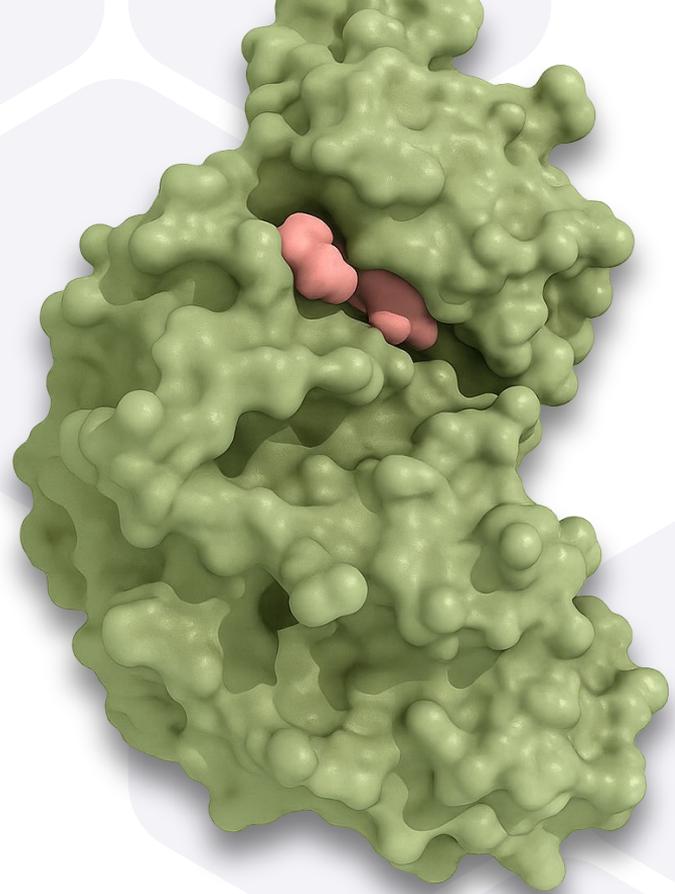




**AI-Guided Engineering of Biotherapeutic
Enzyme Mimetic: Discovery,
Optimization & Validation**

www.medvolt.ai

www.linkedin.com/company/medvolt-ai



Overview of the Project

Oncolytic enzymes and their mimetics have shown immense therapeutic promise across hematological and solid tumors. However, existing clinical enzymes often suffer from high immunogenicity, off-target toxicity, poor pharmacokinetics, and limited efficacy in solid tumor microenvironments.

Key Challenge

- High immunogenicity of existing enzyme therapies
- Low selectivity and short half-life in solid tumors
- PEG-dependence & glutaminase toxicity in current formulations
- Lack of tunable variants with validated activity profiles

Target Class: Amidohydrolase-like enzymes

Objective

- **Low K_m** and high substrate turnover
- **Reduced immune reactivity** and PEG-independence
- **Thermal and structural stability**
- Compatibility with **closed-loop AI-experimental workflows**

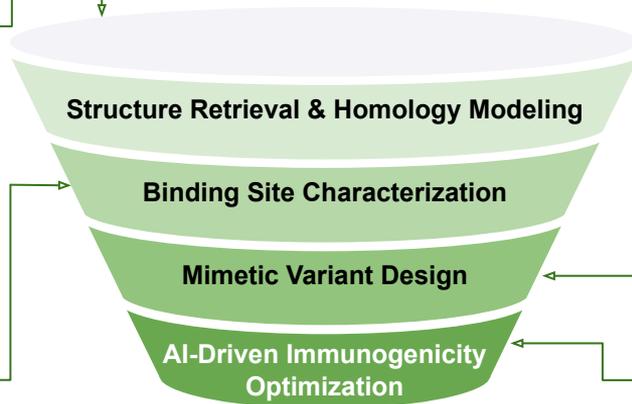
Application: Leukemia, lymphoma, and select solid tumors

Approach & Methodology

Medvolt's integrated AI-platform enabled rapid and rational design of optimized variants through a closed-loop design-evaluate-optimize cycle:

- Multiple sequence alignment across clinically used variants
- De novo 3D structure modeling using AlphaFold3 + in-house refinement for isoforms with no solved structure

- Active site annotation via co-crystal structures and literature-derived catalytic residues
- Pocket analysis for mutational tolerance and steric hindrance



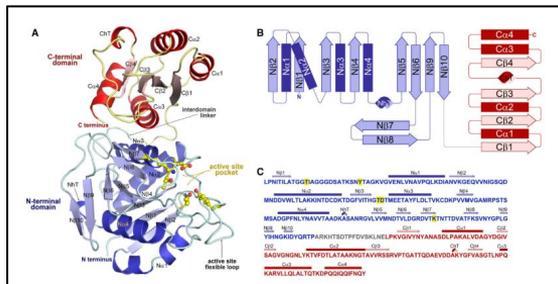
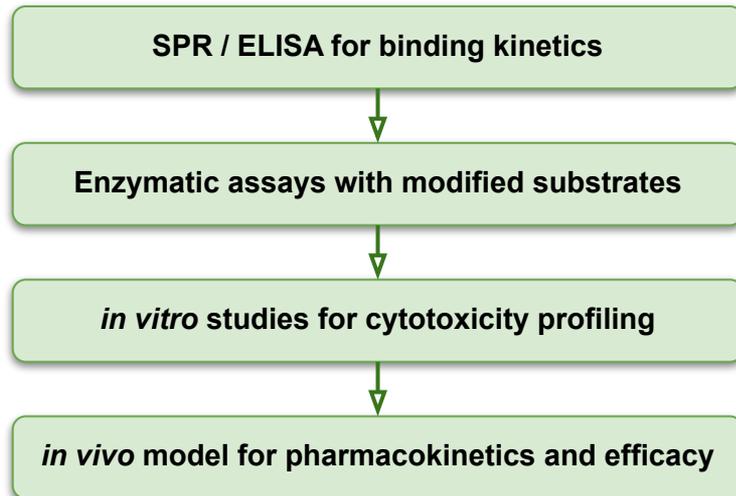
- Design of peptidomimetics via Medvolt's generative engine and structural pharmacophore preservation
- Engineered to exhibit reduced immunogenicity, enhanced half-life and protease resistance
- Use of transformer-based models for epitope prediction and immunogenic hotspot minimization
- In silico HLA class I/II binding predictions across population coverage

Evaluation & Insights

Multi-Parametric Scoring of Designed Variants

Evaluation Parameter	Outcome
Structural Stability (ΔG)	All mimetics $\Delta G < -45$ kJ/mol
Proteolytic Resistance	Improved half-life (>2 \times native)
Epitope Burden Reduction	Up to 85% drop in MHC II binding
Isoform Selectivity	Optimized binding to target isoform
Ensemble Docking Score	Top mimetic outperformed reference
Solubility & Aggregation	No significant aggregation hotspots

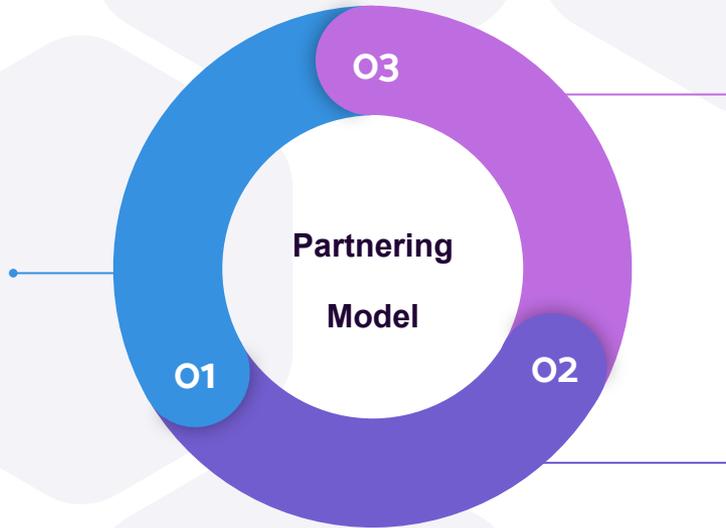
Experimental Planning



Medvolt's Distinctive Capabilities

- **Multi-modal AI stack:** Combines generative models, epitope prediction, ensemble docking, and multi-objective optimization
- **Fast & Iterative Cycles:** Rapid transition from hypothesis to validated in silico candidates
- **Customizability:** Humanized, PEG-free, or modified amino-acid inclusion based on downstream need
- **Clinical Readiness:** Built-in consideration for toxicity, solubility, and developability

Co-development for novel mimetics and protein scaffolds



AI-design + Synbio synthesis + shared IP or licensing

Application across solid tumor immunometabolism and metabolic oncology



THANK YOU

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