

***FUT2* and *FUT3* PCR-SSP for multi-ethnic Lewis phenotype prediction**

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Background

Lewis antigens are ABO related carbohydrates and their expression is regulated by interaction of the two fucosyltransferases *FUT2* (Secretor enzyme) and *FUT3* (Lewis enzyme). In principle, active *FUT3* transfers fucose to Type 1 acceptor substrates resulting in Le(a+b-) phenotypes. Addition of another fucose by active *FUT2* transforms Le^a to Le^b, resulting in Le(a-b-). The third phenotype, Le(a-b-), is the result of an inactive *FUT3*, completely independent of *FUT2* activity. Enzymatic inactivity of *FUT2* and *FUT3* is caused by a variety of inactivating single nucleotide polymorphisms (SNPs), whose distribution differs in various ethnic groups. Since adsorbed onto red blood cells only, serological phenotyping of Lewis antigens is difficult under certain physiological conditions. Therefore, rapid and correct *FUT2/FUT3* genotyping in different ethnic groups would be of interest ^(1,2,3,4).

Methods

The Lewis phenotype was defined using standard serological procedures. An in-house PCR-SSP kit was developed to detect inactivating SNPs 428G>A of *FUT2* and 59T>G, 202T>C, 484G>A and 1067T>A of *FUT3*, respectively. Individuals investigated were 140 blood donors of the Zurich area and 16 individuals of presumptive African ancestry, e.g. estimated by the presence of *FY*02N.01* homozygosity. All had existing serological prevalues of all Lewis phenotypes, including a strong statistical overrepresentation of 100 and 8 Le(a-b-) phenotypes for individuals of Zurich and Africans, respectively.

Results

Considering above mentioned inactivating mutations and well-known expression-negative haplotypes of *FUT3*, e.g. $le^{59,202}$, $le^{202,484}$, $le^{59,1067}$, for Caucasians⁽¹⁾, Africans⁽²⁾, Asians⁽³⁾ and Amazonian populations⁽⁴⁾, eight specific PCR-SSPs (2 for *FUT2* and 6 for statistically relevant *FUT3* haplotypes) were developed and delivered 100% concordance with serological prevalences for all samples.

Summary/Conclusions

The Lewis blood group system comprises the three common phenotypes Le(a+b-), Le(a-b+) and Le(a-b-). The kit provides a helpful and highly accurate diagnostic tool for Lewis genotyping with consecutive phenotype prediction. Since the Lewis blood group phenotype is difficult to assess in situations when affected by certain diseases and in atypical physiological conditions, genotyping the Secretor and Lewis genes *FUT2* and *FUT3* is therefore an attractive and accurate alternative.