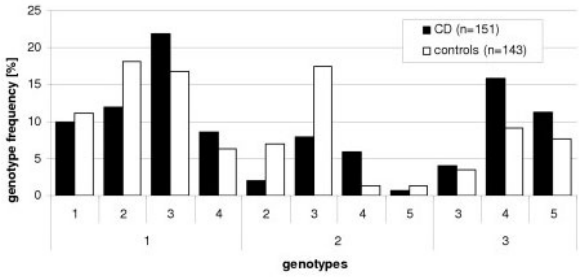

Figure 1
Genotype frequencies of the microsatellite representing the *TNFRSF17* gene. Only genotypes with a frequency of > 0.01 are included. Alleles of the respective microsatellite are indicated as numbers in the X-axis according to their length in bp. For example: 1–1 (read from the number below the numerical series and the first number of the numerical series) means homozygous genotype for microsatellite allele number one and 1–4 heterozygous genotype for allele 1 and 4. Genotypes comprising allele 2 are over-represented within the control group (47% *vs*. 29%; $p_c = 0.0042$ with c = 2), whereas allele 3 genotypes are more frequent in the patient cohort (58% *vs*. 52% $p^c = 0.3130$; c = 2). Therefore, allele 2 might imply a protective effect and/or allele 3 a predisposing effect on CD. Interestingly, the genotype 2–3 is more prevalent in the control group. This result can be interpreted by a different effect size of allele 2 (↑) as compared to allele 3, or the significant difference of this microsatellite is only due to linkage of allele 2 with a protective factor.

The most promising markers (reflected by a significant p-value) were included in further analyses regardless of the correction procedure. Individual genotyping rejected most markers found to be significantly different in the initial step of our approach and only three markers remained significant representing the *TNFRSF17*, *FLIP*, *CARD15* genes (Tab. 2). Obviously, pooled and individual genotyping yield somewhat contradictory results. Eight microsatellites revealed significantly differences between the patient and control cohorts after the pooling procedure, whereas individual genotyping results in the confirmation of 'only' 2 markers. These conspicuous differences might be due to several artefacts caused by analyses with pooled DNA. For example, a typical artefact is the length-dependent amplification of short alleles or the presence of null-alleles. Additionally, consistency of the analyses by a slab-gel system might reflect a further hindrance in this subtle procedure. Nevertheless, individual genotyping eliminates false positive results due to pooling artefacts and, in case of significant results, enables the thorough analyses of the marker alleles in detail (see Fig.1). In order to confirm the aforementioned positive results further markers (SNPs, Tab. 3) were genotyped located in the respective genes in the vicinity of the microsatellites representing *TNFRSF17* and *FLIP*. Yet, RFLP analyses did not reveal any association of the selected SNPs and, therefore, the microsatellite data were not confirmed. On the other hand, these SNPs might not represent regions properly that encompass regulatory elements.

In some instances, the LD of distinct microsatellite alleles covers long genetic distances, thus further gene variations might be in linkage with these alleles. Since the significantly associated '*TNFRSF17*' marker is located at the IBD8 region with 1MBp distance to the major histocompatibility class (MHC) II transactivator (*MHCIITA*), a previously reported functional variation of the *MHC2TA* gene was analysed (see Tab. 4; [30]). MHC2TA regulates the expression of *human leukocyte antigen* (*HLA*) genes regulating the adaptive immune system by presenting antigens to CD4+ T cells, thereby re-activating these cells. The *HLA* region has been implicated in IBD [32]. In addition to the localisation of *MHC2TA* at IBD8 and the associated marker in the adjacent region, the putative biological relevance of the functional rs3087456 polymorphism for CD motivated us to genotype this variation. The analyses did reveal a marginal association in our CD patients when allele or genotype frequencies were compared between the combined control and patient cohorts (see Tab. 4). Yet

Table 4: Allele and genotype frequencies of the functional *MHC2TA* polymorphism (rs3087456).

	Allele frequencies		p value	OR (CI)	Genotype frequencies		p value
CD (n = 147)	C	0.32	0.05	1.33 (0.90–2.01)	CC	0.08	0.54
	T	0.68			CT	0.48	0.06
					TT	0.44	0.03
controls (n = 463)	C	0.26			CC	0.07	
	T	0.74			CT	0.39	
					TT	0.54	

OR: odds ratio; CI: 95% confidence interval