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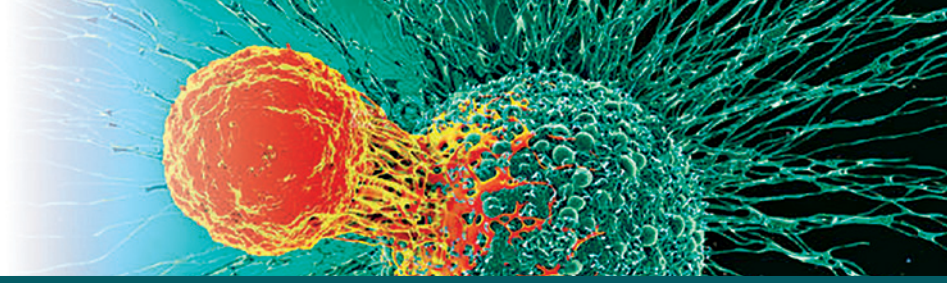

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Immune Checkpoint Reagents

Focus: T cells

Regulation and activation of T lymphocytes depend on signaling by the T cell receptor (TCR) and also by cosignaling receptors that deliver negative or positive signals (see page 5 for an **overview chart**). The amplitude and quality of the immune response of T cells is controlled by an equilibrium between costimulatory and inhibitory signals called immune checkpoints. Under normal physiological conditions, immune checkpoints are crucial for the maintenance of self-tolerance and to protect tissues from damage during pathogenic infection. Manipulations of stimulatory or inhibitory immune checkpoints using monoclonal antibodies, soluble receptors (fusion proteins) or small molecules may provide therapeutic strategies for autoimmune diseases, tumor growth, infectious diseases and transplantation by decreasing or enhancing T cell activity. IHC-competent antibodies and highly sensitive immunoassays are of great importance for diagnostic and therapeutic control purposes.

COLLABORATING WITH

Chimerigen Laboratories

The Experts for High Quality Fusion Proteins

SELECTED REVIEW ARTICLES

The future of immune checkpoint therapy: P. Sharma & J.P. Allison; Science **348,** 56 (2015) • Immune checkpoint blockade in infectious diseases: M.N. Wykes & S.R. Lewin; Nat. Rev. Immunol. **18,** 91 (2018) • Fundamental Mechanisms of Immune Checkpoint Blockade Therapy: S.C. Wei, et al.; Cancer Discov. **8,** 1069 (2018)

Highly Sensitive PD-1/PD-L1 ELISA Kits

JUST RELEASED

Biomarker for Immuno-Oncology & Autoimmune Diseases

NEW PD-1 (human) ELISA Kit

AG-45B-0015 — 96 wells

Specificity: Detects soluble human PD-1 (sPD-1) in biological fluids.
Sensitivity: 1.6 pg/ml **Range:** 3.125 to 200pg/ml
Sample: Cell Culture Supernatant, Plasma, Serum

Tumor Biomarker for Poor Survival Prognosis

NEW PD-L1 (human) ELISA Kit

AG-45B-0016 — 96 wells

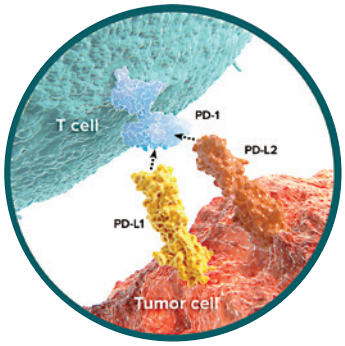
Specificity: Detects soluble human PD-L1 (sPD-L1) in biological fluids.
Sensitivity: 0.8 pg/ml **Range:** 2.34 to 150pg/ml
Sample: Cell Culture Supernatant, Plasma, Serum

Coming Soon: New ELISA Kits for CD40L, B7-H3 and B7-H4!
In collaboration with Suzhou Bright Scistar Biotechnology

CONTENTS

PD-1/PD-L1 Pathway

PD-1 (Programmed Cell Death Protein 1; CD279) is a type I transmembrane protein belonging to the CD28/CTLA-4 family of immune receptors. PD-L1 (CD274; B7-H1) and PD-L2 (B7-DC; CD273) are immuno-coinhibitory ligands of the B7 family binding to PD-1. The PD-1/PD-L1 or PD-L2 signaling pathway is a negative regulatory mechanism that inhibits T cell proliferation and cytokine production. Blockade of the PD-1/PD-L1 interaction enhances antitumor immunity. The PD-1 pathway plays a major role in the inhibition of self-reactive T cells and protection against autoimmune diseases. PD-1 and PD-L1 also exist as soluble forms. Elevated levels of soluble PD-1 (sPD-1) are shown in rheumatoid arthritis, skin sclerosis and autoimmune hepatitis. Levels of sPD-L1 are increased in the plasma of cancer patients as well as in cerebrospinal fluid of gliomas. sPD-L1 is a biomarker of poor survival in patients with B cell lymphoma, renal cell carcinoma, metastatic melanoma or lung cancer and is associated with advanced tumor stages.



SELECTED REVIEWS: PD-1/PD-L1 blockade in cancer treatment: perspectives and issues: J. Hamanishi, et al.; Int. J. Clin. Oncol. **21,** 462 (2016) • PD-1/PD-L1 immune checkpoint: Potential target for cancer therapy: F.K. Dermani, et al.; J. Cell Physiol. **234,** 1313 (2019)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
PD-1 (mouse):Fc (mouse) (rec.)	CHI-MF-110PD1	100 µg	CHO cells	<0.06EU/µg	Ms
PD-1 (mouse):Fc (human) (rec.)	CHI-MF-111PD1	100 µg	HEK 293 cells	<0.06EU/µg	Ms
PD-1 (human) (rec.) (untagged)	CHI-HF-200PD1	50 µg	HEK 293 cells	<0.01EU/µg	Hu
PD-1 (human) (rec.) (His)	CHI-HF-201PD1	100 µg	HEK 293 cells	<0.01EU/µg	Hu
PD-1 (human):Fc (human) (rec.)	CHI-HF-210PD1	100 µg	CHO cells	<0.06EU/µg	Hu
PD-1 (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220PD1	200 µg	CHO cells	<0.06EU/µg	Hu
PD-1 (human):Fc (mouse) (rec.)	CHI-HF-211PD1	100 µg	HEK 293 cells	<0.005EU/µg	Hu
PD-L1 (mouse):Fc (mouse) (rec.) (non-lytic)	CHI-MF-120PDL1	100 µg	CHO cells	<0.06EU/µg	Ms
PD-L1 (human) (rec.) (untagged)	CHI-HF-200PDL1	50 µg	HEK 293 cells	<0.01EU/µg	Hu
PD-L1 (human) (rec.) (His)	CHI-HF-201PDL1	100 µg	HEK 293 cells	<0.01EU/µg	Hu
PD-L1 (human):Fc (human) (rec.)	CHI-HF-210PDL1	100 µg	CHO cells	<0.06EU/µg	Hu
PD-L1 (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220PDL1	100 µg	CHO cells	<0.06EU/µg	Hu
PD-L1 (human):Fc (mouse) (rec.)	CHI-HF-211PDL1	100 µg	HEK 293 cells	<0.005EU/µg	Hu
PD-L2 (mouse):Fc (mouse) (rec.)	CHI-MF-110PDL2	100 µg	CHO cells	<0.06EU/µg	Ms
PD-L2 (human):Fc (human) (rec.)	CHI-HF-210PDL2	100 µg	CHO cells	<0.06EU/µg	Hu
PD-L2 (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220PDL2	100 µg	CHO cells	<0.06EU/µg	Hu
PD-L2 (human):Fc (mouse) (rec.)	CHI-HF-211PDL2	100 µg	CHO cells	<0.06EU/µg	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
NEW PD-1 (mouse), mAb (blocking) (1H10) (PF)	AG-20B-0075PF	100 µg | 500 µg	Rat IgG2aκ	FACS, FUNC	Ms
PD-1 (human), mAb (ANC4H6)	ANC-279-020	100 µg	Mouse IgG1κ	FACS	Hu
NEW PD-1 (human), mAb (AG-IHC001)	AG-20B-6020	100 µl | 1 ml	Mouse IgG1κ	IHC GRADE	Hu
PD-L1 (human), mAb (ANC6H1)	ANC-274-020	100 µg	Mouse IgG1κ	FACS	Hu
NEW PD-L1 (human), mAb (AG-IHC411)	AG-20B-6022	100 µl | 1 ml	Mouse IgG1κ	IHC GRADE	Hu
PD-L2 (human), mAb (ANC8D12)	ANC-273-020	100 µg	Mouse IgG2aκ	FACS, FUNC	Hu

BULK

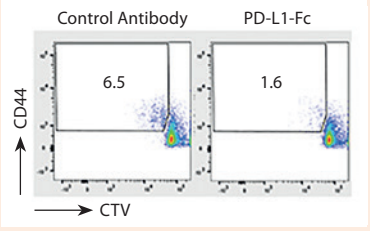
PD-L1 (mouse):Fc (mouse) (rec.)

CHI-MF-110PDL1 100 µg

BIOLOGICAL ACTIVITY: Recombinant PD-L1 (mouse):Fc (mouse) (Prod. No. CHI-MF-110PDL1) inhibits anti-CD3/CD28 antibody-induced proliferation of mouse T lymphocytes

METHOD: T cells from C57BL/6 mice were activated with coated anti-CD3/CD28 and PD-L1-Fc or control antibody (10µg/ml). Plots illustrate the percentage of dividing cells by using anti-CD44 and the dye Cell Trace Violet (CTV).

Picture Courtesy G. Guarda and A. Zenobi, Institute for Research in Biomedicine, Bellinzona (Switzerland).



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APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot **FORMULATION: PF** = Preservative free

SPECIES: Hu = Human; **Mk** = Monkey; **Ms** = Mouse; **Rt** = Rat

NEW

anti-PD-1 (mouse), mAb (blocking) (1H10)

AG-20B-0075		100 µg
AG-20B-0075PF	Preservative Free	100 µg | 500 µg

Functional Application: Blocks PD-1 binding. Induces a rapid activation and proliferation of T cells at concentration of 0.25µg/2x10^5 cells.

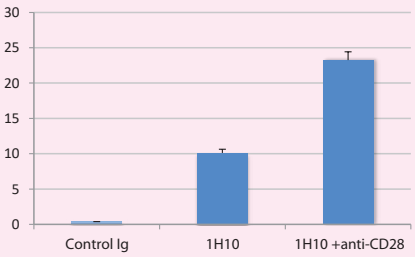


FIGURE: PD-1 receptor-induced CD4 T cell activation and proliferation by PD-1 (mouse), mAb (blocking) (1H10) (AG-20B-0075).

METHOD: Magnetic bead affinity purified CD4+ T cells from C57BL/6 mice are stimulated *in vitro* with PD-1 (mouse), mAb (blocking) (1H10), anti-CD28 and rat IgG2a isotype (control Ig) (0.25µg/2x10^5 cells) for 48h. Proliferation is determined by [3H] thymidine incorporation. The presence of anti-CD28 mAb increases 1H10 mAb-mediated proliferation.

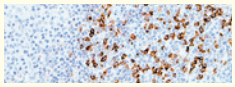
IHC GRADE

NEW IHC-Competent Antibodies for PD-1 and PD-L1 Staining

anti-PD-1 (human), mAb (AG-IHC001)

AG-20B-6020 — 100 µl | 1 ml

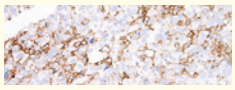
FIGURE: IHC Staining of PD-1 in human tonsil tissue using anti-PD-1 (human), mAb (AG-IHC001) (Prod. No. AG-20B-6020).



anti-PD-L1 (human), mAb (AG-IHC411)

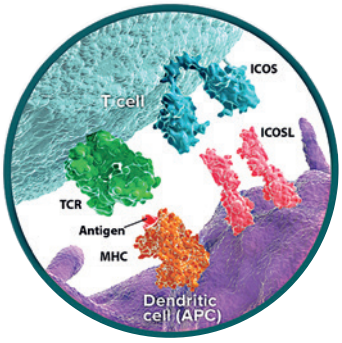
AG-20B-6022 — 100 µl | 1 ml

FIGURE: IHC Staining of PD-L1 in human lung tissue using anti-PD-L1 (human), mAb (AG-IHC411) (Prod. No. AG-20B-6022).



ICOS – ICOSL Pathway

Inducible T Cell Co-Stimulator (ICOS; CD278) is an activating receptor expressed on the surface of activated cytotoxic T cells, regulatory T cells (Tregs), NK cells and other types of T cells, having a distinct and opposing function than CTLA-4. The ligand ICOSL (B7-H2; CD275) is expressed on antigen-presenting cells (APCs) such as dendritic cells (DCs) and macrophages. ICOS/ICOSL signaling leads to the activation, proliferation and survival of cytotoxic T cells, as well as the survival of memory T cells. Recently, it has been shown that ICOS expression could be a useful predictive biomarker of response to checkpoint inhibitor treatments (e.g through the CTLA-4 axis).

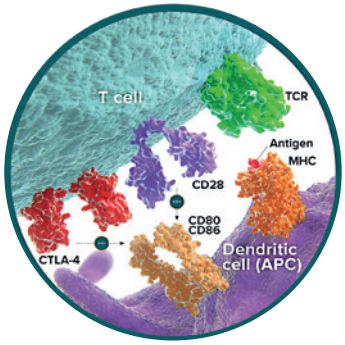


SELECTED REVIEWS: ICOS Co-Stimulation: Friend or Foe? D.J. Wikenheiser & J.S. Stumhofer; Front. Immunol. **7**, 304 (2016) • Inducible Co-Stimulator (ICOS) as a potential therapeutic target for anti-cancer therapy: F. Amatore, et al.; Expert Opin. Ther. Targets **22**, 343 (2018)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
ICOSL [B7-H2] (mouse):Fc (mouse) (rec.)	CHI-MF-110B7H2	100 µg	CHO cells	<0.06EU/µg	Ms
ICOSL [B7-H2] (mouse):Fc (mouse) (rec.) (non-lytic)	CHI-MF-120B7H2	100 µg	CHO cells	<0.06EU/µg	Ms
ICOSL [B7-H2] (human) (rec.) (His)	CHI-HF-201B7H2	50 µg	HEK 293 cells	<0.01EU/µg	Hu
ICOSL [B7-H2] (human):Fc (human) (rec.)	CHI-HF-210B7H2	100 µg	CHO cells	<0.06EU/µg	Hu
ICOSL [B7-H2] (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220B7H2	100 µg	CHO cells	<0.06EU/µg	Hu
ICOSL [B7-H2] (human):Fc (mouse) (rec.)	CHI-HF-211B7H2	100 µg	CHO cells	<0.06EU/µg	Hu
ICOS (mouse):Fc (mouse) (rec.)	CHI-MF-110ICOS	100 µg	CHO cells	<0.06EU/µg	Ms
ICOS (human):Fc (human) (rec.)	CHI-HF-210ICOS	25 µg | 100 µg	CHO cells	<0.06EU/µg	Hu
ICOS (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220ICOS	25 µg | 100 µg	CHO cells	<0.06EU/µg	Hu
ICOS (human):Fc (mouse) (rec.)	CHI-HF-211ICOS	100 µg	CHO cells	<0.06EU/µg	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
ICOSL [B7-H2] (human), mAb (ANC4E3)	ANC-263-020	100 µg	Mouse IgG1κ	ELISA	Hu
ICOS (human), mAb (ANC6C6)	ANC-265-020	100 µg	Mouse IgG1κ	FACS, FUNC	Hu

CTLA-4 [CD152] – CD80 – CD86 – CD28 Network

Cytotoxic T Lymphocyte Antigen 4 (CTLA-4; CD152) is an immune checkpoint receptor expressed on the surface of activated T cells. During immune response, T cell activation is initiated when an antigen is presented to the T cell receptor (TCR) by the major histocompatibility complex (MHC) on antigen-presenting cells (APCs). Antigen presentation alone, however, is not sufficient to induce an immune response. Completing the activation process requires a second signal. To maintain activation of an immune response, the primary costimulatory receptor on T cells CD28 binds to the ligands CD80 (B7-1) and CD86 (B7-2) on APCs. When CTLA-4 is upregulated, it competes with CD28 and has a greater affinity for CD80/86. Binding of CTLA-4 to CD80/86 inhibits T cell activation, preserving balance when the immune system is overactive.



CTLA-4 can also be found on regulatory T cells (Tregs), where it is a key driver of their ability to suppress T cell activity. With an almost indefinite lifespan, memory T cells provide long-term immunity. After they have been exposed to tumor antigen, memory T cells immediately mount an immune response against the tumor. The presence of memory T cells is associated with long-term survival and low risk of tumor recurrence in cancer. Tumor cells utilize the CTLA-4 pathway to suppress initiation of an immune response, resulting in decreased T cell activation and a reduced ability to proliferate into memory T cells. Targeting CTLA-4 can restore an immune response through the increased accumulation, function and survival of T cells and memory T cells, as well as the depletion of Tregs, and consequently improve the antitumor response.

SELECTED REVIEWS: CTLA-4 and PD-1 Pathways: Similarities, Differences, and Implications of Their Inhibition: E.I. Buchbinder & A. Desai; Am. J. Clin. Oncol. **39,** 98 (2016) • CTLA-4: a moving target in immunotherapy: B. Rowshanravan, et al.; Blood **131,** 58 (2018) • Evolving Roles for Targeting CTLA-4 in Cancer Immunotherapy: Y. Zhao, et al.; Cell Physiol. Biochem. **47,** 721 (2018)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
CD28 (mouse):Fc (mouse) (rec.)	CHI-MF-110CD28	200 µg	CHO cells	<0.06EU/µg	Ms
CD28 (human) (rec.) (His)	CHI-HF-201CD28	100 µg	HEK 293 cells	<0.06EU/µg	Hu
CD28 (human):Fc (human) (rec.)	CHI-HF-210CD28	200 µg	CHO cells	<0.06EU/µg	Hu
CD28 (human)-muIg Fusion Protein	ANC-508-020	25 µg	CHO cells	n.d.	Hu
CD80 (mouse):Fc (mouse) (rec.)	CHI-MF-110CD80	100 µg	CHO cells	<0.06EU/µg	Ms
CD80 (human):Fc (human) (rec.)	CHI-HF-210CD80	100 µg	CHO cells	<0.06EU/µg	Hu
CD80 (human):Fc (mouse) (rec.)	CHI-HF-211CD80	100 µg	CHO cells	<0.06EU/µg	Hu
CD86 (mouse):Fc (mouse) (rec.)	CHI-MF-110CD86	100 µg	CHO cells	<0.06EU/µg	Ms
CD86 (human):Fc (human) (rec.)	CHI-HF-210CD86	100 µg	CHO cells	<0.06EU/µg	Hu
CD86 (human):Fc (mouse) (rec.)	CHI-HF-211CD86	100 µg	HEK 293 cells	<0.005EU/µg	Hu
CD86 (var) (human)-muIg Fusion Protein	ANC-589-020	25 µg	CHO cells	n.d.	Hu
CD86 (P2) (human)-muIg Fusion Protein	ANC-579-020	25 µg	CHO cells	n.d.	Hu
CTLA-4 (mouse):Fc (mouse) (rec.)	CHI-MF-110A4	100 µg | 500 µg | 1 mg	NS1 cells	<0.06EU/µg	Ms
CTLA-4 (mouse):Fc (mouse) (rec.) (non-lytic)	CHI-MF-120A4	100 µg | 500 µg | 1 mg	NS1 cells	<0.06EU/µg	Ms
CTLA-4 (human):Fc (human) (rec.)	CHI-HF-210A4	100 µg | 500 µg | 1 mg	CHO cells	<0.06EU/µg	Hu
CTLA-4 (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220A4	100 µg | 500 µg | 1 mg	CHO cells	<0.06EU/µg	Hu
CTLA-4 (human):Fc (mouse) (rec.)	CHI-HF-211A4	100 µg	CHO cells	<0.06EU/µg	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
CD28 (human), mAb (ANC28.1/5D10)	ANC-177-020	100 µg	Mouse IgG1κ	FACS, FUNC	Hu
CD80 (human), mAb (P1.H1.A1.A1)	ANC-110-020	100 µg	Mouse IgG1	FACS, FUNC	Hu
CD86 (human), mAb (BU63)	ANC-307-020	100 µg	Mouse IgG1	FACS, FUNC (Blocking)	Hu, Primate
CD152 (human), mAb (ANC152.2/8H5)	ANC-359-020	100 µg	Mouse IgG1κ	FACS, FUNC (Blocking)	Cat, Cow, Dog, Hu, Pig

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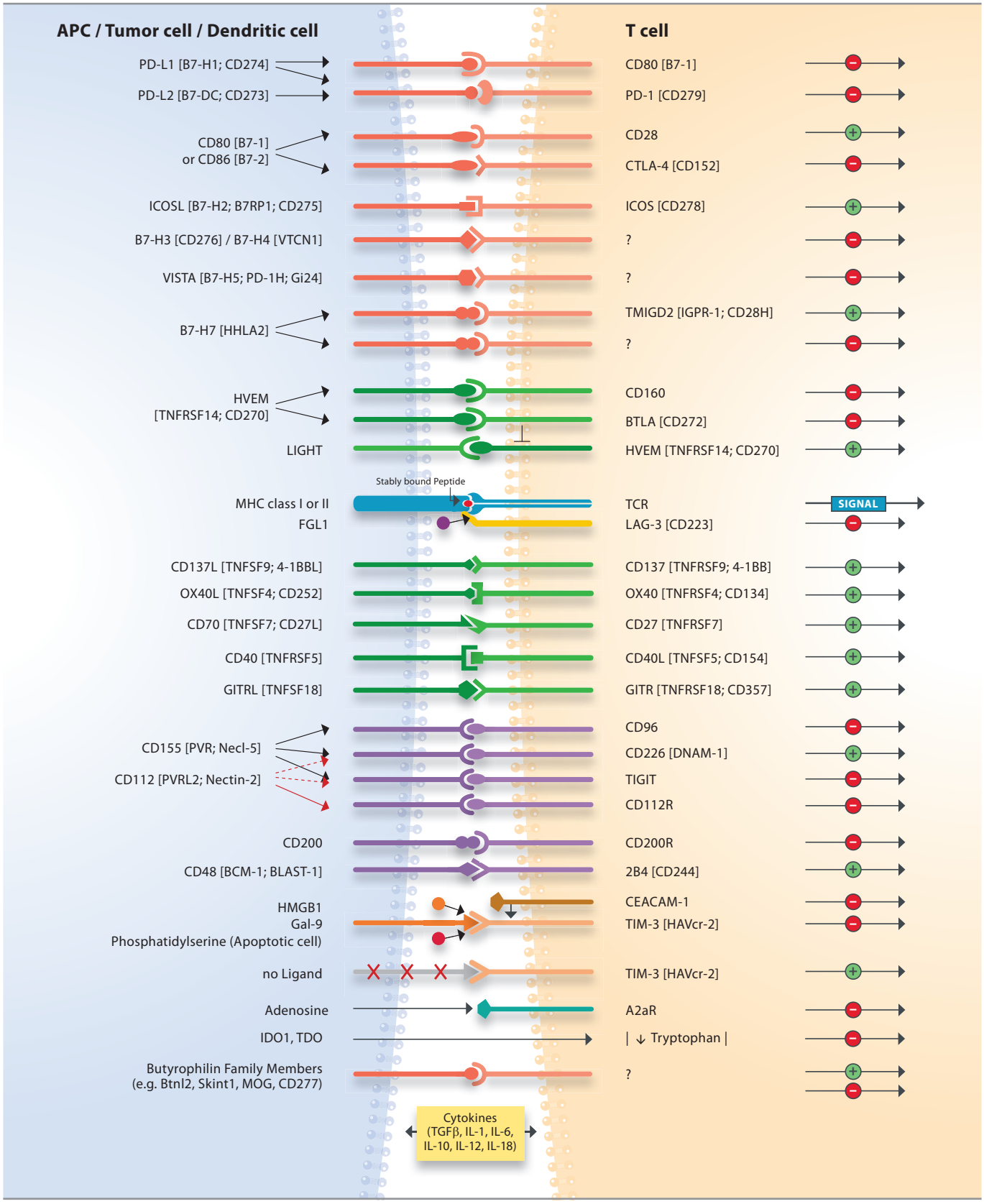
APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot **FORMULATION: PF** = Preservative free

SPECIES: Hu = Human; **Mk** = Monkey; **Ms** = Mouse; **Rt** = Rat

Overview on Immune Checkpoints



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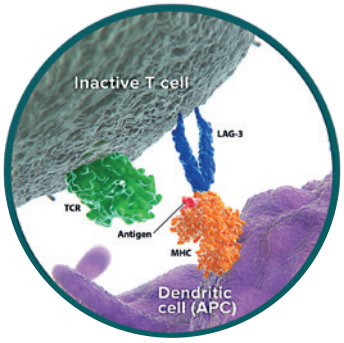
LAG-3 – MHC – TCR Pathway



Lymphocyte-activation Gene 3 (LAG-3; CD223) is an immune checkpoint receptor expressed on the surface of both activated cytotoxic T cells and regulatory T cells (Tregs). LAG-3 selectively inhibits the activation of T cells responsive to stable but not unstable major histocompatibility complex (MHC) class II (pMHCII). LAG-3 binds also to the newly discovered ligand of the fibrinogen family protein, Fibrinogen-Like Protein 1 (FGL1). LAG-3 negatively regulates T cell proliferation and the development of lasting memory T cells.

LAG-3 synergizes with PD-1 in suppressing autoimmunity, tumor immunity and infection immunity and can also trigger the immunosuppressive activity of Tregs. Increased LAG-3 expression has been associated with poorer prognosis in multiple tumor types. Dual inhibition of LAG-3 and other checkpoint pathways may synergistically increase T cell antitumor activity.

SELECTED REFERENCES: The CD4-like molecule LAG-3, biology and therapeutic applications: S. Sierro, et al.; Expert Opin. Ther. Targets **15,** 91 (2011) • LAG-3 in Cancer Immunotherapy: M.V. Goldberg & C.G. Drake; Curr. Top. Microbiol. Immunol. **344,** 269 (2011) • The promising immune checkpoint LAG-3: from tumor microenvironment enes Cancer **9,** 176 (2018) • Fibrinogen-like protein 1 is a major immune inhibitory ligand of LAG-3: J. Wang, et al.; Cell **176,** 334 (2019)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
LAG-3 (mouse):Fc (mouse) (rec.)	AG-40B-0039	50 µg	CHO cells	<0.01EU/µg	Hu, Ms
LAG-3 (human):Fc (human) (rec.)	AG-40B-0031	50 µg	CHO cells	<0.001EU/µg	Hu, Mk, Ms
LAG-3 (human):Fc (human) (rec.)	CHI-HF-210LAG3	50 µg	HEK 293 cells	<0.005EU/µg	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
LAG-3, mAb (blocking) (11E3) (PF)	AG-20B-0011PF	100 µg	Mouse IgG1	FUNC, ICC, IHC, IP, WB	Hu, Mk
LAG-3 (human), mAb (blocking) (17B4) (PF)	AG-20B-0012PF	100 µg	Mouse IgG1	FACS, FUNC, ICC, IHC, IP, WB	Hu
NEW LAG-3 (human), mAb (AG-IHC103)	AG-20B-6023	100 µl | 1 ml	Mouse IgG1	IHC GRADE	Hu
MHC Class I (human), mAb (3F10)	ANC-121-020	100 µg	Mouse IgG2a	ELISA, FACS, IHC	Hu
MHC Class II (human), mAb (TDR31.1)	ANC-131-020	100 µg	Mouse IgG1	FACS, IHC, WB	Hu
TCR Cb1 (human), mAb (Jovi-1)	ANC-101-020	100 µg	Mouse IgG2a	FACS	Hu
TCR Vb3 (human), mAb (Jovi-3)	ANC-102-020	100 µg	Mouse IgG2aλ	FACS	Hu
CD3 (human), mAb (UCHT1)	ANC-144-020	100 µg	Mouse IgG1	FACS, WB, FUNC	Hu
CD3 (mouse), mAb (145-2C11)	ANC-703-020	100 µg	Hamster IgG	FACS, IP, WB	Ms
CD4 (human), mAb (QS4120)	ANC-147-020	100 µg	Mouse IgG1κ	FACS, FUNC	Hu
CD4 (human), mAb (M-T441)	ANC-148-020	100 µg	Mouse IgG2b	FACS	Hu, Mk
CD4 (mouse), mAb (GK1.5) (PF)	ANC-704-820	100 µg	Rat IgG2bκ	FACS, FUNC, IHC, IP	Ms
CD8 (human), mAb (UCHT4)	ANC-153-020	100 µg	Mouse IgG2a	FACS, ICC, WB	Hu
CD8 (human), mAb (14)	ANC-154-020	100 µg	Mouse IgG1κ	FACS	Hu
CD8-α (mouse), mAb (53-6)	ANC-260-020	100 µg	Rat IgG2aκ	FACS	Ms

COMING SOON: Unique High Affinity Mouse LAG-3:COMP Protein!

LATEST INSIGHT

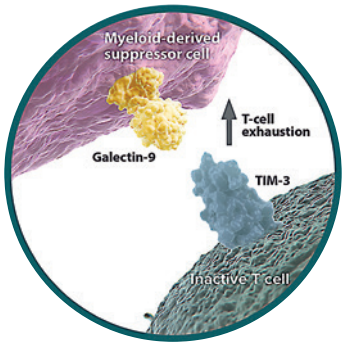
LAG-3 – A Selective Immune Checkpoint Protein

A new study from the lab of Taku Okazaki (Tokushima University, Japan) reveals how LAG-3 inhibits the activation of T cell response. It does not recognize MHC class II universally, but instead recognizes selectively MHC class II proteins presenting only stably bound peptides. In addition, the same study shows that LAG-3 does not compete CD4 for MHC-II interaction, but it blocks T cells by transducing inhibitory signals via its intracellular region. This recent study gives a new view on LAG-3 that might function more selectively than previously thought and probably acts to maintain immune tolerance to dominant autoantigens.

LIT: LAG-3 inhibits the activation of CD4+ T cells that recognize stable pMHCII through its conformation-dependent recognition of pMHCII: T. Maruhashi, et al.; Nat. Immunol. **19,** 1415 (2018)

APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot **FORMULATION: PF** = Preservative free
SPECIES: Hu = Human; **Mk** = Monkey; **Ms** = Mouse; **Rt** = Rat

TIM-3 – Galectin-9 Pathway

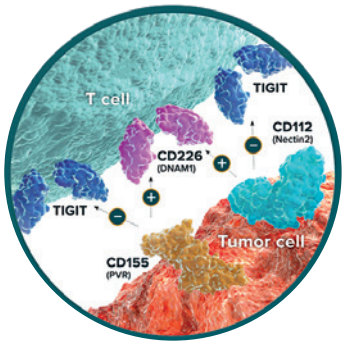


T Cell Immunoglobulin and Mucin-3 (TIM-3; HAVcr-2) is an immune checkpoint receptor involved in the suppression of both innate and adaptive immune cells. It is expressed on a wide variety of immune cells, including cytotoxic T cells, regulatory T cells (Tregs), natural killer (NK) cells and antigen-presenting cells (APCs) such as dendritic cells (DCs). TIM-3 suppresses effector cells through the interaction with a broad array of ligands: carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1), galectin-9, phosphatidylserine (PS) and high mobility group box 1 (HMGB1). Blockade of TIM-3 can rescue NK-cell activity, promotes tumor antigen processing and reinvigorates exhausted T cells, restoring their proliferation and function.

SELECTED REVIEWS: Tim-3 and its role in regulating anti-tumor immunity: M. Das, et al.; Immunol. Rev. **276,** 97 (2017) • TIM-3, a promising target for cancer immunotherapy: Y. He, et al.; Onco Targets Ther. **11,** 7005 (2018)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
Galectin-9 (human):Fc (human) (rec.)	CHI-HF-210GAL9	50 µg	HEK 293 cells	<0.005EU/µg	Hu
HMGB1 (human) (rec.) (His)	CHI-HR-200HMGB1	25 µg	E. coli	<0.1EU/µg	Hu
HMGB1 (rat) (rec.) (His)	CHI-RR-300HMGB1	25 µg	E. coli	<0.1EU/µg	Rt
HMGB1 (rat):Fc (human) (rec.)	CHI-RF-311HMGB1	50 µg	CHO cells	<0.06EU/µg	Rt
Tim-3 (mouse):Fc (mouse) (rec.)	CHI-MF-110T3	100 µg	HEK 293 cells	<0.005EU/µg	Ms
Tim-3 (mouse):Fc (human) (rec.)	CHI-MF-111T3	100 µg	CHO cells	<0.06EU/µg	Ms
Tim-3 (human):Fc (human) (rec.)	CHI-HF-210T3	100 µg	CHO cells	<0.06EU/µg	Hu
Tim-3 (human):Fc (mouse) (rec.)	CHI-HF-211T3	100 µg	CHO cells	<0.06EU/µg	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
Tim-3 (mouse), mAb (TI 142F)	AG-20A-0030	50 µg | 100 µg	Rat IgG2aκ	ELISA, FACS	Ms
NEW Tim-3 (human), mAb (AG-IHC003)	AG-20B-6021	100 µl | 1 ml	Mouse IgG1	IHC GRADE	Hu

TIGIT – CD155 – CD112 – CD226 Network



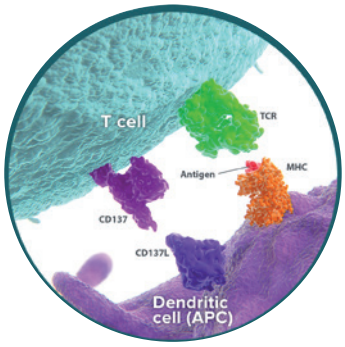
T Cell Immunoreceptor with Immunoglobulin and ITIM domains (TIGIT) is an immune checkpoint receptor expressed on the surface of cytotoxic, memory and regulatory T cells (Tregs) as well as natural killer (NK) cells. TIGIT binding to CD155 (PVR) and CD112 (Nectin-2) suppresses immune activation on cytotoxic T cells and NK cells. In the normal immune system, the suppressive effect of TIGIT is counterbalanced by the immune-activating receptor CD226 (DNAM1), which competes with TIGIT to bind CD155 and CD112. The inhibitory signal provided by TIGIT overpowers the ability of CD226 to stimulate T cell activation. Tumor cells exploit the dominance of the inhibitory TIGIT pathway to avoid immune-mediated destruction. Recently, a new regulator of the immune system CD112R has been described and may become a new attractive cancer immunotherapy target.

SELECTED REVIEWS: Identification of CD112R as a novel checkpoint for human T cells: Y. Zhu, et al.; J. Exp. Med. **213,** 167 (2016) • Interaction of PVR/PVRL2 with TIGIT/DNAM-1 as a novel immune checkpoint axis and therapeutic target in cancer: H. Stamm, et al.; Mamm. Genome **29,** 694 (2018)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
NEW CD112R (mouse):Fc (human) (rec.)	AG-40B-0170	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Ms
CD155 [PVR] (human)-mulg Fusion Protein	ANC-555-020	25 µg	CHO cells	n.d.	Hu
TIGIT (human):Fc (human) (rec.)	AG-40B-0162	50 µg	HEK 293 cells	<0.01EU/µg	Hu
TIGIT (human)-mulg Fusion Protein	ANC-556-020	25 µg	CHO cells	n.d.	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
NEW CD112R (mouse), pAb (IN109)	AG-25B-0035	100 µg	Rabbit	ELISA, WB	Ms
CD155 [PVR] (human), mAb (ANC2B2)	ANC-255-020	100 µg	Mouse IgG1κ	ELISA, FACS	Hu
CD155 [PVR] (human), mAb (ANC6A3)	ANC-350-020	100 µg	Mouse IgG1κ	ELISA, FACS	Hu
TIGIT (human), mAb (ANCTG6/10A6)	ANC-340-020	100 µg	Mouse IgG1κ	ELISA, FACS	Hu

CD137 – CD137L Pathway

CD137 (4-1BB; TNFRSF9) is an activating receptor binding to CD137L (4-1BBL; TNFSF9). Because CD137 is expressed on both natural killer (NK) cells and T cells, it can trigger both innate and adaptive immunity. After these cells have been activated by exposure to tumor antigen, CD137 signals stimulate them to reproduce and to generate antitumor activity. CD137 has been shown to play a critical role on T cells in the development of immune memory and the creation of a durable immune response. On lymphocytes, the presence of CD137 appears to be a marker for tumor reactivity. Activation of CD137 signaling can stimulate both cytotoxic T cell and NK cell activity and generate a lasting memory response.



SELECTED REVIEWS: 4-1BB (CD137), an inducible costimulatory receptor, as a specific target for cancer therapy: D.S. Vinay & B.S. Kwon; BMB Rep. **47,** 122 (2014) • CD137 and CD137L signals are main drivers of type 1, cell-mediated immune responses: B. Dharmadhikari, et al.; Oncoimmunology **5,** e1113367 (2015)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
CD137 (mouse):Fc (human) (rec.)	AG-40A-0025	50 µg	HEK 293 cells	<0.1EU/µg	Ms
CD137 (human) (rec.) (His)	CHI-HR-200CD137	25 µg	E. coli	<0.1EU/µg	Hu
CD137 (human):Fc (human) (rec.)	AG-40B-0060	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Hu
CD137 (human):Fc (human) (rec.)	CHI-HF-210CD137	100 µg	CHO cells	<0.06EU/µg	Hu
CD137 (human):Fc (mouse) (rec.)	CHI-HF-211CD137	100 µg	HEK 293 cells	<0.005EU/µg	Ms
CD137L, Soluble (mouse) (rec.)	AG-40A-0020Y	50 µg	HEK 293 cells	<0.01EU/µg	Ms
CD137L, Soluble (human) (rec.)	AG-40A-0198T	50 µg	HEK 293 cells	<0.06EU/µg	Hu
Fc (human):CD137L, Soluble (human) (rec.)	AG-40B-0173	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu
CD137L (human)-muCD8 Fusion Protein	ANC-503-020	25 µg	CHO cells	n.d.	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
CD137 (human), mAb (4B4-1)	ANC-360-020	100 µg	Mouse IgG1κ	FACS, FUNC	Hu, Mk
CD137 (human), pAb	AG-25A-0018	100 µg	Rabbit	FACS, WB	Hu
CD137L (human), mAb (41B436)	AG-20A-0031	50 µg | 100 µg	Mouse IgG1κ	FACS, ICC, WB	Hu
CD137L (human), mAb (ANC5D6)	ANC-365-020	100 µg	Mouse IgG2aκ	FACS, WB	Hu

GITR – GITRL Pathway

Glucocorticoid-induced TNFR-related protein (GITR; CD357; TNFRSF18) is an activating receptor on the surface of T cells and other immune cells, binding to its ligand GITRL (TNFSF18). Once exposure to tumor antigen activates a T cell, the number of GITR receptors on its surface increases. On the activated T cell, GITR acts as a costimulatory receptor, meaning that it is a receptor whose signaling enhances cell reproduction and the generation of cancer-killing activity. Activation of GITR signaling can also help to enhance immunity through the activation of cytotoxic T cells and inhibition of Treg activity.

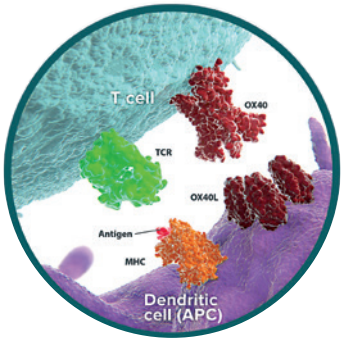
SELECTED REVIEWS: Modulation of GITR for cancer immunotherapy: D.A. Schaer, et al.; Curr. Opin. Immunol. **24,** 217 (2012) | Rationale for anti-GITR cancer immunotherapy: D.A. Knee, et al.; Eur. J. Cancer **67,** 1 (2016)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
GITR (mouse):Fc (human) (rec.)	AG-40B-0002	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Ms
GITR (human):Fc (human) (rec.)	AG-40B-0028	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Hu
GITRL, Soluble (mouse) (rec.)	AG-40A-0008	50 µg	HEK 293 cells	<0.1EU/µg	Ms
GITRL, Soluble (human) (rec.)	CHI-AG-40A-0019	50 µg	HEK 293 cells	<0.06EU/µg	Hu
GITRL, Soluble (human) (rec.) (His)	AG-40A-0024T	10 µg | 50 µg	HEK 293 cells	<0.06EU/µg	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
GITR (human), mAb (ANC7D6)	ANC-268-020	100 µg	Mouse IgMκ	FACS	Hu
GITR (human), mAb (ANC5E3)	ANC-368-020	100 µg	Mouse IgG3κ	FACS	Hu
GITR (human), mAb (AIT 158D)	AG-20A-0017	50 µg | 100 µg	Rat IgG2aκ	FACS	Hu
GITR (human), pAb	AG-25A-0017	100 µg	Rat	FACS	Hu
GITRL (human), pAb	AG-25A-0023	100 µg	Rabbit	IHC, WB	Hu

For *in vivo* Studies

APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free
SPECIES: Hu = Human; **Mk** = Monkey; **Ms** = Mouse; **Rt** = Rat

OX40 – OX40L Pathway



OX40 (CD134; TNFRSF4) is an activating receptor expressed on the surface of activated cytotoxic T cells and regulatory T cells (Tregs). OX40 plays a dual role in the immune response, both activating and amplifying T cell responses. On cytotoxic T cells, OX40 binds to its ligand OX40L (CD252; TNFSF4), resulting in stimulatory signals that promote T cell reproduction, function and survival. OX40/OX40L signaling blocks the ability of Tregs to suppress T cells and reduces Treg generation. By inhibiting the immunosuppressive effect of Tregs and limiting their population, OX40 further amplifies the impact of T cell activation. The dual effects of OX40 help to create a tumor microenvironment that is more favorable to the antitumor immune response.

SELECTED REVIEWS: OX40: Structure and function - What questions remain? J. Willoughby, et al.; Mol. Immunol. **83,** 13 (2017) • The immunobiology of CD27 and OX40 and their potential as targets for cancer immunotherapy: S.L. Buchan, et al.; Blood **131,** 39 (2018)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
OX40 (mouse):Fc (human) (rec.)	CHI-MF-111CD134	100 µg	HEK 293 cells	<0.005EU/µg	Ms
OX40 (human) (rec.) (His)	CHI-HR-200CD134	25 µg	E. coli	<0.1EU/µg	Hu
OX40 (human):Fc (human) (rec.)	AG-40B-0014	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
OX40 (human):Fc (human) (rec.)	CHI-HF-210CD134	50 µg	CHO cells	<0.06EU/µg	Hu
OX40 (human):Fc (mouse) (rec.)	CHI-HF-211CD134	100 µg	HEK 293 cells	<0.005EU/µg	Hu
OX40L (mouse) (multimeric) (rec.)	AG-40B-0029	10 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
Fc (human):OX40L, Soluble (human) (rec.)	AG-40B-0172	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu
OX40L (human) (rec.) (His)	CHI-HF-201CD252	50 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
OX40L (human):Fc (mouse) (rec.)	CHI-HF-211CD252	100 µg	HEK 293 cells	<0.005EU/µg	Hu, Ms
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
OX40 (human), mAb (BerAct35)	ANC-355-020	100 µg	Mouse IgG1	ELISA, FACS, IHC	Hu
OX40L (human), mAb (rec.) (blocking) (R4930) (PF)	AG-27B-6001PF	100 µg	Human IgG1κ	FACS, FUNC	Hu
OX40L (human), mAb (ANC10G1)	ANC-400-020	100 µg	Mouse IgG1κ	FACS, FUNC	Hu

HVEM – BTLA – LIGHT – CD160 Network

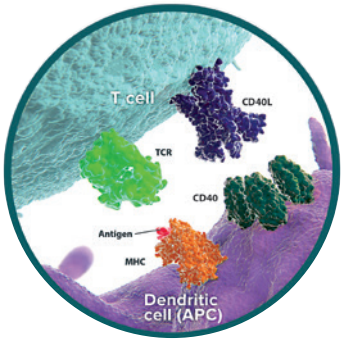
HVEM (CD270; TNFRSF14) is a molecular switch that acts both as an immune system stimulator and as an inhibitor. It is expressed in T cells, B cells, natural killer cells, dendritic cells and endothelial cells. LIGHT is an immune stimulator that contributes to dendritic cell maturation and T cell expansion. The immune suppressor BTLA functions in opposition to LIGHT in suppression of naïve T cell expansion and induction of Treg cells. CD160 acts as an immune suppressor through its interactions with HVEM. The checkpoint receptors/ligands system HVEM, LIGHT, CD160, and BTLA (CD272) is part of a complex network of overlapping receptor interactions that function in both immune stimulation and suppression and which is a potential therapeutic target for treatment of autoimmune diseases and allergies and controlling antitumor responses.

SELECTED REVIEWS: Identification of CD112R as a novel checkpoint for human T cells: Y. Zhu, et al.; J. Exp. Med. **213,** 167 (2016) • Cosignaling molecules around LIGHT-HVEM-BTLA: from immune activation to therapeutic targeting: C. Pasero, et al.; Curr. Mol. Med. **9,** 911 (2009) • HVEM/LIGHT/BTLA/CD160 cosignaling pathways as targets for immune regulation: M.L. del Rio, et al.; J. Leukoc. Biol. **87,** 223 (2010)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
BTLA (human):Fc (human) (rec.)	CHI-HF-210CD272	100 µg	CHO cells	<0.06EU/µg	Hu
BTLA (human):Fc (mouse) (rec.)	CHI-HF-211CD272	100 µg	CHO cells	<0.06EU/µg	Hu
CD160 (HUMAN):FC (HUMAN) (REC.)	CHI-HF-210CD160	100 µg	CHO cells	<0.06EU/µg	Hu
LIGHT, Soluble (human) (rec.)	AG-40B-0009	10 µg | 3 x 10 µg	CHO cells	<0.01EU/µg	Hu, Ms
HVEM (human)-mIgG Fusion Protein	ANC-531-020	25 µg	CHO cells	n.d.	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
BTLA (human), mAb (6F4)	AG-20B-0049	100 µg	Rat IgG1	FACS, FUNC	Hu
BTLA (human), mAb (ANC6E9)	ANC-272-020	100 µg	Mouse IgG1κ	FACS, FUNC	Hu
BTLA (human), mAb (ANC5A5)	ANC-372-020	100 µg	Mouse IgG1κ	FACS	Hu
HVEM (human), mAb (ANC3B7)	ANC-270-020	100 µg	Mouse IgG2aκ	FACS	Hu

CD40 – CD40L Pathway

CD40 is a member of the TNF receptor family expressed by antigen-presenting cells (APCs) and B cells whereas its ligand, CD40L (CD154), is expressed by activated T cells. Interaction between CD40-CD40L stimulates cytokines secretion of B cells with subsequent T cell activation and antitumor immunity. This T cell priming effect of the CD40-CD40L pathway might be a useful approach in anticancer immunotherapy.



SELECTED REVIEWS: Cancer immunotherapy: activating innate and adaptive immunity through CD40 agonists: G.L. Beatty, et al.; Expert Rev. Anticancer Ther. **17,** 175 (2017) • Multiple effects of CD40-CD40L axis in immunity against infection and cancer: A. Ara, et al.; Immunotargets Ther. **7,** 55 (2018)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
CD40 (human):Fc (human) (rec.)	AG-40B-0083	50 µg | 3 x 50 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
CD40 (human):Fc (human) (rec.)	CHI-HF-210CD40	100 µg	CHO cells	<0.06EU/µg	Hu
CD40 (human)-muIg Fusion Protein	ANC-504-020	25 µg	CHO cells	n.d.	Hu
CD40L (mouse) (multimeric) (rec.)	AG-40B-0020	10 µg | 3 x 10 µg	CHO cells	<0.01EU/µg	Hu, Ms
CD40L (human) (multimeric) (rec.)	AG-40B-0010	10 µg | 3 x 10 µg	CHO cells	<0.01EU/µg	Hu
CD40L (human):Fc (human) (rec.)	CHI-HF-210CD40L	50 µg	CHO cells	<0.06EU/µg	Hu
CD40L (human)-muCD8 Fusion Protein	ANC-505-020	25 µg	CHO cells	n.d.	Hu
CD40L (rat) (multimeric) (rec.)	AG-40B-0107	10 µg | 3 x 10 µg	CHO cells	<0.02EU/µg	Hu, Ms, Rt
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
CD40 (mouse), mAb (FGK45) (PF)	AG-20B-0036PF	100 µg | 500 µg	Rat IgG2a	FACS, FUNC	Ms
CD40 (human), mAb (BE-1)	ANC-189-020	100 µg	Mouse IgG1	FACS, FUNC, IP	Hu
CD40 (human), mAb (EA-5)	ANC-300-020	100 µg	Mouse IgG1	FACS, FUNC	Hu, Rt
CD40L (human), mAb (rec.) (blocking) (hu5c8) (PF)	AG-27B-6002PF	100 µg	Human IgG1κ	FUNC, WB	Hu, Dog
CD40L (human), mAb (24-31)	ANC-353-020	100 µg	Mouse IgG1	FACS, FUNC, IHC, WB	Hu, Primate

LATEST INSIGHT B Cell Expansion

Highly Potent B Cell Activators and T Cell Priming Reagents

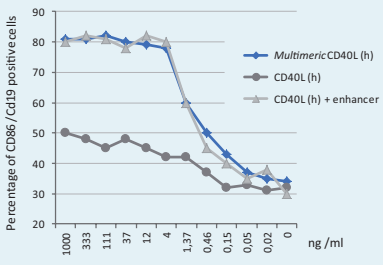
CD40 activation tools can be used to expand B cells (EBCs), which, as antigen-presenting cells (APCs), are as effective as dendritic cells and promises to streamline the generation of antitumor $CD8^+$ T cells. Several studies show that usage of the agonistic anti-CD40 antibody (FGK45) (Prod. No. AG-20B-0036PF) and MultimericCD40L (Prod. No. AG-40B-0010) are strong stimulators of antitumor immunity.

LIT: R.S. Kornbluth, et al.; Int. Rev. Immunol. **31,** 279 (2012) • K.T. Byrne & R.H. Vonderheide; Cell Rep. **15,** 2719 (2016)

CD40L (human) (multimeric) (rec.)

AG-40B-0010 — 10 µg | 3 x 10 µg

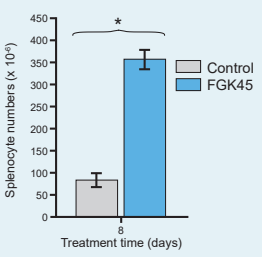
FIGURE: CD40L (human) (multimeric) (rec.) (Prod. No. AG-40B-0010) does not need an enhancer to induce B cell activation.



anti-CD40 (mouse), mAb (FGK45)

AG-20B-0036 — 100 µg | 500 µg
AG-20B-0036PF — Preservative Free — 100 µg | 500 µg | 5 mg

FIGURE: Systemic immune activation by CD40 ligation. Mice were sacrificed on day 8 after daily treatment on day 4-7 with FGK45 or control. FGK45 treatment elevated splenocyte numbers in both groups. *P < 0.005. Data represent mean ± SD for three to four mice per group.



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For *in vivo* Studies

APPLICATIONS: FUNC: Functional Application; **ICC:** Immunocytochemistry; **IHC:** Immunohistochemistry; **IP:** Immunoprecipitation; **WB:** Western blot
FORMULATION: PF = Preservative free
SPECIES: Hu = Human; **Mk** = Monkey; **Ms** = Mouse; **Rt** = Rat

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Other Immune Checkpoint Proteins

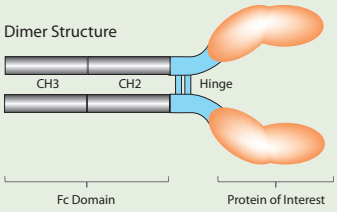
PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
CD27 (human) (rec.) (His)	CHI-HR-200CD27	50 µg	E. coli	<0.1EU/µg	Hu
CD27 (human):Fc (human) (rec.)	CHI-HF-210CD27	100 µg	CHO cells	<0.06EU/µg	Hu
CD27 (human)-muIg Fusion Protein	ANC-543-020	25 µg	CHO cells	n.d.	Hu
CD200 (mouse):Fc (mouse) (rec.) (non-lytic)	CHI-MF-120CD200	50 µg	CHO cells	<0.06EU/µg	Ms
CD200 (human):Fc (human) (rec.) (non-lytic)	CHI-HF-220CD200	100 µg	CHO cells	<0.06EU/µg	Hu
CD244(2B4) (human)-muIg Fusion Protein	ANC-544-020	25 µg	CHO cells	n.d.	Hu
ANTIBODIES	**PID**	**SIZE**	**ISOTYPE**	**APPLICATION**	**SPECIES**
CD27 (human), mAb (M-T271)	ANC-176-020	100 µg	Mouse IgG1	ELISA, FACS	Hu
CD48 (human), mAb (5-4.8)	ANC-199-020	100 µg	Mouse IgG2a	FACS	Hu

TECHNICAL NOTE AdipoGen's Technologies of Protein Multimerization

Ig-based Fusion Cytokines – Long Circulating Half-life

The potential clinical application of cytokines to modulate immune responses is very high. Unfortunately, most cytokines have short circulating half-lives. Therefore, to facilitate the study of cytokine effects *in vivo*, a variety of non-lytic immunoglobulin-based chimeric cytokine Fc-fusion proteins have been created.

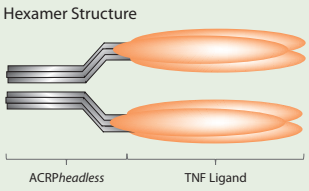
- The genetically fusion of a cytokine sequence to the hinge, CH2 and CH3 regions of an immunoglobulin (Fc domain), determines a prolonged circulating half-life.
- From a biophysical perspective the Fc domain folds independently and can improve the solubility and stability of the partner molecule both *in vitro* and *in vivo*.
- **Non-lytic:** Mutations to the complement (C1q) and FcγR I binding sites of the IgGs Fc fragment render the fusion proteins incapable of antibody directed cytotoxicity (ADCC) and complement directed cytotoxicity (CDC).



TNF Ligands Multimeric Proteins – Higher Activity, Lower Endotoxin

*Multimeric*Ligands™ are high activity constructs in which two trimeric TNFSF ligands are linked via the oligomeric collagen domain of ACRP30 [ACRP30*headless*] and therefore mimic the membrane-bound forms of the proteins.

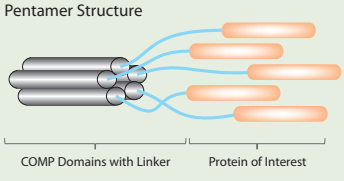
Endogenous TNF superfamily ligands are either active as membrane-form (e.g. FasL, TRAIL, CD40L, OX40L) or are secreted and activated through oligomerization by the binding of proteoglycans at the surface of cells (e.g. APRIL). To mimic endogenous TNF ligands activity, the oligomerization of recombinant TNF ligands can be triggered by fusing the TNF superfamily ligands, to the collagen domain of the protein ACRP30 (which itself has no functional activity) to form a hexameric structure and therefore creating "Multimeric Proteins".



COMP-Fusion Proteins – Improved Avidity & Biological Activity

The avidity (binding) and activity of certain proteins is improved by addition of a oligomerization domain fused at the N- or C-terminus of the protein of interests. To improve avidity and activity of some key proteins, AdipoGen Life Sciences uses the "COMP"-Technology.

COMP-Fusion Proteins are based on the pentamerization domain (minimal coiled-coil domain) of the cartilage oligomeric matrix protein (COMP) which is fused through a specific linker to proteins of interest. Using this technology it is possible to generate a five-stranded α-helical bundle with improved avidity and biological activity.



New B7 Family Immune Checkpoint Proteins

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
B7-H3 [CD276] (mouse):Fc (mouse) (rec.)	CHI-MF-110B7H3	100 µg	CHO cells	<0.06EU/µg	Ms
B7-H3 [CD276] (human) (rec.) (untagged)	CHI-HF-200B7H3	50 µg	HEK 293 cells	<0.01EU/µg	Hu
B7-H3 [CD276] (human):Fc (human) (rec.)	CHI-HF-210B7H3	100 µg	CHO cells	<0.06EU/µg	Hu
B7-H3 [CD276] (human):Fc (mouse) (rec.)	CHI-HF-211B7H3	100 µg	CHO cells	<0.06EU/µg	Hu
B7-H3(4Ig) [B7-H3b] (human) (rec.) (His)	CHI-HF-201B7H3B	50 µg	HEK 293 cells	<0.01EU/µg	Hu
B7-H3(4Ig) [B7-H3b] (human):Fc (mouse) (rec.)	CHI-HF-211B7H3B	100 µg	HEK 293 cells	<0.005EU/µg	Hu
B7-H4 (mouse):Fc (mouse) (rec.)	CHI-MF-110B7H4	100 µg	CHO cells	<0.06EU/µg	Ms
B7-H4 (human) (rec.) (untagged)	CHI-HF-200B7H4	50 µg	HEK 293 cells	<0.01EU/µg	Hu
B7-H4 (human) (rec.) (His)	CHI-HF-201B7H4	50 µg	HEK 293 cells	<0.01EU/µg	Hu
B7-H4 (human):Fc (human) (rec.)	CHI-HF-210B7H4	100 µg	CHO cells	<0.06EU/µg	Hu
B7-H4 (human):Fc (mouse) (rec.)	CHI-HF-211B7H4	100 µg	CHO cells	<0.06EU/µg	Hu
B7-H4 (human):Fc (rabbit) (rec.)	CHI-HF-212B7H4	100 µg	HEK 293 cells	<0.005EU/µg	Hu
VISTA [B7-H5] (mouse):Fc (human) (rec.)	AG-40B-0164	50 µg	HEK 293 cells	<0.01EU/µg	Ms
VISTA [B7-H5] (human) (rec.) (His)	AG-40B-0177	10 µg | 3 x 10 µg	HEK 293 cells	<0.01EU/µg	Hu
VISTA [B7-H5] (human) (rec.) (His)	CHI-HF-201B7H5	50 µg	HEK 293 cells	<0.01EU/µg	Hu
VISTA [B7-H5] (human):Fc (human) (rec.)	AG-40B-0163	50 µg	HEK 293 cells	<0.01EU/µg	Hu, Ms
VISTA [B7-H5] (human):Fc (mouse) (rec.)	CHI-HF-211B7H5	100 µg	HEK 293 cells	<0.005EU/µg	Hu
B7-H6 (human):Fc (mouse) (rec.)	CHI-HF-211B7H6	100 µg	HEK 293 cells	<0.005EU/µg	Hu

LATEST INSIGHT

VISTA:COMP – Immunosuppressive *In Vivo* Agonist

VISTA is a new negative checkpoint regulator that potently suppresses T cell activation. Recently, it has been reported that recombinant VISTA protein needs to be **multimerized to be active** as soluble ligand. The protein VISTA (mouse):COMP (mouse) (with the extracellular domain of mouse VISTA fused to the pentamerization domain from the cartilage oligomeric matrix protein (COMP), but not VISTA-Fc, functions as an immunosuppressive agonist *in vivo* inhibiting the proliferation of $CD4^+$ T cells.

LIT: VISTA.COMP - an engineered checkpoint receptor agonist that potently suppresses T cell-mediated immune responses: A. Prodeus, et al.; JCI Insight **2,** e94308 (2017)

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
NEW VISTA (mouse):COMP (mouse) (rec.) (His)	AG-40B-0181	50 µg	HEK 293 cells	<0.01EU/µg	Ms

NEW

Butyrophilin-like 2 [BTNL2]

Butyrophilin-like 2 (BTNL2-Ig fusion protein) recognizes a putative receptor whose expression on B and T cells was significantly enhanced after activation. BTNL2 inhibits T cell proliferation and is the first member of the butyrophilin family that was shown to regulate T cell activation, which has implications in immune diseases and immunotherapy.

PROTEINS	PID	SIZE	SOURCE	ENDOTOXIN	SPECIES
BTNL2 (mouse):Fc (mouse) (rec.)	CHI-MF-110BTNL2	100 µg	CHO cells	<0.06EU/µg	Ms

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