

"ASSESSMENT OF CHROMOSOME INSTABILITY IN TRIPLE-NEGATIVE BREAST CANCERS USING NUCLEI HARVESTED FROM FROZEN TISSUES"

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Chromosomal instability (CIN), defined as ongoing chromosome mis-segregation, is prevalent in the majority of solid tumors and potentially contributes to cancer progression and hazardous genetic changes.

Optimization of a common laboratory technique to assess CIN in isolated nuclei will benefit basic research and possibly be useful for clinical diagnostic purposes. Preliminary studies have demonstrated a successful protocol for performing fluorescence in situ hybridization (FISH) on nuclei harvested from frozen tumor and normal breast tissues. The frozen breast tumors were of the triple-negative breast cancer (TNBC) sub-type that does not express estrogen receptor (ER), progesterone receptor (PR), or human epidermal growth factor-2 (HER2). Six TNBCs analyzed to date (20-50 nuclei per tumor) exhibited chromosome instability using centromere specific probes in FISH analysis. Modal centromere number deviation (MCD)/sample was used to calculate CIN levels. Percent MCD ranged from 32-68% in TNBCs and contrasted with the normal breast tissue sample that exhibited 2% MCD. Previous FISH studies on tissue sections by others have shown that ER negative breast tumors with greater than 45% MCD had a better prognosis. Further study will be required to determine whether CIN levels (measured by MCD) can serve as a biomarker for stratifying TNBC patients into likely responders and non-

responders to treatment. Chromatin immunoprecipitation (ChIP) assays performed in parallel from the same frozen tissue revealed that centromeric heterochromatin structure is altered in TNBCs and may contribute to chromosome instability. The ability to perform both FISH and ChIP analysis on frozen human breast tissue has provided a foundation for further exploration of the relationship between CIN and centromere malfunction in tumor tissues and opens up therapeutic possibilities targeting the CIN phenotype in TNBCs.