Association between p47phox pseudogenes and inflammatory bowel disease

We read with great interest the recent article by Heyworth et al., which describes the ratio between the p47phox pseudogenes (ψNCF1) and the p47phox gene (NCF1). Gene duplication has prevented elucidation of the genomic sequence at 7q11.23, although the ψNCF1/NCF1 ratio had been assumed to be 2:1. Specifically, the location and quantity of ψNCF1 pseudogenes is unknown. Heyworth et al. demonstrated the ratio to be 1:1 and 1:2 in 13% and 4% of healthy individuals, respectively, the rest being 2:1. Using a family study, they elegantly showed that variability in the ratio probably occurred following DNA exchange by recombination or, conceivably, gene conversion between NCF1 and ψNCF1, to produce a gene hybrid (type II ψNCF1). Similar to NCF1, type II ψNCF1 contains a GT repeat (GTGT) at the start of exon 2, and therefore its transcription product encodes a full-length protein that is homologous to NCF1. ψNCF1, however, contains a dinucleotide deletion at this allele (ΔGT) that results in a premature stop codon. The functional significance of type II ψNCF1 remains unknown.


Figure 1. Ratio of ΔGT/GTGT sequence in patients with CD and UC and 3 parents of CGD patients. Three ratio populations were apparent, approximating to 2:1, 1:1, and 1:2. There was a significant excess of the 1:1 ratio in CD (P < .05), implying an excess of the type II ψNCF1 pseudogene. Each point represents the mean of triplicate measurements.