mutations in BRCA1/2 are point mutations and small insertion/deletions, but recently increasing number of large genomic rearrangements in BRCA genes have been reported in different populations with various prevalence. However, little is known about the prevalence and types of genomic rearrangements of BRCA genes in the Korean population. In this study, we have analyzed for the presence of BRCA1/2 large genomic rearrangements in Korean breast cancer patients.

Methods: Multiplex ligation-dependent probe amplification (MLPA) was used to screen BRCA1/2 large genomic rearrangements in Korean breast cancer patients (249 for BRCA1 and 215 for BRCA2) at a priori risk of BRCA1/2 mutations due to known risk factors. The patients have been comprehensively analyzed for germline mutation in the entire regions of the BRCA1 and BRCA2 genes, using using a combination of fluorescent-conformation sensitive capillary electrophoresis (F-CSCE) and direct sequencing, and were found negative. Positive MLPA result was confirmed and located by long-range PCR and sequencing.

Results: We identified one large deletion in BRCA1, deleting exon 13−15, in one patient with family history of breast cancer. Breakpoints of this deletion are novel. However, we could not find any large deletion in BRCA2.

Conclusion: Our results suggest that the large genomic rearrangements in BRCA1/2 genes are not a major cause for increased breast cancer susceptibility in Korean population.

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Ki67 in Breast Cancer Patients and Its Correlation with Clinico Pathological Factors

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Background: Ki-67 is a nuclear protein universally expressed in all proliferative tissues. Large number of studies have confirmed the potential use of Ki-67 as a prognostic indicator and in predicting response to treatment in early breast cancer. However, due to variation in analytical practice, measurement of Ki-67 is still not recommended for management of early breast cancer patients. The aim is to study our initial results of measurement of Ki67 in breast cancer patients and correlate its significance with known prognostic factors.

Table 1. Clinico pathologic indicators and the Ki-67 index in primary breast cancer patients

Ki-67 index	<20%	20−50%	>50%
Mean tumour size, in cm	2.7	3.4	3.0
Mean age, in years	60.2	59.9	58.1
Breast Cancer Subtypes			
Luminal A (%)	80.9	10.7	8.4
Luminal B (%)	64.3	21.4	14.3
HER 2 type (%)	55.6	22.2	22.2
Triple Negative (%)	44.4	0	55.6
Total (%)	74.1	12.1	13.8
Positive Nodes (%)			
0	67.2	20.9	11.9
1−3	30.8	38.5	30.8
⩾ 4	40.0	30.0	30.0
Nuclear Grade (%)			
1	100	0	0
2	84.8	13.0	2.2
3	43.5	26.1	30.4
Estrogen receptor (%)			
Positive	78.2	12.9	8.9
Negative	44.4	16.7	38.9
Progesterone receptor (%)			
Positive	83.1	14.5	2.4
Negative	50.0	11.1	38.9
HER2 (%)			
1+	75	10	15
2+	74.6	13.4	11.9
3+	54.5	27.3	18.9

Materials and Methods: The Ki67 index was measured in all patients with early breast cancer in our breast unit over a period of six months. Prognostic factors such as Estrogen Receptor, Progesterone Receptor and HER-2 Receptors were simultaneously measured. Ki 67 index was categorised based on median value of 20% and analysed in accordance with breast cancer subtypes.

Results: Ki67 index was measured in 119 patients from February 2011 to July 2011. Age ranges from 29 to 89 with the mean tumour diameter of 2.8 cm (range from 0.6 to 11 cm). The median value of Ki-67 index was 20% and of the subtypes were Luminal A 12.5%, Luminal B 20%, HER 2 type 30% and Triple Negative tumours was 70%. Table 1 shows the relationship between the different groups of Ki67 index (<20%, 20−50% and >50%) and the clinic-pathological indicators of primary breast cancer.

Conclusion: The Ki-67 index ranged from 1−98% and the median was 20%, similar to other studies. The median Ki-67 values were different among subtypes, being low for the good prognostic Luminal A type tumours and high for the triple negative tumours. A higher Ki-67 index correlated with negative ER/PR, higher nuclear grade, younger age, larger tumour and positive HER 2. These data suggest that patients with a higher Ki-67 index have a poorer prognosis. It is therefore important to measure Ki-67 index and to be considered in the treatment and follow up of breast cancer patients.

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The NF-kappa B Signalling Pathway and the Response to Doxorubicin in Hormone-resistant Breast Cancer Cells

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Background: Oestrogen is an intrinsic regulator of the breast cancer growth and progression. Many breast cancers are initially sensitive to estrogen and antiestrogen treatment. The acquired tolerance of breast cancers to growth stimulating estrogen action may provokes the paradoxical tumor sensitization to estrogen apoptotic action. The phenomenon of the cell sensitization to estrogen-induced apoptosis has been demonstrated for the breast cancer cells undergoing long-term estrogen withdrawal or antiestrogen treatment. NF-kB is a transcriptional factor that controls apoptosis and cell responses to stress. Earlier studies have shown that estradiol suppress NF-kB, demonstrating the possible NF-kB involvement in the estrogen apoptotic action. The goal of this work is to study the influence of estrogens on the sensitivity of the resistant breast tumors to doxorubicin, and to evaluate the role of NF-kB signaling in the regulation of the survival of the resistant breast cancer cells.

Material and Methods: MCF-7/LS subline was developed by long-term cultivation of the parental cell line MCF-7 in steroid-free medium. The transcriptional activity of NF-kB and estrogen receptor was determined using luciferase reporter gene assay. The apoptosis level was evaluated by flow cytometry using staining with propidium iodide.

Results: It has been demonstrated that estradiol enhances the apoptotic action of doxorubicin in the resistant MCF-7/LS breast cancer cells. The proapoptotic estrogen action is mediated by NF-kB suppression when NF-kB knock-down sensitizes the resistant cells to both estrogen and doxorubicin.

Conclusions: Thus estrogen-induced NF-kB suppression in the resistant breast cancers results in a imbalance between pro- and anti-apoptotic pathways and cell sensitization to anti-tumor drugs. Additional inhibition of NF-kB by siRNA increases the apoptotic action of estrogen and doxorubicin, demonstrating that NF-kB may be considered as a potential target in the therapy of the resistant breast cancers.

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Quantitative Analysis of RORalpha mRNA Expression in Human Breast Cancer

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Objectives: The retinoic acid receptor-related orphan receptor (ROR) α is a member of the steroid/thyroid hormone nuclear receptor superfamily, which plays an important role on growth and differentiation of many organs by regulating transcription of target genes. We previously reported that RORα directly activated aromatase expression in breast cancer cells through a newly-identified ROR response element located within the promoter region of the aromatase gene. According to previous studies including ours, RORα mRNA is expressed in breast cancer cell lines, such as MCF7. However,