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Large Scale HapMap Genotyping and the Possibility of Genome Center-Specific Effects

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ABSTRACT HapMap samples are currently being genotyped using different high throughput protocols at various international genome centres. To determine if there are any differences between SNP genotypes that may be related to these protocols, we analysed an initial set A consisting of 2,200 SNPs (100 SNPs from each autosome) typed in 90 HapMap CEU samples. Although SNP composition in terms of percentage of transitions and transversions was similar across protocols, one (termed "PI") yielded a high prevalence (39.9%) of mono-morphic SNPs (i.e. those with heterozygosity = 0) which was generally double that observed for the other protocols (corrected P-value (P_c) < 0.01). To examine this issue further, we enlarged the dataset to include a total of 22,000 SNPs (1000 SNPs per autosome). While results in this larger dataset B remained similar for all other protocols, the prevalence of mono-morphic SNPs genotyped using "PI" declined by nearly half from 39.9% to 19.1% ($P_c < 1x10^{-7}$). Stratifying both the initial and larger datasets by genome centres, it was observed that the prevalence of polymorphic SNPs (defined as those with heterozygosity >0 and <= 0.5) genotyped using "PI" increased from 42% to more than 70% at two locations while staying relatively consistent at the remaining centres. Although our analysis does not allow us to pinpoint the precise cause for this discrepancy, our findings clearly advocate greater caution when using high throughput technologies in order to ensure consistent genotype calls.