Recombinant Conformational Proteins

Novel Bioactive Soluble Dimer and Multi-Pass Membrane Proteins to Enhance Drug Discovery

conigen bioscience

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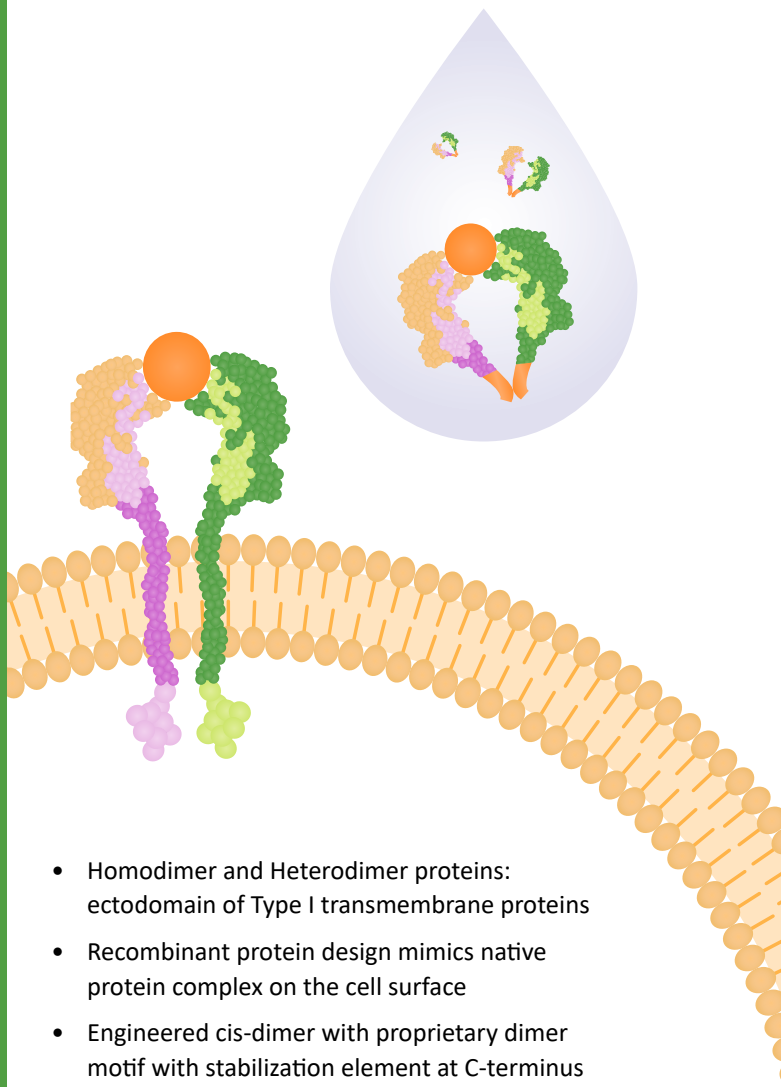
Recombinant Soluble Dimeric Proteins

CSP™ Technology Platform

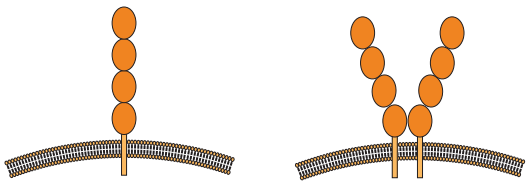
proprietary Conigen Soluble Protein



- Homodimer and Heterodimer proteins: ectodomain of Type I transmembrane proteins
- Recombinant protein design mimics native protein complex on the cell surface
- Engineered cis-dimer with proprietary dimer motif with stabilization element at C-terminus
- Expressed in mammalian cells using the Conigen Soluble Protein (CSP™) platform

Why Dimers?

The Power of Two: Dimerization Enhances Protein Functionality and Stability



Schematic illustration of CD4 monomer (left) and CD4 dimer (right)

Type I Transmembrane Protein Dimer and Dimerization

Over 2,000 Type I transmembrane proteins have been identified by human proteomics[1]. Many of them are dimers, including homodimers and heterodimers, playing a key role in their structural integrity, regulation, and signaling functions. This process is critical for the activity of numerous receptors, adhesion molecules, and enzymes, facilitating ligand binding, enzymatic activation, and immune signaling. By forming dimers, these proteins can achieve greater stability, enhance their specificity in interactions, and dynamically regulate their functional states. The ectodomain often provides multiple contact points for ligand and receptor interactions, improving binding efficiency and signal transduction by dimerization.

Dimerization in Disease: When Proteins Go Wrong[2]

While dimerization is crucial for normal cellular function, dysregulated dimerization can contribute to pathological conditions.

- Aberrant dimer formation is linked to oncogenic signaling, neurodegenerative disorders, and metabolic diseases.
- In cancer, uncontrolled receptor dimerization leads to constitutive activation of growth factor pathways.
- Neurodegenerative diseases involve toxic aggregate formation from misfolded dimeric proteins.

Understanding these mechanisms assists in developing targeted therapies to correct dimer-related dysfunctions.

Therapeutic Targeting of Protein Dimers: Why Drug Design Focuses on Dimeric Interactions[3]

Protein dimers serve as strategic targets in drug discovery due to their functional relevance in disease pathways.

- Many therapies aim to stabilize or disrupt dimeric interactions to regulate signaling cascades.
- Targeting dimerization can be an important innovative approach for receptor tyrosine kinases, cytokine receptors, and immune checkpoints.
- Small molecule drugs, monoclonal antibodies, and peptide inhibitors can selectively modulate dimer formation, especially pathological dimers, to be more effective and precise in reducing potential off-target side effects.
- Dimer-targeted drug development can potentially improve therapeutic interventions for cancer, autoimmune diseases, and inflammatory conditions.

Dimerization of Type I transmembrane proteins critically influences cancer progression and treatment. These complexes drive oncogenic signaling (e.g., HER2/EGFR dimerization in breast cancer) by amplifying growth signals and enabling uncontrolled proliferation. Simultaneously, immune checkpoint dimers like PD-1/PD-L1 suppress anti-tumor immunity, facilitating immune evasion. Therapeutic strategies target these dimers: monoclonal antibodies (e.g., trastuzumab) disrupt oncogenic receptor pairs, while checkpoint inhibitors (e.g., pembrolizumab) block immunosuppressive interactions.

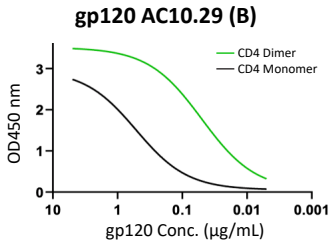
Advances in structural biology and engineered proteins enable precise targeting of dimer interfaces, enhancing therapeutic specificity. By inhibiting tumor-promoting dimers or reprogramming immune-regulatory complexes, these approaches improve cancer treatment efficacy, positioning dimer disruption as a cornerstone of precision oncology.

Conigen Dimers Focus on Type I Transmembrane Proteins

The ectodomains of Type I transmembrane proteins play a central role in receptor/ligand binding and cell signaling, and are prime targets for therapeutic intervention. Dimerization plays a critical role for many of them and their biological functions. However, recombinant protein generation of them as dimer proteins is notoriously challenging, as intricate folding demands often result in low yields, instability, or loss of functional activity.

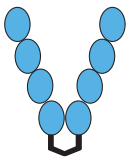
Conigen addresses these limitations through its proprietary dimerization platform. By engineering cis-dimer motifs into the homodimeric or heterodimeric ectodomains, Conigen stabilizes their native conformation, preserving structural integrity and enhancing biological potency. Leveraging advanced mammalian expression systems, the platform achieves high-yield and high purity of conformational proteins. This ensures reliability for research and provides a robust foundation for therapeutic discovery, accelerating the development of biologics, antibody therapies, and precision drug candidates.

Homodimer vs Monomer



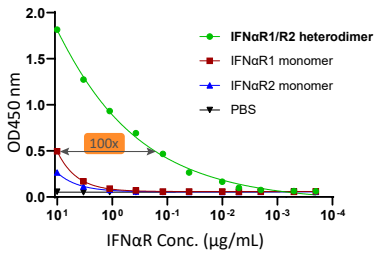
CD4 Dimer Binding to Ligand HIV-1 gp120

- *10-fold increase in binding potency compared to monomer*
- *Conigen CD4 dimer (EC50 0.05 µg/ml)*
- *CD4 monomer (EC50 0.52 µg/ml)*



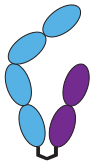
CSP™ Homodimers with proprietary motif at C-terminus

Heterodimer vs Monomer



Cytokine IFNα Binding to IFNα Receptor Molecules

- *Conigen IFNαR1/R2 heterodimer (EC50 4.1 µg/ml)*
- *R1 monomer (too weak to calculate EC50)*
- *R2 monomer (too weak to calculate EC50)*



CSP™ Heterodimers with proprietary motif at C-terminus

The Conigen Difference – Dimer Protein Advantages

Conigen's conformational dimer proteins are engineered to replicate native protein structures with unprecedented accuracy, bridging the gap between recombinant models and physiological reality. These proteins deliver:

- **Native Structural Fidelity** Validated by computational modeling, Conigen's dimers exhibit near-identical alignment with native crystal structures, ensuring authentic folding and domain orientation.
- **Enhanced Functional Activity** The preserved architecture increases ligand-binding affinity and receptor activation kinetics, mirroring natural signaling mechanisms for physiologically relevant outcomes.
- **Optimized Therapeutic Discovery** By stabilizing receptor/ligand interaction interfaces, the platform uncovers novel drug binding epitopes and accelerates the identification of high potency biologics or small-molecule therapies.
- **Broadened Assay Utility** The increased stability and activity of Conigen dimers expand dynamic ranges in functional assays, improving sensitivity for antibody characterization, drug candidate screening, and mechanistic studies.
- **Fc-free Solution with Critical Benefits**
  1. Compact size: <50 aa motif (vs. 230-250 aa Fc) minimizes steric interference, preserving native structure and ligand access.
  2. No Fc artifacts: Eliminates off-target Fc receptor binding, immune activation, and assay noise.
  3. Glycosylation free motif: Ensures batch consistency and reduces immunogenicity and epitope masking risks.
  4. Custom tags: Add small, non-disruptive tags (His, FLAG) without compromising function.
  5. Lower background: Enhances assay sensitivity for precise drug screening and antibody validation.
  6. Therapeutic safety: Ideal for applications where Fc-mediated toxicity is a concern.

Applications

As an Immunogen

Presents more conformational epitopes compared to monomers, to generate antibodies for translational research and therapeutic discovery

As an Antigen

Screen and characterize antibodies targeting diverse epitopes including quaternary conformational epitopes

Drug Screening

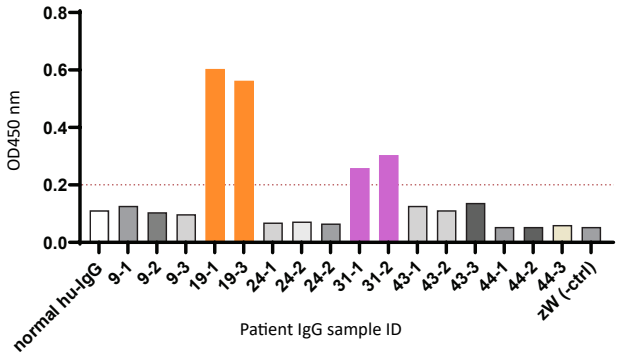
Agonist or antagonist screening for research and therapeutic discovery

Characterization

Antibody and drug bioactivity

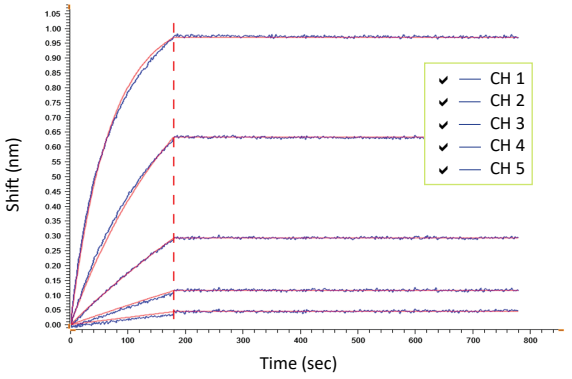
Applications Using Conigen CD4 Homodimer

Using CD4 Dimer to Screen for CD4-specific Antibodies in HIV-1 Infected Autoimmune Patients



Using Conigen's CD4 cis-dimer protein, CD4-specific antibodies were clearly detected in 2 patients' IgG samples: orange bars (19-1, 19-3), and pink bars (31-1, 31-2), that were not able to be detected using CD4 monomer protein. (Collaboration with Medical University of South Carolina)

Using CD4 Dimer for Label Free BLI Assay to Study the Receptor Binding Activities of HIV-1 Envelope Glycoproteins from Various Subtypes



HIV-1 Env protein (subtype)	koff(1/s)	kon(1/Ms)	KD (M)
gp120-IIIB (B)	1.94E-04	1.05E+05	1.85E-09
gp140-JRFL-CF (B)	1.92E-05	9.96E+04	1.92E-10
gp120-96ZM651 (C)	2.49E-04	2.63E+04	9.44E-09
gp140-C1086 (C)	<1.00E-006	1.09E+05	<1E-12
gp120-CM235 (AE)	7.26E-04	6.84E+04	1.06E-08
gp120-93TH975 (AE)	1.37E-04	2.43E+05	5.64E-10
RSC3	1.22E-04	6.75E+04	1.81E-09
RSC3-G367R	2.03E-04	3.17E+04	6.42E-09

HIV-1 envelope glycoprotein's CD4 binding activities are crucial for their functions. The biolayer interferometry (BLI) assays were part of a collaboration with Gator Bio.

Dimeric Immune Checkpoint Receptors

"Transmembrane domain-driven PD-1 dimers mediate T cell inhibition"

- Philips et al., Science Immunology 2024

Examples: CD28, CD80, CTLA-4, PD-1, TIGIT

Immune checkpoint receptors and ligands regulate immune homeostasis by balancing activation and suppression. They prevent autoimmunity and excessive inflammation while enabling immune responses against pathogens and cancer. Advances in understanding their structure and function have driven immune-oncology and immunotherapy breakthroughs.[4]

Dimerization in Checkpoint Regulation

Checkpoint receptors are transmembrane proteins with extracellular ligand-binding domains, transmembrane regions, and intracellular signaling motifs. Dimerization stabilizes ligand interactions and modulates intracellular signaling. Upon ligand binding, dimerization recruits phosphatases like SHP-2, downregulating T-cell receptor (TCR) signaling and inhibiting activation.[4] Structural studies show that PD-1, CTLA-4, and LAG-3 share immunoreceptor tyrosine-based inhibitory motifs (ITIMs), essential for immune suppression and tolerance maintenance. The structural arrangement is critical for its role in dampening T-cell activation, making it a key immunotherapy target.[5]

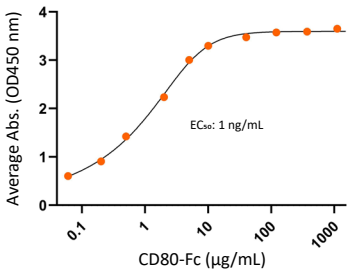
Dimerization and Immune Suppression

Checkpoint dimerization is critical for immune regulation, suppressing excessive activation while maintaining peripheral tolerance. CTLA-4 competes with CD28 for CD80/CD86 binding, reducing co-stimulatory signals necessary for full T-cell activation. PD-1, acting later in the immune response, inhibits TCR signaling upon PD-L1 or PD-L2 binding.[4] LAG-3 further modulates immune activity by associating with TCR–CD3 complexes, disrupting co-receptor signaling and restricting T-cell proliferation.[5] While these mechanisms prevent autoimmunity, tumors often exploit them to evade immune detection.

Targeting Dimerization in Immunotherapy

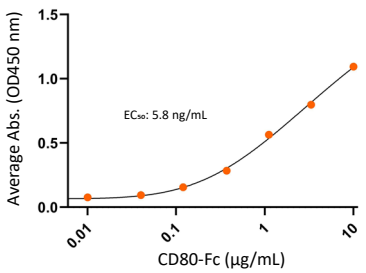
Dysregulated checkpoint signaling contributes to autoimmunity, chronic infections, and cancer. Overactive suppression promotes tumor immune evasion, while insufficient inhibition leads to inflammation and tissue damage. Checkpoint inhibitors such as pembrolizumab (anti-PD-1) and ipilimumab (anti-CTLA-4) block dimerization-driven suppression, restoring T-cell function.[4] Emerging targets like LAG-3 and TIGIT follow similar pathways, expanding therapeutic options. Combination checkpoint blockade, such as the LAG-3/PD-1 inhibitor relatlimab, is under investigation to enhance immune activation while reducing resistance.[5]

CD80 Binding to its Receptor CTLA-4



CD80 protein dimer, Fc-Tag (CD80-Fc, CSP-24033-04) potently binds to its receptor CTLA-4 dimer (CSP-24031) as measured by ELISA. CTLA-4 protein dimer (0.2 µg/well) was coated on 96-well microtiter plates and detected by serial dilutions of CD80-Fc.

CD80 Binding to its Receptor CD28



CD80 protein dimer, Fc-Tag (CD80-Fc, CSP-24033-04) binds well to its receptor CD28 protein dimer (CSP-24032) as measured by ELISA. CD28 protein dimer (0.2 µg/well) was coated on 96-well microtiter plates and detected by serial dilutions of CD80-Fc.

Spotlight: TIGIT

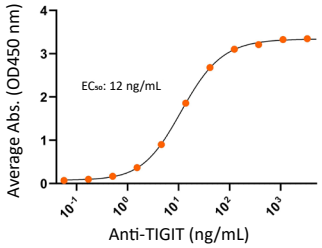
TIGIT, or T-cell immunoreceptor with immunoglobulin and ITIM domain, is an inhibitory immune checkpoint receptor modulating immune responses, especially within the tumor microenvironment (TME). Targeting TIGIT has emerged as a promising therapeutic strategy in cancer immunotherapy due to its effects on T-cells, NK cells, and regulatory T-cells (Tregs).

TIGIT acts by binding to ligands including CD155, Nectin-2 and Nectin-4 which are often overexpressed on tumor cells. This binding sends an inhibitory signal to immune cells, suppressing their cytotoxic activity and promoting immune tolerance within tumors. TIGIT's role as an immune checkpoint helps the immune system to avoid overactivation, which can prevent autoimmune responses but also allows cancer cells to evade immune surveillance.[6,7,8]

TIGIT cis-homodimer protein from Conigen

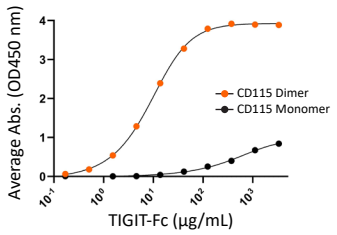
To mimic the TIGIT homodimer on the cell surface, three forms of cis-homodimer proteins are designed and generated by Conigen with Fc tag, His-tag, or His-tag+Avitag fused at the C-terminus. These TIGIT cis-homodimer proteins are bioactive in potently binding to ligands CD155, and Nectin-4. These innovative TIGIT dimer proteins can be used for drug discovery and basic research, as an immunogen/antigen to generate specific antibodies targeting the natural dimer and study the TIGIT and ligand interactions.

TIGIT Specific Antibody Binding



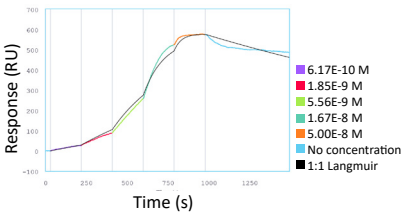
Human TIGIT protein dimer, His-Avi Tag (CSP-24028-03) potently binds to TIGIT specific monoclonal antibody (mAb) as measured by ELISA. The TIGIT protein dimer (0.2 μg/well) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human TIGIT mAb.

TIGIT Binding its Ligand CD155 Dimer or Monomer



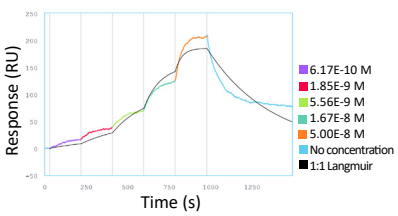
Human TIGIT protein dimer, Fc-Tag (TIGIT-Fc, CSP-24028) binds to its ligand human CD155 protein dimer (CSP-24029) or monomer as measured by ELISA. CD155 dimer significantly enhances the binding to TIGIT compared to CD155 monomer. CD155 dimer or monomer (0.2 μg/well) was coated on 96-well microtiter plates and detected by serial dilution of TIGIT-Fc.

TIGIT Binding to CD155 Dimer



Human TIGIT protein dimer, Fc-Tag (CSP-24028) potently binds to its ligand human CD155 protein dimer (CSP-24029) by surface plasmon resonance (SPR) label-free analysis. CD155 dimer/TIGIT binding Kd: 0.1 nM, 57-fold more potent binding than CD155 monomer.

TIGIT Binding to CD155 Monomer



Human TIGIT protein dimer, Fc-Tag (CSP-24028) potently binds to its ligand human CD155 protein monomer by surface plasmon resonance (SPR) label-free analysis. CD155 monomer/TIGIT binding Kd: 5.7 nM, 57-fold less potent binding than CD155 dimer.

Dimeric Immune Checkpoint Receptors									
Protein	Tag	Product Code	Species	Homodimer/ Heterodimer	Protein	Tag	Product Code	Species	Homodimer/ Heterodimer
CD28	His	CSP-24032	Human	Homodimer	PD-L1-hFc	Fc	CSP-2594-04	Human	Homodimer
CD80	Fc	CSP-24033-04	Human	Homodimer	TIGIT	Fc	CSP-24028	Human	Homodimer
CD80	Flag-His	CSP-24033-02	Human	Homodimer	TIGIT	His	CSP-24028-01	Human	Homodimer
CD80	His	CSP-24033	Human	Homodimer	TIGIT	His-Avi	CSP-24028-03	Human	Homodimer
CD155	His	CSP-24029	Human	Homodimer	CD80-hFc	Fc	CSP-25187-04	Mouse	Homodimer
CTLA-4	His	CSP-24031	Human	Homodimer	PD-L1	His	CSP-25190-01	Mouse	Homodimer
PD1	His-Avi	CSP-24093-03	Human	Homodimer					

Dimeric Tumor-Associated Antigens

"Trop2 ectodomain forms a dimer"

Vidmar et al., Protein Expression and Purification 2013, 91(1):69

Examples: HER2, Trop-2, Nectin-4, Nectin-2

Tumor-associated antigens (TAAs) are proteins aberrantly expressed in cancer cells, serving as biomarkers and therapeutic targets. Their structural features and functional roles, and clinical relevance have shaped the development of targeted therapies, including monoclonal antibodies, CAR-T therapies, and bispecific immune modulators.[9]

Dimerization and Tumor Progression

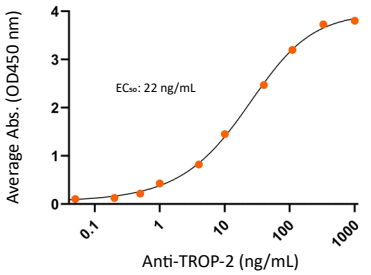
TAAs are broadly classified as oncofetal antigens (e.g., AFP, CEA) and differentiation antigens (e.g., HER2, MUC1), with their expression tightly linked to tumor progression.[9] Many TAAs rely on dimerization, stabilizing receptor-ligand interactions and enhances oncogenic signaling.[10] HER2 and EGFR undergo ligand-independent dimerization, activating the PI3K/AKT and MAPK pathways to drive proliferation, while MUC1 dimers form a glycosylated barrier, shielding tumor cells from immune surveillance dimerization in cancer. [10]

Dimerization plays a pivotal role in oncogenic signaling, immune suppression, and apoptosis resistance dimerization in cancer.[10] Immune checkpoint TAAs, including PD-L1 and Nectin-4, exploit dimerization to suppress T-cell activation and evade immune destruction.[11] In urothelial carcinoma and breast cancer, Nectin-4 interacts with immune checkpoint receptors such as TIGIT, inhibiting NK and T-cell activity, thus supporting tumor immune evasion.[11]

Therapeutic Targeting of TAAs

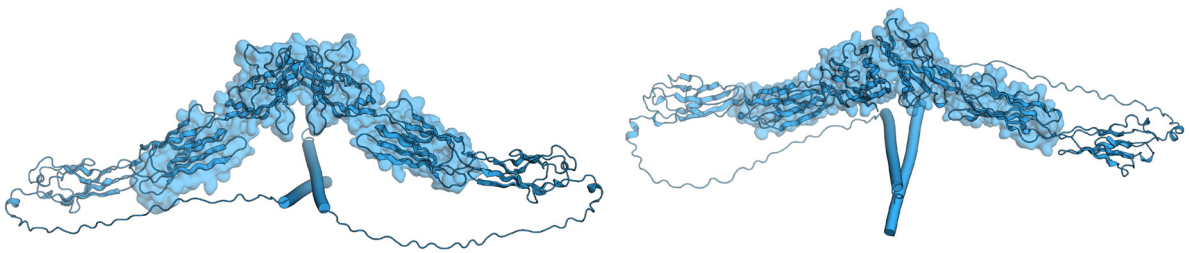
TAAs are overexpressed in breast, lung, colorectal, and urothelial cancers, making them prime targets for precision medicine. Monoclonal antibodies such as trastuzumab and pertuzumab disrupt HER2 dimerization, blocking downstream oncogenic signaling. CAR-T therapies, engineered against targets like MUC1, enhance immune-mediated tumor clearance. Bispecific antibodies and checkpoint inhibitors further manipulate TAA interactions to restore anti-tumor immunity. Emerging strategies, such as antibody-drug conjugates (ADCs) and engineered dimeric ligands, aim to refine targeting specificity and overcome antigen heterogeneity.[9]

TROP-2 Specific Antibody Binding



Human TROP-2 protein dimer, Flag-His Tag (CSP-24041-02) potently binds to TROP-2 specific monoclonal antibody as measured by ELISA. The TROP-2 protein dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human TROP-2 mAb.

Nectin-4 Homodimer Superimposed with Crystal Structure 4FRW



The ectodomain of human Nectin-4 was genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting Nectin-4 homodimer CSP closely aligns with the experimentally determined crystal structure (PDB ID: 4FRW), shown as an isosurface of electron density.*

Spotlight: Nectin-4

Nectin-4: A Key Player in Tumor Biology and Immune Regulation

Nectin-4 is a member of the Nectin family of cell adhesion molecules within the immunoglobulin superfamily. Unlike other Nectins, its expression is largely restricted to embryonic tissues but becomes aberrantly overexpressed in various cancers. [9,11]

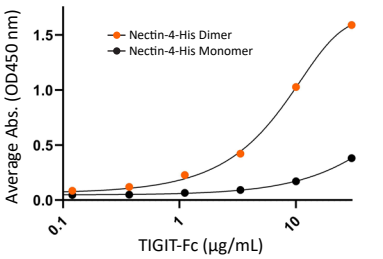
In cancer, Nectin-4 supports tumor growth, invasion, and immune evasion by interacting with immune checkpoint receptors like TIGIT, which inhibits NK and T-cell activity against tumors. While essential for normal tissue structure, its overexpression promotes tumor progression, making it a high-value therapeutic target.[9,10,11]

Conigen's Novel Nectin-4 Cis-Dimer: Advancing Cancer Research with Native Quaternary Conformation

Nectin-4 forms cis-dimers on the cell surface, a conformation often lost in commercial recombinant proteins, which are typically monomeric. These native dimeric structures are essential for maintaining critical target epitopes for therapeutics.

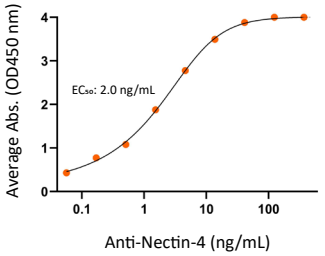
Conigen's Nectin-4 cis-dimer protein is engineered to mimic the native quaternary structure, containing the full-length extracellular Ig-like domains fused with a proprietary cis-dimer motif. Produced in HEK 293T cells, it undergoes a post-translational process similar to native expression, ensuring biological relevance. The cis-dimer exhibits significantly enhanced binding to TIGIT compared to monomeric forms, providing a superior antigen for cancer biology research and therapeutic discovery.

Nectin-4 Binding to its Receptor TIGIT



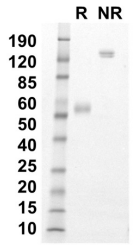
Human Nectin-4 protein dimer, His-Tag (CSP-24016) or Nectin-4 protein monomer binding to TIGIT protein dimer, Fc-Tag (TIGIT-Fc, CSP-24028) as measured by ELISA. Nectin-4 protein dimer significantly enhances the binding to TIGIT compared to Nectin-4 monomer. The Nectin-4 protein dimer or monomer (0.2 μg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of TIGIT-Fc.

Nectin-4 Specific Antibody Binding



Human Nectin-4 protein dimer, His Tag (CSP-24016) potently binds to Nectin-4 specific monoclonal antibody (mAb) as measured by ELISA. The Nectin-4 protein dimer (0.2 μg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human Nectin-4 mAb.

SDS-PAGE Analysis of Nectin-4 Protein Dimer



SDS-PAGE analysis example of Nectin-4 protein dimer, His-Tag (CSP-24016) under reduced (R) and non-reduced (NR) conditions, 1 μg/lane.

Dimeric Tumor-Associated Antigens									
Protein	Tag	Product Code	Species	Homodimer/ Heterodimer	Protein	Tag	Product Code	Species	Homodimer/ Heterodimer
B7H3	His-Avi	CSP-240982lg	Human	Homodimer	CD117	His-Avi	CSP-25193-03	Mouse	Homodimer
B7H3	His-Avi	CSP-240984lg	Human	Homodimer	CD117	His-Avi	CSP-25194-03	Rhesus Macaque	Homodimer
CD2	His-Avi	CSP-24095-03	Human	Homodimer	Nectin-4	His	CSP-24016	Human	Homodimer
CD117	Fc	CSP-25123-04	Human	Homodimer	TROP-2	Flag-His	CSP-24041-02	Human	Homodimer
CD117	His-Avi	CSP-24123-03	Human	Homodimer	TROP-2	Flag-His	CSP-25191-02	Mouse	Homodimer

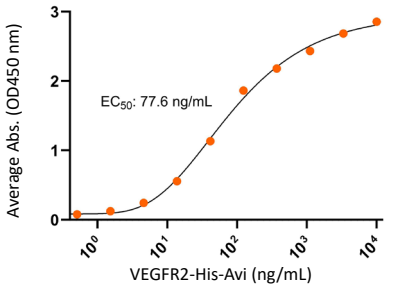
Dimeric Growth Factor Receptors

Examples: VEGFR2, FGFR1

Growth factor receptors bind to specific growth factors to regulate cell proliferation, differentiation, migration, and survival and often have intrinsic enzymatic activities. Many are single-pass Type I transmembrane proteins including enzyme-linked receptors, Receptor Tyrosine Kinases (RTKs) and Receptor Serine/Threonine Kinases (RSTKs). These receptors often function as dimers to activate intracellular signaling pathways, typically forming heterodimers or homodimers upon ligand binding to trigger intracellular signaling cascades that play crucial roles in immune function, development and disease progression.

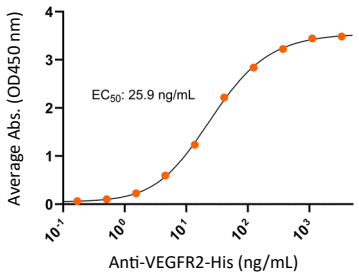
Growth factor receptor dimerization dysregulation is central to cancer, developmental disorders, and metabolic diseases.[12] The dysregulation includes ligand-independent dimerization associated with overexpression and mutations leading to constitutive signaling and non-functional dimers. For example, VEGFR-2 (Vascular Endothelial Growth Factor Receptor-2) overexpression is observed in multiple cancers, including gliomas, colorectal, pancreatic, and breast cancers.[13] Therapies targeting dimerization have revolutionized treatment but face challenges like resistance. Advances in structural biology and personalized medicine hold promise for next-generation therapies that precisely modulate dimerization states.

VEGFR2 Binding to its Ligand VEGF-A



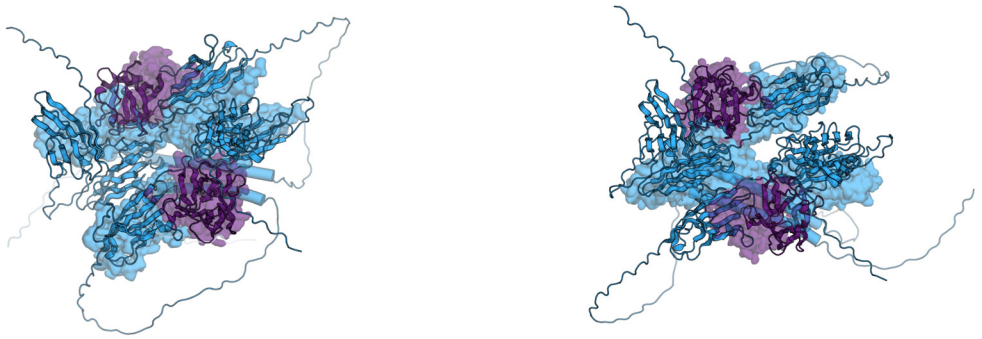
Human VEGFR2 protein homodimer, His-Avi Tag (CSP-25127-03) potently binds to its ligand vascular endothelial growth factor A (VEGF-A) as measured by ELISA. The VEGF-A (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of VEGFR2 homodimer protein.

VEGFR2 Specific Antibody Binding



Human VEGFR2 protein dimer, His-Avi Tag (CSP-24127-03) potently binds to VEGFR2 specific monoclonal antibody (mAb) as measured by ELISA. The VEGFR2 protein dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human VEGFR2 mAb.

IFGFR1 and FGF2 Superimposed with Crystal Structure 1CVS



The ectodomain of human FGFR1 was genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting FGFR1 homodimer CSP bound to its ligand FGF2 aligned with the experimentally determined crystal structure (PDB ID: 1CVS), shown as an isosurface of electron density. FGFR1 is shown in blue; FGF2 is shown in purple.*

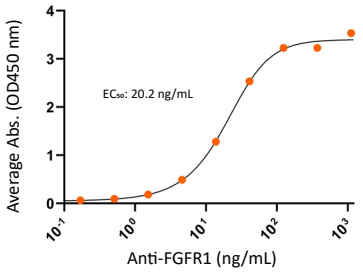
Spotlight: FGFR1-FGFR4

Fibroblast growth factor receptors (FGFRs) are single-pass transmembrane proteins that play a key role in cell growth, differentiation, and development. The FGFR family includes four receptors (FGFR1–FGFR4) that bind to fibroblast growth factors (FGFs) using heparin as a co-factor.[14] While traditionally believed to require ligand-induced dimerization for activation, recent findings show that FGFRs can form dimers even in the absence of ligands, with these unliganded dimers exhibiting basal phosphorylation activity.[14]

Upon FGF binding, FGFRs undergo structural rearrangements that enhance phosphorylation, initiating downstream signaling cascades. Interestingly, different ligands induce distinct conformational changes. For example, FGF2 promotes tighter transmembrane domain packing than FGF1, leading to higher phosphorylation levels.[14] This variability in receptor activation may explain the diverse biological effects of different FGFs. Pathogenic mutations, such as the A391E substitution in FGFR3, can mimic FGF2's effect, locking the receptor in a hyperactive state and driving disease.[14]

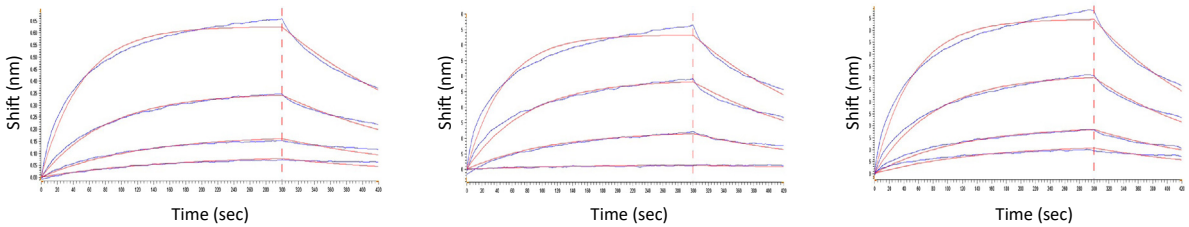
These insights reshape our understanding of FGFR signaling, highlighting how ligand-specific receptor conformations influence activation and disease mechanisms. Given FGFR mutations' role in skeletal disorders and cancers, targeting these structural dynamics could offer new therapeutic avenues.[14]

FGFR1 Specific Antibody Binding



Human FGFR1 protein dimer, His-Avi Tag (CSP-25129-03) potently binds to FGFR1 specific monoclonal antibody (mAb) as measured by ELISA. The FGFR1 protein dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human FGFR1 mAb.

FGFR1, FGFR3, and FGFR4 Dimer Binding to the Ligand Fibroblast Growth Factor



Human FGFR1 protein dimer (CSP-25129-03) (left), FGFR3 (CSP-25131-03) (center), and FGFR4 (CSP-25132-03) (right) protein dimers, His-Avi Tag bind similarly well to their ligand fibroblast growth factor 1 (FGF-1) as measured by biolayer interferometry (BLI). Left: FGFR1/FGF-1 binding Kd: 221 nM; Center: FGFR3/FGF-1 binding Kd: 277nM; Right: FGFR4/FGF-1 binding Kd: 237nM.

Dimeric Growth Factor Receptors									
Protein	Tag	Product Code	Species	Homodimer/ Heterodimer	Protein	Tag	Product Code	Species	Homodimer/ Heterodimer
FGFR1	His-Avi	CSP-25129-03	Human	Homodimer	FGFR4	His-Avi	CSP-25132-03	Human	Homodimer
FGFR2	His-Avi	CSP-25130-03	Human	Homodimer	VEGFR2	His-Avi	CSP-25127-03	Human	Homodimer
FGFR3	His-Avi	CSP-25131-03	Human	Homodimer					

Dimeric Cytokine Receptors

"Receptor dimerization is a universal mechanism to initiate signal transduction, and is utilized by many growth factors such as cytokines, and ligands for tyrosine kinase receptors."

- Moraga et al., Cell 2015, 160(6):1196

Examples: IFNγR1, IL10Rα, IFNαR1/R2, IL-7Rα/TSLPR

Cytokine receptors regulate immune signaling and homeostasis by translating extracellular cytokine interactions into intracellular responses. They maintain immune equilibrium and serve as key therapeutic targets in autoimmune diseases, cancer, and inflammation.

Dimerization as a Switch for Activation

Cytokine receptors share a modular structure, consisting of an extracellular ligand-binding domain (ectodomain), a transmembrane domain, and an intracellular signaling domain.[15] Lacking intrinsic kinase activity, they rely on Janus kinase (JAK) proteins for intracellular signaling.

Dimerization is essential for activation, occurring via:

- Preformed dimers (e.g., EpoR, TpoR), exist in an inactive state until ligand binding induces conformational shifts, triggering signaling[16]
- Ligand-induced dimerization (e.g., IL-6R), requires sequential binding of ligand molecules to drive dimer assembly[15]

The site 1/site 2 model describes how site 1 binds cytokines with high affinity, facilitating site 2 recruitment of a secondary receptor subunit, stabilizing the signaling complex. Structural analyses reveal that receptor flexibility and membrane anchoring play critical roles in stabilizing dimerization, influencing ligand specificity and signaling efficiency. Mutations at dimerization interfaces can lead to constitutive activation, driving oncogenic transformation.[17]

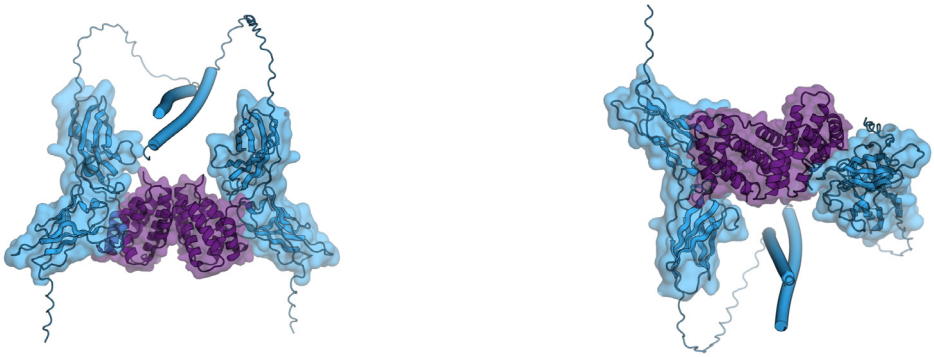
Dimerization and Immune Regulation

Cytokine receptor dimerization orchestrates immune activation, proliferation, and differentiation via JAK-STAT, MAPK, and NF-κB pathways. IL-2 receptor dimerization enhances T-cell proliferation and survival, while TNF receptor trimerization dictates apoptosis or inflammatory responses based on cellular context. These mechanisms ensure precise immune modulation, preventing both excessive inflammation and immune suppression.

Targeting Dimerization in Immunotherapy

Aberrant dimerization underlies immune disorders and cancer. IL-6R overactivation fuels chronic inflammation in rheumatoid arthritis, while defective interferon receptor dimerization impairs antiviral immunity. Therapies such as tocilizumab (IL-6R blockade) and engineered CAR T-cell receptors leverage dimerization control to restore immune homeostasis and enhance therapeutic precision. Advances in receptor engineering are exploring optimized ligand-receptor interactions and altered dimerization kinetics, paving the way for next-generation immunotherapies.[15,16,17]

IFNγR1 and IFNγ Superimposed with Crystal Structure 6E3K



The ectodomain of human IFNγR1 was genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting IFNγR1 homodimer CSP bound to its ligand IFNγ closely aligns with the experimentally determined crystal structure (PDB ID: 6E3K), shown as an isosurface of electron density. IFNγR1 is shown in blue; IFNγ is shown in purple.*

Spotlight: IFNαR1/R2 Heterodimer

IFNαR1 and IFNαR2 form a heterodimeric receptor complex that mediates type I interferon (IFN) signaling, a critical pathway in antiviral defense, immune modulation, and tumor surveillance. As members of the class II cytokine receptor family, they contain fibronectin type III domains that facilitate ligand binding and dimerization. Unlike other cytokine receptors, IFNαR1 has a low-affinity cytokine interaction, relying on IFNαR2 for stable ligand engagement.

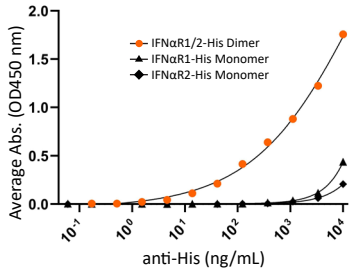
Upon IFN-α or IFN-β binding, IFNαR1/R2 undergoes a conformational change, recruiting JAK1 and TYK2 kinases to activate STAT1/STAT2, driving interferon-stimulated gene (ISG) transcription. This cascade enhances antiviral immunity, antigen presentation, and tumor cell apoptosis. Dysregulation contributes to autoimmune disease, viral persistence, and tumor immune escape, making it a key therapeutic target.

Conigen's IFNαR1/R2 Heterodimer: Advancing Research with Native Structural Integrity

Conventional recombinant IFNαR proteins lack proper structural assembly, limiting biological relevance. Conigen's IFNαR1/R2 heterodimer preserves native receptor conformation, ensuring accurate ligand binding and signal transduction. Engineered with full-length extracellular domains and a proprietary heterodimerization motif, it mimics physiological receptor assembly. Produced in HEK 293T cells, it undergoes post-translational modifications critical for ligand affinity and activation kinetics.

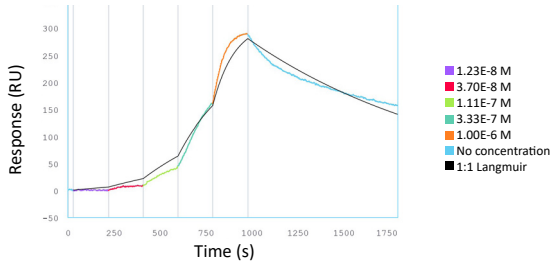
This structurally optimized IFNαR1/R2 complex provides a superior tool for interferon biology studies, antiviral research, and immunotherapy development.

IFNαR Proteins Binding to Type I Interferon



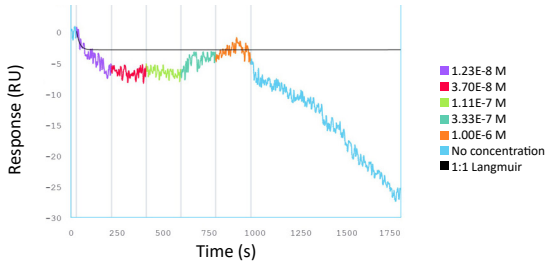
Human IFNαR1/R2 heterodimer, His-Tag (CSP-24025-A1B1), IFNαR1 or IFNαR2 monomer binding to Type I interferon (IFN) as measured by ELISA. IFNαR1/R2 heterodimer significantly enhances the binding to IFN compared to each monomer. The IFN (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of IFNαR heterodimer or monomers.

IFNαR Heterodimer Binding to Type I Interferon



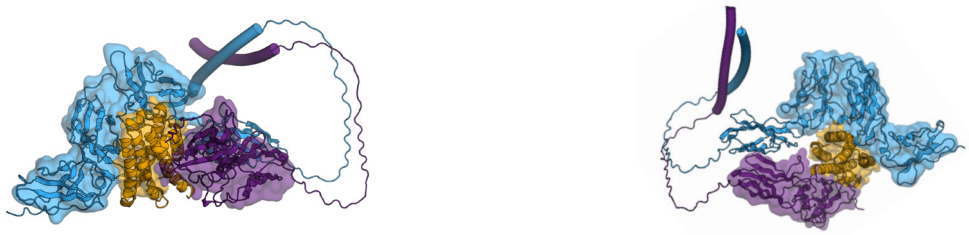
Human IFNαR1/R2 heterodimer, His-Tag (CSP-24025-A1B1) binding to Type I interferon (IFN) as measured by surface plasmon resonance (SPR) label-free analysis. IFNαR1/R2 dimer/Type I interferon binding Kd: 111 nM.

IFNαR1 Monomer Binding to Type 1 Interferon



Human IFNαR1 monomer, His-Tag binding to Type I interferon (IFN) as measured by surface plasmon resonance (SPR) label-free analysis. IFNαR1/IFN binding Kd: not detected.

IFNαR1 / IFNαR2 and IFN2α Superimposed with Crystal Structure 3SE3



The ectodomains of human IFNαR1 and IFNαR2 were genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting IFNαR1 / IFNαR2 heterodimer CSP bound to its ligand IFN2α closely aligns with the experimentally determined crystal structure (PDB ID: 3SE3), shown as an isosurface of electron density. IFNαR1 is shown in blue; IFNαR2 is shown in purple; IFN2α is shown in yellow.*

Spotlight: IFNγR1 Homodimer

Interferon Gamma Receptor 1 (IFNγR1) is a critical component of the immune response, mediating the effects of interferon-gamma (IFNγ), a cytokine with potent immunomodulatory and anti-microbial functions. Together with IFNγR2, it forms the interferon-gamma receptor complex, which activates immune cells to respond to infections and malignancies.

Structurally, IFNγR1 contains an extracellular domain that binds IFNγ, a transmembrane domain, and an intracellular domain that interacts with Janus kinases (JAKs) to propagate signals within the cell. IFN-γ, a homodimer, binds two IFNγR1 molecules triggering receptor dimerization and recruitment of IFNγR2 leading to transcription of interferon-stimulated genes.[18, 19]

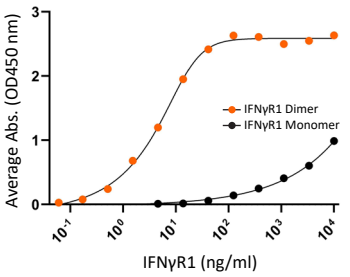
IFNγR1 in Immunity and Infection

IFNγR1 is vital for host defense against intracellular pathogens such as mycobacteria and viruses. Genetic mutations in IFNγR1 can impair immune responses causing Mendelian susceptibility to mycobacterial disease (MSMD), making individuals highly vulnerable to non-tuberculous mycobacteria infections.[20]

IFNγR1 in Cancer

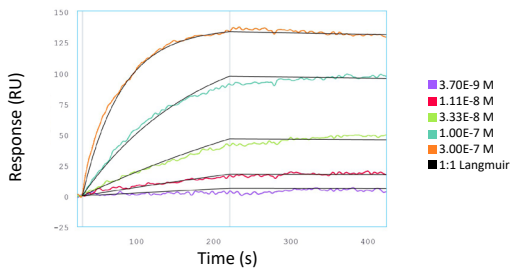
IFNγ signaling through IFNγR1 can have both pro- and anti-tumor effects. It enhances immune surveillance by stimulating T-cell responses, yet chronic IFNγ exposure can drive immune exhaustion, weakening T-cell efficacy in tumors. Modulating IFNγR1 expression in T-cells may improve anti-tumor immunity, making it a potential target for cancer immunotherapy.[20, 21]

IFNγR1 Binding to IFNγ



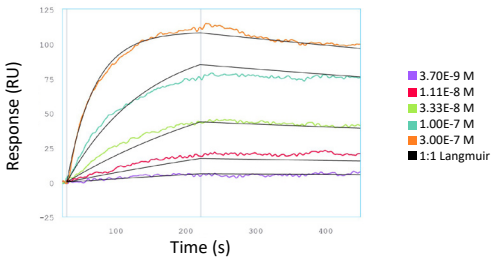
Human IFNγR1 protein homodimer, His-Tag (CSP-24015) or monomer protein binding to its ligand IFNγ cytokine, as measured by ELISA. IFNγR1 homodimer significantly enhances the binding to IFNγ compared to the monomer. The IFNγ (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of IFNγR1 homodimer or monomer.

IFNγR1 Homodimer Binding to IFNγ



Human IFNγR1 protein homodimer, His-Tag (CSP-24015) binding to IFNγ as measured by surface plasmon resonance (SPR) label-free analysis. IFNγR1 dimer/ IFNγ binding Kd: 0.049 nM, which is over 100 fold more potent than the IFNγR1 monomer.

IFNγR1 Monomer Binding to IFNγ



Human IFNγR1 protein homodimer, His-Tag (CSP-24015) binding to IFNγ as measured by surface plasmon resonance (SPR) label-free analysis. IFNγR1 monomer/IFNγ binding Kd: 5.54 nM, which is over 100 fold less potent than the IFNγR1 dimer.

Dimeric Cytokine Receptors									
Protein	Tag	Product Code	Species	Homodimer/ Heterodimer	Protein	Tag	Product Code	Species	Homodimer/ Heterodimer
CD4	His	CSP-24004	Human	Homodimer	IL-2Rβ/γ	His-Avi	CSP-24045-A1B5	Human	Heterodimer
EpoR	His-Avi	CSP-24087	Human	Homodimer	IL10Rα	His	CSP-24018	Human	Homodimer
GCSFR	His-Avi	CSP-24086	Human	Homodimer	IL15Rα	His-Avi	CSP-24064	Human	Homodimer
gp130	His-Avi	CSP-24081-03	Human	Homodimer	PRLR	His-Avi	CSP-24089	Human	Homodimer
IFNα-R1/R2	His	CSP-24025-A1B1	Human	Heterodimer	PRLR	His-Avi	CSP-25160-01	Mouse	Homodimer
IFNγR1	His	CSP-24015	Human	Homodimer					

Receptor Tyrosine Kinase Family

Receptor tyrosine kinases (RTKs) belong to the growth factor receptor family, regulate cell growth, differentiation, and survival by converting extracellular signals into intracellular responses.

Similar to other growth factor receptors, RTKs consist of an extracellular ligand-binding domain, a transmembrane helix, and an intracellular tyrosine kinase domain. Dimerization is essential for activation, that activates kinase domains, leading to mutual phosphorylation of tyrosine residues. These phosphotyrosines recruit adaptor proteins (e.g., Grb2, PI3K), initiating downstream signaling (MAPK/ERK, PI3K/Akt). RTK dimers including homodimers and heterodimers demonstrate ligand-induced dimerization (e.g., EGFR, VEGFR) and preformed inactive dimers (e.g., FGFR). Glycosylation and membrane interactions fine-tune dimerization efficiency and signaling.[22]

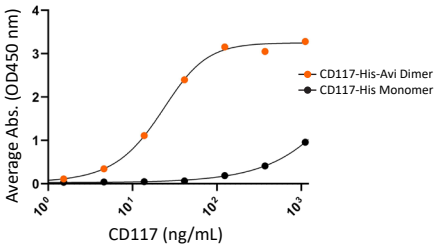
RTK dimerization dysregulation drives cancer, metabolic disorders, and neurodegenerative diseases. Hyperactive RTKs drive tumor growth and resistance. Targeted therapies include trastuzumab (HER2) and osimertinib (EGFR). Understanding the structural and dynamic aspects of RTK dimers will continue to drive innovation, enabling therapies tailored to individual dimerization-driven pathologies. Advances in receptor engineering optimize dimerization kinetics, enhancing precision therapeutics.[22]

Spotlight: CD117

CD117, also known as KIT and c-Kit, is a Type III RTK that plays a crucial role in cell signaling pathways regulating cell survival, proliferation, and differentiation.[23] CD117 is a Type I transmembrane protein, expressed in various cell types, including hematopoietic stem cells, mast cells, melanocytes, and interstitial cells of Cajal.[24]

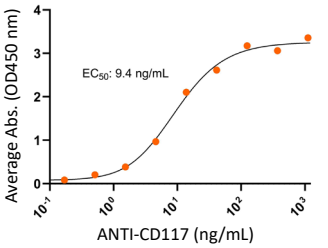
The primary function of CD117 is to regulate cellular processes through interaction with its ligand, stem cell factor (SCF). CD117 is unique due to its ability to dimerize upon ligand binding, a critical mechanism for signal transduction. However, oncogenic mutations can cause ligand-independent pathological dimerization and constitutive activation.[25] CD117 is frequently overexpressed or dysregulated in cancers, including gastrointestinal stromal tumors, acute myeloid leukemia, melanoma, and small cell lung cancer. It is a promising drug target, especially in precision oncology and regenerative medicine. Understanding the CD117 dimerization and its activation is crucial for developing targeted therapeutics. Conigen's recombinant CD117 protein dimers are cis-homodimers and contain a CD117 extracellular domain fused with a dimer motif. The CD117 protein dimers can potently bind to the respective SCF ligand and CD117-specific antibody.

Human CD117 Dimer and Monomer Binding to Human Ligand Stem Cell Factor (SCF)



Human CD117 protein homodimer, His-Avi Tag (CSP-24123-03) or monomer protein binding to its ligand SCF as measured by ELISA. CD117 homodimer significantly enhances the binding to SCF compared to the monomer. The SCF (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of CD117 homodimer or monomer.

CD117 Specific Antibody Binding



Human CD117 protein homodimer, His-Avi Tag (CSP-24123-03) potently binds to human CD117 specific monoclonal antibody (mAb) as measured by ELISA. The CD117 protein dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human CD117 mAb.

Dimeric T Cell Receptor & Co-Receptors

Examples: CD4, CD3 epsilon/delta

T-cell receptors (TCRs) are heterodimeric membrane proteins that recognize antigens and initiate immune responses. They exist as αβ or γδ heterodimers, each with extracellular, transmembrane, and cytoplasmic regions. TCRs lack intrinsic signaling capacity and rely on the CD3 complex (CD3γε, CD3δε, and CD3ζζ dimers) for stability and activation.[26] Dimerization is critical for maintaining receptor integrity, optimizing antigen engagement, and facilitating ITAM phosphorylation, which drives downstream signaling.[26] CD4 and CD8 act as co-receptors for the TCR, enhancing antigen recognition and signaling.

Cryo-electron microscopy studies reveal that TCR transmembrane helices form a tightly packed bundle with CD3 subunits, ensuring structural cohesion.[26] Disrupting these dimer interactions weakens T-cell activation, while stabilizing them enhances immune responses, making CD3-targeting therapies a key focus in immunotherapy.[27] Strategies that modulate dimerization are being explored to either amplify T-cell activity against tumors or suppress overactive responses in autoimmune diseases, highlighting the importance of receptor assembly in immune regulation.[27]

Spotlight: CD4 Homodimer

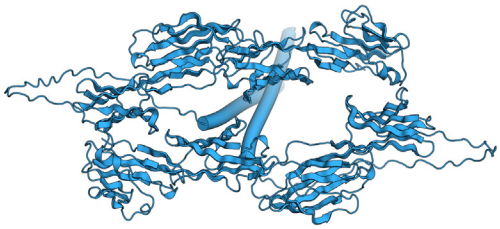
CD4: A Key Co-Receptor for TCR and Receptor for HIV

CD4 is a glycoprotein expressed on $CD4^+$ T cells, macrophages, and dendritic cells, playing a critical role in adaptive immunity. As a coreceptor for the TCR, CD4 binds to MHC class II molecules on antigen-presenting cells, stabilizing immune synapse formation and enhancing T-cell activation. Beyond its role in antigen recognition, CD4 is the primary cellular receptor for HIV entry and also serves as the receptor for interleukin-16 (IL-16), mediating chemotactic responses in CD4+ T cells.[28, 29]

Conigen's Bioactive CD4 Protein Dimer

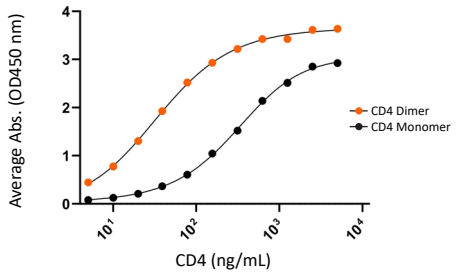
Since the discovery of CD4 nearly five decades ago, several recombinant forms have been developed for research, including monomeric CD4-2D (first two Ig-like domains), CD4-4D (four Ig-like domains), and CD4-Ig (CD4-2D fused to an IgG Fc domain). Conigen's CD4 protein dimer is a novel recombinant protein featuring four Ig-like domains fused to a proprietary cis-dimer motif at the C-terminus. Expressed in HEK293T cells, it undergoes human-like post-translational modifications, enhancing its structural and functional fidelity. This engineered protein dimer exhibits significantly improved binding to HIV-1 envelope glycoproteins across multiple subtypes, making it a valuable reagent for HIV and immunology research.

Prediction of CD4



The ectodomain of human CD4 was genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting CD4 homodimer CSP.*

CD4 Binding to its Ligand HIV-1 gp120



Human CD4 protein homodimer, His-Tag (CSP-24004) potently binding to HIV-1 envelope glycoprotein gp120-JR-FL as measured by ELISA. The CD4 dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of gp120 protein.

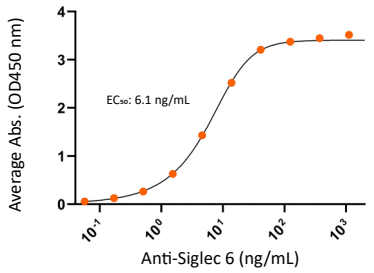
Siglecs

Siglec (sialic acid-binding immunoglobulin-type lectin) proteins are immune-regulatory proteins, a subset of the immunoglobulin superfamily that specifically recognize sialylated glycans on cell surfaces. Siglec dimerization or oligomerization is critical for modulating immune responses, and dysregulation of these processes is implicated in various diseases. Their dimerization can be through different mechanisms including ectodomain, transmembrane domain and ligand-induced clustering. Examples include:

- Siglec-3, Siglec-7 can dimerize via interactions between immunoglobulin (Ig) domains, particularly the V-set domain responsible for ligand binding
- Hydrophobic residues in transmembrane helices in Siglec-3 can promote dimerization
- Binding to multivalent sialylated ligands forces Siglecs into proximity, mimicking dimerization

Siglec dimerization can have different functional outcomes including inhibitory signaling and activating signals. For inhibitory signaling, dimerization/clustering enhances phosphorylation of ITIM/ITAM motifs, recruiting phosphatases (e.g., SHP-1/SHP-2) to suppress immune cell activation. For activating signals: some Siglecs (e.g., Siglec-14/15) pair with adaptor proteins (e.g., DAP12) to trigger pro-inflammatory responses. Siglec dimerization is a pivotal mechanism for immune regulation, with profound implications in cancer, autoimmunity, neurodegeneration, and infection. Targeting these interactions offers promising avenues for precision therapies.

Siglec 6 Specific Antibody Binding

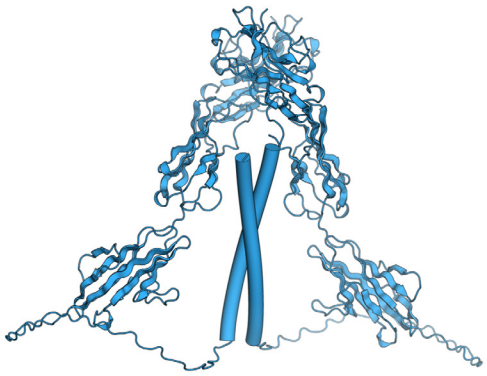


Human Siglec 6 protein dimer, His-Avi Tag (CSP-25203-01) potently binds to Siglec 6 specific monoclonal antibody (mAb) as measured by ELISA. The Siglec protein dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human Siglec 6 mAb.

Spotlight: Siglec-6

Siglec-6 is a member of the CD33-related Siglec family, an inhibitory receptor primarily expressed on human mast cells, certain B-cell subsets, and placental trophoblasts. It plays a role in modulating immune responses and maintaining immunological homeostasis. The ectodomain of Siglec-6 binds specifically to α2,6-linked sialic acid-containing glycans. Its cytoplasmic tail contains immunoreceptor tyrosine-based inhibitory motifs (ITIMs) and switch motifs (ITSMs), enabling it to downregulate cellular activation upon ligand binding. Siglec-6 is identified to dimerize via IgC1, analogously to CD33.[30] Siglec-6 is overexpressed on cancer cells, including those from chronic lymphocytic leukemia (CLL), making it an attractive target for immunotherapy.[31] Conigen's Siglec-6 protein dimer is designed to mimic the natural dimer conformation, potently binding to its specific antibody. It can potentially serve as a very useful immunogen and antigen for basic research and drug discovery.

Prediction of Siglec-6



The ectodomain of human Siglec-6 was genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting Siglec-6 homodimer CSP.*

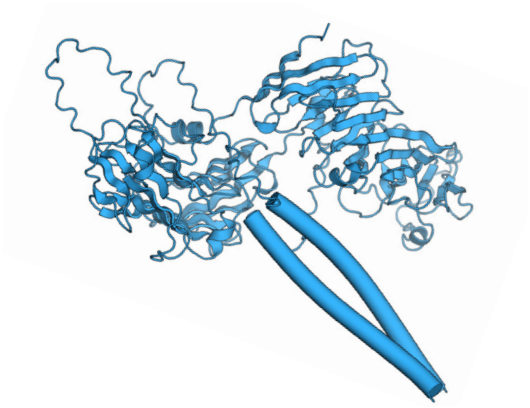
B Cell Receptors and Surface Markers

The B cell antigen receptor (BCR) is essential for B lymphocyte development, survival, and activation. Structurally, it consists of a membrane-bound immunoglobulin (mIg) noncovalently associated with the Ig-α/Ig-β heterodimer, enabling antigen recognition and intracellular signaling.[32] B cells differ from T cells in their ability to recognize native, unprocessed antigens without requiring antigen-presenting cells or MHC molecules.[33]

BCR signaling leads to B cell activation, differentiation into antibody-secreting plasma cells, and the formation of memory B cells, which ensure a faster and stronger response upon subsequent antigen encounters.[33]

CD19 and CD27, Type I transmembrane proteins, are important markers on B cells involved in B cell function. CD19 is important for B cell development and acts as a co-receptor with the BCR to enhance signaling and activation. CD27 is a dimeric membrane protein on T cells and a subset of B cells, especially memory B cells, a co-stimulatory molecule crucial for B cell activation and survival.

Prediction of CD19

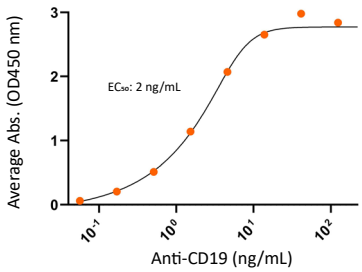


The ectodomain of human CD19 was genetically fused to a proprietary linker and dimerization motif to promote soluble dimer formation. An AlphaFold2 prediction (cartoon representation) of the resulting CD19 homodimer CSP.*

Spotlight: CD19 Homodimer

CD19 is a Type I transmembrane glycoprotein expressed on the surface of B cells, serving as a critical marker for their identification. It acts as a co-receptor in the B cell receptor (BCR) complex, alongside CD21, CD81, and CD225. It amplifies BCR signaling, enhancing B cell activation and differentiation in response to antigens and the functional activity relies on heteromultimeric interactions within the B cell receptor (BCR) complex. CD19 is also a key target in B-cell malignancies, central to CAR T-cell therapies and antibody-based treatments.[34] While anti-CD19 CAR T cells have transformed outcomes for diseases like diffuse large B-cell lymphoma (DLBCL) and acute lymphoblastic leukemia (ALL), challenges such as antigen escape and therapy resistance persist.[34] Efforts to refine CD19-targeted therapies include engineering stabilized extracellular domain (ECD) variants to improve expression and structural integrity. Although CD19 doesn't form a dimer under physiological conditions, the CD19 overexpression and potential clustering in cancer cells enhance pro-survival signaling while posing challenges to immunotherapies. Targeting the overexpressed clustering CD19 may improve the therapeutic precision and overcome resistance.

CD19 Specific Antibody Binding

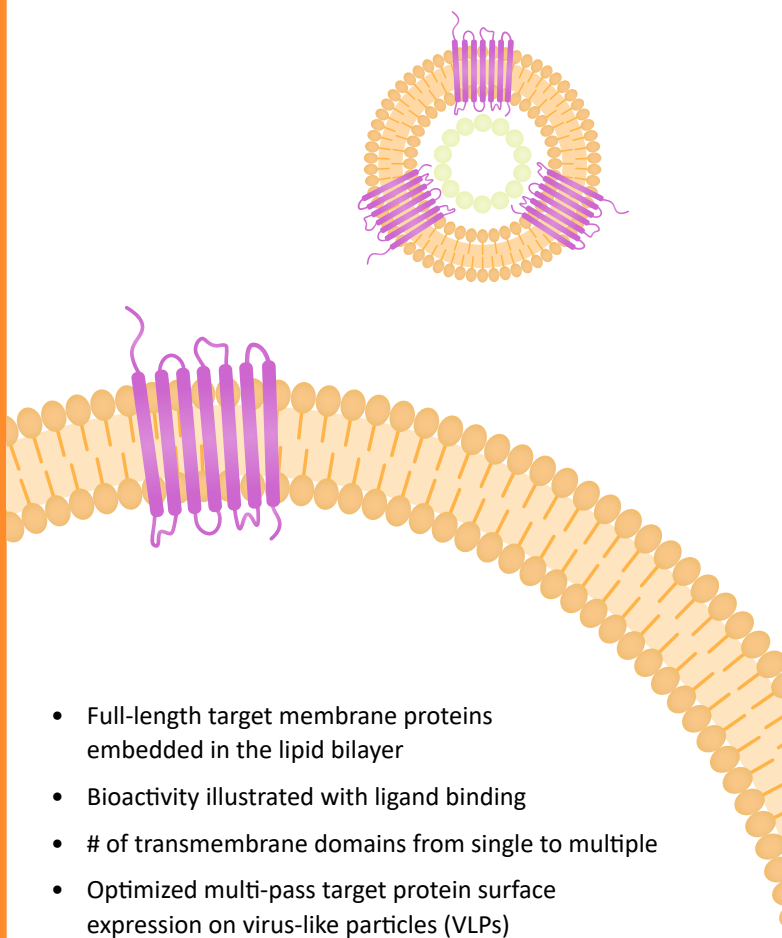


Mouse CD19 protein dimer, His Tag (CSP-124-01) potently binds to CD19 specific monoclonal antibody (mAb) as measured by ELISA. The CD19 protein dimer (0.2 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-mouse CD19 mAb.

B Cell Receptors and Surface Markers									
Protein	Tag	Product Code	Species	Homodimer/ Heterodimer	Protein	Tag	Product Code	Species	Homodimer/ Heterodimer
CD19	His	CSP-24125-01	Human	Homodimer	CD19	His-Avi	CSP-24125-03	Human	Heterodimer
CD19	His	CSP-124-01	Mouse	Homodimer					

Multi-Pass Transmembrane Target Proteins Displayed on Virus-Like Nanoparticles

CMP™ Technology Platform
proprietary Conigen Membrane Protein



- Full-length target membrane proteins embedded in the lipid bilayer
- Bioactivity illustrated with ligand binding
- # of transmembrane domains from single to multiple
- Optimized multi-pass target protein surface expression on virus-like particles (VLPs)
- Viral capsid backbone engineering to increase VLP release for higher production yield

7-Transmembrane GPCRs in Drug Discovery

7-Transmembrane Domain GPCRs and 4-Transmembrane Domain Claudins in Cancer

Many multi-pass transmembrane proteins including G-protein-coupled receptors (GPCRs) and Claudins (CLDNs) are involved in cancer progression through distinct yet interrelated pathways. GPCRs, such as CXCR4 and CXCR5, possess seven transmembrane domains and regulate tumor cell migration, immune evasion, and metastasis. In contrast, Claudins are four-transmembrane domain proteins that contribute to tumor progression through tight junction regulation, invasion, and chemoresistance.

CXCR4 and CXCR5: Chemokine-Driven Tumor Dynamics

CXCR4, a well-characterized 7-transmembrane domain GPCR, promotes tumor survival, angiogenesis, and metastasis by engaging CXCL12, leading to enhanced invasiveness and immune suppression in various cancers.[35] Similarly, CXCR5 plays a dual role—while its expression on tumor cells is linked to poor chemotherapy response, its presence on tumor-infiltrating lymphocytes (TILs) correlates with improved survival, highlighting its immunomodulatory potential.[36]

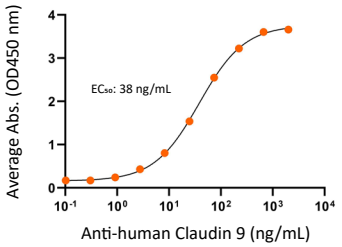
Claudins: Regulators of Tumor Progression

Claudins are a family of four-transmembrane domain proteins primarily responsible for forming tight junctions. Among them, CLDN9 is aberrantly expressed in multiple malignancies, including endometrial cancer, where its overexpression is associated with poor prognosis and metastatic potential.[37] CLDN9 functions through tight junction regulation and intracellular signaling pathways, often working in concert with CLDN6, another cancer-associated Claudin. Their co-expression predicts significantly worse survival outcomes, implicating these proteins in tumor aggressiveness.[37]

Therapeutic Potential

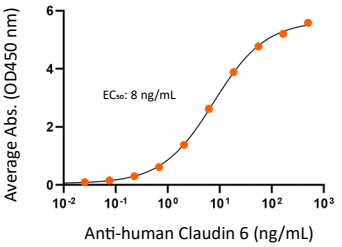
Targeting GPCRs and Claudins represents a promising cancer treatment strategy. CXCR4 antagonists, such as AMD3100, are under clinical investigation, while Claudin-based therapies, including antibody-drug conjugates and CAR-T cells, are being explored for their ability to disrupt tumor-promoting interactions.[35,37] Given their role in cell adhesion, migration, and immune modulation, these transmembrane proteins offer novel avenues for therapeutic intervention.

Claudin 9 Specific Antibody Binding



Human Claudin 9 protein CMP (CMP-24009) potently binds to Claudin 9 specific monoclonal antibody (mAb) as measured by ELISA. The Claudin 9 protein dimer (0.5 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human Claudin 9 mAb.

Claudin 6 Specific Antibody Binding



Human Claudin 6 protein CMP (CMP-24006) potently binds to Claudin 6 specific monoclonal antibody (mAb) as measured by ELISA. The Claudin 6 protein dimer (0.5 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human Claudin 6 mAb.

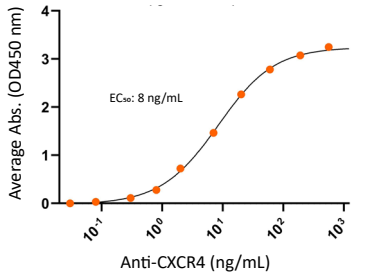
Spotlight: CXCR4

Recombinant expression of CXCR4 is notoriously difficult due to its complex structure, poor stability, and low expression levels. To address these challenges, Conigen developed CXCR4-CMP using the innovative Conigen Membrane Protein platform technology that displays CXCR4 on non-infectious viral-like particles (VLPs).

CXCR4-CMP incorporates CXCR4 into a lipid bilayer supported by a viral capsid core, mimicking its natural conformation on mammalian cell membranes. These 150–200 nm VLPs present a high density of bioactive CXCR4, maintaining its structural integrity and functionality. The displayed receptors specifically bind CXCL12, HIV-1 envelope glycoproteins, and CXCR4-targeting antibodies, making them ideal for studying receptor-ligand interactions.

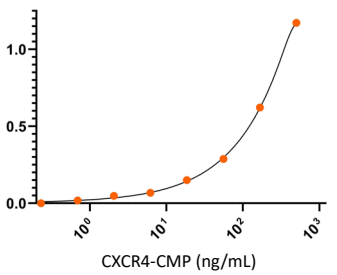
With enhanced stability and bioactivity, CXCR4-CMP provides a reliable and scalable platform for *in vivo* immunization, *in vitro* bioassays, drug screening, and mechanistic studies. Its safety, ease of production, and adaptability make it a powerful tool for both fundamental research and pharmaceutical applications, facilitating the development of therapeutics targeting CXCR4-mediated pathways.

CXCR4 Specific Antibody Binding



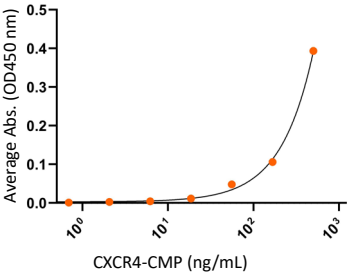
Human CXCR4 protein CMP (CMP-24005) potently binds to CXCR4 specific monoclonal antibody (mAb) as measured by ELISA. The CXCR4 protein dimer (0.5 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of anti-human CXCR4 mAb.

CXCR4 Binding to CXCL12 Chemokine



Human CXCR4 protein CMP (CMP-24005) binds well to its ligand CXCL12 chemokine as measured by ELISA. The CXCL12 protein dimer (0.5 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of CXCR4-CMP.

CXCR4 Binding to HIV-1 gp120



Human CXCR4 protein CMP (CMP-24005) binds well to its ligand HIV-1 envelope glycoprotein gp120 as measured by ELISA. The gp120 protein dimer (0.5 µg/ml) was coated on 96-well microtiter plates and detected by serial dilutions of CXCR4-CMP.

GPCRs and Claudins							
Protein	Product Code	Species	Family	Protein	Product Code	Species	Family
Claudin 3	CMP-24008	Human	Claudin	Claudin 18.2	CMP-24001	Human	Claudin
Claudin 4	CMP-24006	Human	Claudin	CMP Isotype Control	CMP-24000	NA	Control
Claudin 6	CMP-24007	Human	Claudin	CXCR4	CMP-24005	Human	GPCR
Claudin 9	CMP-24009	Human	Claudin	CXCR5	CMP-24014	Human	GPCR

Product Catalog

Protein	Tag	Product Code	Species	Protein Category	Homodimer/ Heterodimer
B7H3	His-Avi	CSP-240982lg	Human	Tumor Associated Antigen	Homodimer
B7H3	His-Avi	CSP-240984lg	Human	Tumor Associated Antigen	Homodimer
CD2	His-Avi	CSP-24095-03	Human	Tumor Associated Antigen	Homodimer
CD4	His	CSP-24004	Human	Cytokine Receptor	Homodimer
CD19	His	CSP-24125-01	Human	B-cell Receptor	Homodimer
CD19	His	CSP-124-01	Mouse	B-cell Receptor	Homodimer
CD19	His-Avi	CSP-24125-03	Human	B-cell Receptor	Homodimer
CD28	His	CSP-24032	Human	Immune Checkpoint	Homodimer
CD80	Fc	CSP-24033-04	Human	Immune Checkpoint	Homodimer
CD80	Flag-His	CSP-24033-02	Human	Immune Checkpoint	Homodimer
CD80	His	CSP-24033	Human	Immune Checkpoint	Homodimer
CD80-hFc	Fc	CSP-25187-04	Mouse	Immune Checkpoint	Homodimer
CD117	Fc	CSP-25123-04	Human	Tumor Associated Antigen	Homodimer
CD117	His-Avi	CSP-24123-03	Human	Tumor Associated Antigen	Homodimer
CD117	His-Avi	CSP-25193-03	Mouse	Tumor Associated Antigen	Homodimer
CD117	His-Avi	CSP-25194-03	Rhesus Macaque	Tumor Associated Antigen	Homodimer
CD155	His	CSP-24029	Human	Immune Checkpoint	Homodimer
Claudin 3	NA	CMP-24008	Human	Claudin	NA
Claudin 4	NA	CMP-24006	Human	Claudin	NA
Claudin 6	NA	CMP-24007	Human	Claudin	NA
Claudin 9	NA	CMP-24009	Human	Claudin	NA
Claudin 18.2	NA	CMP-24001	Human	Claudin	NA
CMP Isotype Control	NA	CMP-24000	NA	Control	NA
CTLA-4	His	CSP-24031	Human	Immune Checkpoint	Homodimer
CXCR4	NA	CMP-24005	Human	GPCR	NA
CXCR5	NA	CMP-24014	Human	GPCR	NA
EpoR	His-Avi	CSP-24087	Human	Cytokine Receptor	Homodimer
FGFR1	His-Avi	CSP-25129-03	Human	Growth Factor Receptor	Homodimer

Protein	Tag	Product Code	Species	Protein Category	Homodimer/ Heterodimer
FGFR2	His-Avi	CSP-25130-03	Human	Growth Factor Receptor	Homodimer
FGFR3	His-Avi	CSP-25131-03	Human	Growth Factor Receptor	Homodimer
FGFR4	His-Avi	CSP-25132-03	Human	Growth Factor Receptor	Homodimer
GCSFR	His-Avi	CSP-24086	Human	Cytokine Receptor	Homodimer
gp130	His-Avi	CSP-24081-03	Human	Cytokine Receptor	Homodimer
IFNα-R1/R2	His	CSP-24025-A1B1	Human	Cytokine Receptor	Heterodimer
IFNγR1	His	CSP-24015	Human	Cytokine Receptor	Homodimer
IL-2Rβ/γ	His-Avi	CSP-24045-A1B5	Human	Cytokine Receptor	Heterodimer
IL10Rα	His	CSP-24018	Human	Cytokine Receptor	Homodimer
IL15Rα	His-Avi	CSP-24064	Human	Cytokine Receptor	Homodimer
Nectin-4	His	CSP-24016	Human	Tumor Associated Antigen	Homodimer
PD1	His-Avi	CSP-24093-03	Human	Immune Checkpoint	Homodimer
PD-L1-hFc	Fc	CSP-2594-04	Human	Immune Checkpoint	Homodimer
PD-L1	His	CSP-25190-01	Mouse	Immune Checkpoint	Homodimer
PRLR	His-Avi	CSP-24089	Human	Cytokine Receptor	Homodimer
PRLR	His-Avi	CSP-25160-01	Mouse	Cytokine Receptor	Homodimer
TIGIT	Fc	CSP-24028	Human	Immune Checkpoint	Homodimer
TIGIT	His	CSP-24028-01	Human	Immune Checkpoint	Homodimer
TIGIT	His-Avi	CSP-24028-03	Human	Immune Checkpoint	Homodimer
TROP-2	Flag-His	CSP-24041-02	Human	Tumor Associated Antigen	Homodimer
TROP-2	Flag-His	CSP-25191-02	Mouse	Tumor Associated Antigen	Homodimer
VEGFR2	His-Avi	CSP-25127-03	Human	Growth Factor Receptor	Homodimer

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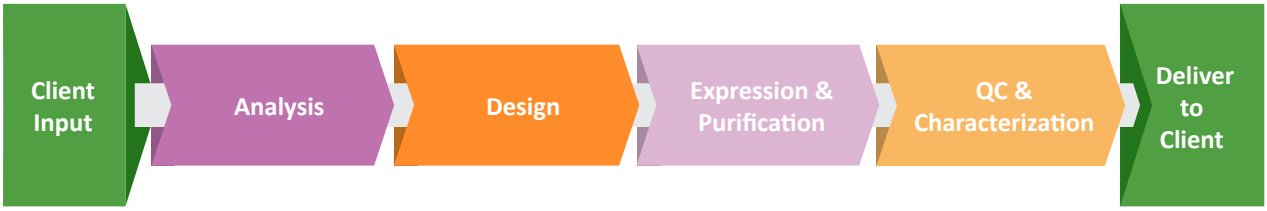

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Innovator in genetic prime-protein boost and immunofocusing immunization regimens, generated antibodies against diverse targets in mouse, rabbit, and human

Antibody binding and functional evaluations including solid phase binding assays, label-free affinity measurements, flow cytometry, neutralizing and Fc-mediated activities

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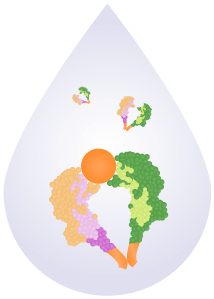
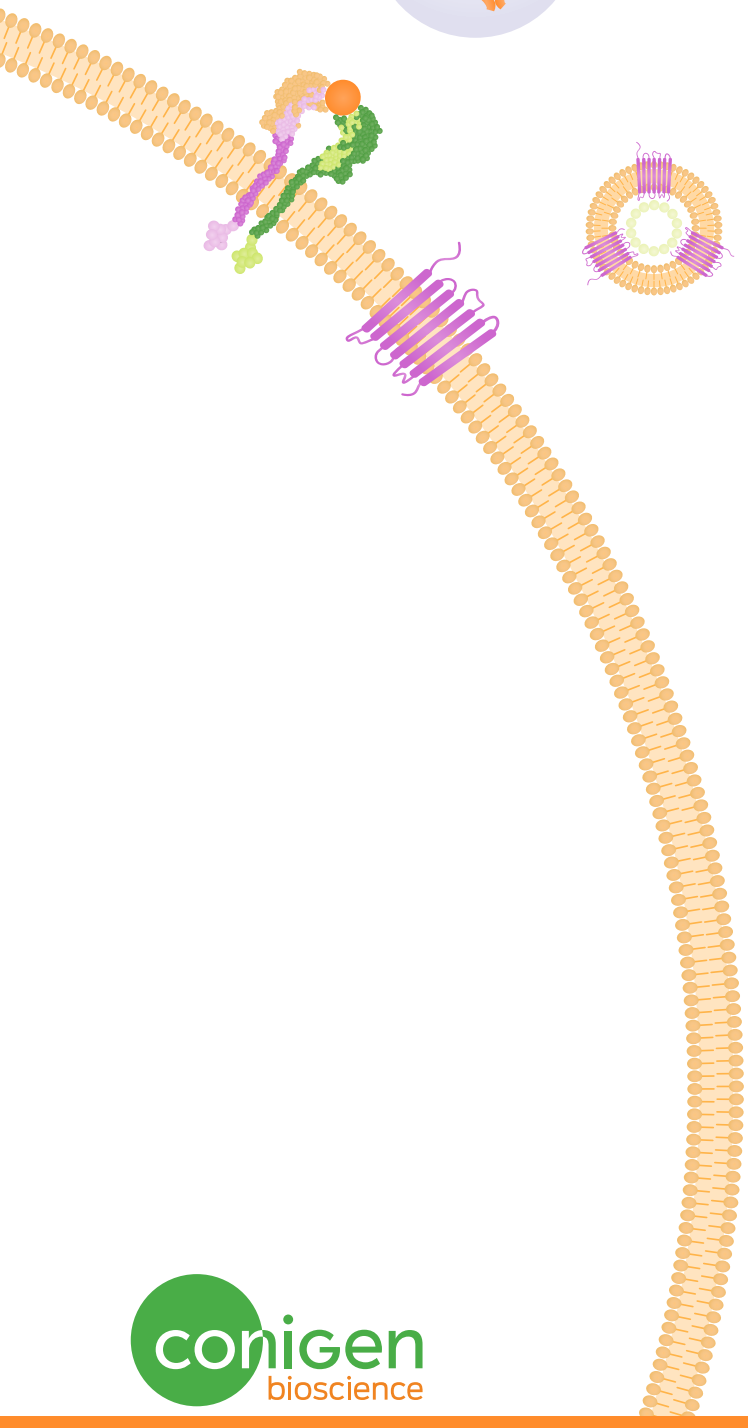
*Computational Modeling: Structures were predicted using the ColabFold implementation of AlphaFold2. Predictions were run in PDB100 template mode with MMseqs2 (UniRef + environmental databases), using the AlphaFold2-multimer v3 model and 12 recycles. Experimental crystal structures were retrieved from the RCSB Protein Data Bank (PDB), and all structural alignments and visualizations were performed in PyMOL.



Soluble Proteins

Single-pass ectodomain dimers

- Cytokine Receptors
- Immune Checkpoint Receptors
- Tumor Associated Antigens
- Growth Factor Receptors



Membrane-Associated Proteins

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