ANTIBODIES

MOUSE *IN VIVO* ANTIBODIES

Improve *in vivo* antibody performance

- Mouse and murinized anti-mouse mAbs to reduce *in vivo* toxicity
- Recombinant antibodies for high sensitivity and reproducibility
- High quality InvivoFit™ grade for pre-clinical studies

Monoclonal antibodies (mAbs) for mouse pre-clinical studies are typically produced in other species (e.g. rat and hamster) and hence, are recognized as foreign when injected into mice. Upon repeated administration, these xenogeneic mAbs trigger the production of host anti-species antibodies, also known as anti-drug antibodies (ADAs). This leads to limited efficacy of the administered mAb and eventually fatal pro-inflammatory hypersensitivity reactions. InvivoGen offers an expanding collection of recombinant anti-mouse mAbs, specifically engineered to limit their immunogenicity and increase their *in vivo* performance.

Choose from our growing list of targets:

Immune Checkpoints

Cytokines

Lymphocyte Markers

Tumor-Associated Antigen

INVIVOGEN.COM/IN-VIVO-RECOMBINANT-MOUSE-ANTI-MOUSE-ANTIBODIES

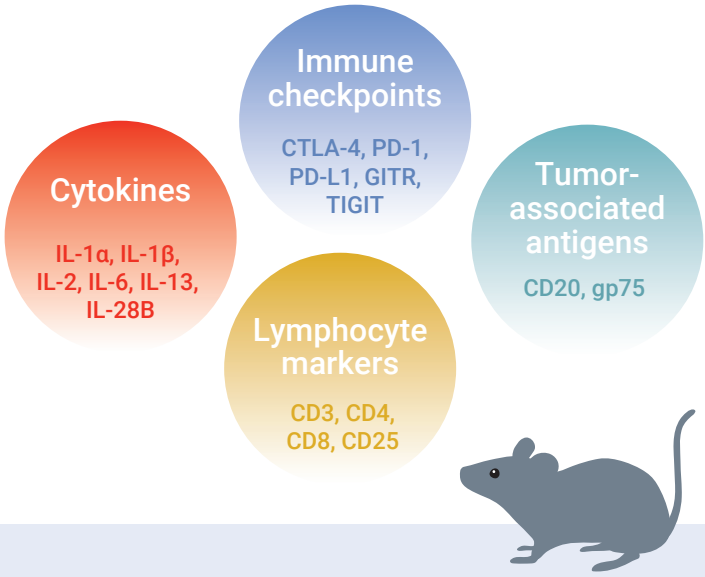
InvivoGen

OPTIMIZED ANTIBODIES FOR MOUSE IN VIVO STUDIES

InvivoGen provides a growing collection of mouse or murinized monoclonal antibodies for *in vivo* studies in mice. These recombinant mAbs have been specifically engineered to limit their immunogenicity and to maintain constant efficacy upon repeated injections in mice.

Monoclonal antibodies (mAbs) are extensively used therapeutics to treat autoimmune diseases and certain types of cancer[1]. They function through various mechanisms with the ultimate effect of recruiting, blocking, or priming immune cells[2].

Most of InvivoGen's murinized and mouse mAbs derive from well-referenced antibody clones recognizing important targets (e.g. clone RMP1-14 for PD-1). Our extensive collection includes mAbs directed against immune checkpoints, cytokines, lymphocyte markers, and tumor-associated antigens. The corresponding isotype controls are also available.



Pre-clinical InvivoFit™ grade

To ensure consistently high-quality mAbs for your research, InvivoGen performs rigorous quality control of each lot. Our collection is provided in a **pre-clinical InvivoFit™ grade**, a high-quality standard specifically adapted for *in vivo* studies.

- **Suitable for parenteral delivery in mice (azide-free)**
- **Filter-sterilized with an endotoxin level <1 EU/mg**
- **Produced in defined and animal-free media**
- **Low aggregation < 5%**

Recombinant mAb production for increased quality and efficacy

Most mAbs on the market for *in vivo* research are produced in hybridomas, which have a number of drawbacks including the exchange of light chains and cellular derivations[3]. InvivoGen uses recombinant technology to overcome these issues.

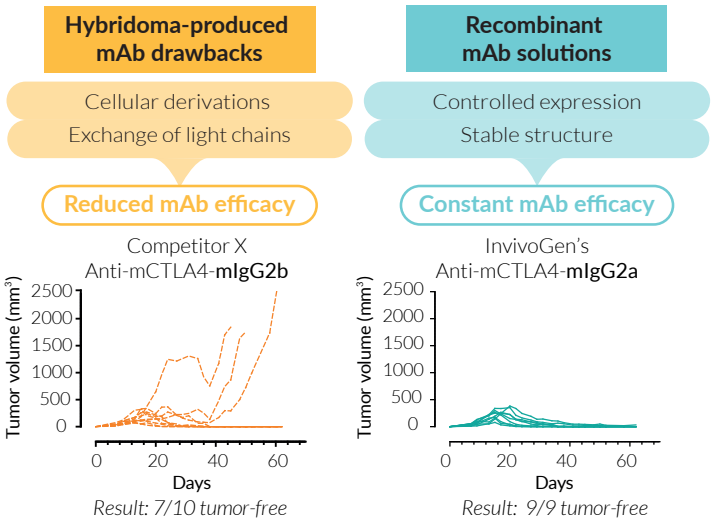


Figure 1. Benefit of recombinant mAbs *in vivo*: BALB/c mice aged 10 weeks were challenged with CT26 cells. After 8 days, Competitor X's Anti-mCTLA4 -mIgG2b (hybridoma-produced) or our Anti-mCTLA4-mIg2a (recombinant) (200 µg/mouse) was administred intraparenterally (IP) into the mice. Tumor growth was monitored for 60 days.

InvivoGen's recombinant mouse or murinized mAbs are expressed and produced in Chinese hamster ovary (CHO) cells (virus-free status confirmed), ensuring structural stability and proper protein glycosylation. Production of recombinant mAbs guarantees the highest purity and batch-to-batch consistency. Additionally, this technology allows us to replace the original isotype with an optimal format for proven increased *in vivo* efficacy *(see figure 1 and table below)*[4].

Certain blocking mAb Fc-mediated effects, such as antibody-dependent cell-mediated cytotoxicity/phagocytosis (ADCC/ADCP) or complement-dependent cytotoxicity (CDC), should be avoided[2]. Therefore, InvivoGen offers an Fc-silent mouse IgG1 isotype (IgG1e3) containing a point mutation D265A. This results in the complete loss of Fc-mediated effector functions.

	IgG1	IgG2a	IgG1e3
ADCC	+/-	++	-
ADCP	+	+++	-
CDC	-	++	-

1. Mall, C. *et al.* 2016. Oncoimmunology 5, e1075114. 2. Li, M. *et al.* 2022. Sci Rep. 11(1):5774. 3. Bradbury, A. *et al.* 2018. 10(4), 539–546. 4. Selby, M.J. *et al.* 2013. Cancer Immunol Res. 1(1):32-42.

Murinization for reduced *in vivo* toxicity

Two major pitfalls encountered in mouse *in vivo* studies upon repeated mAb injections are: 1) anti-species antibody generation and 2) decreased antibody performance. InvivoGen has limited these pitfalls by murinizing the constant regions.

Murinization of a mAb requires the replacement of sequences of non-murine origin with murine counterparts. InvivoGen has successfully replaced the entire non-murine constant region sequence of commonly used anti-human, anti-rat, and anti-hamster mAbs with murine sequences for reduced toxicity *in vivo (see figure 2)*. Such engineered mAbs offer multiple advantages:

- **Sequence 65% to 100% of mouse origin**
- **Reduced anti-species responses**
- **Prolonged circulation of administered mAb**
- **Reduced toxicity and/or hypersensitivity reactions**

Upon repeated injection of xenogeneic mAbs, mice mount a dose-dependent immune response initially directed against the constant region. Ultimately, this response is directed against the whole molecule. The production of mouse anti-species antibodies, also known as ADAs (anti-drug antibodies), removes the administered mAb from circulation, thereby reducing its *in vivo* efficacy[2,5].

Furthermore, this immunogenicity can lead to fatal hypersensitivity reactions. In particular, this response has been noted in studies of xenogeneic mAbs targeting immune checkpoints (e.g. PD-1/PD-L1[1] and GITR[6,7]). In these studies, upon the 3rd or 4th injection of the mAb, the mice exhibited signs of hypersensitivity-associated distress, such as lethargy, and a rapid drop in body temperature[4,6] *(see figure 3)*.

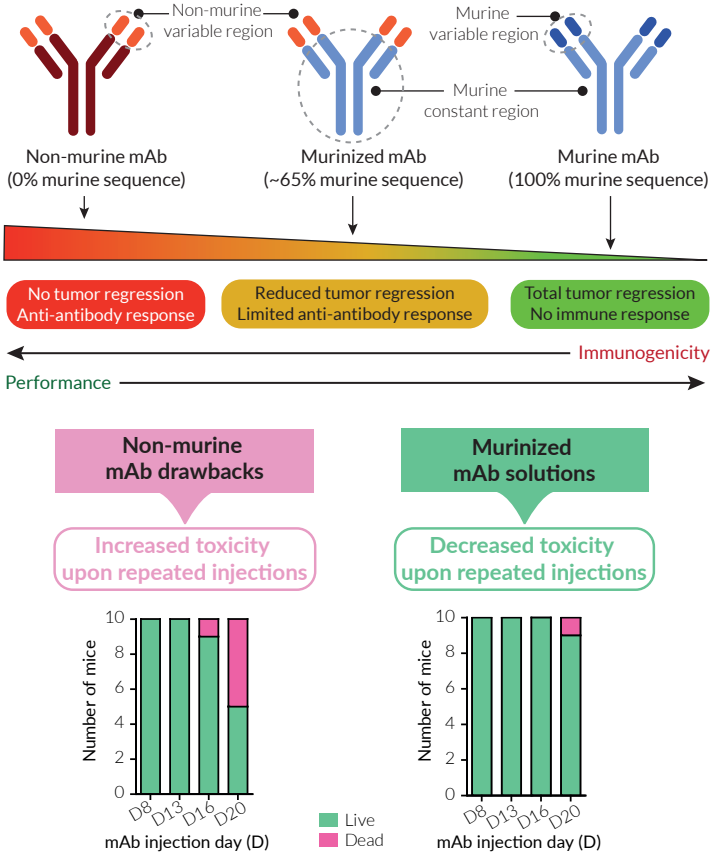


Figure 2. Importance of murinized mAbs *in vivo*: 2 groups of 10 BALB/c mice were challenged with CT26 cells. After 8 days, Anti-PD-L1-hIgG1 (non murine) or Anti-PD-L1-mIgG1e3 (chimeric/murine) (200 µg/mouse) was administred IP into the mice. This was repeated on day 13, 16, and 20.

LIMITED RISK OF A HYPERSENSITIVITY REACTION WITH A MURINIZED ANTIBODY

To demonstrate the induction of an anti-species response in mice, we compared the effectorless human Atezolizumab-derived Anti-PD-L1 mAb against our murinized version *(see figure 3)*. Approximately 30 minutes after the 4th injection, a drop in body temperature (red line), along with other symptoms of a hypersensitivity reaction, were observed in the non-murine mAb-treated group. With intervention (e.g. external heating), these mice survived. On the other hand, the murinized mAb-treated group (purple line) maintained stable body temperature comparable to the negative control group (blue line), with no signs of hypersensitivity reaction.

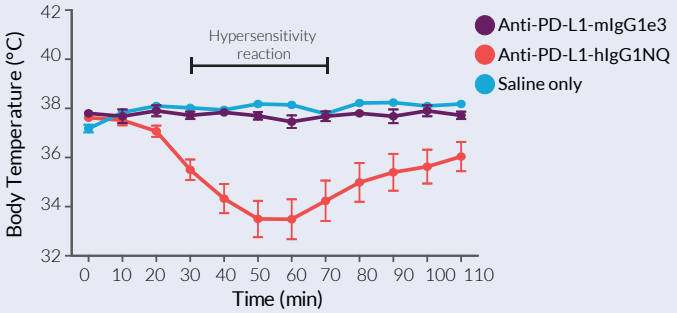


Figure 3. Body temperature comparison between human and murinized Anti-PD-L1 mAbs. BALB/c mice were challenged with CT26 cells. After 8 days, our murinized Anti-PD-L1-mIgG1e3 or Anti-PD-L1-hIgG1NQ (human) was administered IP (200 µg/mouse). IP injections were then performed twice a week for 3 weeks. After IP4, rectal temperature measurements were taken every 10 minutes for all groups. Data are presented as mean ± SEM.

5. Suh K, *et al.* 2022; J Sep Sci. 45(12):2077-2092. 6. Murphy, J.T. *et al.* 2014. Blood 123, 2172-2180. 7. Belmar, N.A. *et al.* 2017. J Immunol 198, 4502-4512.

CHOOSE FROM OUR COLLECTION OF IN VIVO MABS

TARGET	PRODUCT	DESCRIPTION	CAT. CODE
IMMUNE CHECKPOINTS			
CTLA-4	Anti-mCTLA4-mIgG2a	9D9-derived mouse mAb against murine CTLA-4	mctla4-mab10-1
GITR	Anti-mGITR-mIgG2a	DTA-1-derived murinized mAb against murine GITR	mgitr-mab10-1
PD-1	Anti-mPD-1-mIgG1e3 (D265A)	RMP1-14-derived murinized mAb against murine PD-1 - Fc effectorless	mpd1-mab15-1
PD-L1	Anti-PD-L1-mIgG1e3 (D265A)	Atezolizumab-derived murinized mAb against PD-L1 - Fc effectorless	pdl1-mab15-1
	Anti-mPD-L1-mIgG1e3 (D265A)	10F.9G2-derived mouse mAb against PD-L1 - Fc effectorless	mpdl1c2-mab15-1
TIGIT	Anti-mTIGIT-mIgG2a	10A7-derived murinized mAb against murine TIGIT	mtigit-mab10-1
CYTOKINES			
IL-1α	Anti-mIL-1α-mIgG1	6H7-derived mouse mAb against murine IL-1α	mil1a-mab9-1
IL-1β	Anti-mIL-1β-mIgG1	7E3-derived mouse mAb against murine IL-1β	mil1b-mab9-1
IL-2	Anti-mIL-2-mIgG1e3 (D265A)	S4B6-derived murinized mAb against murine IL-2 - Fc effectorless	mil2-mab15-1
IL-6	Anti-mIL-6-mIgG1e3 (D265A)	10F9-derived murinized mAb against murine IL-6 - Fc effectorless	mil6-mab15-1
IL-13	Anti-mIL-13-mIgG1	8H8-derived mouse mAb against murine IL-13	mil13-mab9-1
IL-28B	Anti-mIL-28b-mIgG1	3C11-derived mouse mAb against murine IL-28B	mil28b-mab9-1
LYMPHOCYTE MARKERS			
CD3	Anti-mCD3-mIgG2a	145-2C11-derived murinized mAb against murine CD3	mcd3-mab10-1
CD4	Anti-mCD4-mIgG2a	GK1.5-derived murinized mAb against murine CD4	mcd4-mab10-1
CD8	Anti-mCD8-mIgG2a	YTS169.4-derived murinized mAb against murine CD8	mcd8-mab10-1
CD25	Anti-mCD25-PC-mIgG2a	PC-61.5.3-derived murinized antibody against murine CD25 (blocking)	mcd25c1-mab10-1
	Anti-mCD25-7D4-mIgG2a	7D4-derived murinized antibody against murine CD25 (non-blocking)	mcd25c2-mab10-1
TUMOR-ASSOCIATED ANTIGENS			
CD20	Anti-mCD20-mIgG2a	18B12-derived mouse mAb against murine CD20	mcd20-mab10-1
gp75	Anti-mgp75-mIgG2a	TA99-derived mouse mAb against murine gp75	mgp75-mab10-1
ISOTYPE CONTROLS			
β-Gal	Anti-β-Gal-mIgG1	Mouse isotype controls against *E. coli* β-Galactosidase (β-Gal)	bgal-mab9-1
	Anti-β-Gal-mIgG1e3 (D265A)		bgal-mab15-1
	Anti-β-Gal-mIgG2a		bgal-mab10-1

They trust InvivoGen

More than 30 peer-reviewed publications

Ueki H, et al., 2023. Sci Rep. 13(1):9994.
An oral cancer vaccine using Bifidobacterium vector augments combination of anti-PD-1 and anti-CTLA-4 antibodies in mouse renal cell carcinoma model.

Liou GY, et al., 2017. Cell Rep. 19(7):1322-1333. The Presence of Interleukin-13 at Pancreatic ADM/PanIN Lesions Alters Macrophage Populations and Mediates Pancreatic Tumorigenesis.

Bulk Quantity Available

InvivoGen offers bulk quantities of our mouse anti-mouse mAb collection upon request.
Please contact us for more information:
tech.eu@invivogen.com

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