

# Diagnosis and Treatment of Synchronous Bilateral Breast Carcinoma

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## DESCRIPTION

Synchronous Bilateral Breast Cancer (sBBC) occurs when the same germline genetics and environmental exposures affect both breasts. Regarding immune infiltration and treatment response in sBBCs, there is scant evidence. Here, demonstrated that the impact of breast cancer subtype on Tumour Infiltrating Lymphocyte (TIL) levels (n=277) and pathologic complete response (pCR) rates (n=140) varied depending on whether the subtype of breast cancer in the contralateral tumor was concordant or discordant; TIL levels and pCR rates were higher in luminal breast cancers with a discordant contralateral tumor than in those with a concordant contralateral tumor. While primary tumor and residual disease were closely associated from the somatic mutation and transcriptome points of view, tumor sequencing showed that left and right cancers (n=20) were independent regarding somatic mutations, copy number changes, and clonal phylogeny. This study shows that the characteristics of the contralateral tumor are likewise related to immune infiltration and therapeutic response, suggesting that tumor-intrinsic properties may play a role in the relationship between tumor immunity and pCR.

The incidence of Bilateral Breast Cancers (BBCs), which make up about 2-11% of all breast cancers, is rising as a result of improvements in breast cancer imaging. Both Synchronous Bilateral Breast Cancers (sBBCs), which develop simultaneously in both breasts, and metachronous Bilateral Breast Cancers (mBBCs), which develop in the opposite breast after the main index cancer, are included in this category. Studies show that sBBCs have a worse prognosis than unilateral cancer. Just 5% of individuals with BBC had BRCA1 (BReast CAncer gene 1) or BRCA2 (BReast CAncer gene 2) mutations, and neither synchronous nor metachronous breast cancer is strongly influenced by genetic factors.

From a genetic basis, a number of studies, some using outdated technology, investigated the clonal relationships among BBCs. Only one pair of 39 sBBCs was recently determined to be clonally related (two shared mutations out of three mutations observed), leaving the issue of the independence of sBBCs unresolved. This was determined by evaluating a focused sequencing panel of 254 genes.

In the past ten years, a lot of studies have focused on the immune microenvironment and, in particular, the function of Tumor-Infiltrating Lymphocytes (TILs) in breast cancer. Breast cancer immunosurveillance is influenced by a combination of tumor-specific characteristics, such as the subtype of the disease, proliferative patterns, and tumor mutational burden, and environmental or host-related extrinsic factors, such as sex, age, and body mass index (for example, tobacco, alcohol and commensal microbiota). It is yet unknown how much anti-tumor immunity is influenced by the tumor, the host, or how the host and the tumor interact.

Currently, patients with locally advanced breast cancer get neoadjuvant chemotherapy. Breast cancer molecular subtypes and the quantity of immune cells infiltrating the tumor are both regarded as significant prognostic and predictive variables. High TIL levels at diagnosis have been linked to both greater neoadjuvant chemotherapy response and improved prognosis in numerous studies.

After several decades of the same environmental exposures, reproductive life events, and germline genetic influences on both breasts, sBBCs occur. When two tumors develop simultaneously in a host, it simulates a scenario in which the same host shares almost all extrinsic factors, the intrinsic factors are unique to each tumor, and the immune tumoral microenvironment produced by the interaction between the same host and the two different tumors can be compared.

In this study, identified an unusual supply of 20 tumors derived from six individuals with sBBCs treated with neoadjuvant chemotherapy, with left and right pre-NAC and post-NAC material readily available. So, carried out Whole-Exome Sequencing (WES), Copy Number Changes (CNAs), and RNA sequencing (RNA-seq) in order to thoroughly investigate somatic modifications, the immunological milieu, and the evolution of the tumour under treatment.

## CONCLUSION

Synchronous bilateral breast cancer (sBBC) is a type of breast cancer that occurs when the same germline genetics and environmental exposures affect both breasts. Combination of

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tumor-specific traits, proliferative patterns, and tumour mutational burden affect breast cancer immunosurveillance. Neoadjuvant chemotherapy is currently given to patients with locally advanced breast cancer. Greater NAC response and

effective prognosis have been associated with high TIL levels at the time of diagnosis. sBBCs develop on both breasts over several decades of the same environmental exposures, reproductive life events, and germline genetic factors.