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Abstract of Doctoral Dissertation

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Title of Doctoral Dissertation

Study on the Effect of Chemical Structures of Photo-Responsive Non-Nucleoside Triphosphates on the Interaction with Motor Proteins

(光応答性非ヌクレオシド三リン酸の化学構造がモータータンパク質との相互作用に与える影響に関する研究)

Linear motor proteins including kinesin and myosin are promising biomaterials for developing the artificial nano-devices. Photoswitchable substrates of these biomotors can be used to optically regulate the motility of their associated cytoskeletal filaments in *in vitro* systems. Recently, our group has made significant contribution to optically control the motor protein function in reversible manner with high spatio-temporal control. We previously reported the azobenzene-tethered triphosphates as photo-reversible substrates of bio-molecular motors to control the motile function with light. However, their substrate specificity in molecular motors and the mechanism of substrate recognition and their photoreversibility remain unclear. And the inhibitory effect of non-hydrolysable analogs of the photo-reversible substrates were unknown.

In this thesis, author describe several azobenzene-tethered triphosphates to photoreversibly drive kinesin and myosin in microtubules-kinesin and actin-myosin *in vitro* motility assays. Through the motility assays, the myosin-selective photo-responsive substrate is successfully discovered. Using this substrate, the myosin motility is selectively photomanipulated in the kinesin-myosin composite motility assay, while it shows almost no kinesin motility. This mechanistic insight of driving myosin selectively with photoswitchability is explained through the docking simulation study.

Further, the author describes four non-hydrolysable triphosphate analogs of the photo-reversible substrates, where the oxygen atom bridging the β to the γ phosphate is replaced by a nitrogen or carbon atom to explore their photo-responsive inhibitory activity in actin-myosin and microtubules-kinesin *in vitro* motility assays. The non-hydrolysable azo-triphosphate molecule showed inhibitory activity towards myosin and kinesin with photo-reversible manner. These reversible inhibitory activities of non-hydrolysable azo-triphosphate molecules could be well explained by reversible change in affinity of the azo-triphosphate molecules to motor proteins upon photo isomerization.

Finally, the study has indicated the advances for controlling bio-molecular machines *ad arbitrium*, and presented technique can be a chemical tool for unveiling the motor-based biological processes and constructing nanotechnological system using the microtubule and actin composite system.