Titel des Beitrags:
Polymorphisms in the Janus kinase 2 (JAK)/signal transducer and activator of transcription (STAT) genes: putative association of the STAT gene region with familial breast cancer.

Abstract:
The Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway mediates the signals of a wide range of cytokines, growth factors and hormones. Thus, aberrant activation of the JAK/STAT pathway may predispose to malignancy due to deregulation of proliferation, differentiation or apoptosis. In this study, we investigated whether genetic variation in the JAK2 gene and the STAT gene region (STAT3, STAT5A and STAT5B) is associated with breast cancer (BC) risk. We carried out a case-control study using a German sample set with 441 familial, unrelated BC cases and 552 controls matched by age, ethnicity and geographical region. A second similar set (381 cases, 460 controls) was applied to validate the findings. Haplotypes in the JAK2 gene were not associated with the risk of BC. In the STAT gene region, the rare haplotype CAGCC containing the variant alleles of each single nucleotide polymorphism (SNP) was associated with an increased risk odds ratio (OR = 5.83, 95% confidence interval (CI) 1.51-26.28). According to Akaike's information criterion, the best model to describe the relationship between the haplotypes and BC was based on the SNPs rs6503691 (STAT5B) and
rs7211777 (STAT3). Carriers of the AC haplotype, which represents the variant alleles of both SNPs, were at an increased risk (OR = 1.41, 95% CI 1.09-1.82). A decreased risk was observed for carriers of the AT haplotype (OR = 0.60, 95% CI 0.38-0.94). Furthermore, individuals with the AC/GC diplotype were at a significantly increased risk (OR = 1.88, 95% CI 1.13-3.14). The observed genetic variation may also influence the inter-individual variation in response to STAT-signalling targeted therapy.