SMP: Genetic Epidemiological Methods (GEM)

Project: Assessment and Optimisation of Quality Control for Genotyping

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Introduction

The primary objective of this project is the external validation and the improvement of genotyping quality for the clinical networks within the NGFN. To realize this, we intend to get duplications for a part of the genotyping results with replications primarily made by at least a second independent genotyping centre (GTC) and, if possible, with a different genotyping method. It is known, that some of the SNP genotyping techniques tend to specific problems. [Kwok PY (2001) Methods for genotyping single nucleotide polymorphisms. Ann Rev GEnomics Hum Genet2: 235 - 258] Error rates have been estimated within one genotyping procedure in the size of 0.1 to 0.8% by internal checks. Notwithstanding of the fact that these problems can be and are treated by internal procedures of the different GTCs there is a need for an external validation of the genotyping results.

Marker	Person				
D6S344	002	154	154	154	156
D15S165	001	182	198	182	182
D17S1876	001	101	103	101	101
D11S1393	002	205	213	205	205
D14S53	002	147	149	149	149
D16S764	003	94	102	102	102
D17S2180	003	121	121	118	121
D4S2632	003	140	152	140	140

Fig 1: *Replication of STR typing in two families*

Results/Project Status

At the present time two experiments have been performed.
Two ASP-families were duplicated and typed for approximately 450 markers each.
A total of 3636 genotypes from 8 persons were genotyped with 8 differences. This results in an estimated error rate of 1.10×10^{-3}.
The genotypes always differed in such a way that one was heterozygous and the other was homozygous (allelic drop out).
3 SNPs were replicated in the NGFN Genomic Control Project. 3 differences in 4155 genotypes were found. That gives us an estimate of 3.6×10^{-4} errors per SNP genotype.

Outlook

Presently, one additional duplication experiment for STR typing is running. For this experiment we duplicated several persons out of some smaller families being genotyped as part of a genome scan. The duplicated persons are chosen in such a way that Mendelian check procedures cannot be applied to these duplicates. Apart from a confirmation of our previous error estimations for STR typing, by this experiment we intend to get an estimation of the effect of Medelian checks by the genotyping center on the error rates.

Lit.: ***1.*** *Albers P, Weissbach L, Krege S, Kliesch S, Hartmann M, Heidenreich A, Walz P, Kuczyk M, Fimmers R; German Testicular Cancer Study Group.: Prediction of necrosis after chemotherapy of advanced germ cell tumors: results of a prospective multicenter trial of the German Testicular Cancer Study Group. J Urol. 2004 May;171(5):1835-8.* ***2.*** *Felsberg J, Erkwoh A, Sabel MC, Kirsch L, Fimmers R, Blaschke B, Schlegel U, Schramm J, Wiestler OD, Reifenberger G.. Oligodendroglial tumors: refinement of candidate regions on chromosome arm 1p and correlation of 1p/19q status with survival. Brain Pathol. 2004 Apr;14(2):121-30.*