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How to monitor and to estimate genetic drift

Full genome STR genotyping

Our full genome genotyping test is based on the analysis of 230 - 250 STR markers (Short-Tandem-Repeats, microsatellites), which are distributed relatively even over all chromosomes, including X and Y chromosomes. Genetic drift can be monitored by detection of new STR alleles as result of mutation events, subsequent fixation of this new allele and loss of the original.

The full genome genotyping of samples is carried out with the objective to find out about the genetic diversity between the individuals of one generation within the particular line, but also to determine the genetic divergence from the reference substrain, e.g. C57BL/6J, or from same transgenic line at different numbers of generations.

1 Genetic homogeneity/variability within strain

For this comparison, we initially determine the allele which occurs most frequently for each STR marker and which we refer to as „consensus allele“. The series of consensus alleles for all STR markers defines the consensus profile for the specific mouse line.

In order to determine the homogeneity/variability, the STR allele profiles of all individuals from the respective line are compared with the consensus allele. An example is given in pdf file „1_Samples vs Consensus“. Here we analyzed 10 different samples of an in-house bred C57BL/6J (Jax) and compared them to their consensus profile “Consensus NNT”.

As one can see, the individual allele profiles match the consensus profile at a percentage between 97.8% and 98.9%. These percentages represent an excellent result and will be observed in the same range for individuals originally bought from the breeders (96-99%).

2 Comparison of “Consensus Nnt” profile with the STR profile of original C57BL/6J

“Consensus Nnt” STR profile can be compared with the consensus allele profile of the original C57BL/6J (see pdf “2_BL6J vs Consensus Nnt”). The degree of resemblance with C57BL/6J is 94.16%. The degree of resemblance of individual STR profiles of samples 21 to 30 with C57BL/6J is between 92.8% and 94.5% (data not shown).

These results show that all samples are quite homogenous within their respective group, but also that the STR profiles differ somewhat from the original C57BL/6J. This may be an indication for a subtle genetic drift having occurred.

3. Transgenic lines and genetic drift

In the same way, original consensus profiles of transgenic lines can be compared with samples/consensus profiles after N generations to estimate the size of the genetic drift having occurred. The mismatch between two consensus profiles is a measure for the genetic drift, the larger the difference, the more drift has occurred. Lines with a match of less than 90% should be associated with a significant genetic drift which requires attention such as backcrossing or refreshing.