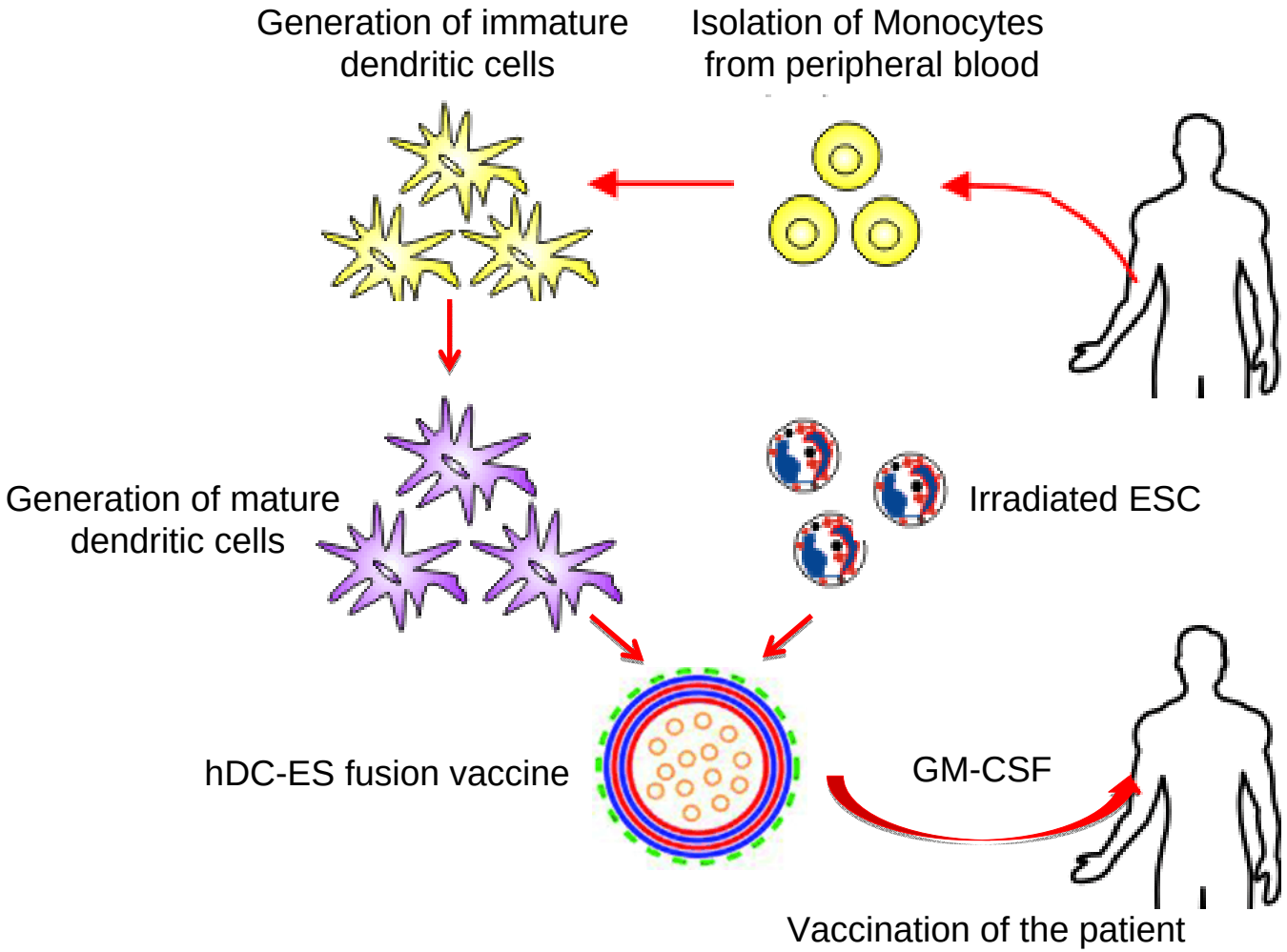
ESC vaccination-induced effector responses are maintained in long-term surviving animals



ESC vaccination-induced CD4⁺ T memory responses are maintained in long-term surviving animals

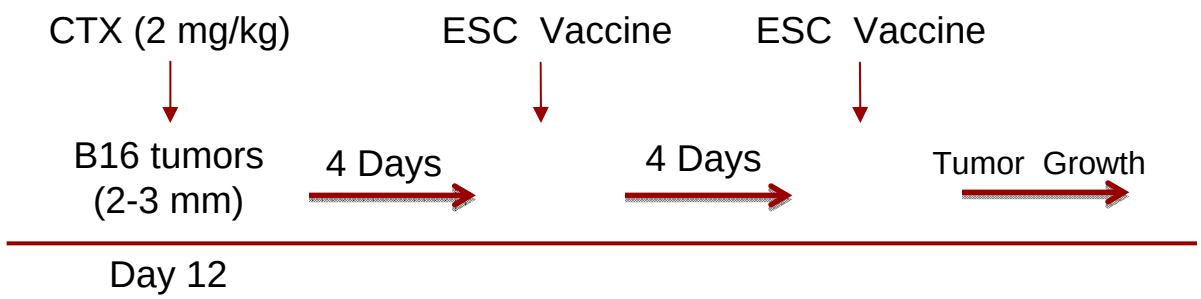


Vaccination with allogeneic dendritic cell/embryonic stem cell fusion hybrids



Combination Treatment with Cyclophosamide and ESC Vaccine

A



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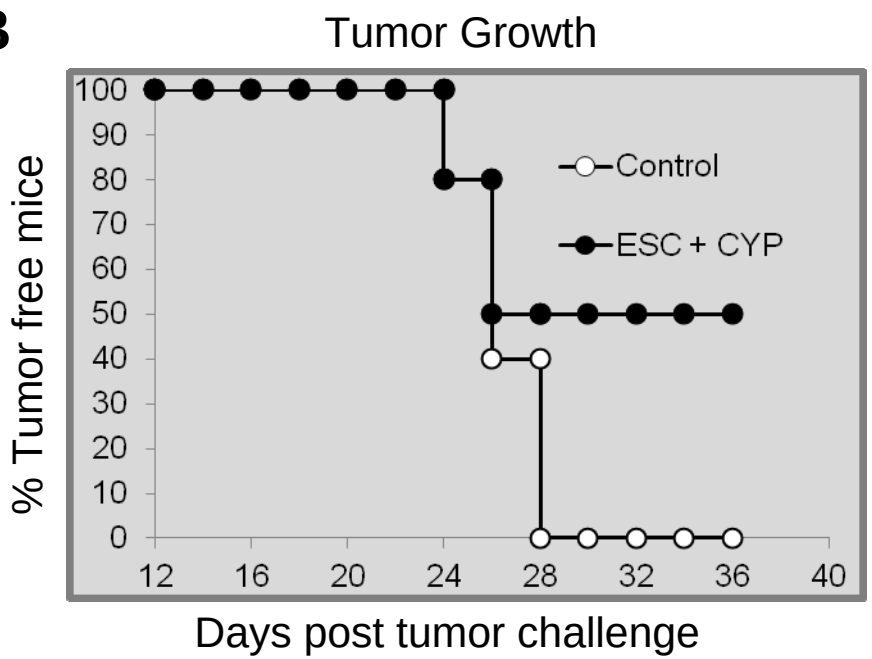

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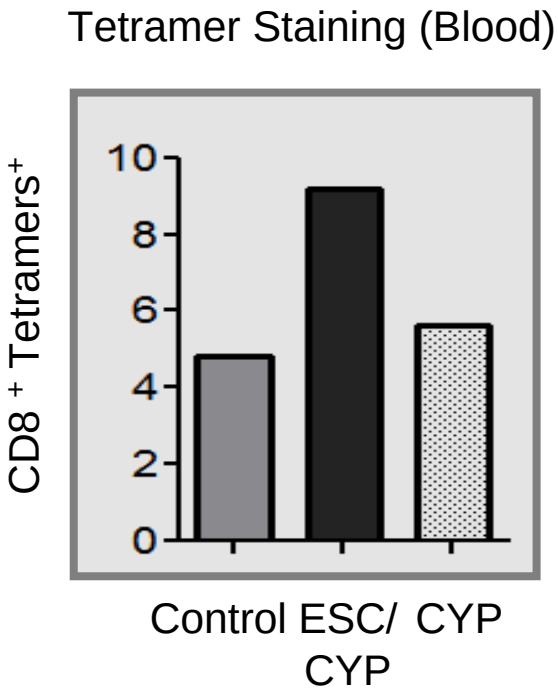
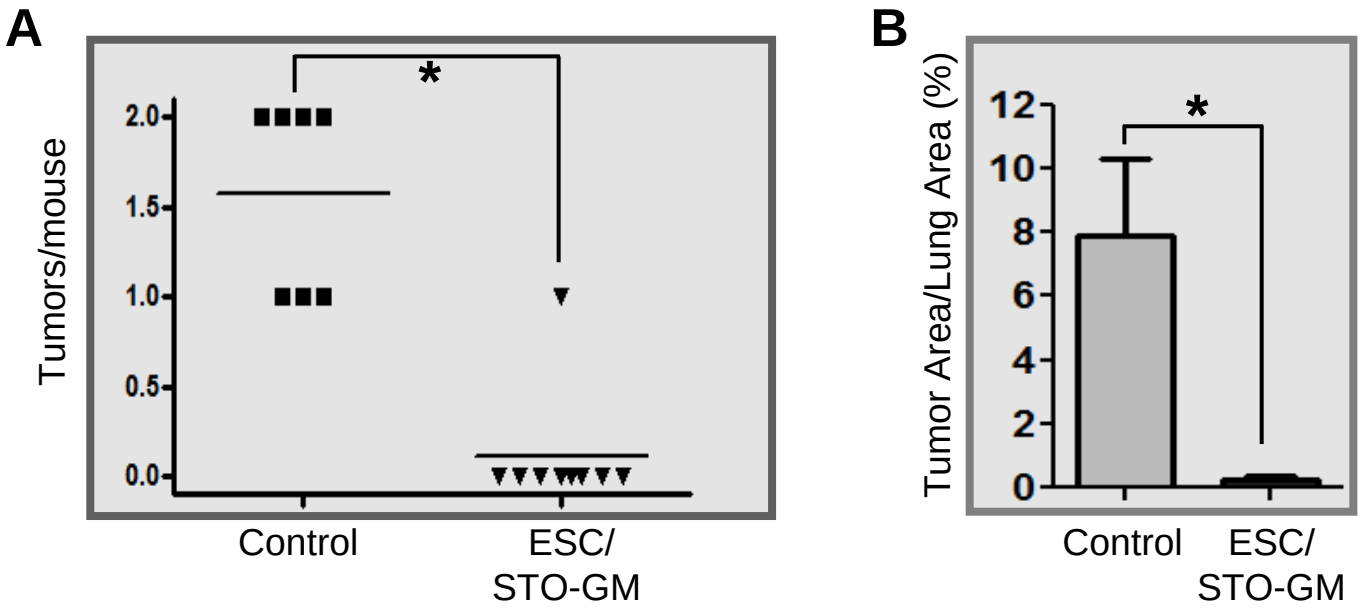
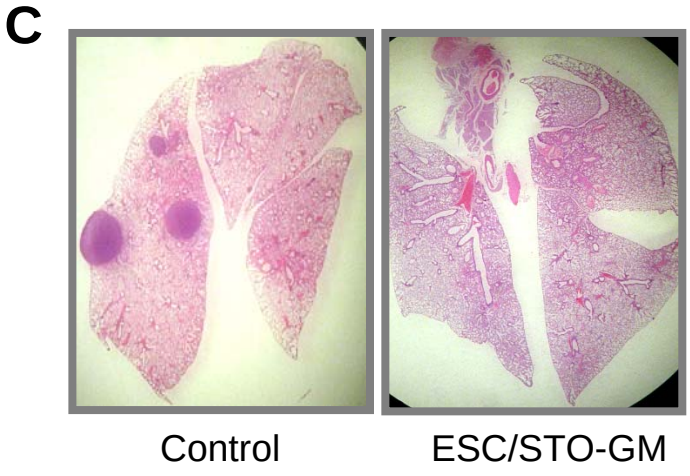


ESC Vaccination in a Spontaneous, Carcinogen-induced Mouse Pulmonary Carcinoma





Conclusions

- Vaccination with ESC and a source of GM-CSF inhibits lung and melanoma tumor outgrowth.
- Tumor inhibition and retardation may be due to expansion of TNF-α/IFN-γ producing $CD8^+$ T cells in the spleen.
- ESC vaccine induces higher intratumoral $CD8^+$ T effector/$CD4^+CD25^+Foxp3^+$ T regulatory cell ratio, and reduces myeloid derived suppressor cells in the spleen.
- ESC vaccination-induced $CD8^+$ T cell-mediated effector responses are maintained in long-term surviving animals