CHEMICAL SYNTHESIS AND INVESTIGATION OF BIOLOGICAL SYSTEMS

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To elucidate the energy metabolism in biological systems, we have synthesized biologically active compounds, which are key elements in a range of topics. With rationally designed molecular probes in hand, we have been investigating their dynamic actions at the cell and enzyme levels.

Exploring the structure and function of NADH-quinone oxidoreductase (complex I)

Mitochondrial NADH-quinone oxidoreductase (complex I), the first energy-converting enzyme in the respiratory chain, plays a central role in cellular energy metabolism. Using rationally designed analogues of specific complex I inhibitors such as acetogenin and quinazoline, we are investigating the mechanism of complex I which remain to be elucidated. So far, we have identified the binding sites of three complex I inhibitors at amino acid level.

Comprehensive survey of ubiquinone-binding proteins using synthetic ubiquinone probes

Ubiquinone is an essential electron carrier, which functions as a substrate of various redox-enzymes in most prokaryotic and eukaryotic cells. We are synthesizing various functionalized ubiquinone probes for identification of novel ubiquinone-binding proteins as well as for characterization of ubiquinone reaction mechanism in the respiratory enzymes.

Characterization of the biological role of cardiolipin in mitochondria

Cardiolipin (CL) is a major phospholipid found in mitochondria. To elucidate the molecular mechanism of diverse functions of CL in mitochondria, we are synthesizing a variety of cardiolipins having different fatty acid combinations.

The structure of bacterial complex I and the inhibitor binding site identified by photoaffinity labeling.

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Synthetic cardiolipin bearing linoleic acids

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Key words

Organic Synthesis, Mitochondria, Respiratory Enzymes, NADH-Ubiquinone Oxidoreductase (complex I), Ubiquinone, Acetogenin, Quinazoline, Cardiolipin, Photoaffinity Labeling

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