GENETICS

MY COMPLIMENTS

8.02.2007

My compliments to Nicole, the latest Ph.D. student from our lab who succesfully passed her final exam today in Freising at TU München-Weihenstephan. Here is the semi-official document:

The title of her thesis is *High-resolution snp scan of chromosome 6p21 in pooled samples from patients with complex diseases* , a topic that has recently attracted new interest.

We apply a high-throughput protocol of chip-based mass spectrometry (matrix-assisted laser desorption/ionization time-of-flight; MALDI-TOF) as a method of screening for differences in single-nucleotide polymorphism (SNP) allele frequencies. Using pooled DNA from individuals with asthma, Crohn's disease (CD), schizophrenia, type 1 diabetes (T1D), and controls, we selected 534 SNPs from an initial set of 1435 SNPs spanning a 25-Mb region on chromosome 6p21. The standard deviations of measurements of time of flight at different dots, from different PCRs, and from different pools indicate reliable results on each analysis step. In 90% of the disease-control comparisons we found allelic differences of <10%. Of the T1D samples, which served as a positive control, 10 SNPs with significant differences were observed after taking into account multiple testing. Of these 10 SNPs, 5 are located between DQB1 and DRB1, confirming the known association with the DR3 and DR4 haplotypes whereas two additional SNPs also reproduced known associations of T1D with DOB and LTA. In the CD pool also, two earlier described associations were found with SNPs close to DRB1 and MICA. Additional associations were found in the schizophrenia and asthma pools. They should be confirmed in individual samples or can be used to develop further quality criteria for accepting true differences between pools. The determination of SNP allele frequencies in pooled DNA appears to be of value in assigning further genotyping priorities also in large linkage regions.