Fusion BioLabs Fc Engineering Vector Datasheet

Human IgG1 (V308P) — V308P Fc Variant

SKU#: AFV-32

Plasmid Information

- **Plasmid name:** `pHC-IgG1-V308P`
- **Backbone:** Human IgG1 heavy-chain expression vector
- **Insert:** Signal peptide–MCS-C_H1-hinge-C_H2(V308P)-C_H3
- **Resistance marker:** Ampicillin
- **Promoter:** CMV
- **Product Configuration:** Fc-engineered heavy-chain expression vector (single-vector format).
- **Compatible Light-Chain Vector:** A matching light-chain expression vector is required for complete IgG antibody expression and is available separately or as part of the optional Fc Engineering Set/Pair.

Fc Engineering Summary

- **Mutation set:** `V308P` (C_H2 domain)
- **Common name:** V308P Fc Variant
- **Engineering purpose:** Single-point mutation to modulate FcRn dissociation kinetics, enabling controlled/accelerated systemic clearance without completely abrogating FcRn engagement.

Functional Profile

Property	Effect
FcγR binding	Maintained / WT Baseline
ADCC	Maintained / WT Baseline
CDC	Maintained / WT Baseline
FcRn binding	Altered / Reduced ↓
Serum half-life	Shortened / Accelerated clearance ↓
PK profile	Controlled fast-clearance (~ 2-5 days)

Note: Functional properties are based on published Fc-engineering studies and may vary with antibody specificity, expression system, glycosylation, and assay conditions. Unless otherwise indicated, these results have not been independently validated for this specific Fusion BioLabs expression construct.

Mechanism of Action

The V308P Fc variant introduces a single point substitution—**Val308 to Pro**—within the loop region of the C_H2 domain at the FcRn binding interface. The rigid proline substitution alters local backbone conformation and perturbs optimal hydrogen bonding and hydrophobic contact with FcRn. This speeds up endosomal dissociation and reduces intracellular recycling efficiency, resulting in accelerated clearance while avoiding the immediate, complete ablation seen with total FcRn knockout variants like I253A.

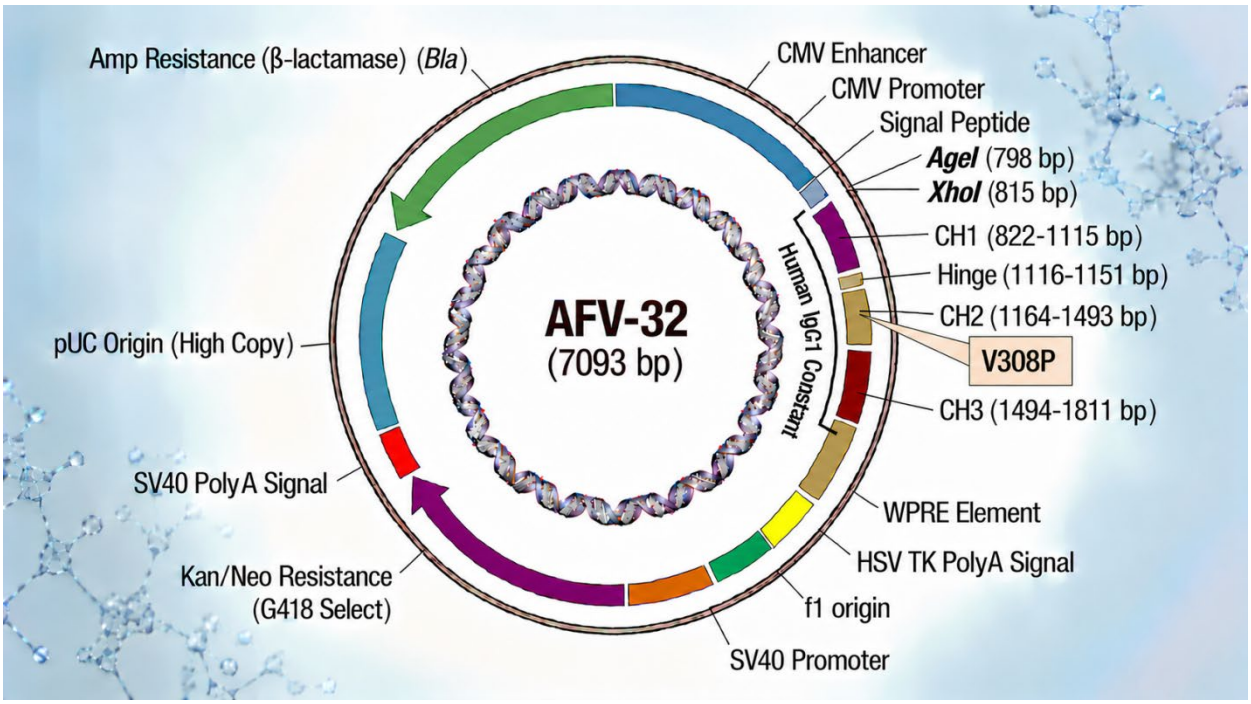
Phenotypic Effects

- Moderately reduced FcRn binding affinity at endosomal acidic pH (pH 6.0)
- Accelerated systemic clearance rate (2 -5-day serum half-life in human/primate models)
- Provides intermediate clearance rate between wild-type IgG1 (~ 21 days) and FcRn-null variants (hours)
- Retains wild-type effector functions (ADCC, ADCP, and CDC)
- Preserves overall conformational stability and expression yields

Applications

- Antibody-drug conjugates (ADCs) designed to minimize systemic toxicity from long circulation
- Immuno-PET imaging and diagnostic radioimmunotherapy requiring clear background contrast within days
- Bispecific or toxic biologics requiring rapid off-target clearance windows
- Mechanistic control for calibrating FcRn recycling threshold models

Vector Map



Feature annotation:

- C_H1 — constant heavy 1
- **Hinge** — native IgG1 hinge
- C_H2(V308P) — **FcRn-modulating fast-clearance mutation**
- C_H3 — constant heavy 3

Vector Specifications

Antibiotic Resistance	Ampicillin (Amp^R)
Constitutive or Inducible System	Constitutive
Delivery Type	Transfection
Promoter	CMV
Product Type	Mammalian Expression Vector
Cloning Method	Restriction Enzyme (5'-AgeI; 3'-XhoI) or Homologous Assembly
Available Configurations	Single Heavy-Chain Vector or Fc Engineering Set/Pair
Content — Single Vector	5.0 µg Fc-engineered heavy-chain plasmid in TE buffer
Content — Set/Pair	Two separate plasmids: 5.0 µg Fc-engineered heavy-chain expression vector and 5.0 µg compatible light-chain expression vector, supplied individually in TE buffer.

Cloning Map



Primer Design for Restriction Enzyme Cloning (Traditional)

Forward primer: 5'- CTAGTAGCAACTGCAACCGGTGTACATTCAN_{VHF}(15-18)-3'

Reverse Primer: 5'- GGCCCTTGGTGGAGGCGCTCGAGACN_{VHR}(15-18)-3'

N_{VHF}(15-18): append 15-18 bases encoding 5-6 amino acids starting from the beginning of the VH region to the end of the forward primer.

N_{VHR}(15-18): append the Reverse Complement DNA Sequence of 15-18 base encoding 5-6 amino acids of starting from the end of the VH region to the reverse primer (i.e. from 9th--8th to 4th from the VH end, VSS has already been included in the reverse primer).

Primer Design for Homologous Recombination Cloning (Seamless)

Forward primer: 5'- CTAGTAGCAACTGCAACCGGTGTACATTCAN_{VHF}(15-18) -3'

Reverse Primer: 5'- GGCCCTTGGTGGAGGCN_{VHR}(15-18) -3'

N_{VHF}(15-18): append 15-18 bases encoding 5-6 amino acids starting from the beginning of the VH region to the end of the forward primer.
N_{VHR}(15-18): append the Reverse Complement DNA Sequence of 15-18 bases encoding 5-6 amino acids starting from the end of the VH region to the reverse primer.

Sequencing primer for confirming the correct VH insert (included in the Kit)

pFB forward: 5'- ATGGGCGGTAGGCGTGTA-3'

Storage & Handling

- Store plasmid at –20°C
- Avoid repeated freeze–thaw cycles
- Use sterile technique when handling
- Suitable for transient or stable mammalian expression

Product Notes

- Complete Antibody Expression — Fc Engineering Set/Pair

For expression of a complete Fc-engineered IgG antibody, the Fc-engineered heavy-chain expression vector must be co-transfected with a compatible light-chain expression vector containing the corresponding antibody light-chain variable region.

Fusion BioLabs offers matching light-chain expression vectors through its Antibody Expression Vector product category. Customers may purchase the Fc-engineered heavy-chain vector individually or select the optional Fc Engineering Set/Pair, which includes the Fc-engineered heavy-chain expression vector and a compatible light-chain expression vector.

Note: The Fc Engineering Set/Pair provides compatible heavy-chain and light-chain expression vectors. Antibody-specific VH and VL sequences must be cloned into the corresponding vectors unless the product is explicitly supplied with pre-inserted variable-region sequences.

- The V308P Fc variant is an essential tool for applications where long serum persistence is undesirable or toxic. It provides a finely tuned "middle ground" for accelerated clearance, ensuring that circulating therapeutic or diagnostic constructs clear within several days rather than several weeks or a few hours.

Comparison within Fusion BioLabs FcRn / PK-Modulated Fc Variant Family

Variant	Mechanism	Strength (PK Extension)	Primary Application & Notes
human IgG1 (WT) (Wild-Type)	Native FcRn binding	★★☆☆☆	Baseline Control. Standard physiological baseline (~21-day half-life in humans).
human IgG1 (N434A) N434A	Single-point FcRn-enhanced	★★★☆☆	Single-point mutation providing a moderate 1.5–2× PK boost with low immunogenicity risk and easy manufacturing integration.
human IgG1 (LA) M428L / N434A	FcRn-enhanced	★★★★☆	Strong PK Extension. Dual mutation combining M428L and N434A; enhances acidic FcRn binding with minimal neutral binding.
human IgG1 (LS) M428L / N434S	FcRn-enhanced	★★★★★	Very Strong PK Extension. Extends human serum half-life up to 3–5× (>70–90 days; e.g.,

			tixagevimab/ cilgavimab).
human IgG1 (YTE) M252Y / S254T / T256E	FcRn-enhanced	★★★★★	Benchmark PK Extension. Industry-standard benchmark delivering ~3–4× PK boost in humans (e.g., nirsevimab / Beyfortus®).
human IgG1 (QL) T250Q / M428L	FcRn-enhanced	★★★★☆	Moderate-to-Strong PK Extension. Increases acidic FcRn affinity with favorable intellectual property freedom to operate.
human IgG1 (YTE + KF) M252Y/S254T/T256E + H433K/N434F	Hyper-FcRn-enhanced / FcRn Blocker	★★★★★	FcRn Antagonist / Autoimmune Control. Binds tightly across pH 6.0 and 7.4 to block FcRn recycling and clear endogenous IgGs.
human IgG1 (V308P) V308P	Controlled/Accelerated Clearance	★★☆☆☆	Tunable Fast-Clearance Variant. Modulates FcRn dissociation kinetics to yield accelerated clearance (2–5-day half-life); ideal for ADCs and immuno-PET imaging to limit non-target toxicity.
human IgG1 (I253A)I253A	FcRn-null / Abrogated	★☆☆☆☆	Ultra-Fast Clearance Control. Complete knockout of the core FcRn binding triad; rapidly cleared within hours.

References

- *Shields RL, Namenuk AK, Hong K, Meng YG, Rae J, Briggs J, Xie D, Lai J, Stadlen A, Li B, Fox JA, Presta LG. High resolution mapping of the binding site on human IgG1 for Fc gamma RI, Fc gamma RII, Fc gamma RIII, and FcRn and design of IgG1 variants with improved binding to the Fc gamma R. J Biol Chem. 2001;276(9):6591-6604.*
- *Datta-Mannan A, Witcher DR, Tang Y, Watkins J, Jiang W, Wroblewski VJ. Humanized IgG1 variants with differential binding properties to the neonatal Fc receptor: relationship to pharmacokinetics in mice and primates. Drug Metab Dispos. 2007;35(1):86-94.*

Document Version

- **Datasheet version:** 3.1
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