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Autor(en) des Beitrags:
Kirchhoff, T; Gaudet, MM; Antoniou, AC; McGuffog, L; Humphreys, MK; Dunning, AM; Bojesen, SE; Nordestgaard, BG; Flyger, H; Kang, D; Yoo, KY; Noh, DY; Ahn, SH; Dork, T; Schürmann, P; Karstens, JH; Hillelmanns, P; Couch, FJ; Olson, J; Vachon, C; Wang, X; Cox, A; Brock, I; Elliott, G; Reed, MW; Burwinkel, B; Meindl, A; Brauch, H; Hamann, U; Ko, YD; GENICA Network; Broeks, A; Schmidt, MK; Van't Veer, LJ; Braaf, LM; Johnson, N; Fletcher, O; Gibson, L; Peto, J; Turnbull, C; Seal, S; Renwick, A; Rahman, N; Wu, PE; Yu, JC; Hsiung, CN; Shen, CY; Southey, MC; Hopper, JL; Hammet, F; Van Dorpe, T; Dieudonne, AS; Hatse, S; Lambrechts, D; Andruulis, IL; Bogdanova, N; Antonenkova, N; Rogov, JI; Prokofieva, D; Bermisheva, M; Khusnutdinova, E; van Asperen, CJ; Tollenaar, RA; Hooing, MJ; Devilee, P; Margolin, S; Lindblom, A; Milne, RL; Arias, JI; Zamora, MP; Benitez, J; Severi, G; Baglietto, L; Giles, GG; kConFab: AOCs Study Group; Spurdle, AB; Beesley, J; Chen, X; Holland, H; Healey, S; Wang-Gohrke, S; Chang-Claude, J; Mannermaa, A; Kosma, VM; Kauppinen, J; Kataja, V; Agnarsson, BA; Caligo, MA; Godwin, A; Nevanlinna, H; Heikkinen, T; Fredericksen, Z; Lindor, N; Nathanson, KL; Domchek, SM; SWE-BRCA; Loman, N; Karlsson, P; Stenmark Askmalm, M; Melin, B; von Wachenfeldt, A; HEBON; Hogervorst, FB; Verheus, M; Rookus, MA; Seynaeve, C; Oldenburg, RA; Ligtenberg, MJ; Ausems, MG; Aalfs, CM; Gille, HJ; Wijnen, JT; Gómez García, EB; EMBRACE; Peock, S; Cook, M; Oliver, CT; Frost, D; Luccarini, C; Pichert, G; Davidson, R; Chu, C; Eccles, D; Ong, KR; Cook, J; Douglas, F; Hodgson, S; Evans, D; Eeles, R; Gold, B; Pharoah, PD; Offit,
Breast cancer risk and 6q22.33: combined results from Breast Cancer Association Consortium and Consortium of Investigators on Modifiers of BRCA1/2.

Abstract:
Recently, a locus on chromosome 6q22.33 (rs2180341) was reported to be associated with increased breast cancer risk in the Ashkenazi Jewish (AJ) population, and this association was also observed in populations of non-AJ European ancestry. In the present study, we performed a large replication analysis of rs2180341 using data from 31,428 invasive breast cancer cases and 34,700 controls collected from 25 studies in the Breast Cancer Association Consortium (BCAC). In addition, we evaluated whether rs2180341 modifies breast cancer risk in 3,361 BRCA1 and 2,020 BRCA2 carriers from 11 centers in the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). Based on the BCAC data from women of European ancestry, we found evidence for a weak association with breast cancer risk for rs2180341 (per-allele odds ratio (OR) = 1.03, 95% CI 1.00–1.06, p = 0.023). There was evidence for heterogeneity in the ORs among studies (I² = 49.3%; p =<0.004). In CIMBA, we observed an inverse association with the minor allele of rs2180341 and breast cancer risk in BRCA1 mutation carriers (per-allele OR = 0.89, 95%CI 0.80–1.00, p = 0.048), indicating a potential protective effect of this allele. These data suggest that that 6q22.33 confers a weak effect on breast cancer risk.