Virtual Cyclic Peptide Generation using DL Model Construction

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1. Project Purpose

Cyclic peptides offer significant advantages in drug development due to their rigid structure, which enhances target specificity, enzymatic stability, and, in some cases, cell membrane permeability. They serve as antibiotics, antifungals, anticancer agents, and immunosuppressants (e.g., cyclosporine), making them promising candidates compared to linear peptides, small molecules, or antibodies. Currently, around 19 approved cyclic peptide drugs target a range of proteins, including intracellular and membrane-bound targets. While experimental and computational methods exist for designing new cyclic peptides, most rely on mimicking known peptides or existing data. These approaches remain limited and time-consuming. This research aims to accelerate cyclic peptide drug discovery using AI, improving bioactivity prediction, reducing costs, and expanding candidate diversity. Additionally, we are developing a user-friendly platform to enable experimental researchers to perform virtual screening easily, bridging the gap between computational and laboratory work.

2. Results

This research project has already led to one publication (*In press*) based on the proposed approach, demonstrating the feasibility and impact of AI-driven cyclic peptide prediction. The project is currently ongoing, with continued development of the user-friendly screening tool and expansion of the peptide dataset to improve model accuracy and accessibility for non-computational researchers.

3. Roles of the MCRP and its significance

The role of MCRP for this project is to enable large-scale AI model training, high-throughput peptide screening, and complex molecular simulations. It significantly accelerates data processing and enhances the accuracy of cyclic peptide prediction.

4. Future plan

Using the ML model, we plan to work on the docking data that contains about 100,000 structures.

5. Publications and conference presentations

(1) Journal papers

Manik, M. C.; Kiewhuo, K.; Rungrotmongkol, T., Duan, L.; Harada, R.; Shigeta, Y.; Hengphasatporn, K.*; Darai N.; Vangnai, A.*, Rational Designed and Engineered Antimicrobial Peptides with High Selectivity and Efficiency Against Phytopathogenic Ralstonia Solanecearum. **2025,** *Science of the Total Environment, In press*.

(2) Presentations

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(3) Others

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Supercomputer	Use	Allocated resources*		
		Initial resources	Transferred resources**	Additional resources
Cygnus	Yes	20000	-	-
Pegasus	Yes	18000	-	-
Wisteria/BDEC-01	No			
	*in units of node-hour product ** If the budget transfer was performed, fill in here, such as "+2000" and "−1000".			