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Characterization of structural variants and germline mutations in early-onset breast cancer leveraging whole genome data

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Studying early-onset breast cancer is crucial for understanding genetic predisposition, as variations accumulate over a shorter period compared to typical breast cancer onset. To investigate this, we analyzed whole-genome sequencing (WGS) data from 100 breast cancer patients diagnosed before the age of 40 (Young group) and 76 patients diagnosed after the age of 46 (Old group). Our aim was to characterize early-onset breast cancer by identifying genetic predisposing factors such as structural variants and germline mutations. Here's what we discovered from the WGS analysis of these 176 patients:

1. The total number of accumulated structural variants was significantly higher in the early-onset group compared to the late-onset group.
2. Two factors—deficiency in homologous recombination-related DNA repair and the occurrence of complex structural variants—were more prevalent in the early-onset group than in the late-onset group.
3. Conversely, the proportion of patients exhibiting whole genome duplication was significantly higher in the late-onset group.
4. Further analysis of the total accumulated structural variants and complex structural variants, key contributors to genetic instability, revealed distinct differences between early- and late-onset patients. Notably, the early-onset group exhibited complex structural variants predominantly on chromosomes 1, 17, and 19, while in the late-onset group, chromosome 6 was primarily affected.

In summary, our results delineate the genetic characteristics of early-onset breast cancer, including an increased total genetic variation, heightened genetic instability, and distinct complex structural alterations. These findings provide a foundation for further investigations into the mechanisms underlying these genetic features.