Message from the Director

Nearly 20 years have passed since I began working to develop drugs that target extracellular targets to treat diseases. I have been working on the production of monoclonal antibodies against High Mobility Group Box-1 (HMGB1), which is now considered to be a representative of Damage-associated Molecular Patterns (DAMPs), and oxidative stress-modified protein structures, and have been able to identify several diseases that are suitable for use in animal model experiments. During these studies, I became strongly attracted to the biological reaction generally called the "inflammatory response." The reason is that inflammatory responses exist at the base of almost all disease pathologies, from life-threatening ARDS pathologies such as sepsis and the current COVID-19, to local wounds such as injuries, and in the former case, I came to believe that finding an appropriate drug intervention method could lead to a life-saving treatment. In analyzing systemic inflammation, I began to deal with a breakdown of the system that must be essential for maintaining physiological functions, namely the interaction between blood cells (white blood cells, red blood cells, and platelets) and vascular endothelial cells, and I became aware of the importance of plasma proteins as regulators. One of the results is the research into the formulation of plasma protein histidine-rich glycoprotein (HRG), which we are currently working on with a company. The blood coagulation and fibrinolysis systems are well-known representative functions of plasma proteins, but from the perspective of maintaining homeostasis, if we consider that plasma proteins control the entire interface between blood, blood cells, and vascular endothelial cells, we feel that there is a large area of unexplored information about plasma proteins that we do not yet know. It is only natural to think that the primary receptor structure for DAMPs derived from living organisms and PAMPs derived from pathogenic microorganisms is in plasma proteins. Sometimes I imagine that plasma proteins are like the flow of a river that is responsible for maintaining homeostasis at each interface.

About 10 years ago, I had the opportunity to talk with a researcher from a supercomputer company, and I remember being surprised to hear about the efforts and feasibility of comprehensive analysis of blood factors as a new disease diagnostic method. I was surprised not only by the idea of developing a comprehensive measurement method, but also by the confidence that it was close to being realized. The disease definitions and disease diagnoses that we follow will probably be made possible by the large-scale data collection of factor analysis, such as blood factor measurement, and the development of computer algorithms. However, I feel that there is still a gap that cannot be easily bridged between making diagnosis easier with such methods and finding a treatment. The difficulty of drug development remains unchanged.

The Human Genome Project was completed at the beginning of this century, and we have witnessed the rapid development of genome-level gene analysis technology and the explosive growth of secondary databases obtained through such research. In this situation, understanding the process that we call "pathophysiology of disease" has only become more complex, not easier. Antibody drugs, which appeared at the end of the 20th century, have opened up new horizons for medicine, and many libraries, such as modified antibodies, small molecule nucleic acid drugs, peptide aptamers, and natural compounds, are considered treasure troves for the search for new drug candidates. We would like to continue the challenge of drug discovery by devising various drug discovery approaches while incorporating cutting-edge technologies.