

***In vivo* antitumor evaluation model for immune checkpoint inhibitors**

Use NOG- Δ MHC transplanted with
Peripheral Blood Mononuclear Cells (PBMC)

In-Vivo Science Inc.

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Summary

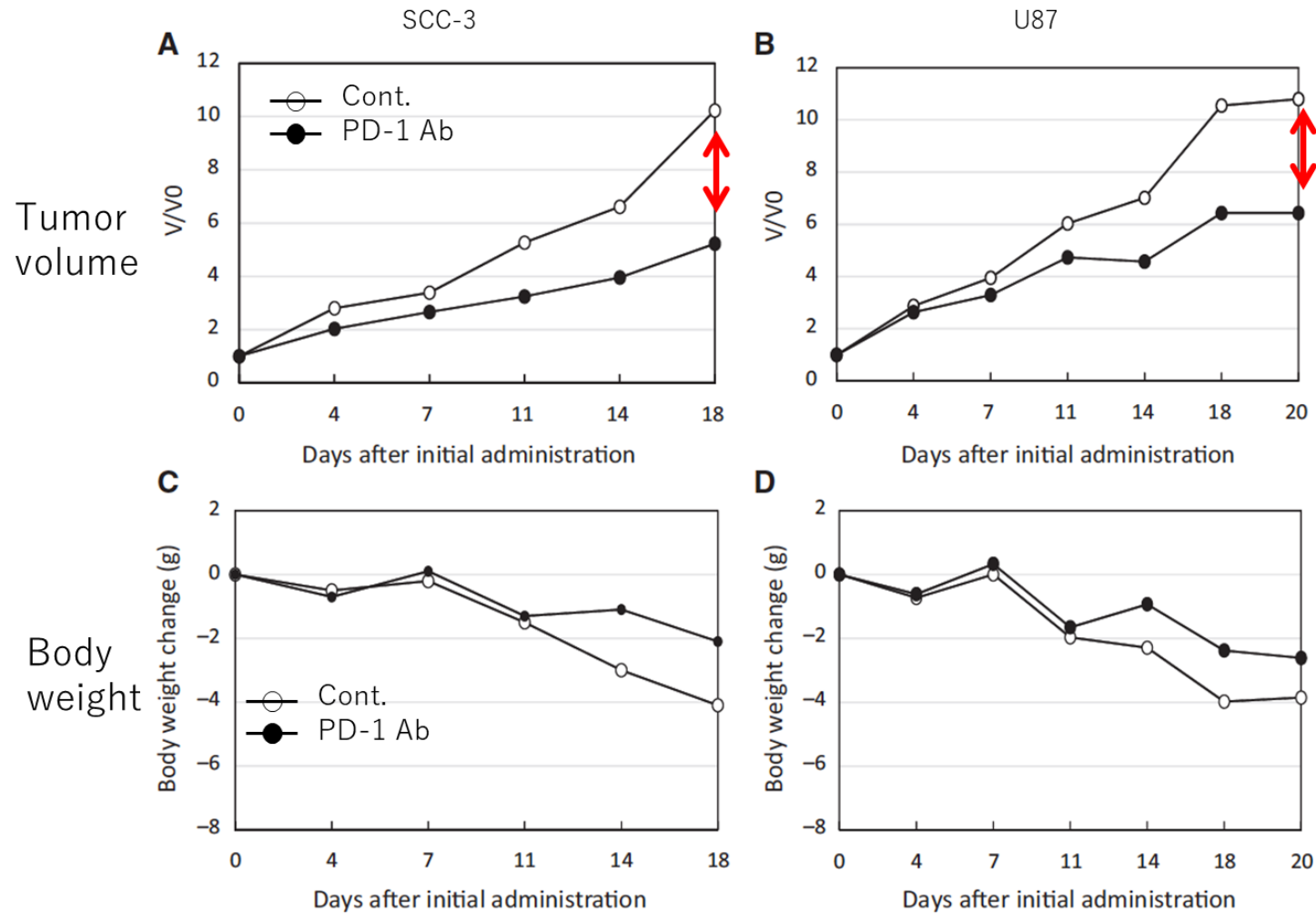
- An *in vivo* antitumor evaluation experiment for immune checkpoint inhibitors (hereinafter referred to as ICI) using PBMC* transplanted humanized NOG- Δ MHC mice has been established.
- **Background:**
 - When PBMCs are transplanted into severely immunodeficient NOG mice, mature lymphocytes engraft.
 - On the other hand, NOG mice develop GVHD, so only short-term studies could be performed.
 - Using NOG- Δ MHC** (NOG-dKO) mice, the development of GVHD was significantly attenuated, confirming the antitumor effect of her ICI against cancer cell lines.

PBMC*:Peripheral Blood Mononuclear Cells

NOG- Δ MHC**:NOG mice with mouse MHC class I and II knocked out. Donor T cells are no longer able to recognize the recipient mouse's MHC, and GVHD is significantly attenuated.

Anti-tumor effect by ICI (Result)

—Tumor growth inhibition effect of anti-PD-1 antibody nivolumab biosimilar—



ICI *in vivo* evaluation model experiment protocol

Humanized mice production
Cancer cell lines transplantation

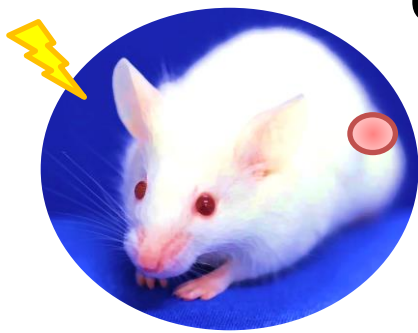
ICI evaluation experiment

0 1w 2w 3w 4w 5w 6w 7w 8w

hPBMC (HLA-A*0201)

X-ray
~2.5Gy

1x10⁷ i.v.



Cancer Cell Lines*

S.C.

*SCC-3 human Lymphoma	2 × 10 ⁵ SC
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*U87 human glioblastoma	2 × 10 ⁵ SC
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NOG-ΔMHC
(=NOG-dKO)



Anti PD-1 antibody

2mg/kg Ab i.p. × 6times, 2times/week

PBMC

- FACS
- Cytokine (IL2, 4, 10, TNFα, IFNγ, TGFβ1)

Tumor, Spleen
Harvest

- | | |
|-----------|---|
| 1. Tumor | <ul style="list-style-type: none"> • IHC (CD4, CD8, Granzyme, Treg, etc.) • Real Time PCR (antigens, cytokines) • TIL FACS (hCD45) |
| 2. Spleen | <ul style="list-style-type: none"> • Cytotoxicity Assay (CTL, NK Assay) • Real Time PCR (Cytokines) |

Orders and Inquiries, questions

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