Low-risk variants FGFR2, TNRC9 and LSP1 in German familial breast cancer patients.

To validate common low-risk variants predisposing for breast cancer (BC) in a large set of BRCA1/2 negative familial or genetically enriched cases from Germany, we genotyped 1,415 cases and 1,830 healthy women by MALDI-TOF in 105 candidate SNPs. Significantly higher ORs than previously reported for heterozygous unselected cases were found for the minor allele in FGFR2 (OR = 1.43, 95% CI 1.30-1.59, p-value = 1.24 x 10(-12)) and for TNRC9 (OR = 1.33, 95% CI 1.19-1.46, p-value = 1.54 x 10(-7)). Most intriguing, however, were the ORs for homozygous carriers from high-risk families for FGFR2 (OR = 2.05, 95% CI 1.68-2.51), LSP1 (OR = 0.49, 95% CI 0.28-0.86) and TNRC9 (OR = 1.62, 95% CI 1.27-2.07). Moreover, the additional validation of 99 CGEMS-SNPs identified putative novel susceptibility alleles within the LSP1 gene (OR = 0.73, 95% CI 0.61-0.87, p-value = 5.23 x 10(-4)).

Finally, we provide evidence for the first time that a low-risk variant located at 6q22.33 (rs6569479) is associated with estrogen receptor negative BC in familial cases (OR = 1.33, 95% CI 1.06-1.66; p-value = 0.012). Our data confirm the impact of the previously identified susceptibility loci and provide preliminary evidence for novel
susceptibility loci in familial BC cases and correlate them to specific histopathological subtypes defined by estrogen receptor status.