INTRODUCTION

The 12th International Symposium of the Foundation for Promotion of Cancer Research, entitled ‘Basic and Clinical Research in Breast Cancer’ was held from April 26 to 29, 1999, at the International Lecture Hall located in the Tsukiji campus of the National Cancer Center (NCC), Tokyo. The organizing committee members were Kaoru Abe (Chairman, NCC), Kent Osborne (University of Texas at San Antonio), Toru Watanabe (NCC), Takashi Fukutomi (NCC), Minako Nagao (Tokyo University of Agriculture) and Ken Yamaguchi (NCC).

Breast cancer is one of the leading causes of cancer death among females, especially in Western countries. Although its incidence in Japan is still relatively low, an increasing trend has been manifest over recent decades. This symposium was designed to highlight the current problems of the disease from both basic and clinical viewpoints and to give researchers a chance to try to solve them.

The first day was opened with a welcome address and an introduction by Takashi Sugimura (NCC) and an opening address by Kent Osborne, followed by a keynote address entitled ‘Is Japanese breast cancer different?’ by Kaoru Abe. Based on his 40 years of experience as an endocrine oncologist, Abe mentioned drastic changes in lifestyles in Japan after World War II that were characterized by ‘westernization’. These changes brought to Japanese women a prolongation of lifespan, early menarche and late menopause with increase in breast cancer incidence. He emphasized the importance of primary treatments of breast cancer, explaining how difficult it was to cure the spread of the disease in spite of the recent developments in chemo- and hormonotherapy.

SESSION 1: EPIDEMIOLOGY AND RISK FACTOR

Suketami Tominaga (Aichi Cancer Center, Nagoya) summarized epidemiological studies and risk factors of breast cancer in Japan. He showed a steady increase in breast cancer incidence that would soon reach the level of those observed in Western countries. Many factors appear to be related to this trend, including westernized foods, increasing fat intake, late marriage and no pregnancy. Regina G. Ziegler (National Cancer Institute, USA) showed in her paper ‘Migration patterns, life style and breast cancer risk in Asian-American women’ that, over several generations, Asian-American women could have a risk comparable to that of American whites. This study highlighted the impact of the exposure of Asian women to Western lifestyles on breast cancer risk and suggested new etiological aspects of the disease.

SESSION 2: PREVENTION, BASIC AND CLINICAL APPROACH

Minako Nagao overviewed experimental models of carcinogenesis under the title ‘Induction and prevention of mammary cancers by food factors in the experimental animal system’. She reported that HCA-induced mammary carcinogenesis was suppressed by soy-hypocotyl, chlorophyllin, indole-3-carbinol, a naturally occurring phytochemical in cruciferous vegetables, and plant phenols. She suggested that modification of cooking conditions and addition of various anti-carcinogenic agents are a feasible way to delay onset of cancer in humans. Norman Wolmark (NSABP, USA) summarized a well-known trial in a presentation entitled ‘The role of tamoxifen in breast cancer prevention: results of the NSABP breast cancer prevention trial (P-1)’. The conclusion was that tamoxifen decreased the incidence of invasive and non-invasive breast cancer, but at the price of an increased incidence of endometrial carcinoma and thrombotic disease. The benefits definitely outweighed the risks in certain patient categories.

SESSION 3: SCREENING PROGRAM

A screening program is crucial for the early detection of breast cancer and two speakers presented their recent data in this session. Laszlo Talbar (Falun Central Hospital, Sweden), gave a talk with the title ‘Control of breast cancer through early detection: the natural history of breast cancer. What we have learned from screening’. He showed a significant reduction in breast cancer mortality achieved through mammographic screening in a
Swedish trial. This was due to a significant decrease in the incidence of advanced-stage breast cancer. Noriaki Ohuchi presented a paper ‘Perspective of mammographic screening of breast cancer in Japan’. He reported a Japanese case-control study of clinical breast examination which had failed to show its effectiveness as a screening method and stressed the importance of mammography. He described a current Japanese trial to evaluate mammographic screening and discussed a new direction in the organization of screening delivery.

SESSION 4: FAMILIAR BREAST CANCER AND GENE COUNSELING

In this session, recent progress in BRCA1 and BRCA2 studies were reported. Piri L. Welch (University of Washington, USA) presented a paper entitled ‘Genetic analysis of breast and ovarian cancer’, in which she mentioned genomic-scale expression technologies and suggested that BRCA1 target genes may be novel genes involved in either inherited or sporadic breast or ovarian cancer. Takashi Fukutom (NCC, Japan) gave a paper entitled ‘BRCA1 and BRCA2 germline mutations in Japanese breast cancer families’. They examined germline mutations in Japanese breast cancer families and found that only 30% of the families had a mutation in one of the two genes, which was definitely low compared with those observed in Caucasian families. This suggested a different role of these genes in breast carcinogenesis between Japanese and Caucasian women.

SESSION 5: PATHOLOGY

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SESSION 6: PROGNOSTIC FACTORS

No cancer other than breast cancer has been shown to have so many prognostic factors. Two speakers contributed to this

Figure 1. The Twelfth International Symposium of the Foundation for Promotion of Cancer Research, Tokyo, 1999.
SESSION 7: IMAGING DIAGNOSTICS AND SENTINEL NODE BIOPSY

Four papers were presented in this session, namely 'Diagnostic value of contrast-enhanced computed tomography for diagnosing the intraductal component and small invasive foci of breast cancer' by Sadako Akashi-Tanaka (NCC, Tokyo), 'Sentinel node evaluation for breast cancer' by David Krag (University of Vermont, USA), 'Japanese experience of sentinel node biopsy in 600 patients' by Masakuni Noguchi (Kanazawa University, Kanazawa) and 'Problems in sentinel node biopsy' by Tadashi Ikeda (Keio University, Tokyo). Akashi-Tanaka reported experience of contrast-enhanced helical CT in diagnosing intraductal components and small invasive foci of breast cancer. A high sensitivity as compared with conventional ultrasound or mammography was shown. Sentinel node biopsy is currently a hot subject in breast cancer surgery to achieve a minimally invasive lymphadenectomy. Technical aspects together with retrospective clinical data were discussed and the ongoing NCI-sponsored randomized trial which will recruit 4000 patients was presented.

SESSION 8: SURGERY AND POST-SURGICAL FOLLOW-UP

Three breast surgeons contributed to this session. Fujio Kasumi (Cancer Institute Hospital, Tokyo) presented 'Safe breast conservation without radiotherapy sustained by serial pathological examination of resected specimens'. He demonstrated by showing their experience of 1073 cases of breast conservative surgery that unnecessary post-operative irradiation could be avoided by examining the resected specimens serially. A problem with this method is that such meticulous pathological examination is possible only in selected institutions. Norman Wolmark of NSABP reported on 'The addition of tamoxifen to lumpectomy and radiotherapy in the treatment of ductal carcinoma in situ (DCIS): preliminary results of NSABP Protocol B-24'. He concluded that radiotherapy following lumpectomy for DCIS significantly reduced the subsequent incidence of invasive and non-invasive ipsilateral breast tumor recurrence and the addition of further reduces the cumulative 5 year incidence of subsequent breast cancer-related events.

SESSION 9: CHEMOTHERAPY TAILORED FOR INDIVIDUAL PATIENTS AND HIGH DOSE CHEMOTHERAPY

In his presentation entitled 'Construction of a prognostic index for patients with metastatic breast cancer', Toru Watanabe (NCC, Tokyo) showed highly variable survival in patients with metastatic breast cancer. He proposed a prognostic index with which metastatic breast cancer patients could be categorized into three risk groups and the treatment might be individualized in each patient. Alan Coates (University of Sydney, Australia) presented 'Metastatic breast cancer: survival and quality of life'. Although continuous efforts have been made to improve the treatment efficacy, the progress is modest and cure is rarely achieved in patients with metastatic breast cancer. He emphasized the importance of maintaining or improving the quality of life (QOL) of breast cancer patients who receive systemic therapy. William Peters (Carmanos Cancer Institute, USA) presented 'High-dose chemotherapy and autologous bone marrow support for primary breast cancer'. Phase II trials suggested the survival advantage of high-dose chemotherapy in patients with breast cancer not only in a post-operative adjuvant setting but also in metastatic disease. Prospective randomized trials will give answers to the questions of the efficacy of high-dose chemotherapy in breast cancer. Yutaka Tokuda (Tokay University, Kanagawa) presented, in his paper entitled 'High-dose chemotherapy with autologous hematopoietic stem cell support in Japan', the 3-year progression-free survival rate of 14% of metastatic breast cancer patients who had been shown a complete response (CR) or partial response (PR) to induction therapy and were treated with high-dose chemotherapy with autologous stem cell support. He suggested the necessity for developing more efficacious induction regimens to achieve higher CR rates.

SESSION 10: HORMONE RECEPTOR FUNCTION AND ENDOCRINE THERAPY

Suzanne A. W. Fuqua (University of Texas at San Antonio, USA) presented 'Molecular mechanisms of estrogen receptor action'. She reported recent data on the nuclear receptor co-regulator in transcriptional activation of estrogenic effects on breast cancer. She focused on the mechanisms for acquired resistance to tamoxifen, which is most frequently prescribed for breast cancer, and also described the mechanism of the pure anti-estrogen faslodex. Shigeaki Kato (University of Tokyo, Tokyo) presented 'Cross-talk of estrogen receptor function with growth factors'. He reported that MAP kinase activated by growth factors modulates the estrogen receptor molecule and modifies its function. This may be a novel cross-talk between estrogenic stimulation and the growth factor signaling pathway.

SESSION 11: BONE METASTASIS

This session dealt with bone metastasis as an issue of both basic and clinical importance. Isamu Adachi (NCC, Tokyo) presented 'Possibilities and limitations of medical therapy for bone metastases'. The incidence of bone metastases as the initial
recurrence site is 30% and it reaches 70% during the clinical course of metastatic breast cancer patients. Etsuro Ogata (Cancer Institute Hospital, Tokyo) presented ‘Newer modalities in diagnosis, treatment and monitoring of bone metastasis’. Modulation of the function of osteoclasts and osteoblasts at the site of bone metastasis is the focus of effective treatment of this complication.

SESSION 12: NEW TREATMENTS BASED ON BIOLOGY

In this session, five papers on recent progress in the treatment of breast cancer were presented. Daniel F. Hayes (Lombardi Cancer Center, USA) presented ‘HER-2 as a predictive factor’. HER-2 over-expression or amplification is a significant prognostic factor in breast cancer. In addition, recent clinical investigations demonstrated that it was a positive predictive factor for anthracycline-containing chemotherapeutic regimens and a negative predictive factor for endocrine therapy. I. Craig Henderson (University of California at San Francisco, USA) presented ‘Application of STEALTH technology in oncology’. Adriamycin encapsulated in liposomes with polyethylene glycol (PEG) on the outer surface remains longer in circulation and has reduced cardiac toxicity. This technique may also prove to be a powerful tool for the delivery of gene therapy, small molecules and monoclonal antibody. ‘Herceptin and other therapies based on biology’ was presented by Richard M. Elledge (University of Texas at San Antonio, USA). Herceptin, a humanized monoclonal mouse antibody against HER2/neu protein overexpression, is a novel modality of breast cancer treatment and is now clinically useful for treating breast cancer patients. Masakazu Toi (Tokyo Metropolitan Komagome Hospital, Tokyo) presented ‘Novel strategy of adjuvant therapy based on inhibition of angiogenesis’.

He suggested that high levels of thymidine phosphorylase and low levels of vascular endothelial growth factor characterize patients with node-positive breast cancer treated with adjuvant CMF who had the highest likelihood of a favorable outcome. Ken Yamaguchi (NCC, Tokyo) presented ‘Chemopreventive and anti-tumor effects of a synthetic progestational steroid, dienogest, in experimental mammary carcinoma models’. Based on a well designed in vivo model system, it was suggested that dienogest can be a potential candidate as an agent for hemoprevention and also endocrine therapy for breast cancer.

SESSION 13: SUMMARY OF THE SYMPOSIUM

Kent Osborne (University of Texas at San Antonio) comprehensively summarized the symposium. During the past 30 years, various therapeutic and diagnostic agents have been developed and brought into breast cancer clinics. Owing to these developments, what was unknown or thought to be impossible has now become well known and possible. Continuing effort in both basic and clinical investigation into the 21st century has cardinal importance. Throughout this symposium, several issues in breast cancer have become clear, mainly on the basis of mutual understanding of the Japanese delegates and guests from the overseas. The symposium was very useful and productive.

Acknowledgements

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