

Library Evaluation and Ingestion

High-Throughput NGS Quality Control, Clonal Deduplication, and Kinetic Selection

Transform massive, noisy NGS datasets (FASTQ, FASTA, multi-file ZIP) and multi-round screening libraries directly into curated lead candidates. AbLead automatically validates 7-region IMGT completeness, checks Phred quality scores, detects molecular formats, and computes biopanning enrichment kinetics—eliminating custom bioinformatic scripting bottlenecks.

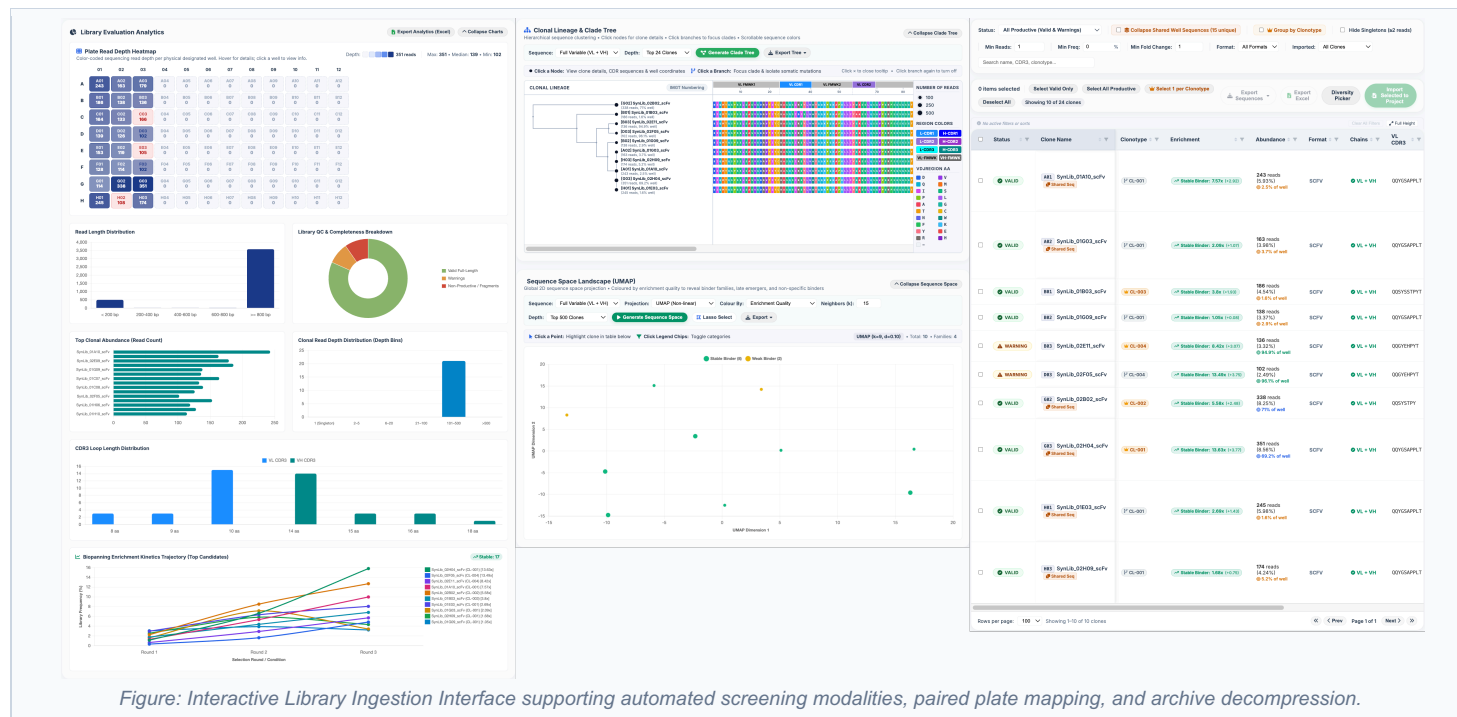


Figure: Interactive Library Ingestion Interface supporting automated screening modalities, paired plate mapping, and archive decompression.

CORE CAPABILITIES

- **Universal Archive Ingestion:** Parses FASTQ (.gz), FASTA, GenBank, TSV, and nested ZIP archives directly in memory with zero manual pre-formatting.
- **Screening Workflows:** Optimized for Hit Picking (with/without plate maps), Biopanning Kinetics, Cross-Reactivity, DMS, FACS Sort-Seq, and Single-Cell AIRR.
- **Architecture Auto-Detect:** Automatically identifies scFv, single-domain VHH, and paired Fv/Fab constructs from raw read length and domain landmarks.
- **Rigorous Sequencing QC:** Translates per-base Phred ASCII scores to numeric quality, flags frameshifts and premature stop codons, and decodes dual barcodes.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Longitudinal Kinetics:** Calculates log2(Fold-Change) enrichment and depletion trajectories across panning rounds to isolate true high-affinity binders.
- **Eliminate Sequencing Noise:** Filters out non-productive amplicons, primer-dimers, and aberrant clones before committing costly wet-lab resources.
- **Pre-Flight Plate Validation:** Automatically reconciles well coordinates, barcode adapters, and clone IDs to prevent expensive tracking errors.
- **Platform Handoff:** Promotes prioritized clones directly into AbLead for rank ordering, liability triage, and optimization design.

The AbLead Advantage: By unifying high-throughput sequencing QC, multi-round selection kinetics, and automated architecture validation into a single pipeline, AbLead bridges the gap between raw sequencing reads and prioritized lead molecules.

Accelerate Your Antibody Lead Optimization and De-Risk Development

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Unified Lead Prioritization, Custom Scoring Presets, and Multi-Parameter Optimization

	Lineage						Genetic Origin									
	Name ▾	Parent ▾	LC Leader ▾	LC Leader %Id ▾	VL Species ▾	VL V-Gene ▾	VL V-Gene %Id ▾	VL J- Gene ▾	VL J- Gene %Id ▾	LC Constant ▾	LC Constant %Id ▾	HC Leader ▾	HC Leader %Id ▾	VH Species ▾	VH	
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- **Composite Multi-Attribute Scoring:** Interactive multi-tier developability analyses evaluating potential conformational and colloidal stability aspects.
- **Customizable KBC Scoring Presets:** Tailor developability scoring weights to project goals, saved as named presets with instant recalculation.
- **Custom Metadata Ingestion:** Merge experimental wet-lab data directly into the grid, allowing rank order and lead selection using developability and activity data.
- **Format Presets and Direction Icons:** Named conditional formatting sets with directional icons (↓ lower is better. ↑ higher is better) for instant triage.

- **Holistic Lead Triaging:** Replaces subjective evaluation with an objective composite score balancing multiple developability attributes.
- **Session and State Persistence:** Preserves sort hierarchies, active filters, and custom column configurations across browser sessions and team members.
- **Comprehensive Export Suite:** One-click export to conditionally-formatted Excel workbooks with live formulas, CSV, Word analysis reports, and WIPO ST.26.
- **Rapid Pipeline Alignment:** Enables discovery and developability teams to agree on explicit candidate selection thresholds across campaigns, leading directly to optimization designs.

The AbLead Advantage: AbLead's Results Rank Order transforms lead selection from fragmented, error-prone manual spreadsheets into an objective, preset-driven decision engine that balances biological efficacy with manufacturability.

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Sequence Alignment and Positional Analytics

Multi-Scheme Numbering and CDR Regions, Dynamic Sequence Logos, and Integrated Liability Tracking

Inspect and compare antibody sequences with structural precision using industry-standard numbering schemes across variable, constant, and leader domains. AbLead pairs interactive multi-chain alignments with stacked amino acid Sequence Logos, consensus baselines, and aligned germline reference tracks with live liability overlays.

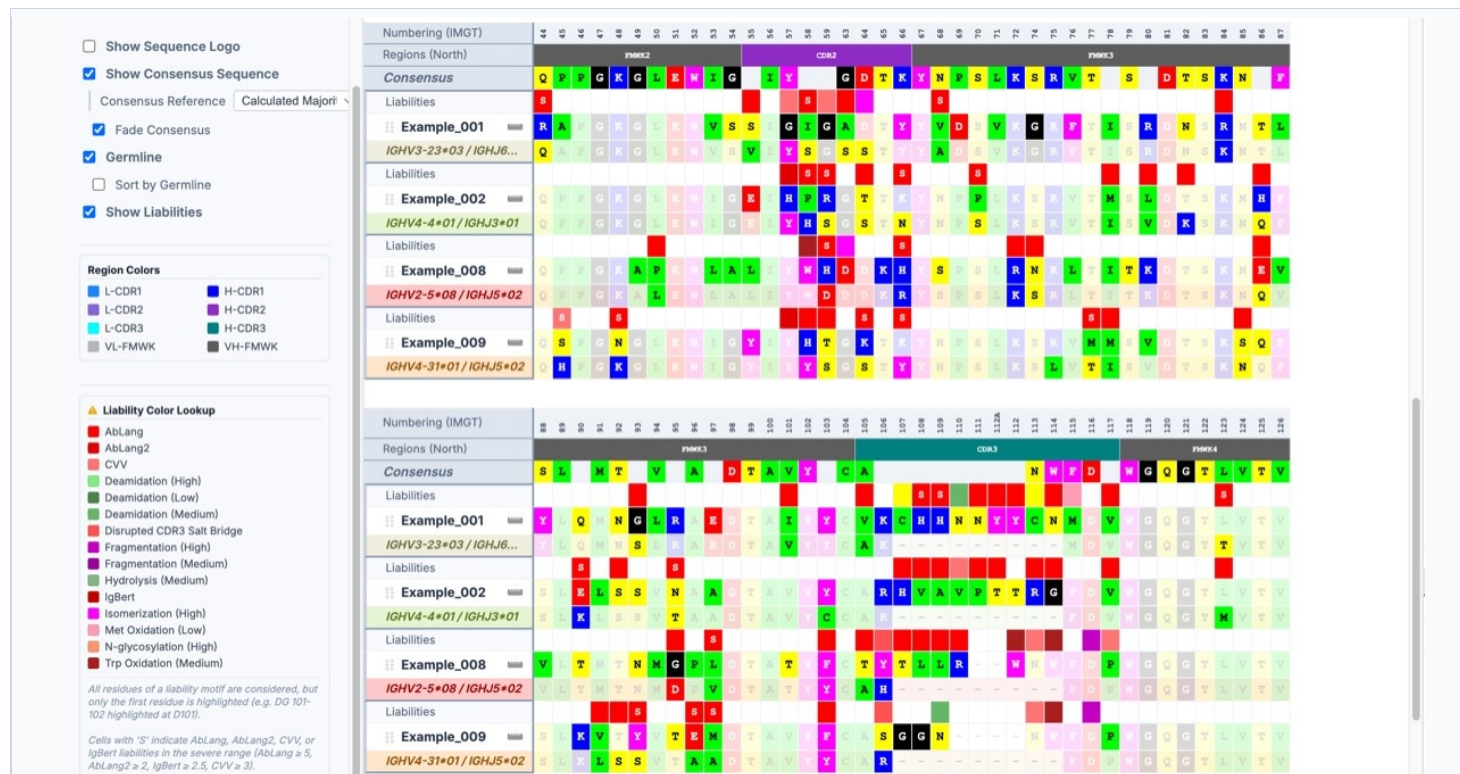


Figure: Interactive multi-chain alignment displaying closest germline deviations, dynamic sequence logos, and flagged developability liabilities.

CORE CAPABILITIES

- **Multi-Scheme Numbering and CDR Region Support:** Dynamically switch or multi-display between numbering and CDR schemes.
- **Dynamic Stacked Sequence Logos:** High-resolution letter stacks proportional to positional frequency, colored by ABHAND physicochemical properties.
- **Consensus Baseline Tracking:** Flexible majority-rule or reference-clone consensus with match fading to instantly spotlight somatic mutations.
- **Integrated Germline and Liability Rows:** Aligns closest V/J germlines beneath queries and overlays sequence liability motifs with severe (S) flags.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Paratope and CDR Conservation:** Pinpoints conserved binding residues versus permissive positions across clonal families to guide engineering.
- **IP Claim Generation:** Facilitates sequence range definitions and consensus drafting for patent applications and freedom-to-operate filings.
- **Direct Design and Observation Pinning:** Click any residue position to record institutional lab observations or queue mutations for variant generation.
- **Publication-Ready Exports:** Generates high-resolution SVG and PNG sequence logo figures and formatted Excel sheets preserving all region annotations.

The AbLead Advantage: By integrating standard numbering schemes, dynamic sequence logos, and aligned germline liabilities into one view, AbLead turns sequence alignment into a diagnostic and engineering command center.

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Repertoire Clading and Lineage Distribution

Phylogenetic Clustering, Germline Rooting, and Parsimonious Liability Tracking

Uncover sequence-distance relationships, B-cell clonal expansion, and ancestral developability modifications across your antibody repertoire. AbLead automatically builds hierarchical cladograms, reconstructs unmutated common ancestor (UCA) germline roots, and parsimoniously maps sequence liabilities along clade branches.

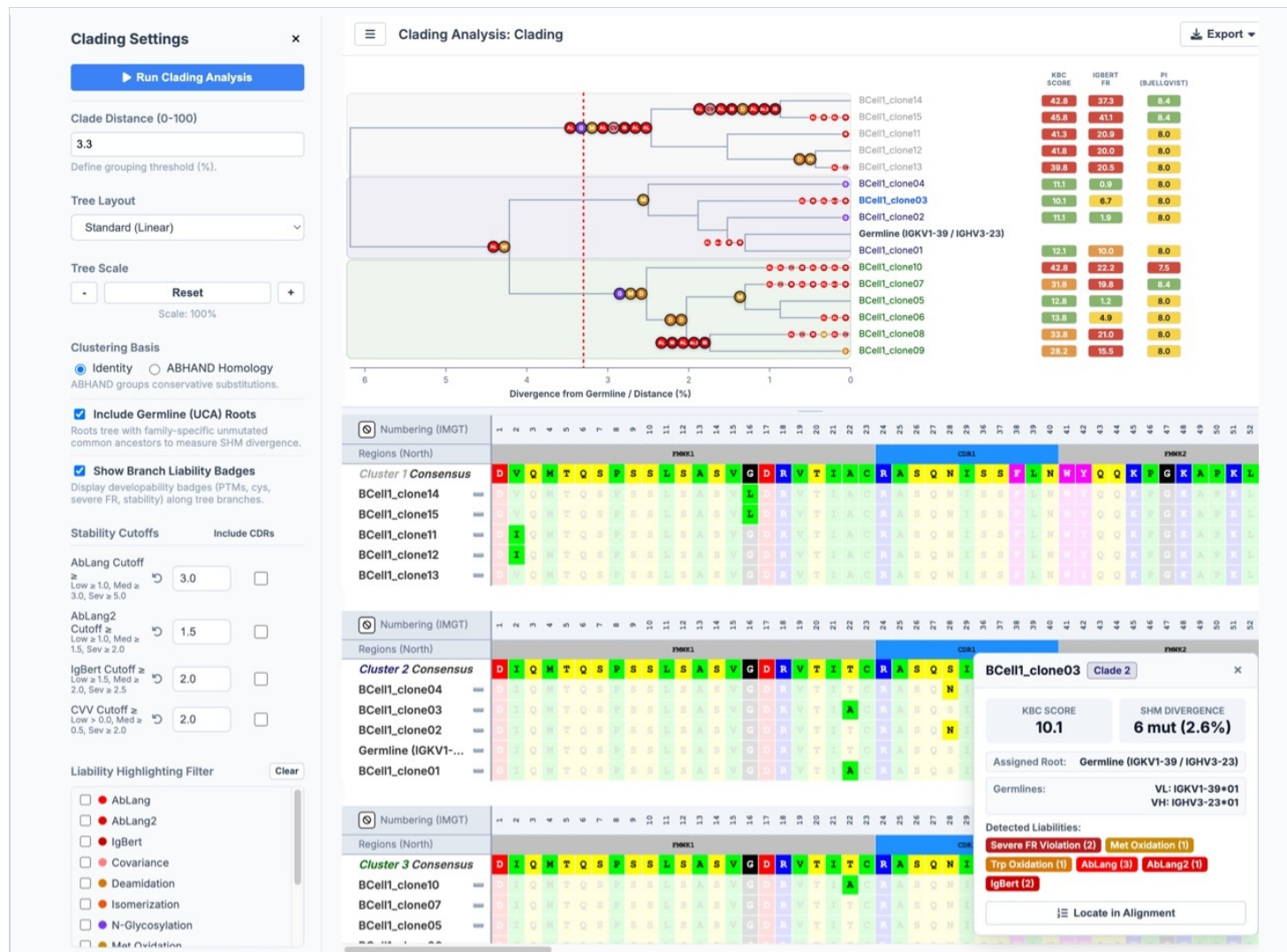


Figure: Phylogenetic Cladogram with interactive distance threshold slider, unmutated common ancestor (UCA) rooting, and ancestral liability branch badges.

CORE CAPABILITIES

- **Dual Tree Layouts:** Switch dynamically between Linear and Circular phylogenetic projections with interactive real-time cutoff distance sliding.
- **Dual Clustering Metrics:** Cluster sequences by Sequence Identity (Hamming distance) or ABHAND Homology (physicochemical property distance).
- **Germline (UCA) Rooting:** Synthesizes multi-family unmutated ancestral germlines to establish B-cell origins and somatic hypermutation (SHM) rates.
- **Parsimonious Liability Mapping:** Automatically distinguishes ancestral liabilities shared across entire sub-lineages from private leaf mutations.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Repertoire Diversity Preservation:** Prevents over-sampling identical clones by clustering repertoires into distinct functional families.
- **Liability Origin De-Risking:** Identifies whether a developability flaw was introduced during affinity maturation or inherited from a germline framework.
- **Cluster Alignment Exports:** Exports multi-chain alignments grouped by clade into formatted Excel workbooks with consensus and developability metrics.
- **Phylogenetic Interoperability:** Exports trees to standard Newick (.nwk) format for seamless publication figure generation in FigTree, iTOL, and MEGA.

The AbLead Advantage: Clading empowers discovery teams to navigate repertoire diversity, intelligently selecting the most potent, developable representatives from every lineage while avoiding clones compromised by ancestral liabilities.

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Developability Liabilities and 3D Structural Mapping

Comprehensive PTM Motif Detection, AI Stability Gating, and Real-Time 3D Visualization

Detect, categorize, and resolve chemical and structural degradation liabilities before advancing leads to production. AbLead combines the comprehensive Satlaw et al. (2024) motif library with cutting-edge antibody language models (AbLang, AbLang2, IgBert) and covariance analysis, synchronized with an interactive 3D molecular viewer.

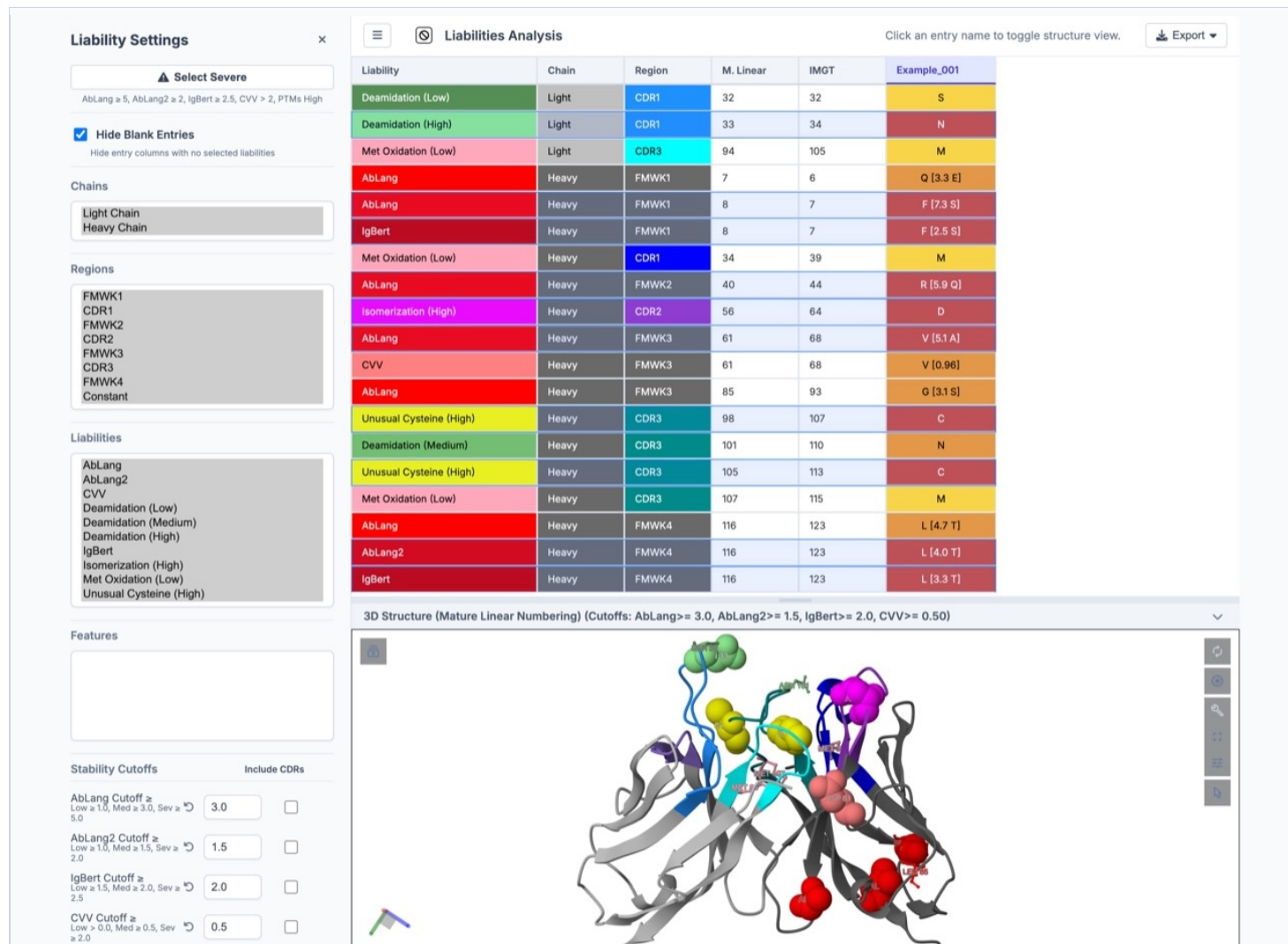


Figure: Interactive Liabilities Dashboard combining residue-level motif tables, AI stability penalty scores, and synchronized 3D structural viewer.

CORE CAPABILITIES

- Comprehensive Motif Detection:** Flags deamidation, isomerization, fragmentation, hydrolysis, unpaired cysteines, as well as user-based motifs.
- Multi-LLM Stability Gating:** Computes residue likelihood differences ($\Delta \ln P$) using AbLang, AbLang2, and IgBert to detect conformational destabilization.
- Covariance Violation Analysis:** Identifies co-varying constraint violations (CVV) that disrupt canonical antibody framework packing.
- Synchronized 3D Molecular Viewer:** Clicking any liability in the grid instantly highlights and spacefills the affected residue on the 3D atomic structure.

DEVELOPABILITY ADVANTAGE and IMPACT

- Improve Product Developability:** Drives optimization designs with direct visualization, allowing for combinatorial design decisions to maintain efficacy.
- Multi-Antibody Comparative Matrix:** Compares liability profiles across discovery cohorts side-by-side to de-select high-risk molecules early.
- 1-Click PyMOL Script Export:** Generates ready-to-run PyMOL visualization scripts with color-coded selections and custom zoom presets.
- Direct Engineering Workflow:** Select any identified liability to launch targeted mutation designs or execute 1-click First Pass Optimization.

The AbLead Advantage: Addressing stability and chemical liabilities computationally can save substantial time and money during cell line and process development, often improving yields and stability.

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Germline Analysis and Allotype Detection

Multi-Species Origin Mapping, Framework Homology, and Automated Constant Allotyping

Deconstruct antibody sequences into Leader, Variable (V and J), and Constant domains aligned against reference databases. AbLead utilizes deterministic framework-first identity and ABHAND homology ranking to identify precise germline origins and automatically calls IgG allotypes and isotypes based on EU numbering.

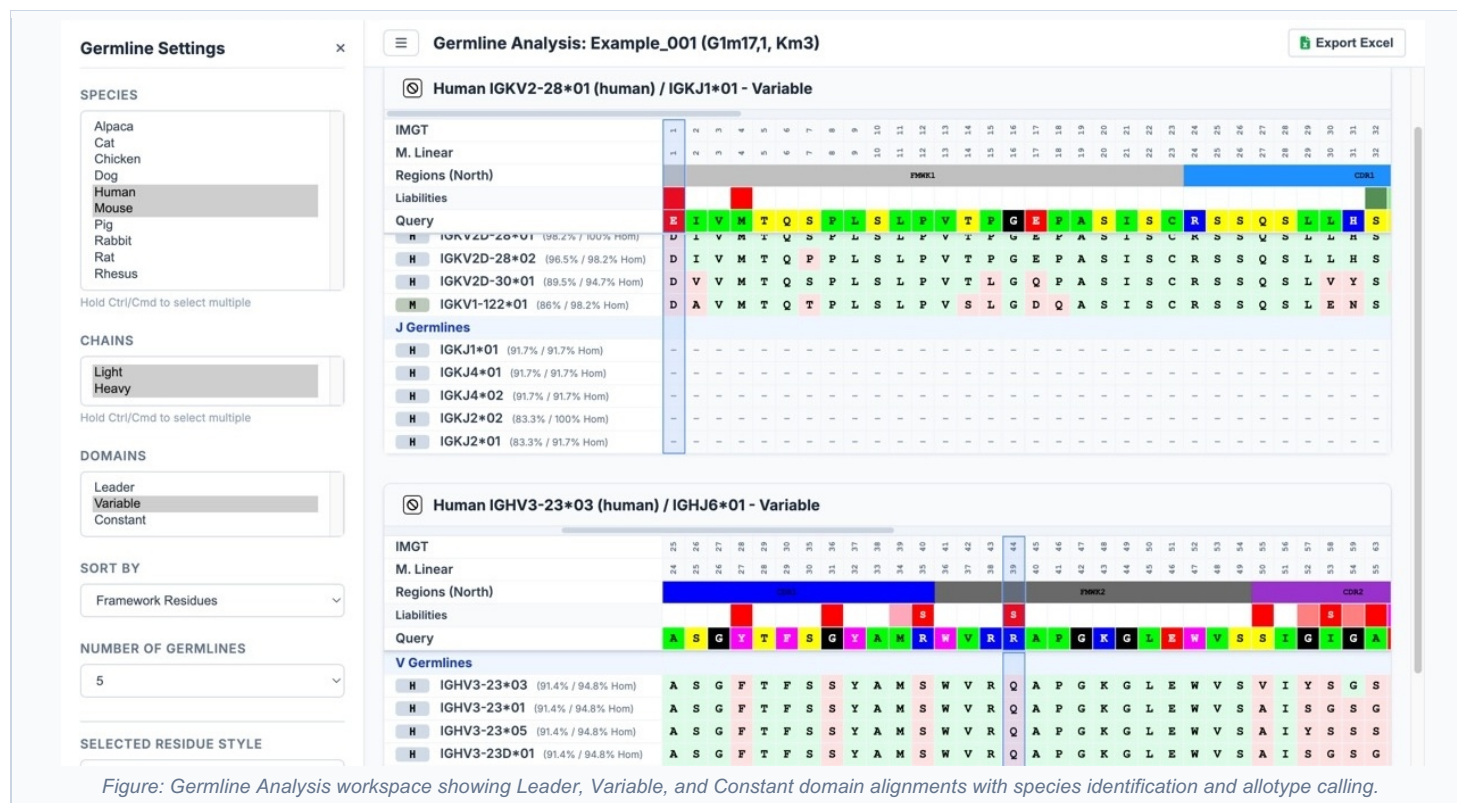


Figure: Germline Analysis workspace showing Leader, Variable, and Constant domain alignments with species identification and allotype calling.

CORE CAPABILITIES

- **Species Reference Database:** Curated germline repertoires for Human, Rhesus, Mouse, Rat, Rabbit, Alpaca, Dog, Cat, Chicken, and Pig.
- **Framework-First Deterministic Ranking:** Evaluates FR1–FR3 (V) and FR4 (J) identity and homology to prevent misclassification from affinity-matured CDRs.
- **Automated Constant Allotyping:** Calls IgG1, IgG2, IgG4 subclasses and human allotypes (G1m17,1, G1m3, Km3) based on EU-numbered constant markers.
- **Multi-Domain Alignment View:** Dissects sequences into Leader, V-domain, J-domain, and Constant domains (CH1, Hinge, CH2, CH3, CL) with aligned matches.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Species Verification and Lineage QC:** Rapidly verifies parental species identity in multi-species hybridoma and transgenic animal discovery campaigns.
- **Immunogenicity Baseline:** Quantifies somatic divergence from unmutated germline precursors to assess baseline immunogenicity risks.
- **Constant Domain Integrity:** Ensures proper constant region subclass assembly, hinge matching, and light chain isotype pairing (Kappa vs Lambda).
- **Integrated Developability Alerts:** Overlays sequence liability motifs and language model stability outliers directly above the query sequence.

The AbLead Advantage: Precision germline mapping and allotype calling establish the essential structural foundation required for reliable humanization, developability assessment, and patent characterization.

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Humanness and Immunogenicity Assessment

Repertoire OASign Humanness and RPEMHC Class II MHC T-Cell Epitope Prediction

Evaluate therapeutic antibody humanness and Anti-Drug Antibody (ADA) risk by combining repertoire self-tolerance with physical Class II MHC presentation. AbLead unites OASign (human 9-mer repertoire frequency) and RPEMHC (DeepMHCII ensemble Class II MHC presentation across 11 global core DRB1 alleles) in a single diagnostic workspace.



CORE CAPABILITIES

- **Dual-Metric Clinical Risk Scoring:** Combines OASign (TCR self-tolerance) with RPEMHC (Class II MHC presenting probability across 11 global HLA alleles).
- **High-Risk MHC-II Hotspots:** Scans 15-mer sliding windows, classifying peptides as 100% Germline (tolerated), Somatic Mutations, or Non-Germline.
- **1-Click Noise Reduction:** Instantly filters out natural germline binders to isolate actionable non-germline de-immunization liabilities.
- **Dual-Track Sequence Alignment:** Displays non-human 9-mer clusters alongside predicted MHC-II binding grooves with mutation trajectories.

The AbLead Advantage: A candidate is only safe if it scores well on both humanness and MHC presentation: AbLead combines OASign self-tolerance with RPEMHC presentation to deliver true clinical immunogenicity de-risking.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Mitigate Clinical ADA Risk:** Prevents neutralizing Anti-Drug Antibody formation that causes rapid clearance, loss of efficacy, and adverse reactions.
- **Predictive De-Immunization Scans:** Evaluates all 20 amino acid substitutions per position across MHC-II binding, germline frequency (PFA), and Sapiens AI.
- **Targeted Lead Optimization:** Preserves critical paratope binding residues while replacing high-risk presenting residues with tolerated human alternatives.
- **Comprehensive Excel Export:** One-click export of complete diagnostic tables, 20 allele affinity profiles, and Fv hotspot inventories for regulatory dossiers.

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Position Frequency Analysis (PFA)

Repertoire Statistical Likelihoods, Language Model Evaluations, and 3D Structural Gating

Guide antibody engineering with positional statistics and large language models. PFA unites human repertoire positional distributions from >127 million antibody sequences with four complementary antibody language models (Sapiens, AbLang, AbLang2, and IgBert), mapped directly onto 3D atomic structures.

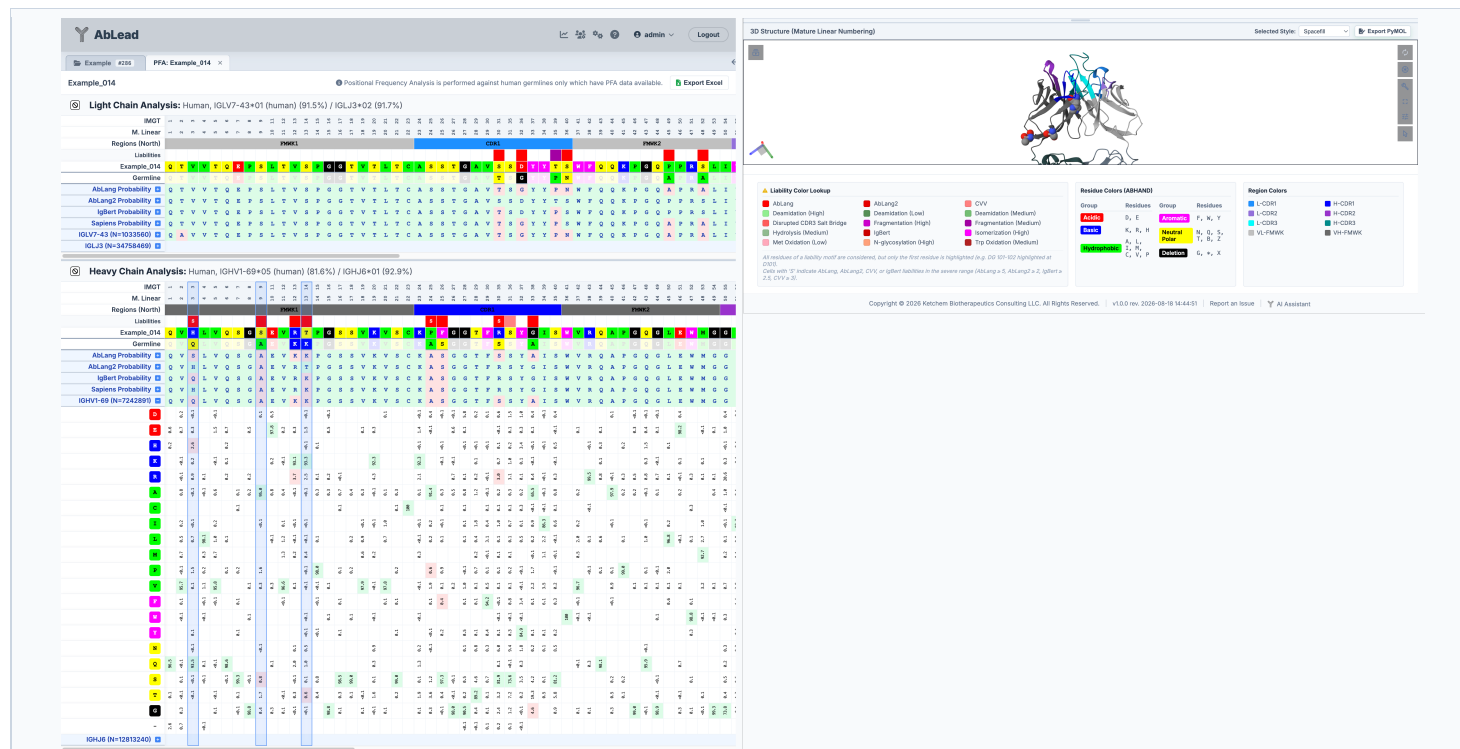


Figure: PFA Workspace showing per-residue repertoire probabilities, multi-model AI likelihood scores, and synchronized PDB Mol* 3D structure viewer.

CORE CAPABILITIES

- **Massive Repertoire Distributions:** Evaluates positional amino acid frequencies derived from millions of light and heavy chains against closest human germlines.
- **4 Integrated AI Language Models:** Combines Sapiens, AbLang, AbLang2, and IgBert.
- **Delta-Likelihood Defect Spotting:** Measures differences between parental residues and AI-preferred amino acids to flag destabilizing framework mutations.
- **Synchronized PDB Mol* 3D Viewer:** Interactive 3D ribbon rendering with CPK element highlighting for selected positions and adjustable split-pane sizing.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Data-Driven Residue Selection:** Replaces speculative mutagenesis with statistically validated, human B-cell preferred amino acid substitutions.
- **Paired Interface Evaluation:** Captures cross-chain VH-VL interface cooperativity using paired deep learning models (AbLang2 and IgBert).
- **Integrated Germline and Liability Tracking:** Displays germline deviations, severe stability violations, and potential PTMs directly above the sequence track.
- **1-Click Engineering Handoff:** Click any position in the probability grid to view 20-amino-acid scores and queue mutation designs into engineering sets.

The AbLead Advantage: By coupling massive natural repertoire statistics with modern paired antibody transformers, PFA guides engineering decisions toward mutations that naturally maximize conformational stability and expression.

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Surface Properties and Structural Developability

Hydrophobic Patches, Charge Densities, and Electrostatic Dipole Profiling

Predict and resolve formulation hurdles directly from 3D structural coordinates. AbLead computes Surface Hydrophobicity (SPH), Positive Charge Patches (SPP), Negative Charge Patches (SPN), and Charge Dipole (SPCD) using solvent-accessible surface area (SASA) and spatial neighbor decay to prevent stickiness, fast clearance, and viscosity liabilities.

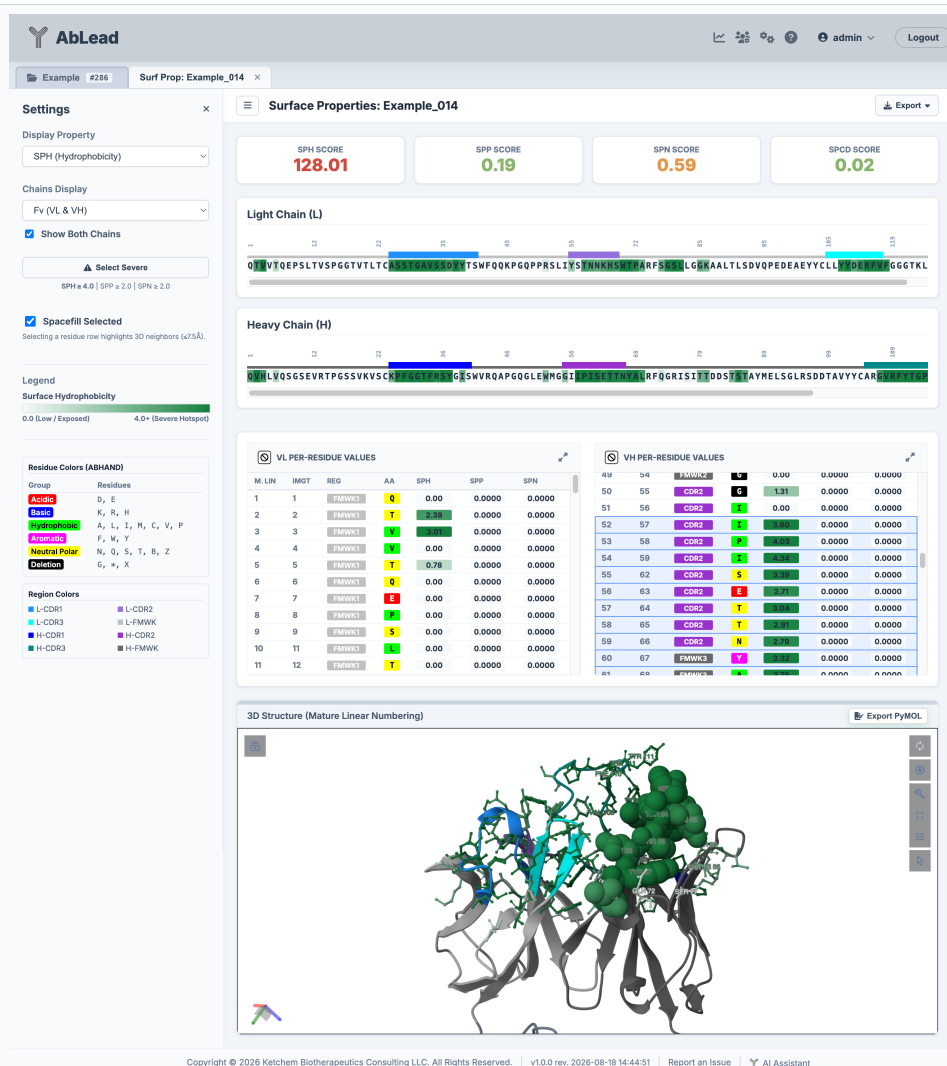


Figure: Surface Properties Workspace detailing spatial hydrophobicity (SPH), charge patches (SPP/SPN), dipole asymmetry (SPCD), and 3D structure.

CORE CAPABILITIES

- **3D Spatial SASA Calculations:** Implements the Shrake-Rupley algorithm with 7.5 Å spatial cutoff decay and pairwise salt-bridge neutralization.
- **Surface Hydrophobicity (SPH):** Measures exposed hydrophobic patches that drive self-association, aggregation, and rapid clearance.
- **Charge Patch Densities (SPP/SPN):** Pinpoints dense basic (Lys/Arg/His) or acidic (Asp/Glu) surface clusters that cause non-specific binding and high viscosity.
- **Electrostatic Dipole (SPCD):** Evaluates inter-chain charge asymmetry and polarization across the VH-VL interface.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Prevent High-Concentration Viscosity:** Identifies dense electrostatic and hydrophobic clusters early, safeguarding high-concentration subcutaneous delivery.
- **Reduce Clearance and Off-Target Binding:** Neutralizes patches responsible for non-specific binding and fast in vivo clearance.
- **Isolated Domain Formulation QC:** Evaluates exposed interface liabilities in non-mAb formats (scFvs, VHH nanobodies) to prevent severe aggregation.
- **Targeted Solubilizing Designs:** Directly launches mutation designs on identified surface hotspots to improve biophysical developability profiles.

The AbLead Advantage: High-concentration viscosity and rapid clearance are frequently rooted in surface charge and hydrophobic patches. AbLead pinpoints these structural liabilities so you can optimize formulation profiles before entering the clinic.

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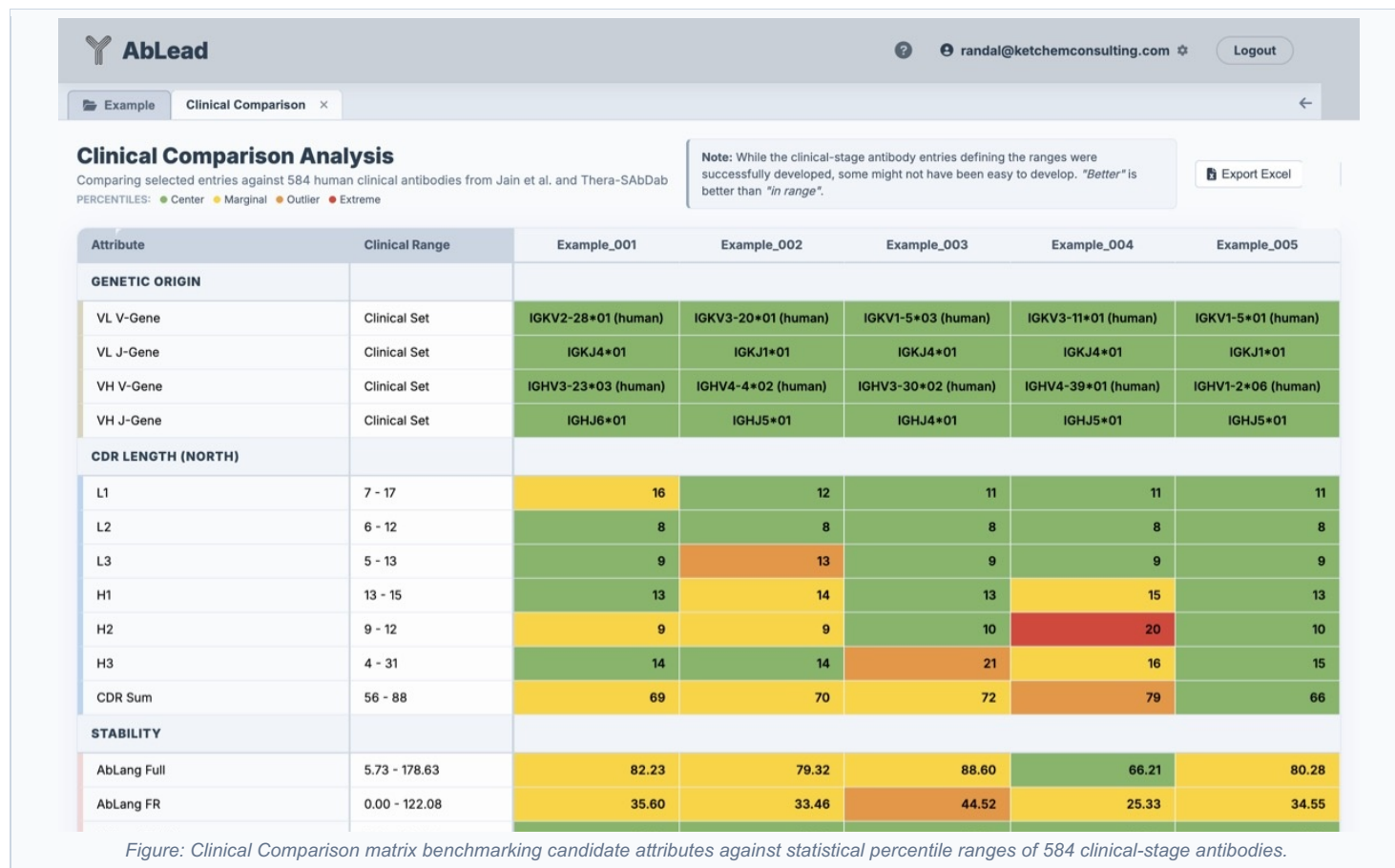
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Clinical Benchmark Comparison

Benchmarking Discovery Leads Against 580+ Clinical-Stage Therapeutics

Contextualize lead candidates against successful commercial therapeutics. AbLead benchmarks project molecules across biophysical attributes, surface metrics, humanness, and immunogenicity against a curated database of 584 clinical-stage antibodies from Thera-SAbDab and Jain et al.



CORE CAPABILITIES

- **584 Curated Clinical Reference Leads:** Curated clinical dataset from Thera-SAbDab and Jain et al., modeled with native Fab constant domains.
- **Multi-Dimensional Attribute Suite:** Benchmarks the AbLead project results values against those of the clinical set.
- **Percentile-Based Statistical Triage:** Categorizes values into Green (25th–75th benchmark window), Yellow (5th–25th / 75th–95th), Orange (atypical), and Red (out-of-bounds).
- **Overall KBC Score:** Evaluates the total rank order score of the AbLead project results against the clinical set.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Objective Drug-Likeness Validation:** Validates whether lead molecules fall within the proven developability envelope of approved commercial therapeutics.
- **Spot Atypical Red Flags Early:** Immediately identifies outlier attributes (e.g. unusually long CDR-H3, extreme charge, or excessive hydrophobicity).
- **Audit-Ready Reporting:** Exports benchmark comparison grids to Excel for inclusion in executive selection reviews, ELNs, and IND filings.
- **Data-Driven Candidate Ranking:** Provides clear rationale for choosing one lead candidate over another based on proven clinical biophysical ranges.

The AbLead Advantage: Rather than guessing whether a lead's developability metrics are acceptable, AbLead benchmarks every candidate against hundreds of clinical-stage antibodies to verify drug-likeness with hard statistical evidence. NOTE: While the clinical-stage antibody entries defining the ranges were successfully developed, some might not have been easy to develop. "Better" is better than "in range".

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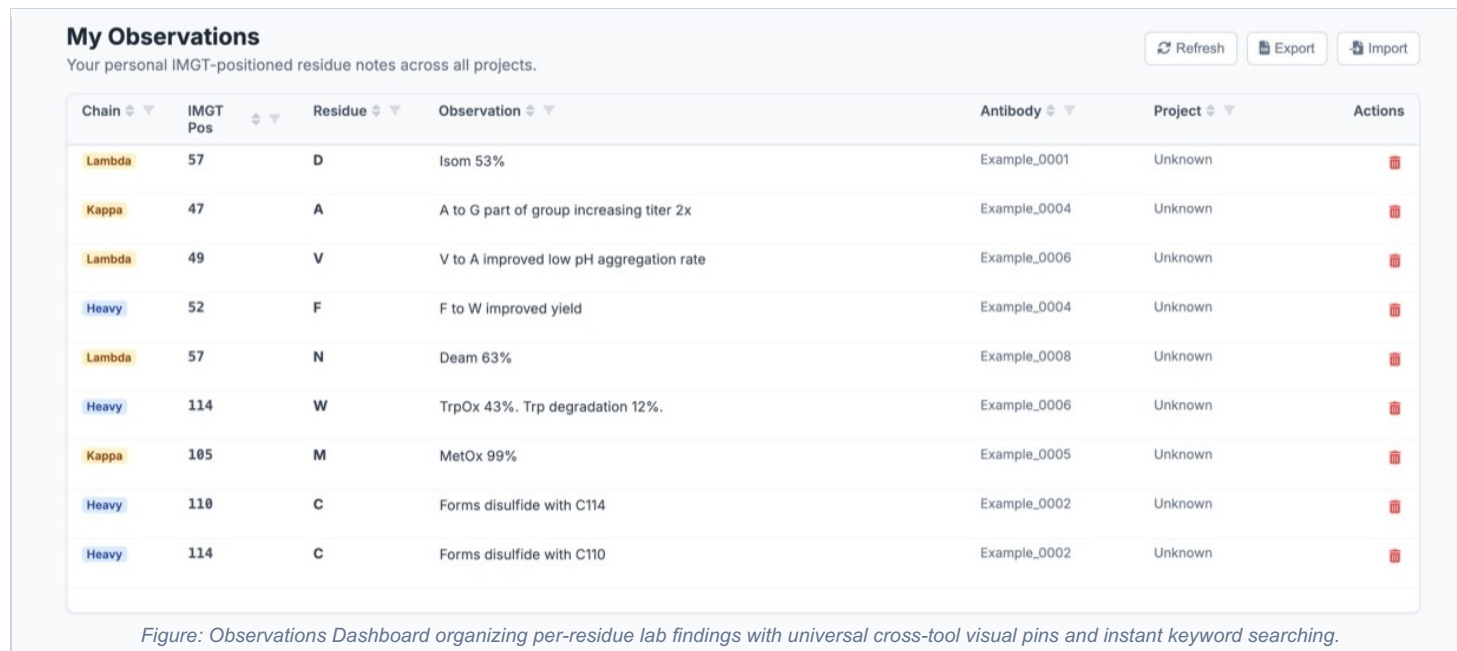
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Institutional Observations Memory

Centralized Per-Residue Lab Knowledge Tracking and Cross-Project Experience Reuse

Retain and leverage critical experimental insights across antibody discovery campaigns. AbLead's Observations tool provides a centralized repository that links user lab notes, assay results, and failure modes to specific IMGT residue positions, displaying contextual warning pins across all platform analysis tools.



CORE CAPABILITIES

- **IMGT-Anchored Knowledge Base:** Associates experimental findings, assay observations, and notes with specific chains and IMGT position coordinates.
- **Universal Cross-Tool Indicator Pins:** Orange indicator dots appear in Alignment, Liabilities, PFA, Humanness, and Engineering whenever observations exist.
- **Cross-User Observations:** Observations may be exported and imported across users.
- **Comprehensive Search and Filtering:** Search the institutional knowledge base by chain, residue, position, clone identity, or experimental keywords.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Eliminate Repetitive Lab Errors:** Prevents re-testing substitutions or motifs previously proven to cause aggregation, deamidation, or loss of binding.
- **Institutional Memory Retention:** Preserves invaluable wet-lab learnings and tacit knowledge across rotating discovery teams and ongoing projects.
- **Bidirectional CSV Data Exchange:** Ingest historical ELN notes via CSV import and export curated knowledge bases for cross-functional review.
- **User-Specific Data Privacy:** Observations are maintained securely per user account, ensuring sensitive client or project notes remain isolated.

The AbLead Advantage: The most expensive mistake in antibody discovery is repeating an experiment that already failed. AbLead's Observations tool captures per-residue institutional memory to make every project smarter than the last.

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Antibody Assembler (Bulk and Multispecific)

Drag-and-Drop mAb Rebuilding, Bispecific Engineering, and Zero-Error Formatting

Reconstruct full-length antibodies, bispecifics, and novel multi-chain formats with modular drag-and-drop ease. The Assembler eliminates manual copy-paste errors and reading-frame shifts in spreadsheets, providing dedicated Batch Mode for rebuilding hundreds of mAbs and Multispecific Mode for complex bi- and multi-specific architectures.

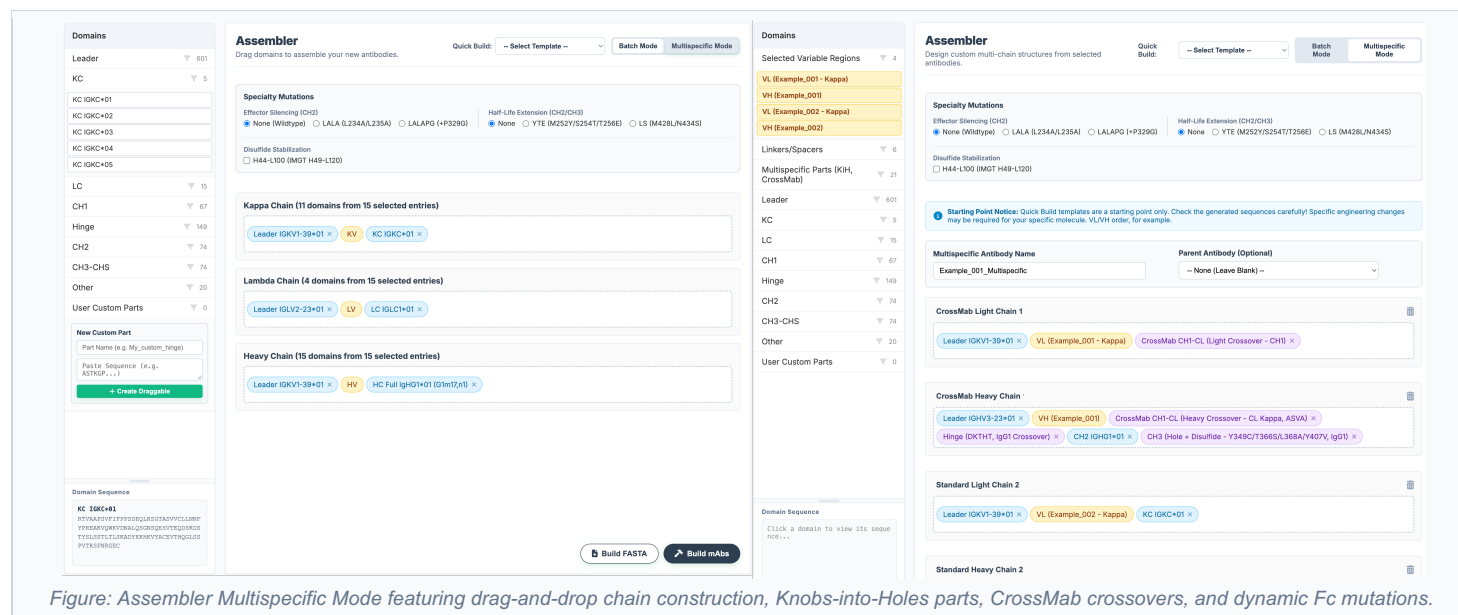


Figure: Assembler Multispecific Mode featuring drag-and-drop chain construction, Knobs-into-Holes parts, CrossMab crossovers, and dynamic Fc mutations.

CORE CAPABILITIES

- **High-Throughput Batch Rebuilding:** Bulk-stitches constant domains (CL, CH1, Hinge, CH2, CH3) across hundreds of variable regions in a single click.
- **Multispecific Chain Architectures:** Drag-and-drop assembly for bispecifics, CrossMabs, scFv-Fcs, BiTEs, and asymmetrical multi-chain constructs.
- **Validated Engineered Parts Library:** Pre-loaded with Knobs-into-Holes (KiH) CH3 pairs, CH1-CL crossover parts, flexible linkers, and user custom parts.
- **Dynamic Fc Mutations:** 1-click insertion of clinically validated effector-silent and extended half-life mutations (LALA, LALAPG, YTE, LS).

DEVELOPABILITY ADVANTAGE and IMPACT

- **Zero Human Copy-Paste Error:** Prevents catastrophic reading-frame shifts, missing junction residues, and transcription errors common in Excel.
- **Lineage Heritage and Fv Extraction:** Tracks parent-variant lineage relationships and enables instant reverse extraction of variable domains via Extract Fvs.
- **Persistent Construct Memory:** Reopening an assembled multispecific restores its exact layout, parts, chain configurations, and custom annotations.
- **Dual Export Formats:** Generates annotated FASTA sequence archives or instantly adds assembled antibodies as new active rows in the project grid.

The AbLead Advantage: Manual sequence assembly in spreadsheets is slow, tedious, and prone to costly frame-shift errors. AbLead's Assembler makes building full-length mAbs and complex bispecifics fast, reliable, and completely error-free.

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Antibody Humanization

Precision Germline Template Matching, BioPhi Sapiens AI, and Structural Exclusions

Humanize non-human leads or convert antibodies across species while protecting binding affinity and paratope integrity. AbLead combines structural annotation with deterministic germline template ranking and BioPhi Sapiens deep learning, complete with configurable structural exclusions for CDRs, Vernier zones, and VHH interfaces.



CORE CAPABILITIES

- **Structural Annotation:** Positional numbering and germline assignment across multiple species.
- **Dual Humanization Modalities:** Choose between deterministic Germline Template Matching or AI-guided BioPhi Sapiens deep learning suggestions.
- **Configurable Structural Exclusions:** Pre-set or custom filters protecting CDR loops, Honegger canonical positions, Vernier zones, and VHH interfaces.
- **Deterministic Ranking:** Ranks candidate germlines by modifiable residue identity, homology, and overall sequence similarity for reproducible selection.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Preserve Binding and Paratope Geometry:** Excludes critical structural framework and Vernier residues to maintain original binding affinity.
- **VHH Solubility Safeguards:** Special VHH interface exclusion preserves hydrophobic tetrad residues to prevent nanobody aggregation.
- **Multi-Species Cross-Conversion:** Rapidly humanize animal antibodies or convert human leads into surrogate animal models for preclinical toxicology.
- **Direct Engineering Transfer:** Transfer selected humanization substitutions directly into the Engineering workspace as a dedicated mutation set in one click.

The AbLead Advantage: AbLead automates antibody humanization by combining rigorous structural exclusions with germline matching, maximizing human sequence identity while safeguarding original target affinity.

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Lead Engineering and First Pass Optimize

Combinatorial Variant Generation, DMS Permissibility, and 1-Click Automated Optimization

Design, track, and build optimized antibody variants seamlessly across AbLead. The platform connects mutation designs across all analytical tools into organized Mutation Sets, integrates Deep Mutational Scanning (DMS) permissibility matrices, and features First Pass Optimize—an automated 1-click algorithm to resolve severe developability liabilities instantly.

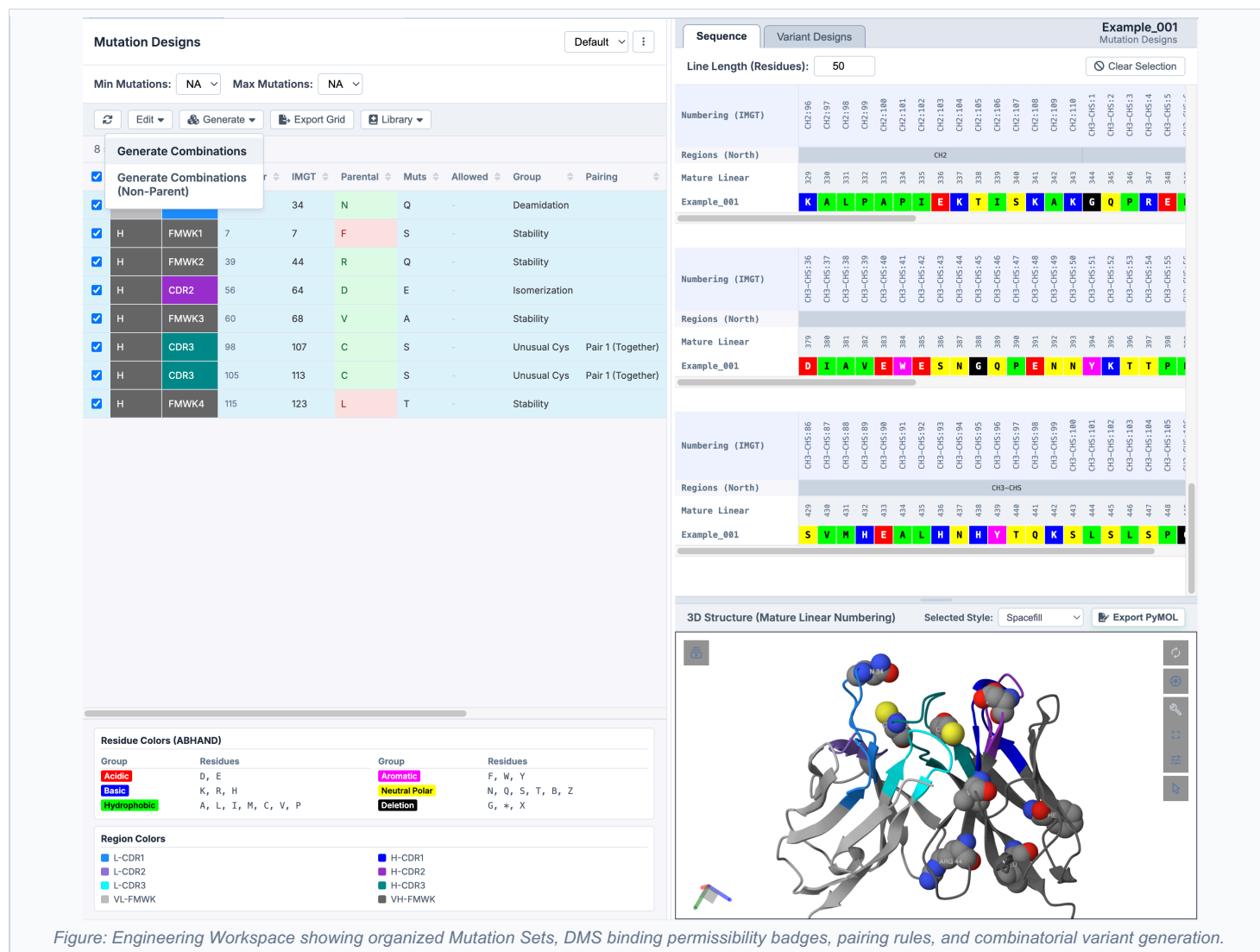


Figure: Engineering Workspace showing organized Mutation Sets, DMS binding permissibility badges, pairing rules, and combinatorial variant generation.

CORE CAPABILITIES

- **Universal Mutation Tracking:** Designs initiated anywhere in AbLead sync into organized Mutation Sets.
- **First Pass Optimize Engine:** 1-click automated algorithm that scans for severe liabilities, applies structural SASA gating, and creates optimized designs.
- **DMS Experimental Permissibility:** Ingests saturation mutagenesis matrices; displays green/red permissibility badges and auto-prunes unsafe substitutions.
- **Pairing Rules and Complexity Limits:** Enforces paired mutations (Together for disulfides/salt bridges, Single for cleavage sites) with Min/Max mutation limits.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Rapid Combinatorial Generation:** Builds tens to thousands of combinatorial variants with parental controls in seconds, bypassing manual sequence drafting.
- **Structural Evaluation:** Evaluates paratope or interface residues to guide targeted combinatorial variant designs.
- **Lineage Tree Inheritance:** Descendant variants recursively inherit ancestor DMS fitness data with explicit lineage provenance tracking.
- **Direct mAb Synthesis Handoff:** Pushes generated combinatorial variants directly into the Project View for comprehensive rank ordering and FASTA export.

The AbLead Advantage: Engineering turns analytical insights into optimized therapeutic leads. With First Pass Optimize and DMS permissibility integration, AbLead automates the resolution of developability flaws while protecting binding function.

Accelerate Your Antibody Lead Optimization and De-Risk Development

Request a Live Demo: ablead@ketchemconsulting.com | Explore Platform: ablead.ketchemconsulting.com

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Isoelectric Point (pI) Engineering

Structure-Based Charge Modification, Formulation Optimization, and Humanness Safeguards

Modulate antibody isoelectric point (pI) to optimize formulation and serum stability. AbLead couples sequence-based Bjellqvist titration with empirical 3D structure-based PROPKA 3 electrostatics, monitoring real-time humanness (Sapiens) and stability (AbLang) during combinatorial charge engineering.

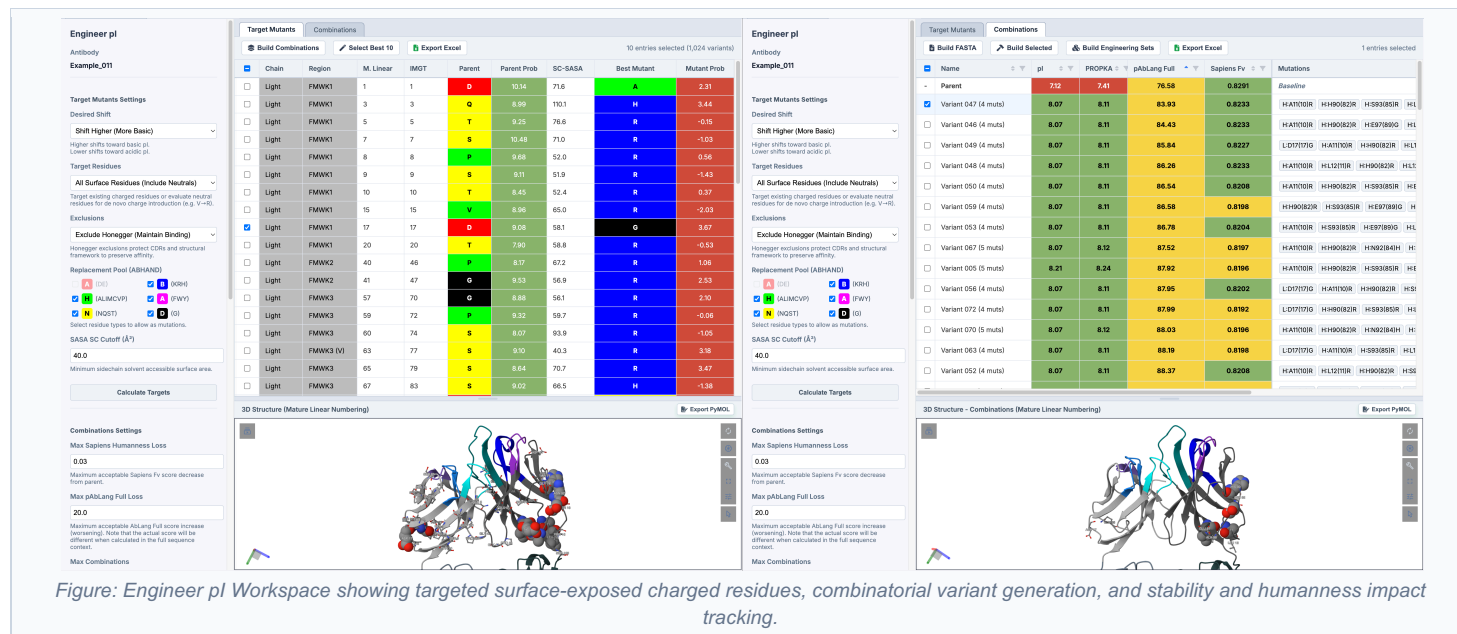


Figure: Engineer pI Workspace showing targeted surface-exposed charged residues, combinatorial variant generation, and stability and humanness impact tracking.

CORE CAPABILITIES

- **Dual Calculation Methodologies:** Combines theoretical sequence Bjellqvist titration with empirical 3D structure-based PROPKA 3 electrostatics.
- **Hybrid Full-Length Modeling:** Evaluates Fv electrostatics in 3D atomic coordinates and couples them with constant domain titration curves.
- **Rapid Delta Titration:** Calculates folded pI predictions for thousands of combinatorial variants instantly on exposed residues.
- **Real-Time Humanness Monitoring:** Monitors every charge-shifting substitution against Sapiens deep learning scores.

DEVELOPABILITY ADVANTAGE and IMPACT

- **Formulation Stability Optimization:** Shifts pI in the desired direction for optimal formulation stability.
- **Reduce Potential Serum Particulation:** Shifts molecular pI away from serum pH to prevent in vivo particulation.
- **Bispecific Heterodimer Purification:** Engineers pI asymmetry between homodimers and heterodimers to enable clean ion-exchange chromatography separation.
- **Direct Engineering Handoff:** Seamlessly exports prioritized charge-engineered combinations into project results or FASTA synthesis lists.

The AbLead Advantage: Shifting antibody isoelectric point has profound impacts on serum particulation, solubility, viscosity, and manufacturing purification. AbLead automates structure-guided charge engineering while safeguarding therapeutic stability and humanness.

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