## Presentation of Foundation-Assisted Research Findings 2002
## Interactive Biotic Activity and Organic Chemistry

On July 16, the 10th presentation of research results was held at the United Nations University. Following Chairman Seya's greetings, Professor Shohei Inoue from the Science University of Tokyo, and a director of the Foundation and chair of Area 1 of the Natural Sciences Selection Committee, gave the opening remarks. Professor Kenji Soda of Kansai University, another member of the committee, and Professor Inoue then served as the chairmen for the following five presentations.

Chairman Seya

Professor Inoue, Selection Committee chair

Professor Soda, Selection Committee member

Performance Enhancement of Non-Cellular Protein Synthesis Systems and Their Applications
Dr. Tsuneo Yamane, Professor, Graduate School of Bio- & Agro-Sciences, Nagoya University

Non-cellular protein synthesis systems are biosynthesis systems that use liquids extracted from cells, but not the living cells themselves, to synthesize proteins in a test tube using the transcription/translation effect of template DNA or mRNA. These systems may also be called *in vitro* protein synthesis systems. They use the cells' ribosomes, the small organs in which protein synthesis is concentrated, outside the cell, completely freeing them from the cells' restraints. This has several merits, including vastly increased flexibility, but these systems have also had some drawbacks in the past.

Increasing the performance of these systems is what our research was intended to achieve. We aimed to increase the production yield, improve disulfide bonding and achieve correct peptide chain folding. Furthermore, in recent years, work is progressing on combinatorial bioengineering technologies, such as high-speed multi-sample screening.

Biosynthesis Mechanisms for New Covalent Coenzymes Derived from Amino Acid Residues
Dr. Katsuyuki Tanizawa, Professor, Institute of Scientific and Industrial Research, Osaka University

Successive covalent quinone coenzymes (TPQ, TTQ, etc.) have been discovered in various enzyme proteins, such as redox coenzymes, in recent times. These coenzymes, which may perhaps best be called built-in peptide coenzymes, are coded by specific amino acid residues that are the precursors in the various enzyme genes, and after some protein is translated in the cell, they are modified and changed into active enzymes. We discovered numerous built-in coenzyme production mechanisms that are formed by certain change factors (activated enzymes) or by the self-modification function that exists in protein precursors, such as certain tyrosine residues that exhibit an automatic oxidation mechanism in the presence of copper ions. Using methods such as x-ray crystallographic analysis, we also clarified the production mechanisms for these coenzymes

and their three-dimensional structures.

Pyrrolo-Quinoline Quinone (PQQ): New Redox Coenzymes and Oxidative Fermentation
Dr. Osao Adachi, Professor, Faculty of Agriculture, Yamaguchi University

The pyrrolo-quinoline quinone (PQQ) that we isolated from acetobacter near the end of the 1970s was discovered at the same time in other bacteria in Europe and North America. There are many redox enzymes, including the new PQQ coenzyme, and quino proteins in acetobacter and other aerobic bacteria. Since the existence of many types of quino proteins (20 or more) has been established in acetobacter exterior cell membranes, research into oxidative fermentation with acetobacter, which have long been important industrially, has undergone a major transformation in recent years from a pure research topic to an applied research topic. As a result, the structure, characteristics and physiological roles of quino proteins from acetobacter have been clarified and the revelation of the oxidative fermentation mechanism has achieved great strides forward. And representative examples of the application of this knowledge in research projects include research into new production methods for ketogluconic acid and vitamin C.

Synthesis of Useful Activated Biotic Compounds Using Nitrogen Gas
Dr. Miwako Mori, Professor, Graduate School of Pharmaceutical Sciences, Hokkaido University

The nitrogen so essential to human existence is generally obtained by reacting gaseous nitrogen and oxygen together to produce ammonia, but the prospect of incorporating nitrogen directly into organic compounds has remained a dream for humankind. Although nitrogen was considered to be an inert gas, nitrogen and metal complexes began to be discovered one after another starting in the late 1960s. Thus, we began to look at how organic metal complexes formed new complexes easily with nitrogen, placed them in catalytic reactions and used them in synthetic organic chemistry. A Ti-nitrogen complex is readily formed when you react Li and nitrogen at a pressure of 1 atmosphere in the presence of $Me_3SiCl$, using $TiX_4$ as the metal. If you add various compounds to this complex and react them, you can obtain a high yield synthesizing nitrogenous compounds. We discovered that you can obtain almost exactly the same results even if you substitute air for the nitrogen gas, and succeeded in synthesizing many useful activated biotic compounds.

# Expansion of Protein Biotic Synthesis Systems through Organic Chemistry
## ---Taking Up the Challenge of Synthesized Life Forms---

Dr. Masahiko Shishido, Professor, Faculty of Engineering, Okayama University

In all the living creatures on the Earth, proteins formed from 20 types of amino acids carry out the chemical functions and nucleic acids formed from four bases carry out the information functions. If we were to expand this framework with organic chemistry and a living creature that had more amino acids or nucleic acid bases or a manmade nucleic acid introduced to it were to survive and multiply, then it would be fair to call it a "synthesized life form." In these synthesized life forms, we could expect to develop various manmade functions that cannot be realized with existing life forms. Examples of taking up the challenge of creating and using synthetic life forms include unnaturally mutated protein biodiagnostic products that have had antigens, hormones or various inhibitors introduced and screened with fluorescent bases with high sensitivity, as well as the use of variant screening with a gene library incorporating unnatural amino acids, or the design of peptide nucleic acids that bond tightly to natural nucleic acids.