Mutations in STAT3 (signal transducer and activator of transcription 3) have recently been found to cause the hyper-IgE syndrome (HIES) - a rare immunodeficiency syndrome including complex somatic features. We now tested whether STAT3 mutations or single-nucleotide polymorphisms (SNPs) within STAT3 may be responsible for increased IgE levels in asthmatic children. We genotyped DNA samples from 918 individuals of 217 core families by MALDI-TOF mass spectrometry. SNPs were selected from previous reports, by functional relevance and haplotype-tagging capacity. In 24 assays, including the recently described HIES mutations, no variant was detected. In another 27 SNP assays, there was no association of any STAT3 variant with asthma, allergic rhinitis or eczema. In addition, neither total and specific IgE and eosinophil count nor any lung function parameter showed any significant association. When combining high eosinophil counts and high total IgE levels to an HIES-like trait, four SNPs in the 5'-UTR of STAT3 were slightly overtransmitted. A minor fraction of asthmatic children may possibly have an alternate STAT3 promoter architecture influencing joined IgE and eosinophil upregulation. While an overall effect of STAT3 mutations on serum IgE is unlikely in asthma children.