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Presentation Title: Common variants in estrogen metabolism and DNA repair genes associated risk of breast cancer in young women

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Background: Breast cancer is a complex disease. The majority of cases occur in women without a family history and are considered sporadic. Currently for most women clinical evaluation of breast cancer risk utilizes epidemiological factors related to endogenous estrogen exposure. Estrogen and its related metabolites affect breast carcinogenesis by serving both as promoters of ductal epithelial cell growth and mutagenic precursors. Genomic instability caused by compromised DNA repair can also contribute to breast cancer development. Multiple low penetrance gene variants in these pathways may have a role in determining breast cancer risk in the general population. **Methods:** A case-control associative study of 5076 Caucasian women, 1812 breast cancer cases and 3264 cancer-free controls, was analyzed for common polymorphisms in fifteen genes involved in estrogen metabolism and DNA repair pathways. All polymorphisms were known to or likely to cause functional alterations and most resulted in non-synonymous amino acid substitutions. Overall analyses and stratification into likely pre-, peri- and post-menopausal age groups (30-44, 45-54, and over 55, respectively) were performed to derive odds ratios (ORs) and p-values. **Results:** Partitioning the study into the three age groups identified strong associations that were confined to the 30-44 age group. A total of nine polymorphisms were significantly ($p \leq 0.05$) associated with risk in this age group. The range of ORs varied from 0.7 to 1.6 with p-values as low as 0.001. **Conclusions:** Common variants in genes involved estrogen metabolism and DNA repair have significant impact on breast cancer risk in the youngest age group. The consideration of these variants could contribute to improved clinical management of breast cancer risk by identifying young women at the highest risk of developing the disease.