Sobol, H; Bourdon, V; Eisinger, F; Coulet, F; Colas, C; Soubrier, F; Coupier, I; Payrat, JP; Fournier, J; Révillon, F; Vennin, P; Adenis, C; Rouleau, E; Lidereau, R; Demange, L; Nogues, C; Muller, D; Fricker, JP; Longy, M; Sevenet, N; Toulas, C; Guimbaud, R; Gladeff, L; Feillel, V; Leroux, D; Dreyfus, H; Rebischung, C; Cassini, C; Olivier-Faire, L; Prieur, F; Ferrer, SF; Frénay, M; Vénat-Bouvet, L; Lynch, HT; Hogervorst, F; Vernhoef, S; Pijpe, A; Van't Veer, L; van Leeuwen, F; Rookus, M; Collée, M; van den Ouweland, A; Krieger, M; Schutte, M; Hoogerbrugge, N; Hooning, M; Seynaeve, C; van Asperen, C; Wijnen, J; Vreesswijk, M; Tollenaar, R; Devilee, P; Ligtenberg, M; Ausems, M; van der Luijt, R; Aalfs, C; van Os, T; Gille, H; Waisfisz, Q; Meijers-Heijboer, H; Gomez-Garcia, E; van Roosendaal, K; Blok, M; Oosterwijk, J; van der Hout, A; Mourits, M; Vasen, H; Szabo, C; Zikan, M; Pohlerich, P; Kleibl, Z; Foretova, L; Machackova, E; Lukesova, M; Claes, K; De Leeneer, K; Poppe, B; De Paepe, A

Titel des Beitrags: Common variants associated with breast cancer in genome-wide association studies are modifiers of breast cancer risk in BRCA1 and BRCA2 mutation carriers.

Abstract:
Recent studies have identified single nucleotide polymorphisms (SNPs) that significantly modify breast cancer risk in BRCA1 and BRCA2 mutation carriers. Since these risk modifiers were originally identified as genetic risk factors for breast cancer in genome-wide association studies (GWASs), additional risk modifiers for BRCA1 and BRCA2 may be identified from promising signals discovered in breast cancer GWAS. A total of 350 SNPs identified as candidate breast cancer risk factors (P< 1 x 10(-3)) in two breast cancer GWAS studies were genotyped in 3451 BRCA1 and 2006 BRCA2 mutation carriers from nine centers. Associations with breast cancer risk were assessed using Cox models weighted for penetrance. Eight SNPs in BRCA1 carriers and 12 SNPs in BRCA2 carriers, representing an enrichment over the number expected, were significantly associated with breast cancer risk (P(trend)< 0.01). The minor alleles of rs6138178 in SNRPB and rs6602595 in CAMK1D displayed the strongest associations in BRCA1 carriers (HR = 0.78, 95% CI: 0.69-0.90, P(trend) = 3.6 x 10(-4) and HR = 1.25, 95% CI: 1.10-1.41, P(trend) = 4.2 x 10(-4)), whereas rs9393597 in LOC134997 and rs12652447 in FBXL7 showed the strongest associations in BRCA2 carriers (HR = 1.55, 95% CI: 1.25-1.92, P(trend) = 6 x 10(-5) and HR = 1.37, 95% CI: 1.16-1.62, P(trend) = 1.7 x 10(-4)). The magnitude and direction of the associations were consistent with the original GWAS. In subsequent risk assessment studies, the loci appeared to interact multiplicatively for breast cancer risk in BRCA1 and BRCA2 carriers. Promising candidate SNPs from GWAS were identified as modifiers of breast cancer risk in BRCA1 and BRCA2 carriers. Upon further validation, these SNPs together with other genetic and environmental factors may improve breast cancer risk assessment in these populations.

Zeitschriftentitel / Abkürzung: Hum Mol Genet
Jahr: 2010
Band: 19
Heft / Issue: 14
Seiten: 2886-97
Sprache: eng
Print-ISSN: 0964-6906
TUM Einrichtung: Frauenklinik und Poliklinik
Occurences: