構造生物 Vol.7 No.2
2001年9月発行

New approaches for cancer treatment

Koji Kawai

Department of Urology, Institute of Clinical Medicine, University of Tsukuba

Cancer management technology, especially in the field of cancer diagnosis, has advanced over the past 25 years. For example, the advent of sensitive tumor marker makes it possible to diagnosis the early stage prostate cancer, which is the most increasing cancer in Japanese men. This results in a high cure rate of early stage cancer. On the other hand, the treatment results of advanced cancer, i.e. metastatic cancer, still remain poor.

The use of anti-tumor cytotoxic drugs for cancer treatment began fifty years ago. The chemotherapy using anti-tumor cytotoxic drugs is still cornerstone of the treatment of metastatic cancer. In the field of cancer treatment, the American Society of Clinical Oncology (ASCO) is the most important clinical and translational meeting worldwide. In this year, the 37th Annual Meeting of ASCO has drawn more than 25,000 participants at San Francisco.

In the meeting, two reports of therapeutic trial considered to represent the top studies. One is large clinical trial of combination chemotherapy (use of four cytotoxic drugs) for advanced bladder cancer. Approximately, 300 patients were randomized to the chemotherapy group or the control group in the study. Outcome of the chemotherapy group was statistically superior to the control group, however, the survival benefit from chemotherapy was too small. The results might suggest the limitation of chemotherapy using classical cytotoxic drugs to improve the survival of advanced cancer patients.

The other important report is a therapeutic use of STI-571 for

gastrointestinal stromal tumors (GIST), a kind of sarcoma. STI-571 is an orally available, small molecule compound, synthesized as an inhibitor of Abl-Bcl tyrosine kinase that responsible for development of Chronic Myelogenous Leukemia (CML). Clinically, STI-571 has already shown activity against CML patients. In addition to inhibiting the Abl kinase, STI-571 effectively inhibits the c-kit kinase. In GIST, c-kit is activated by point mutation in the majority of cases. There is no known histopathological association between CML and GIST. Thus, the GIST trial was based on the concept of the molecular targeted therapy. Early results presented at this meeting, shows that ST-571 also has clinical activity in the GIST.

The successful clinical trials with STI-571 are a dramatic demonstration of the potential of targeting molecular pathogenesis based on structural biology in cancer treatment. The other important point is the selection of target cancer for clinical trials on the basis of the presence of molecular target. The structure analysis of these targets as well as gene analysis is essential to develop new agents to overcome the limitation of cancer treatment. I hope that structural biology would be further advanced and identify many other appropriate candidates for cancer treatment with a specific agent.