UNIVERSITY OF TOYAMA

Proposal

Development of compounds that inhibit amyloid fibril formation

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Amyloidosis is a group of diseases caused by the accumulation of protein aggregates called amyloid fibrils in various organs. It includes Alzheimer's disease, Parkinson's disease, transthyretin amyloidosis, and others, with aggregates of proteins such as amyloid β-peptide, α-synuclein, and transthyretin contributing to the onset of each disease. Compounds that inhibit the formation of amyloid fibrils have the potential to become therapeutic agents for amyloidosis. Our focus has primarily been on developing compounds that inhibit amyloid fibril formation. This master's thesis project aims to build on this effort by exploring new compounds to prevent amyloid aggregation.

Through the master's thesis project, the master's candidate will learn techniques and tools to:

obtain purified proteins for biophysical measurements,
analyze the amyloid inhibitory activities of compounds using various techniques,
analyze the protein structure in complex with compounds.

By the end of the project, the master's candidate will have gained insights into drug development for amyloidosis, in addition to acquiring knowledge of protein purification, biophysical measurements, and structural biology.

References:

Mizuguchi M, Yokoyama T, Okada T, Nakagawa Y, Fujii K, Nabeshima Y, Toyooka N. Benziodarone and 6-hydroxybenziodarone are potent and selective inhibitors of transthyretin amyloidogenesis. *Bioorg Med Chem*. 2023, 90, 117370. doi:10.1016/j.bmc.2023.117370.

Mizuguchi M, Nakagawa Y, Inui K, Katayama W, Sawai Y, Shimane A, Kitakami R, Okada T, Nabeshima Y, Yokoyama T, Kanamitsu K, Nakagawa S, Toyooka N. Chlorinated naringenin analogues as potential inhibitors of transthyretin amyloidogenesis. *J Med Chem*. 2022, 65, 16218-16233. doi:10.1021/acs.jmedchem.2c00511.

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