NuvoBIO
Intellegent peptide design

DARWIN: An evolution-inspired algorithm for target-specific peptide inhibitor engineering

What is DARWIN?

DARWIN is a genetic algorithm that can evolve target-specific peptide binders using sequence information. **Darwin** can generate (1) binding/ therapeutic, (2) anti-viral/ microbial, and (3) target/delivery peptides.

Case Study 1: Can DARWIN independently confirm targets of FDA approved therapeutic peptides?

To evaluate the ability of **DARWIN** to accurately determine therapeutic peptide targets, a total of 13 FDA approved peptides were selected based on their clinical use and validated target protein specificity. **DARWIN** determines predicted peptide-target interaction(s) based solely on primary sequence information within any given proteome. Based within the principles of protein interaction within the training data, **DARWIN** can identify specific peptide targets, and use this information to evolve highly specific peptides that prioritize (1) target interaction, and (2) target specificity.

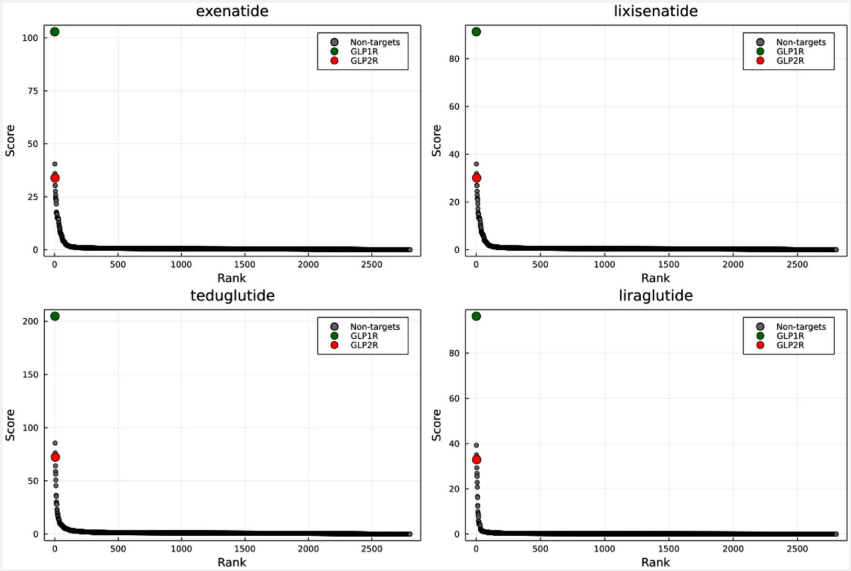
Table 1. FDA approved peptides used for validate test set

Compound name	Molecular target	Chemical basis	Length	Known targets (accession ID)
Corticotropin	MC receptors	Native	39	Q01726;Q01718;P41968;P32245;P33032
Calcitonin (salmon)	Calcitonin receptor	Native	32	P30988
Tetracosactide	MC receptors	Native	24	Q01726;Q01718;P41968;P32245;P33032
Calcitonin (human)	Calcitonin receptor	Native	32	Q16602
Carperitide	NPR-A	Native	28	P16066;P20594;P17342
Bivalirudin	Thrombin	Analog	20	P00734
Nesiritide	NPR-A	Native	32	P16066;P20594;P17342
Pramlintide	Calcitonin receptor	Analog	37	Q16602
Exenatide	GLP-1 receptor	Native	39	P43220
Liraglutide	GLP-1 receptor	Analog	32	P43220
Tesamorelin	GHRH receptor	Analog	44	Q02643
Teduglutide	GLP-2 receptor	Analog	33	O95838
Lixisenatide	GLP-1 receptor	Analog	44	P43220

Peptide Therapeutics

- A compound annual growth rate (CAGR) for peptides drugs represent 11% and the use of artificial intelligence in drug discovery at 30%.
- **DARWIN** has market potential in two expanding market areas.
- In the pharmaceutical industry, main challenges include accelerating discovery and managing target specificity; **DARWIN** designs peptides based on these principles.
- AI platforms can significantly accelerate the process of drug discovery.

DARWIN can successfully predict specific targets of FDA-approved therapeutic peptides



We observe that GLP1R was ranked first for all GLP receptor-targeting peptides. This was the case even for Teduglutide which is a glucagon-like peptide 2 analog. In all cases, **DARWIN** outranks GLP2R by Glucagon Receptor and the Gastric Inhibitory Polypeptide Receptor with which GLP2R shares >40% identity. In summary, **DARWIN** was able to successfully identify therapeutic targets for all FDA approved GLP receptor-targeting peptides from within the surface-exposed human proteome (nearly 3,000 proteins). *For complete study information for all FDA approved peptides shown in Table 1, please reference:*

Charih *et al.* (2022) Assessing sequence-based protein-protein interaction predictors for use in therapeutic peptide engineering (2022). *Scientific Reports* 12(9610), 1-13.