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Preclinical Mouse Models for Cancer Immunotherapy with Anti-PD-1 Highlight the Importance of Using Mouse-Specific Reagents to Reflect Clinical Settings

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ABSTRACT

Immune checkpoint inhibition (ICI) has become a highly effective strategy for reversing cancer-induced immune suppression. Monoclonal antibodies (mAbs) targeting PD-1/PD-L1 are FDA-approved and increasingly used in clinical practice. However, preclinical mouse models have struggled to replicate the significant therapeutic responses and toxicities seen in patients. This discrepancy is largely due to commonly used models, which rely on fast-growing, ex vivo–cultured transplantable tumor cell lines implanted into young, naïve inbred mice. Another challenge arises from the repeated use of xenogeneic reagents in mice, such as rat or hamster mAbs against mouse antigens, which differ from the human or humanized mAbs applied clinically. Building on previous work showing that repeated administration of xenogeneic anti-PD-1 mAbs can trigger fatal hypersensitivity in some tumor-bearing mice, we compared these effects with those of a mouse-specific anti-PD-1 mAb. Treatment with a murine anti-mouse PD-1 (clone MuDX400) did not provoke lethal anaphylaxis in the 4T1 tumor model and demonstrated stronger antitumor activity across multiple models, likely because it avoided generating neutralizing antibodies against the therapeutic mAb, a problem observed with xenogeneic antibodies. These findings underscore the importance of using mouse-specific reagents in preclinical studies to more accurately reflect clinical outcomes, enabling proper assessment of long-term efficacy and toxicity while preventing xenogeneic immune responses that do not occur in patients. Moreover, this work provides a potential explanation for why preclinical murine studies have often failed to reproduce the clinical effectiveness and adverse effects of checkpoint inhibitors as single agents.

Keywords: Immunotherapy, PD-1, Checkpoint, Anti-PD-1

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Introduction

Advances in tumor immunology have enabled the development of innovative therapies aimed at counteracting cancer-induced immune suppression and eliciting T cell–mediated antitumor responses. Immunotherapeutic approaches, including vaccines, checkpoint inhibitors, and chimeric antigen receptor (CAR) T cells, have shown substantial clinical potential [1]. Among these, immune checkpoint blockade targeting the programmed cell death 1/programmed cell death ligand 1 (PD-1/PD-L1) axis represents a major breakthrough in cancer therapy.

PD-1 is a critical inhibitory receptor that modulates immune pathways to control the magnitude and duration of immune responses, prevent tissue damage, resolve inflammation, and maintain self-tolerance [2, 3]. It is expressed on multiple immune cell types, including CD4+ and CD8+ T cells, B cells, natural killer T (NKT) cells, and activated monocytes [2, 4–6]. PD-1 interacts with two known ligands, PD-L1 and PD-L2, with PD-L2 inducibly expressed on dendritic cells (DCs), macrophages, and cultured bone marrow–derived mast cells [7, 8], whereas PD-L1 is more widely expressed across both immune and non-hematopoietic cells [7, 9]. The engagement of PD-1 by PD-L1/PD-L2 serves as an immune checkpoint to restrain immune activity [10], and many tumors exploit this pathway to evade immune destruction [10]. Blocking PD-(L)1 with monoclonal antibodies (mAbs) enhances

T cell cytotoxicity, proliferation, and proinflammatory cytokine production, promoting tumor clearance in preclinical studies and clinical settings, though off-target toxicities remain a concern [3, 11–14].

Given the clinical impact of checkpoint inhibitors, a comprehensive understanding of both their therapeutic effects and associated toxicities is crucial. Preclinical mouse models using transplantable tumor lines have historically formed the backbone of cancer immunology and therapy research, and their central role in experimental cancer therapeutics remains unchallenged [14–18]. However, these models have limitations, particularly in studying immunotherapy. Transplantable tumors often consist of highly cultured, homogeneous, rapidly growing cell lines implanted into young, immunologically naïve inbred mice, which does not fully replicate the human tumor environment. Furthermore, preclinical studies frequently rely on xenogeneic antibodies, as most in vivo mAbs against mouse targets, including PD-1/PD-L1, are generated in other species such as rats or hamsters. Repeated administration of such xenogeneic antibodies in mice can induce neutralizing antibodies or even fatal anaphylaxis, mirroring early clinical failures of mouse-derived antibodies that required humanization for repeated therapeutic use [18, 19]. This poses significant challenges for modeling long-term immunotherapy effects, dosing regimens, and repeated treatment strategies in preclinical studies.

In this study, we demonstrate that repeated intraperitoneal injections (more than 5–6 doses) of a commonly used hamster-derived anti-mouse PD-1 antibody (clone J43) induced fatal hypersensitivity reactions in the highly inflammatory orthotopic 4T1 mammary carcinoma model. Fatal outcomes were associated with massive pulmonary infiltration by polymorphonuclear leukocytes and elevated serum levels of hamster-specific IgG1 antibodies. Conversely, administration of a species-matched mouse anti-mouse PD-1 antibody (clone MuDX400) did not trigger immune-mediated lethality, while exhibiting antitumor activity in both 4T1 and B16 models. Unlike the J43 antibody, MuDX400 did not induce species-specific IgG1 responses and was safely administered long-term. These findings underscore the limitations of xenogeneic checkpoint antibodies in mouse models, which can provoke immune-related adverse events absent in humans. Our results emphasize the importance of using species-compatible reagents in preclinical immunotherapy studies to more accurately assess both long-term efficacy and toxicity profiles.

Results and Discussion

Repeated xenogeneic αPD-1 administration triggers fatal hypersensitivity in the inflammatory 4T1 breast cancer model. The 4T1 model is a widely used representation of triple-negative human breast cancer that spontaneously metastasizes to the lungs, liver, brain, and bone [20–23]. Our previous work demonstrated that 4T1 tumor-bearing mice experience fatal anaphylaxis following repeated administration of xenogeneic hamster or rat αPD-1 antibodies, whereas xenogeneic species-specific antibodies or anti–CTLA-4 mAbs did not induce such responses [18], underscoring the unique immunological role of PD-1/PD-L1 as a therapeutic target. Notably, this hypersensitivity was absent in non-tumor-bearing mice or in other tumor models or strains, and appeared dependent on both the frequency and dose of antibody administration [18]. These findings suggest that fatal anaphylaxis arises from the combination of 4T1's inflammatory tumor environment and PD-1 blockade.

To further investigate, 4T1 cells were orthotopically implanted into the mammary fat pad of female BALB/c mice, and tumor-bearing mice were treated with repeated injections of either hamster anti-mouse αPD-1 (clone J43) or a hamster IgG isotype control, as outlined in the experimental schema **(Figure 1a)**. Due to fatal hypersensitivity following the fifth or sixth J43 injection, administration was limited, and significant antitumor effects were not observed, with tumor volumes remaining comparable between the J43 and hIgG groups **(Figure 1b)**. Cyanosis and labored breathing were observed 30–60 minutes after the fifth–sixth injection, leading to rapid death **(Figure 1c)**. These lethal reactions depended on the number and dose of injections, mouse strain (BALB/c), and the presence of the highly inflammatory 4T1 tumor, which is known for elevated myeloid-derived suppressor cell (MDSC) levels. Such clinical manifestations are consistent with hypersensitivity reactions previously reported in other mouse models following repeated xenogeneic antisera administration (e.g., rabbit anti-mouse ASGM1) [18, 24–26], characterized by increased vascular permeability, respiratory arrest, multi-organ failure, or cardiac collapse [27, 28].

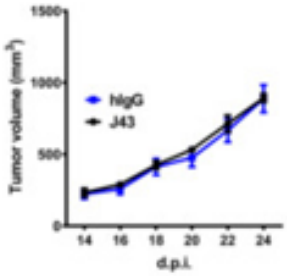
Histopathological analysis revealed marked neutrophil infiltration in the lungs of J43-treated 4T1 mice, with extensive leukostasis within interstitial alveoli and bronchioles **(Figure 1d)**, while hamster IgG-treated mice showed no such changes. Similarly, livers from J43-treated mice displayed significant polymorphonuclear

leukocyte infiltration **(Figure 1e)**. Given the known expansion of MDSCs in 4T1-bearing mice, we previously found that MDSC depletion could prevent anaphylactic death [18].

Serum IgG1 levels measured by ELISA were significantly elevated in J43-treated mice compared to hamster IgG controls **(Figure 1f)**, indicating that αPD-1 treatment enhanced anti-hamster antibody responses. More specifically, J43-treated mice exhibited increased levels of anti-J43-specific IgG1 antibodies **(Figure 1g)**, whereas hamster IgG did not elicit significant neutralizing antibodies. These data indicate that hypersensitivity in 4T1-bearing BALB/c mice receiving prolonged αPD-1 therapy is mediated by anti-hamster antibody responses. Importantly, these effects were not solely attributable to xenogeneic antibody exposure, as hamster IgG controls and non-tumor-bearing mice treated with J43 did not exhibit hypersensitivity [18]. Thus, lethal toxicity resulted from the combined effects of PD-1 blockade, repeated xenogeneic antibody exposure, and the inflammatory tumor environment.

Consistent with 4T1's inflammatory profile, MDSC levels were elevated in the lungs of tumor-bearing mice relative to non-tumor-bearing controls **(Figure 1h)**, and these levels were further increased in mice treated with xenogeneic αPD-1 compared to hIgG **(Figure 1h)**, suggesting that 4T1-induced MDSCs may contribute to anaphylactic responses. Previous studies confirmed that depletion of GR-1+ cells mitigates this toxicity [18]. Collectively, these findings indicate that repeated xenogeneic αPD-1 administration in the 4T1 model triggers fatal hypersensitivity, limits repeated dosing, and likely reduces therapeutic efficacy due to induction of neutralizing antibodies.

a)



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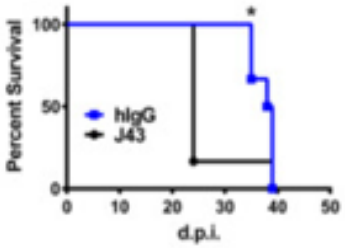

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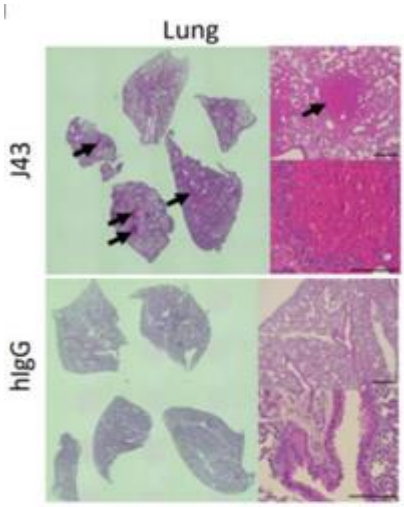

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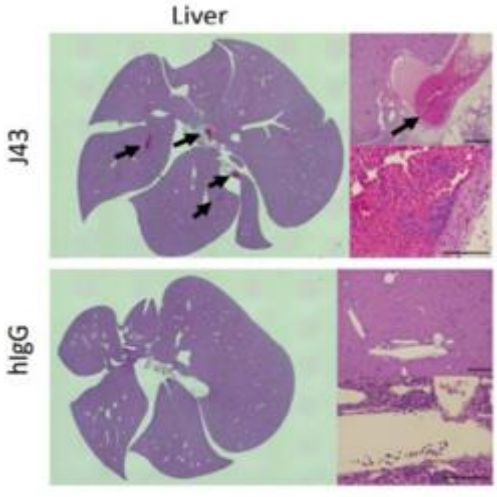

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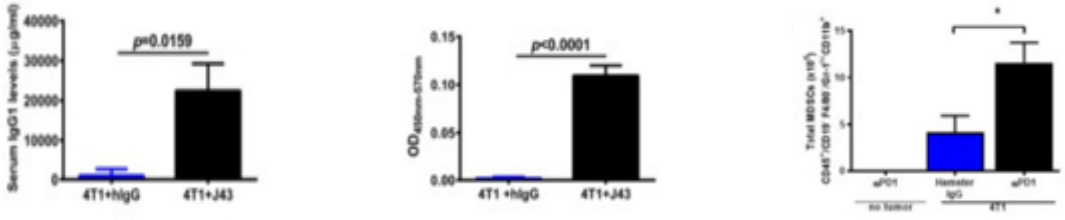
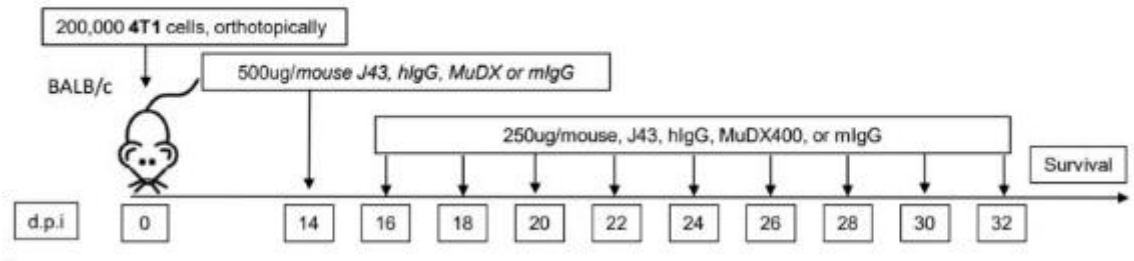


f) g) h)

Figure 1. Repeated administration of xenogeneic αPD-1 antibodies induced fatal hypersensitivity in the 4T1 breast cancer model. (a) Experimental design: BALB/c mice were orthotopically inoculated with 4T1 breast carcinoma cells in the mammary fat pad and treated with either hamster anti-mouse isotype control (hIgG) or αPD-1 (clone J43). (b) Tumor growth of 4T1 in BALB/c mice is shown as mean ± s.e.m. over days post-inoculation (d.p.i.). (c) Kaplan–Meier survival curves of 4T1-bearing mice treated with hIgG or J43, analyzed by log-rank (Mantel–Cox) test. Representative H&E staining of (d) lungs and (e) liver from 4T1 mice treated with hIgG or J43 show inflammation, disrupted tissue architecture, and mononuclear cell infiltration (black arrows). (f) Serum IgG1 levels and (g) J43-reactive IgG1 in treated mice are presented. (h) Absolute numbers of myeloid-derived suppressor cells (MDSCs) in lungs were assessed by flow cytometry. Bars indicate mean ± s.e.m., *p < 0.05, n = 6 per group.

Because xenogeneic αPD-1 monoclonal antibodies caused anaphylaxis, preventing long-term evaluation of their antitumor effects in 4T1 mice, a fully murine αPD-1 antibody (MuDX400) was used instead. Tumor-bearing mice were treated with either J43 or MuDX400 **(Figure 2a)**. Both antibodies showed no difference in primary 4T1 tumor growth compared to controls up to day 24 after six injections, consistent with prior observations that anti-PD-1 monotherapy generally exerts minimal effects on rapidly growing murine tumors **(Figure 2b)**. J43-treated mice developed toxicity after the sixth injection, culminating in 100% lethal anaphylaxis by the eighth injection **(Figures 2c and 2d)**. In contrast, MuDX400 was well tolerated over 10 injections, resulting in modest but statistically significant reductions in tumor growth and improved survival **(Figures 2c and 2d)**, with no signs of hypersensitivity. Unlike J43-treated mice, which exhibited lung and liver pathology **(Figures 1d, 1e, 2e and 2f)**, MuDX400-treated mice showed normal tissue histology. Total serum IgG1 was elevated in J43-treated mice compared to MuDX400 **(Figure 2g)**, and repeated MuDX400 dosing did not elicit antibodies against hamster J43 determinants **(Figure 2h)**. Assessment of lung metastases after six treatments revealed that MuDX400 reduced metastatic burden compared to isotype controls, preserving normal lung architecture **(Figure 2i)**. Overall, murine αPD-1 antibody treatment avoided anaphylaxis, conferred antitumor effects, reduced lung metastases, and improved survival in the 4T1 model, highlighting that toxicities observed with xenogeneic antibodies do not reflect the clinical context where humanized mAbs are used.



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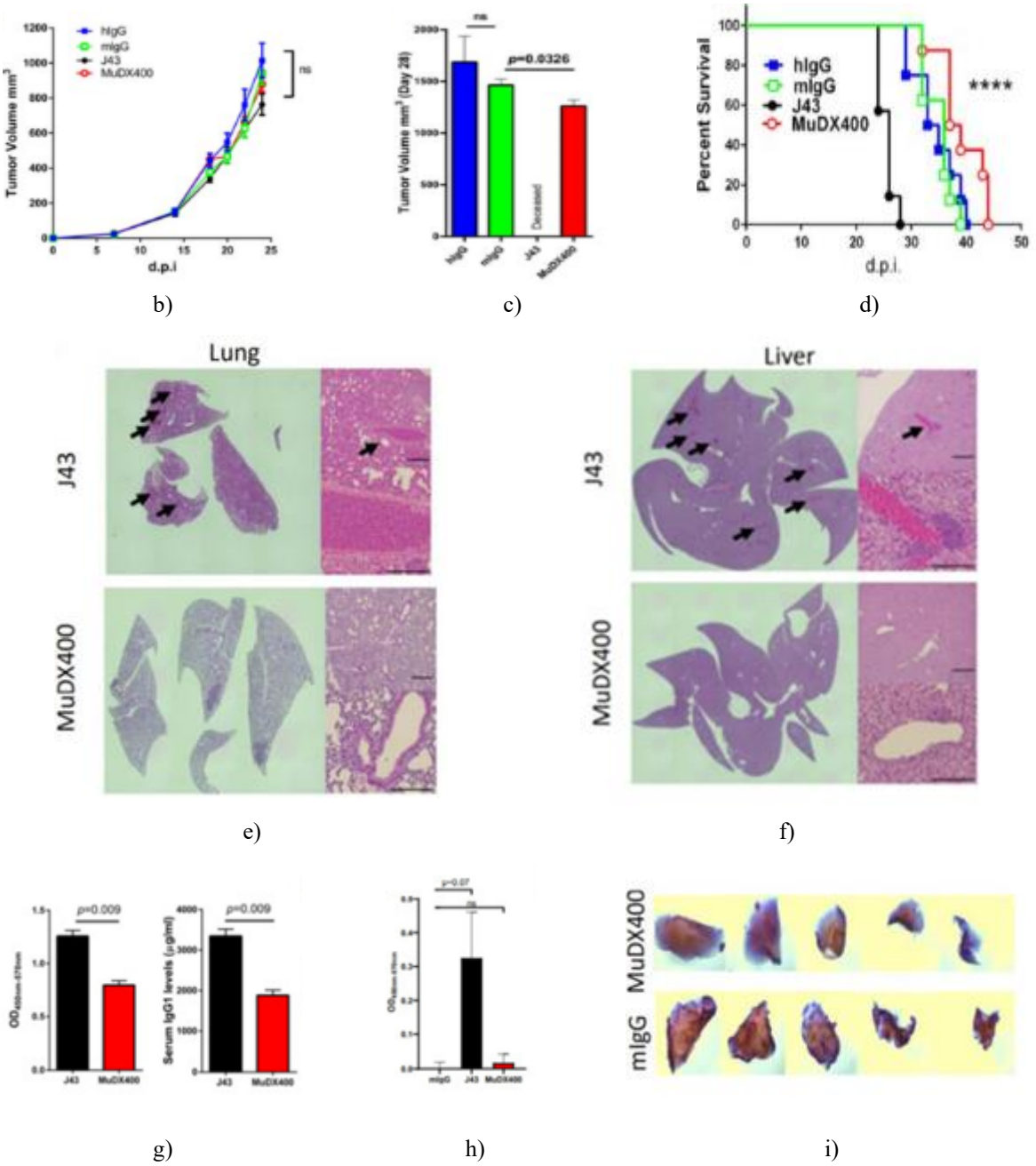

b) c) d)

e) f)

g) h) i)

Figure 2. Murine αPD-1 prevented the lethal hypersensitivity observed with xenogeneic reagents in the 4T1 breast cancer model. (a) Experimental scheme depicting BALB/c mice orthotopically implanted with 4T1 breast carcinoma cells in the mammary fat pad, followed by monotherapy with either mouse αPD-1 (MuDX400) or J43. (b) Tumor growth curves of 4T1 in BALB/c mice, with tumor volumes shown as mean ± s.e.m. (c) Tumor volumes at day 28 presented as mean ± s.e.m. (d) Kaplan–Meier survival curves of 4T1-bearing BALB/c mice treated with MuDX400 or J43, compared using the log-rank (Mantel–Cox) test. Representative H&E staining of (e) lungs and (f) liver in 4T1 mice treated with either J43 or MuDX400, highlighting inflammation, disruption of normal tissue architecture, and mononuclear cell infiltration (black arrows). (g) Total serum IgG1 levels measured by ELISA in 4T1 tumor-bearing mice treated with J43 or MuDX400. (h) Serum levels of J43-reactive IgG in 4T1 tumor-bearing mice. (i) Representative whole-mount lung staining to assess metastases in 4T1 mice treated with MuDX400 or mIgG1. Bar graphs show mean ± s.e.m., **** $p < 0.0001$, n = 7–12 mice per group.

Repeated administration of murine αPD-1 also demonstrated antitumor activity in the B16-F0 melanoma model. Previously, we reported that in less inflammatory tumor models, such as Renca (renal carcinoma) in BALB/c mice or B16 melanoma and 3LL tumors in C57BL/6 mice, repeated treatment with xenogeneic αPD-1 did not trigger

anaphylactic reactions [18]. Nevertheless, the absence of anaphylaxis does not preclude the generation of neutralizing antibodies. To investigate this, we evaluated both the antitumor efficacy and the presence of neutralizing antibodies against murine versus xenogeneic anti-PD-1 mAbs. Although αPD-1 is approved for metastatic melanoma treatment in humans, its monotherapy in mice, particularly in the B16 model, often fails to reproduce the robust clinical responses. Using B16 tumor-bearing mice, we compared the effects of murine (MuDX400) versus xenogeneic (J43) αPD-1 **(Figure 3a)**. Tumor growth progressed rapidly in the J43 and control groups with no significant differences, consistent with previous findings. In contrast, MuDX400-treated mice exhibited significantly smaller tumors compared to J43-treated mice **(Figures 3b and 3c)**. Pooled analysis from two experiments showed that only 1/10 J43-treated mice achieved >1.5-fold tumor reduction versus controls, whereas 7/9 MuDX400-treated mice reached this level **(Figure 3c)**. The reduced efficacy of xenogeneic αPD-1 likely reflects the generation of neutralizing antibodies that alter drug pharmacokinetics, as ELISA revealed elevated anti-hamster IgG in sera from J43-treated mice but not in MuDX400 or control mIgG-treated mice **(Figure 3d)**. These findings highlight the importance of using species-matched reagents for reliable long-term immunotherapy studies in mouse models.

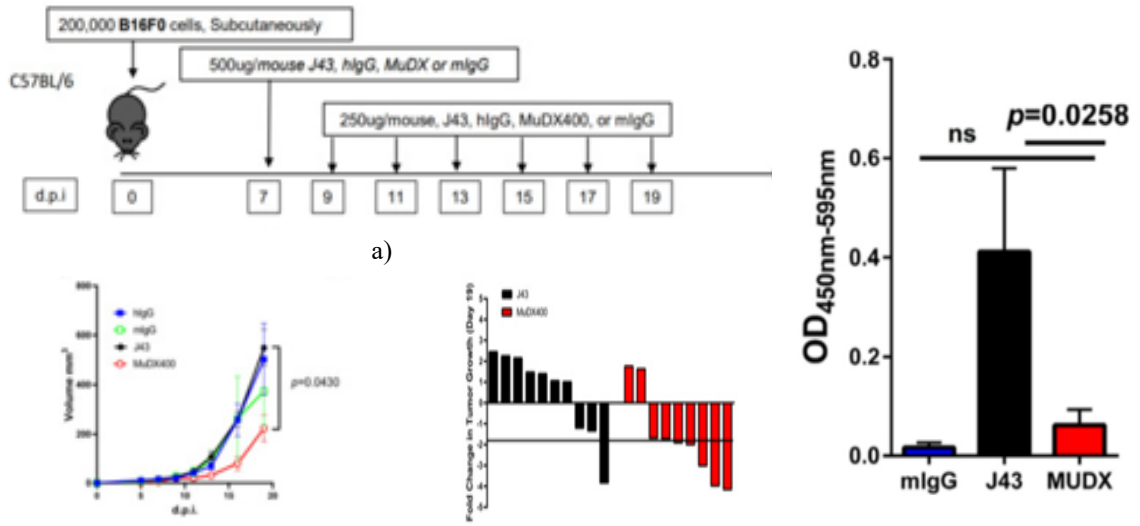

Figure 3. Repeated administration of murine αPD-1 showed antitumor activity in the B16 melanoma model. (a) Experimental design: C57BL/6 mice were subcutaneously implanted with B16-F0 melanoma cells and treated with either J43 or MuDX400. (b) Tumor growth curves of B16-F0 in C57BL/6 mice, with volumes presented as mean ± s.e.m. (c) Waterfall plot showing pooled data for fold change in tumor growth relative to IgG-treated controls. (d) ELISA analysis of J43-reactive IgG in serum of B16-F0 tumor-bearing mice with or without treatment. Bar graphs represent mean ± s.e.m., n = 9–11 mice per group.

In this study, we demonstrate that repeated dosing with xenogeneic PD-1 monoclonal antibodies (mAbs) triggers rapid, fatal hypersensitivity in 4T1 tumor-bearing mice, whereas such reactions are absent in less inflammatory tumor models or with xenogeneic isotype controls. This suggests that the lethal xenogeneic hypersensitivity likely arises from a synergistic inflammatory effect of PD-1 blockade, the xenogeneic antibody, and the 4T1 tumor environment, supported by elevated lung MDSCs in 4T1 mice treated with xenogeneic αPD-1 compared to non-tumor-bearing mice or 4T1 mice treated with isotype controls. Fatal reactions to xenogeneic antibodies can also occur independently, as repeated administration of xenogeneic antisera (e.g., rabbit antisera to asialo GM1 in mice) has been documented to induce anaphylaxis even in naive mice. In the current study, hypersensitivity to xenogeneic αPD-1 was further evidenced by elevated serum IgG1 and severe lung and liver pathology after 5–6 injections [18, 29].

While fatal anaphylaxis was only seen in the 4T1 model, neutralizing antibodies against xenogeneic αPD-1 may impair efficacy in any tumor model. Consistent with this, prolonged treatment with murine αPD-1 (MuDX400) resulted in superior antitumor responses in both 4T1 and B16 models compared to hamster αPD-1 (J43), illustrating that the two antibodies differ in efficacy and toxicity despite targeting the same molecule. Previous

studies with other xenogeneic αPD-1 clones support similar findings [18], though further validation across additional clones and tumor models is warranted. Differences in epitope recognition may contribute, but a more likely explanation is the induction of neutralizing antibodies against xenogeneic αPD-1, a phenomenon that could also impact studies of acquired resistance to checkpoint blockade. Supporting this, ELISA revealed increased serum IgG1 and anti-hamster IgG1 following xenogeneic αPD-1 treatment, likely affecting antibody pharmacokinetics and therapeutic efficacy. In contrast, MuDX400, being a mouse anti-mouse IgG1, complicates direct quantification of neutralizing antibodies via ELISA; confirmation would require measuring antibody concentrations in serum by mass spectrometry.

MuDX400 treatment reduced both primary tumor growth and lung metastases; however, the rapid growth of 4T1 and B16 tumors may limit the ability to fully observe antitumor effects that are clinically relevant, highlighting challenges in modeling human tumor kinetics in mice. Slower-growing or genetically engineered tumor models could provide more clinically relevant conditions, allowing long-term assessment of therapeutic efficacy and immune-related adverse events.

These findings underscore limitations in using mouse tumor models for checkpoint blockade studies. In clinical settings, human anti-mouse antibodies (HAMA) against xenogeneic mAbs impaired efficacy, necessitating the use of human or humanized antibodies for repeated dosing. Similarly, murine αPD-1 antibodies such as MuDX400 enable preclinical models to better recapitulate clinical scenarios, improving evaluation of checkpoint inhibition over prolonged periods or in combination therapies. Other checkpoint targets studied with xenogeneic agents may similarly provoke neutralizing antibody responses, affecting both toxicity and efficacy assessments in murine models.

Materials and Methods

Mice

Female BALB/cAnNCrl mice (6 weeks old) were obtained from Charles River Laboratories, Inc., while female BALB/cAnNTac and C57BL/6NTac mice, along with male C57BL/6NTac mice aged 4–6 weeks, were sourced from Taconic Farms. Animals were maintained under specific-pathogen-free conditions in AALAC-accredited facilities at the University of California, Davis (UC Davis, Sacramento, CA, USA). All experimental procedures were conducted in compliance with ethical standards and approved by the UC Davis Institutional Animal Care and Use Committee (IACUC; approval numbers 20680 and 20707), with strict adherence to humane endpoints.

Tumor cell lines and treatment protocols

The murine breast carcinoma line 4T1 (CRL-2539) and melanoma line B16-F0 (CRL-6322) were obtained from the American Type Culture Collection (ATCC). For tumor establishment, BALB/c mice received subcutaneous injections of 2×10^5 4T1 cells in 100 µL PBS into the right mammary fat pad, whereas C57BL/6 mice were injected subcutaneously in the right flank with 2×10^5 B16-F0 cells in 100 µL PBS. Tumor growth was observed daily and measured every 2–3 days, with tumor volume calculated using the formula: length × width² × 0.5 (mm^3). For immunotherapy, tumor-bearing mice were treated intraperitoneally beginning on day 14 post-inoculation with either 500 µg of αPD-1 monoclonal antibody (clone J43, BioXCell) in 200 µL PBS, or αPD-1 monoclonal antibody (clone 03AHF, MuDX400, Merck, Kenilworth, NJ, USA) in acetate-sucrose buffer (NaAc) provided by Merck. Subsequent doses of 250 µg were administered every other day. Control groups received either Syrian Hamster Gamma Globulin (Jackson ImmunoResearch, West Grove, PA, USA) in 200 µL PBS or mouse IgG1 (clone 61AVY, Merck) in 200 µL 20 mM NaAc. Mice displaying severe hypersensitivity (immobile, prostrate, cyanotic, labored breathing) were humanely euthanized.

Preparation of mouse lung whole-mounts

Lungs from 4T1 tumor-bearing BALB/c mice were first perfused with PBS, separated into five lobes, and fixed in 10% neutral buffered formalin. Following fixation, tissues were sequentially transferred to 70% ethanol (2 h) and 100% ethanol (2 h). Samples were dehydrated using three xylene washes (30 min, 1 h, 1 h) and processed through graded alcohols. After rinsing under running tap water for 30 minutes, lungs were stained with hematoxylin for 2 minutes, then de-stained in 1% HCl for 15 minutes. Lungs underwent additional washes under running water (30 min), immersion in 70% ethanol (1 h), 100% ethanol (1 h), and xylene (1 h), before being stored in methyl salicylate.

Hematoxylin and eosin (H&E) staining

Lungs and livers from 4T1-bearing BALB/c and B16-F0-bearing C57BL/6 mice were fixed in 10% paraformaldehyde, paraffin-embedded, and sectioned at 4 μm. H&E staining was conducted at the UC Davis Pathology Core. Brightfield images (2× magnification, 1/80 s exposure) were captured using a BioRevo BZ-9000 Fluorescence Microscope (Keyence, Osaka, Japan), with 9–18 images per specimen subsequently stitched using Bio-Analyzer software (Keyence) to generate full-specimen views.

Enzyme-linked immunosorbent assay (ELISA)

Serum levels of total IgG1 and J43-specific IgG1 were quantified using the Mouse IgG1 ELISA Ready-SET-GO!® kit (eBioscience). High-affinity 96-well plates (Corning Costar 9018) were coated with either 100 μL of pre-titrated anti-mouse IgG1 monoclonal antibody or 100 μL J43 (10 μg/mL) and incubated overnight at 4 °C. Plates were washed twice with 400 μL Wash Buffer (1 min per wash) and blocked with 250 μL Blocking Buffer overnight at 4 °C. After washing, 100 μL standards and 50 μL prediluted serum samples were added alongside 50 μL Assay Buffer and 50 μL Detection Antibody. Plates were incubated at room temperature for 3 hours, washed four times, and developed with 100 μL TMB substrate for 15 minutes. Absorbance was measured at 450 nm and 570 nm using a VersaMax™ Tunable microplate reader (VWR, Radnor, PA, USA) with SoftMax Pro software (Molecular Devices, Sunnyvale, CA, USA). Final IgG1 concentrations were determined by subtracting the 570 nm readings from 450 nm readings, with absolute changes calculated relative to PBS-treated controls.

Statistical analysis

Survival curves were generated using the Kaplan–Meier approach, with comparisons made via the log-rank test. Results are reported as mean ± standard error of the mean (s.e.m.). Differences between groups were evaluated using either one-way or two-way ANOVA, or Student's t-test, where appropriate. Analyses were carried out using GraphPad Prism 6 (GraphPad Software, La Jolla, CA, USA). Statistical significance is indicated as: **** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$, and * $p < 0.05$, unless otherwise noted.

Conclusion

Administration of xenogeneic αPD-1 can trigger lethal hypersensitivity in highly inflammatory tumor models like 4T1, a response influenced by the tumor's inflammatory nature, the xenogeneic origin of the reagent, and the αPD-1 activity itself. This effect is absent in other tumor models when using xenogeneic control IgG or with mouse-specific αPD-1. Consequently, murine αPD-1 permits long-term therapeutic evaluation in the 4T1 model, revealing modest antitumor activity. In models without anaphylaxis, xenogeneic reagents still pose limitations due to the generation of neutralizing antibodies that reduce efficacy. For instance, in the B16 model, hamster αPD-1 elicits specific antibodies over time, diminishing its effectiveness, whereas murine αPD-1 can be administered repeatedly and produces strong antitumor responses. Overall, employing species-matched reagents is essential for accurately assessing both the efficacy and safety of antibody-based cancer immunotherapies in mouse models.

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Conflict of Interest: None

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Ethics Statement: None

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