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- 1: Am J Hum Genet. 1999 May;64(5):1371-7.

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Modification of BRCA1-associated breast cancer risk by the polymorphic androgen-receptor CAG repeat.

[Rebbeck TR](#), [Kantoff PW](#), [Krithivas K](#), [Neuhausen S](#), [Blackwood MA](#), [Godwin AK](#), [Daly MB](#), [Narod SA](#), [Garber JE](#), [Lynch HT](#), [Weber BL](#), [Brown M](#).

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Compared with the general population, women who have inherited a germline mutation in the BRCA1 gene have a greatly increased risk of developing breast cancer. However, there is also substantial interindividual variability in the occurrence of breast cancer among BRCA1 mutation carriers. We hypothesize that other genes, particularly those involved in endocrine signaling, may modify the BRCA1-associated age-specific breast cancer risk. We studied the effect of the CAG repeat-length polymorphism found in exon 1 of the androgen-receptor (AR) gene (AR-CAG). AR alleles containing longer CAG repeat lengths are associated with a decreased ability to activate androgen-responsive genes. Using a sample of women who inherited germline BRCA1 mutations, we compared AR-CAG repeat length in 165 women with and 139 women without breast cancer. We found that women were at significantly increased risk of breast cancer if they carried at least one AR allele with ≥ 28 CAG repeats. Women who carried an AR-CAG allele of ≥ 28 , ≥ 29 , or ≥ 30 repeats were given a diagnosis 0.8, 1.8, or 6.3 years earlier than women who did not carry at least one such allele. All 11 women in our sample who carried at least one AR-CAG allele with ≥ 29 repeats had breast cancer. Our results support the hypothesis that age at breast cancer diagnosis is earlier among BRCA1 mutation carriers who carry very long AR-CAG repeats. These results suggest that pathways involving androgen signaling may affect the risk of BRCA1-associated breast cancer.

PMID: 10205268 [PubMed - indexed for MEDLINE]

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