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# CzeekD: Fragment-based *de novo* Drug Design System for Drug Discovery

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For early stages in drug development, it is a critical issue to find lead compounds with novel scaffolds. However, the set of all possible small organic molecules has been estimated to consist of more than $10^{60}$ compounds, it is difficult to figure out the best scaffolds from among the vast chemical space through experimental synthetic approaches.

We have developed a computational approach to efficiently generate lead compounds with novel scaffolds using fragment chemical library. The fragment-based drug *de novo* design system with a fast stochastic optimization algorithm, called “CzeekD”, has following functions:

- Generation of novel scaffolds in vast chemical space is achieved by combination of building blocks in fragment library.
- It is easy to synthesize the designed chemical structures because of using basic chemical reactions, i.e. RECAP rule.
- Chemical Genomics-Based Virtual Screening (CGBVS) is implemented as a scoring function, which can efficiently estimate the possibility of molecular interactions between the generated compounds and the target proteins.
- Particle Swarm Optimization (PSO) algorithm was newly developed to swiftly explore druggable molecular seeds and to efficiently find out diverse structures among the vast chemical space.

As a result of bioactivity evaluation of the designed compounds through organic synthesis and *in vitro* assay, we successfully identified novel active compounds with highly hit rate (20－40%) for GPCR proteins. This result suggested that CzeekD provides a powerful solution to guide medicinal chemists into the discovery of novel bioactive molecules.

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