

Research Internship Report

Takeda Pharmaceutical Company Limited

Graduate School of Engineering

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2023(D1), Fluoroorganic Chemistry Lab. 03-5841-6500

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1. Outline of internship

Company: Takeda Pharmaceutical Company Limited

Hosts: Dr. Satoshi Mikami and Mr. Daisuke Inushima

Schedule: 1/1/2024-2/29/2024

Theme: Medicinal Chemistry

Background leading to the internship:

I have been interested in the difference between basic research at academic organizations and research at companies since I was assigned to a laboratory in my fourth year at the university. The goal of the former is to publish a paper, while the goal of the latter is to bring the results of research to the world as a product. Therefore, I sought an internship that would allow me to be involved in cutting-edge research being conducted at a company. The GMSI office, in cooperation with companies in a variety of fields, offers long-term (2 months or more) research internships for doctoral students who can conduct research independently. I applied for the internship because I wanted to have an opportunity to devote myself to research as a member of a research team for a long period of time. I chose the medical chemistry project of Takeda Pharmaceutical Company Limited so that I could make use of the organic synthesis skills that I had cultivated in my master's thesis research. The internship was also conducted as Corporate Internship in the MERIT program.

2. The research during the internship

Background

Central nervous system (CNS) diseases are known as psychiatric and neurological disorders (e.g., Alzheimer's disease, Parkinson's disease). In drug discovery for CNS drugs, it is important whether a candidate compound can penetrate the blood-brain barrier to exert its expected effect in the brain. For this purpose, the following physical properties are said to be conditions for useful molecules:

- (1) Low molecular weight (450 Da or less)
- (2) Moderate lipid solubility (cLogP value: 1-3)
- (3) Small polar surface area (90 Å² or less)
- (4) Hydrogen bond donors: less than 3, hydrogen bond acceptors less than 7

In recent years, drug discovery has been conducted not only with small molecules but also with various modalities. However, in the field of CNS drugs, drug discovery with small molecules is promising because they have been well-studied as mentioned above.

Overview

The following work was performed during this research internship. Confidential information is omitted in this report.

- Optimization studies of candidate compounds were conducted to improve pharmacological activity, selectivity, pharmacokinetics, toxicity, physical properties, etc. for a certain drug target.

3. Comment

I participated in this internship focusing on the question, "How much time, effort, and cost does it take for a product to become available to society? In drug discovery research, a product goes through many steps from preclinical to clinical before it is released to the public, and it takes several years before it is available to patients. In discussions with members from various departments, I realized that a great many people are involved in drug discovery research. Among them, the optimization of candidate compounds, which I was involved in this time, greatly influences the potency of a drug, and I learned "what kind of compounds become good drugs" in the course of my work. I was particularly impressed by the fact that the project team conducts research while communicating closely with each other in order to find drug candidates more quickly, and that the research is conducted while flexibly assigning personnel within the team. At the university, students mainly had discussions with their supervisors and did not often discuss research policies in depth with each other.

4. Message to future interns

When I applied for the internship, I thought that I would make use of my prior research. However, when I actually participated in the internship, there were so many things that I did not know, and I was in a rush at first, listening to the employees and looking for references. As a result, I learned so much in those two months that I honestly feel that there is still much more to learn. I think it may be hard for you to participate in an internship for a few months away from the laboratory, but I think it is a valuable experience that is different from the academic research. If you are interested, why not find out what kind of internships are available?

5. Acknowledgments

I would like to thank everyone at Takeda Pharmaceutical Company Limited for accepting me as an intern. In particular, I would like to thank Mr. Inushima, our host, Dr. Mikami and Dr. Hasui, who frequently checked on the progress of my research and gave me constructive advice, and everyone in each department who kindly explained the details of their work to me. I would also

like to thank the GMSI office for their great cooperation with the internship application and other procedures. Finally, I would like to thank my supervisors, Prof. Kawaguchi, Prof. Aikawa, Prof. Kobayashi, and the MERIT office for their kind cooperation in allowing me to participate in the internship program.